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Chettinad Health City

MEDICAL JOURNAL

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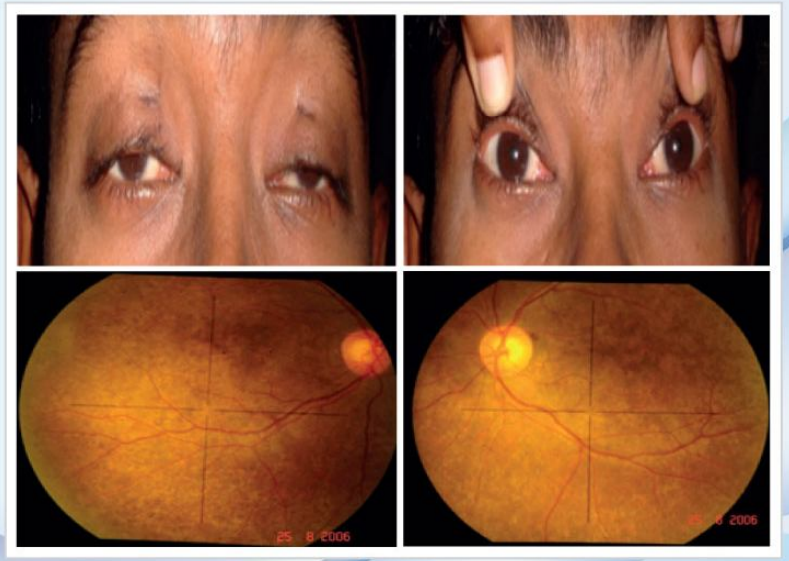

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Chettinad Health City

MEDICAL JOURNAL

Contents

Editorial

Vanakkam.

The journal enters the third year of uninterrupted regular publication with this issue. All your contributions and support has helped us to get the journal indexed with several indexing agencies. The journal is accessible and the full content is readable from anywhere in the world from its website and through all the indexed agencies' websites.

Fertility is the most cherished of all assets. As Thirukkural No 61 aptly says :

> பெறுமவற்றுள் யாமறிவது இல்லை அறிவறிந்த மக்கட்பேறு அல்ல பிற.
>
> Translation: Among all the assets that may be acquired we know of no greater asset than having intelligent children.

Infertility today is a growing global epidemic. There are several causes for this phenomena -environmental, sociological and genetic. Regardless of the cause, Assisted Reproduction serves as a boon for many forms of infertility. However, there were and there are still lots of concerns about the health of the mother and particularly the babies born out of an ART programme as the field of Assisted reproduction is just 36 years old.

The original article in this issue reports on the follow up of these babies.

Chronic renal disease is increasing worldwide. These patients may also have other co-morbid conditions and require appropriate dental treatment. A review article outlines the 'Current trends in dental management of patients with chronic renal disease'.

A case of venous air embolism during paediatric craniotomy in sitting position is described in a case report. Ocular Thelaziasis, a very rare occurrence is described in another case report.Papillary cystadenoma of the minor salivary gland is described in yet another case report.

A great surgical challenge in the form of Giant Dumb bell trigeminal schwannoma is described in a case report.

All seizures in pregnancy are not eclamptic. A series of non-eclamptic seizures are described in an article.

The class room article describes a pragmatic approach in designing a study.

The pages of history describes the origin of the classical neurological sign – Babinski sign.

We hope you will enjoy going through the issue. Please do give us your valuable feedback.

Dr. N. Pandiyan
Chief Editor : Chettinad Health City Medical Journal
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Perspective Article

Whither Varicocelectomy?

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Chettinad Health City Medical Journal 2014; 3(1): 2 - 3

Varicocele was first described as a possible causative factor in male infertility in the year 1885 by the British surgeon Barwell[1]. Tulloch was the first to publish a case report on varicocelectomy documenting a rise in semen parameters after varicocelectomy[2]. More than sixty years later, the role of varicocele in male infertility still remains controversial.

The incidence of varicocele is 15% in the general male population and 19% to 40% among infertile men[3,4]. Varicocele is supposed to alter semen parameters and cause infertility by one or more of the following mechanisms:-

1) Varicocele is believed to increase the scrotal temperature by venous stasis which is considered to impair spermatogenesis. It is presumed that the testes lie in the scrotum because they need lower temperature for effective spermatogenesis[3]. However, in reality, it is not known why the testes are scrotal in some mammals and not in others. It has never been convincingly demonstrated that the scrotal temperature is raised in men with varicocele compared to men without varicocele[5]. Besides, in varicocele, there is stasis of venous blood which is cooler and therefore should cause a cooler scrotum and not a warmer one.

2) In varicocele, reflux of blood from the left renal vein into the left internal spermatic vein is supposed to carry adrenocortical metabolites and these metabolites are supposed to cause suppression of spermatogenesis[3,6]. It is difficult to comprehend how adrenocortical metabolites in the static venous blood would perfuse into testicular tissue and suppress spermatogenesis.

3) Varicocele is supposed to cause a stress pattern in semen parameters often described as oligozoospermia, asthenozoospermia and teratozoospermia[7]. It has never been consistently or clearly shown what this stress pattern is and the definition of oligoasthenoteratozoospermia has changed five times in the last 34 years[8]. Semen analysis is hugely variable from time to time in the same individual[9], the definition of oligozoospermia is uncertain[10] and the sperm morphology assessment is very subjective[11].

Therefore, at this point in time, it is not at all clear if varicocele causes male infertility and if so the mechanism of causation is not known[12,13].

Management

The management of varicocele has had a chequered history. Several studies recommend varicocelectomy[14-17] whereas others find it to be ineffective[12,18]. The NICE guidelines published in 2013 do not recommend surgery for infertile men with varicocele because it does not improve pregnancy rates[19]. There have been several surgical approaches like open surgical, microsurgical, laparoscopic surgical methods and radiological methods like embolisation[17,18]. The effectiveness of all these techniques is debatable. The precise mechanism by which any of these techniques would improve the spermiogram is not known.

In 2014, in my opinion, varicocele, probably a variation in the normal anatomy of testicular venous drainage and a coexistent factor in some infertile men has been overblown as a causative factor in male infertility. Surgery for varicocele in these depressed infertile men with all the attendant risks and with no proven benefits in randomized controlled trials, I feel, is superfluous. A technique which was introduced in the pre assisted reproduction era should no longer serve in the armamentarium of the infertility physician. It should be confined to the museum of infertility treatment along with ventrisuspension and Rubin's tubal insufflation. Men with varicocele and varying sperm pictures should be subjected to assisted reproduction, IUI or ICSI depending on the sperm picture.

Acknowledgements

I thank Dr. Siddharth, fellow in Clinical Andrology for helping me in researching the references and structuring the article . I also thank peer reviewers for their valuable feedback and constructive criticism which has helped improve the article.

References

1) Barwell, R. One hundred cases of varicocele treated by the subcutaneous wire loop. The Lancet 1885; 125(3222): 978.

2) Tulloch WS. Varicocele in subfertility. British Medical Journal 1955; 2(4935): 356.

3) Naughton CK, Nangia AK, Agarwal A. Varicocele and male infertility: Part II: Pathophysiology of varicoceles in male infertility. Human Reproduction update 2001; 7(5): 473-481.

4) Meacham RB, Townsend RR, Rademacher D, Drose JA. The incidence of varicoceles in the general population when evaluated by physical examination, gray scale sonography and color Doppler sonography. The Journal of Urology 1994; 151(6): 1535.

5) Mieusset R, Bujan L, Mondinat C, Mansat A, Pontonnier F, Grandjean H. Association of scrotal

hyperthermia with impaired spermatogenesis in infertile men. Fertility and Sterility 1987; 48(6): 1006-1011.

6) Camoglio FS, Zampieri N, Corroppolo M, Chironi C, Dipaola G, Giacomello L, Ottolenghi A. Varicocele and Retrograde Adrenal Metabolites Flow. Urologia Internationalis 2004; 73(4): 337-342.

7) Simşek F, Türkeri L, Cevik I, Bircan K, Akdaş A. Role of apoptosis in testicular tissue damage caused by varicocele. Archivos españoles de Urología 1998; 51(9): 947-950.

8) World Health Organization. WHO laboratory manual for the examination of human semen and sperm-cervical mucus interaction 2010.

9) Pandiyan N. Semen analysis – A numbers game. CHCMJ 2012; 1(1): 2-3.

10) Prathima T, Pandiyan N. Definition of Oligozoospermia – A Commentary. CHCMJ 2013; 2(4): 108-109.

11) Uma Maheshwari. Inter-observer variability on human sperm morphology assessment. Paper presented at the CAC; Chennai; 2014 March 29.

12) Evers, JL, Collins JA. Assessment of efficacy of varicocele repair for male subfertility: a systematic review. The Lancet 2003; 361(9372): 1849-1852.

13) Charny CW, Baum S. Varicocele and infertility. JAMA 1968; 204(13): 1165-1168.

14) Madgar I, Weissenberg R, Lunenfeld B, Karasik, A, Goldwasser B. Controlled trial of high spermatic vein ligation for varicocele in infertile men. Fertility and Sterility 1995; 63(1): 120-124.

15) French DB, Desai NR, Agarwal A. Varicocele repair: does it still have a role in infertility treatment? Current Opinion in Obstetrics and Gynecology 2008; 20(3): 269-274.

16) Krause W, Müller HH, Schäfer H, Weidner W. Does treatment of varicocele improve male fertility? Andrologia 2002; 34(3): 164-171.

17) Ding H, Tian J, Du W, Zhang L, Wang H, Wang Z. Open non microsurgical, laparoscopic or open microsurgical varicocelectomy for male infertility: a meta analysis of randomized controlled trials. BJU international 2012; 110(10): 1536-1542.

18) Bechara CF, Weakley SM, Kougias P, Athamneh H, Duffy P, Khera, M, Lin PH. Percutaneous treatment of varicocele with microcoil embolization: comparison of treatment outcome with laparoscopic varicocelectomy. Vascular 2009; 17(suppl 3): S129-S136.

19) NICE Clinical guidelines. Fertility: assessment and treatment for people with fertility problems. National Institute for Health and Clinical Excellence; February 2013; 2nd edition: 136.

Mind the diet for a timely delivery

Pre-term birth accounts for around 10% of all live births worldwide and is a leading cause of death and disease in infants. In a new study carried out in Adelaide, South Australia, the researchers investigated the relationship between preconception diet of the women and the occurrence of pre-term birth when they became pregnant. Women who consistently ate high protein foods(lean meat, fish, chicken, whole grains), vegetables and fruits before they became pregnant had less chance of delivering a pre-term baby, while women who ate high fat-high sugar food (take away food, potato chips, cakes, biscuits etc.) had a greater chance of having a pre-term birth. Diet is a modifiable risk factor and it is important to adopt a wholesome diet before as well as during the pregnancy to achieve the best outcome. The results of the study are published in Journal of Nutrition (J. A. Grieger, et al. Preconception Dietary Patterns in Human Pregnancies Are Associated with Preterm Delivery. Journal of Nutrition, 2014; DOI: 10.3945/jn.114.190686,)

- Dr. K. Ramesh Rao

Original Article

Follow up of ART Babies

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Abstract

Assisted reproductive technology (ART) has been accepted as a viable and safe method of treatment for infertile couples. Although a number of studies have been reassuring, there still remains concern about poor perinatal outcomes & congenital anomalies in the babies born. Very few Indian studies on the follow up of ART babies have been reported. Our study evaluates the outcome of babies born as a result of ART treatment at the Department of Reproductive Medicine at Chettinad Medical college and Research Institute, Kelambakkam, Tamil Nadu. A total of 123 babies were included in our 5 years follow up study. The growth mile stones and cognitive development were assessed through personal check up, telephone calls and emails. Congenital anomalies observed in our study were 4%. None of the anomalies could be attributed directly to ART. Growth and development were normal for all these babies. However further long term follow up and comparison with naturally conceived babies during the same period is required to ensure the safety of these advanced techniques.

Key Words: ICSI, Follow up, ART babies, Anomalies

Chettinad Health City Medical Journal 2014; 3(1): 4 - 7

Introduction

Ever since the world's first IVF baby was born in the year 1978[1], there has been a phenomenal growth in the use of A.R.T for the treatment of the infertile couples. Although a large number of studies on the health of babies born using ART have been reassuring[1], no published data exists for the Indian scenario. The Department of Reproductive Medicine at Chettinad Hospitals has strived to conduct a study on the health and well-being of babies born using ART.

Aim of the Study

To assess the well-being of babies born out of IVF/ICSI from Chettinad Health City from March 2008 to April 2014, and to establish the incidence of congenital anomalies in these babies.

Materials & Methods

Babies born either by fresh or frozen embryo transfers as a result of IVF and ICSI treatment in the Department of Reproductive Medicine Chettinad Health City, from March 2008 to April 2014 were included in this study. The babies were individually assessed by a program called "Babies Meet", which is conducted annually. Details from parents regarding antenatal events such as Pregnancy induced hypertension (PIH), Gestational diabetes mellitus (GDM), Ante-partum haemorrhage (APH), History of preterm labour and Premature rupture of membranes (PROM) and use of any medications during pregnancy were collected retrospectively. The perinatal events, mode of delivery, indications for LSCS were also noted. Birth weight, APGAR (1 min and 5 min), NICU admissions and its progress, breast feeding history were recorded.

Clinical follow up of children through the event "Babies Meet"

Babies were examined by a team of Paediatricians. Morphometric features (weight, height) and mile stones were checked. Cognitive function, behaviour were also assessed. Any anomalies observed were also noted. Individual case records were prepared by Paediatricians.

Follow up through phone call

Some children who could not come for the paediatric assessment for personal reasons and who resided out of station/country were followed up by phone calls and e-mails. Parents were requested to provide a paediatric assessment of their children and follow up details were recorded. Periodic phone calls were made to follow up the milestones.

Results

Total number of pregnancies following A.R.T were 221. Of these 111 mothers delivered. All the observations are presented here in tables 1-11.

Pregnancy Outcome - Distribution

Table 1

PREGNANCY OUTCOME	NUMBER OF PATIENTS	PERCENT--AGE
Biochemical pregnancy	35	15.8%
Ectopic Pregnancy	5	2.2%
Spontaneous miscarriage	24	10.8%
Missed miscarriage	14	6.3%
Molar pregnancy	1	0.4%
Ongoing pregnancies	31	14%
Total number delivered	111	50.2%
Total number of pregnancies	221	

Means of follow up

Table 2

FOLLOW UP	NO.TRACED
Total number of deliveries	111
By babies meet	40 (36%)
By phone call	59 (53.1%)
Not traceable	12 (10.8%)

Out of 221, only 111 pregnancies ended up in live births. Among the 111, details of 99 could be traced and the rest (12) were lost for follow up. There were 75 singletons and 24 twins born of 99 deliveries. So the total number of babies on our follow up was 123. There were 3 triplets reduced to twins. 75 mothers could reach the full term before delivery and 24 mothers delivered pre term babies.

Parental Age

Table 3

AGE	MOTHER	FATHER
20-29	33 (33.3%)	6 (6%)
30-39	62 (62.6%)	75 (75.7%)
40 and above	4 (4%)	18 (18.1%)
Total	99	99

Majority of parents were in the age group 30-39 years.

Indications for A.R.T

The indications requiring ART treatment are presented in Table 4.

Table 4

INDICATION FOR A.R.T	NO OF CASES	PERCENTAGE (%)
Male factor	28	28.2%
Female factor	38	38.3%
Unexplained	24	24.2%
Combined	9	9%
Total	99	

Table 5

ANTENATAL COMPLICATIONS	NO OF PATIENTS
GDM	10
Placenta praevia	1
Oligohydramnios	3
PIH	6
GDM and PIH	2
PROM	1
Triplet reduction to twins	3
Total	26 (26.2%)

Of 99 mothers only 26 mothers had antenatal complications. GDM was the most frequently observed complication in our study group, followed by PIH. GDM was prevalent in female factor infertility. Out of 12 patients with GDM, 3 mothers had polycystic ovarian syndrome.

Table 6

AGE VS Complication	20-29 yrs	30 - 39 yrs	>40 yrs.
Placenta previa	1	Nil	Nil
Oligohydramnios	-	3	Nil
GDM	2	6	2
PIH	1	5	Nil
GDM & PIH	1	1	Nil
PROM	-	1	Nil

Antenatal complications were more common in mothers between 30- 39 yrs of age, there were 4 mothers above 40 yrs of age & 2 of them had antenatal complications (GDM).

Mode of Delivery

Table 7

MODE OF DELIVERY	NO OF DELIVERIES	PERCENTAGE
Normal vaginal	7	7.07%
LSCS	92 (33+59)	92.9%
Total	99	

Majority of patients underwent LSCS, of which 59 were elective and 33 emergency.

Weight of the babies at birth

Table 8

WEIGHT	SINGLE	TWINS	PERCENTAGE
<2KG	4 (preterm)	13 (preterm)	13.8%
2.1-3.0KG	52 (8 preterm)	35 (4preterm)	70.7%
>3.1KG	19	-	15.4%
Total	75	48	

NICU treatment

Table 9

INDICATIONS FOR NICU ADMISSION	NO.OF BABIES
Low birth weight	3
Jaundice	5
Preterm	7
Respiratory distress	4
Hypoglycaemia	1
Observation	8
Total	28 (22.7%)

Age of Babies at the Time of Follow Up

Table 10

AGE IN MONTHS	NO OF BABIES	PERCENTAGE (%)
Less than 12	33	33.3%
13-24	22	22.2%
25-36	13	13.1%
37-48	23	23.2%
49-60	8	8%

Oldest baby at follow up was 5 years old. Out of 77 singletons, 33 were male babies and 44 were female babies. Of 46 twin babies, 22 were male and 24 were female babies. There were no known identical twins.

Congenital Anomalies

Table 11

CONGENITAL ANOMALIES	NO OF BABIES	FOLLOW UP
Ovarian cyst	1	Operated
Meningo-myelocoele	1	Expired
Congenital talipes equino varus	2	1-corrected 1-on treatment
Patent foramen ovale	1	On treatment
Total	5 (4%)	

There were 5 babies with congenital anomalies. 2 had congenital talipes equino varus, 1 had ovarian cyst, 1 Meningo-myelocoele, 1 baby had patent foramen ovale. One baby on follow up had an acquired complication of meningitis (normal at birth) at 3 months of age and the baby expired despite treatment.

Discussion

The majority of the women in our study had an uneventful antenatal period. GDM was the most commonly observed medical complication (Table 5). However, mothers more than 30 years of age demonstrated antenatal complications like GDM, PIH, PROM and had an association with the duration of infertility (Table 6). The deliveries were conducted by the Obstetricians who had referred the patients and not by the Reproductive Medicine Specialists in the department. Considering the fact that 75 were singleton pregnancies, the high rate of operative deliveries (92/99) indicates the anxiety of the couples and the care given in dealing with the IVF-ICSI pregnancies.

The birth defects reviewed by Wen et al., 2012 (who had reviewed 46 studies containing 124468 IVF/ICSI children), reported a 2.01% defects for nervous system followed by 1.69% for genitourinary, 1.66% for digestive system, 1.64% for circulatory system, 1.48% for musculoskeletal system and 1.43% for eye, ear, face and neck[1]. The incidence of congenital anomalies in our group is 4%, comparable to naturally conceived children in Indian population 2-3% [2].

Out of the 5 anomalous children (table 11), 2 had CTEV. The reported incidence of CTEV in ICSI babies is 1.48% and in general population is 1-2/1000 live birth[3]. The commonest associated factor is intrauterine compression to fetal parts due to Oligohydramnios / amniotic bands or crowding of fetal parts due to multiple pregnancy[3]. Most of the CTEV are sporadic but in few situations like Edwards syndrome, Ehlers-Danlos syndrome and Loeys-Dietz syndrome it is familial[3]. Because one of the CTEV babies was one of the twins, this could be the contributing factor. The other did not show any associated factors as mentioned above and we conclude that it is sporadic.

Ovarian cysts are estimated to be present in 30% of foetuses and an increase in detection could be attributed to the widespread use of prenatal ultrasound[4]. The fetal and neonatal ovarian cyst are most likely caused by endogenous hormonal stimulation such as fetal gonadotropin, maternal estrogens and placental HCG[5]. Also an association with maternal diabetes, fetal hypothyroidism and fetal ovarian cyst has been observed in certain studies[4,6]. Because after birth the estrogens and HCG decreases rapidly, spontaneous resolution during the neonatal period is seen in most cases[5]. Our baby with the ovarian cyst was born to a mother with GDM and PIH and showed a complex cyst diagnosed at 36 weeks of intrauterine life and persisted till 3 months after birth. As it did not show signs of spontaneous regression it was surgically excised as per the standard recommendations[4] and was found to be benign in nature.

One female child with Meningo-myelocoele died 4 days after birth which was one of the twin babies. Other twin was a male baby and is healthy. Although the exact etiology of Meningo-myelocoele has not been established so far, deficiency of folic acid in women during the early pregnancy is known to be the most important cause[2]. All of the patients in our study were prescribed periconceptional folates and remained compliant with the medication. It is therefore highly unlikely to be the cause for this defect. The most commonly reported complication of cerebral palsy[1,6], was not seen in our cohort of babies.

The baby with patent foramen ovale was one of the twins born to a hypertensive mother at 35 weeks gestational age for uncontrolled hypertension. The incidence of cardiovascular anomalies in ART children is 1.64%[1,6] and the incidence in general population in India is about 2 per 1000 live births.

Twenty eight patients in the study group had male factor infertility. Azoospermia was present in 8 men & oligoasthenoteratozoospermia (OATS) in 20 men.

Although ICSI for severe male factor is associated with increased incidence of genito-urinary abnormalities,[1,6] in our study we have had no urogenital malformations for severe male factor. Because the acceptance for karyotyping and Y-chromosomal deletion studies prior to ART in this group of men is poor or non-existing, it is difficult to associate the possibility of any chromosomal defects in these men.

Several contradicting studies on cognitive and motor development in children of different age groups conceived through ICSI exist. Leunens and Zing[7] in 2006 compared 86 ICSI and 165 IVF conceived children of 4-6 years of age and found no significant difference between the ART group and natural conception group. Bonduelle[8] used Bayley test in children <2 years to assess the psychomotor development and found that the ICSI children were normal and comparable with the natural conception group. However Heineman[9] found the prevalence of autism, autism spectrum disorder to be higher after ICSI. Autism spectrum disorders are a group of neuro behavioural disorders that are marked by social and communication deficit, including repetitive stereotypic behaviour. On the contrary, large study in Denmark by Hvidtjorn[10] between Jan 1995 to Dec 2003 found no increased risk.

Most of our ART children were examined by Paediatricians during our "Babies Meet" for communication skills, work skills, socialization, speech, fine motor development etc. All these babies were found to be normal. The younger babies who are <3 years old were examined for mile stones, speech and were found to be comparable with the natural conception group. Even the behaviour of the children was assessed meticulously and found to be normal so far. The rest was traced through phone calls and e mails to the parents and their well being recorded.

There is always a fear of getting some epigenetic imprinting disorders due to some potential mechanisms by which ART could contribute to the creation of epimutations[11]. The composition of culture media, environment, disruption of maternally imprinted genes with super ovulation, hypomethylation of paternal and maternal genes and the underlying condition of infertility itself could all be associated with imprinting abnormalities. The actual risk for one of the imprinting phenotypes (Silver - Russell syndrome, Beckwith-Wiedemann syndrome, or Angelman syndrome) to occur in an assisted pregnancy is estimated to be low, at less than 1 in 5000[6]. The exact etiology for this imprinting disorder is likely to be heterogeneous and requires more research. We had no child with features suggestive of epigenetic disorders in our series.

Our stringent policy on number of embryos transferred has led to a minimal and acceptable multiple pregnancy rates. This has further limited the consequence of multiple pregnancies like increased incidence of PIH, PROM, prematurity, low birth weight and perinatal complications. Multi fetal reduction can be emotionally very difficult for couples who have conceived through fertility treatment, particularly when the procedure results in the loss of entire pregnancy[12]. We had only 3 patients for whom triplets were reduced to twins and these three patients delivered normal babies.

Conclusion

The observations of babies born in our ART study group have been reassuring and conform with the finding in natural pregnancies in terms of congenital anomalies, growth and development till 5 years of age. The commonly reported genitourinary anomalies in children born after ICSI for severe male factor were not seen. The other anomalies which were seen did not show a positive correlation with ART conception and majority were correctable. Because the number of patients in our study was small, a longer follow up with a larger group is required for confirming the safety of the babies born out of ART.

References

1) Wen J, Jiang J, Ding C, Dai J, Liu Y, Xia Y, Liu J, Hu Z, Birth defects in children conceived by in vitro fertilization and intracytoplasmic sperm injection: a meta-analysis, Fertil Steril 2012; 97(6):1331-1337.

2) Shatanik Sarkar, Chaitali Patra, Malay Kumar Dasgupta, Kaustav Nayek, and Prasanta Ray Karmakar, Prevalence of congenital anomalies in neonates and associated risk factors, Indian journal of Paediatrics 2010;16:159-63.

3) Satish kumar Bhargava, Anupama Tandon, Meenakshi Prakash, Radiography and Sonography of club foot, Indian Journal Orthopedics March 2012, vol 46,229-235

4) Bagolane F, Complex ovarian cyst diagnosis and Management, Journal of Obstet Gynecol 2003; 81:434-438.

5) Klemetti R, Sevon T, Gissler M,Hemminki E, Health of children born after ovulation induction. Fertil Steril 2010; 93: 1157-68.

6) Society of obstetricians and gynaecologists of Canada, clinical practice guidelines 2014: No 302.

7) Leunens LA, Zing RR Klemetti R, Sevon T, Health of children born as a result of in-vitro fertilisation, J Pediatrics 2006; 118:1819-27.

8) Bonduelle M, Joris H, Hofmans K, Mental development of 201 ICSI children at 2 yrs of age, Lancet 2011; 351:1553.

9) Heineman MJ, Leslie Neuromotor, cognitive, language and behavioural outcome in children born following IVF or ICSI–a systematic review Hum. Reprod. Update 2008; 14(3): 219-231.

10) Hvidtjørn D, Schieve L, Schendel D, Jacobsson B, Svaerke C, Thorsen P, Cerebral palsy, autism spectrum disorders, and developmental delay in children born after assisted conception: a systematic review and meta-analysis, Arch Pediatr Adolesc Med 2009; 163(1):72–83.

11) Palermo GD, Neri QV, Monahan D, Kocent J, Rosenwaks Z. Development and current applications of assisted fertilization. Fertil Steril 2012;97:248-59.

12) Evans MI et al, Multi foetal reductions after assisted reproduction, AMJ Obstet Gynecol 2001; 184:97-103.

Review Article

Current Trends in Dental Management of Patients with Chronic Renal Disease

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Abstract

The kidneys perform a wide range of important functions, the prime function of which is to maintain a stable composition of the fluid-bathing cells by selective retention and elimination of water, electrolytes, and other solutes. Chronic renal disease is defined as the presence of kidney damage, or a reduction in the GFR (<90ml/min/1.73m^2), for 3 or more months. Consultation with the nephrologist is essential before any dental treatment is carried out, in order to determine the condition of the patient, define the best moment for dental treatment, introduce the necessary pharmacological adjustments, or to establish other important aspects for preventing complications in the dental clinic.

Key Words: GFR, CKD, Drugs modification, Hemostasis, Infection

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Introduction

The kidneys are essential organs in the urinary system and maintain homeostasis of the body by regulation of electrolytes, maintenance of acid–base balance, and regulation of blood pressure (via maintaining salt and water balance). They serve the body as a natural filter of the blood, and remove water soluble wastes, which are diverted to the urinary bladder. In producing urine, the kidneys excrete wastes such as urea and ammonium, and they are also responsible for the reabsorption of water, glucose, and amino acids. The kidneys also produce hormones including calcitriol, erythropoietin, and the enzyme renin[1].

The glomerular filtration rate (GFR) can be calculated from creatinine clearance, insulin clearance or clearance of isotopes, such as ^{125}I-iothalamate, ^{51}Cr-EDTA or ^{99}mTc-DPTA, or plasma creatinine levels.

In healthy individuals, GFR is around 120ml/min per 1.73m^2 for female and 130ml/min per 1.73m^2 for male[1] (Table 1).

According to the part of renal anatomy involved, kidney diseases can be classified as:-

1.Vascular – diseases of large vessels (e.g. bilateral renal artery stenosis) or small vessels (e.g. ischemic nephropathy, haemolytic –uraemic syndrome and vasculitis)
2. Glomerular – primary (e.g. focal segmental glomerulosclerosis and immunoglobin A nephritis) or secondary (e.g. diabetic nephropathy and lupus nephritis)
3. Tubulointerstitial – polycystic kidney diseases, drug- and toxin- induced chronic tubulointerstitial nephritis and reflux nephropathy.
4. Obstructive – renal and bladder stones and prostate diseases

Table 1: Stages of chronic kidney disease

Stages	Renal Health	GFRml/min/1.73m^2	Features
-	Normal	130	-
1	Diminished renal reserve (early CRF)	>90	Abnormalities in blood or urine test or imaging studies but few overt symptoms
2	Mild CRF (azotaemia)	60-89	Abnormalities in blood or urine tests or imaging studies
3	Moderately severe	30-59	Abnormalities in blood or urine tests or imaging studies
4	Severe CRF	15-29	Uraemic symptoms
5	End stage renal failure(ESRF) or chronic renal failure (CRF)	<15	Life threatening and requires some form of renal replacement therapy

General management of patients with CKD

The progress of CKD is measured by eGFR (estimated GFR ; calculated by taking into account age, gender, serum creatinine level), raise in BUN, rise in serum creatinine. The main treatment goal should be to stop the progress of CKD to stage 5, reduce the cardiovascular risk and thereby reducing the mortality rate. A normal diet with potassium restriction and salt or water control is advocated.

The dosage of drugs excreted renally should be reduced according to the existing kidney function. The least nephrotoxic drugs are preferred. The drugs with active metabolites compromising existing renal function should be avoided.

Table 2: Drug modification in patients with chronic kidney disease

	Usually safe (no dosage change usually required)	**Fairly safe (dosage change only in severe renal failure)**	**Less safe (dosage reduction indicated even in mild renal failure)**	**Avoid (best avoided in any patient with renal failure)**
Antimicrobials	Azithromycin Cloxacillin Doxycycline Flucloxacillin Fucidin Minocycline Rifampicin	Ampicillin Amoxicillin Benzylpencillin Clindamycin Co-trimaxazole Erythromycin Ketoconazole Lincomycin Metronidazole Phenylmethyl penicillin	Acyclovir Cephalosporins Ciprofloxacin Etafloxacin Fluconazole Levofloxacin Ofloxacin vancomycin	Aminoglycosides Carbenicillin Cefadroxil Cefalexin Cefixime Cephalothin Gentamycin Imipenem/cilastatin Itraconazole Sulfonamides Tetracyclines valaciclovir
Anesthetics	Lidocaine	Prilocaine, articaine	-	-
Analgesics	Paracetamol/acetaminophen	Codeine	Aspirin NSAIDs	Dextropropoxyphene opioids, Meperidine, morphine, Pethidine, Tramadol
Anticonvulsants			Carbamazepine Gabapentin Lamotrigine	
Sedatives	Diazepam, Midazolam			

Dental management of CKD

Hemostasis and infection control are the important aspects to be considered in patients with chronic renal disease undergoing dental treatment. The dental procedures like periodontal procedures, minor oral surgeries and dental extractions should be carried out on the day after dialysis, when there is maximal benefit from dialysis and the effect of heparin has worn off. Hemostasis can be achieved in case of prolonged bleeding by-

Desmopressin (DDAVP)	Upto 4hrs
Cryoprecipitate	Peak effect at 4-12hrs and lasts upto 36hrs
Conjugated oestrogen	2-5 days to develop and persists for 30 days

Patients with CKD are more prone for infections and may lead to septicaemia if immunosuppressed. Risk of extrapulmonary tuberculosis is also high. Drugs like tetracyclines which worsen nitrogen retention and acidosis are best avoided. However, doxycycline and minocycline are usually safe. Benzylpenicillin may be neurotoxic due to its high potassium content (Table 2).

Antimicrobial prophylaxis should be considered in patients undergoing dental extractions, scaling or periodontal surgery, especially those with polycystic kidneys (may have mitral valve prolapse), with renal transplants, on PD (peritoneal dialysis) or HD (hemodialysis) with prosthetic bridge grafts of PTFE or tunnelled cuffed catheters. Teicoplanin 400mg may be given intravenously during dialysis, which gives cover for a day[2,3].

Dosage of drugs excreted through kidney should be lowered. Generally prescription of drugs for dental procedures should be considered after consultation with nephrologist. Aspirin and other NSAIDs should be avoided since they aggrevate GI bleeding associated with CKD. Long term use of NSAIDS is associated with risk of acute renal failure, nephrotic syndrome with interstitial nephritis and chronic renal failure[4]. Sodium excretion is reduced and can lead to peripheral oedema, elevated blood pressure and exacerbation of heart failure. Antihypertensive effects of beta-blockers, ACEi (angiotensin converting enzyme inhibitors) or ARBs (Angiotensin II receptor blockers) can be decreased. Short term NSAID use is well tolerated if the patient is well hydrated and has good renal function

and no heart failure, diabetes or hypertension. Serum creatinine should be checked every 2-4 weeks in early treatment.

Topical fluorides can be safely administered for caries prophylaxis. Systemic fluorides are generally avoided due to questionable excretion through damaged kidneys. Antihistamines may cause dry mouth or urinary retention. Antacids with magnesium are avoided as there is risk of magnesium retention. Antacids with calcium or aluminium bases may affect absorption of penicillin V and sulfonamides[5].

In patients on hemodialysis requiring intravenous sedation or withdrawal of blood for investigations, veins of the forearms and saphenous veins are avoided because of risk of fistula infection or thrombophlebitis. Midazolam is preferable to diazepam due to low risk of thrombophlebitis. Local anesthesia is generally safe unless there is severe bleeding tendency.

Conclusion

Patients with chronic renal Disease require special care in relation to dental treatment, not only due to the conditions inherent to the disease but also because of the side effects and characteristics of the treatment they receive. Renal disease influence the use of drugs in dentistry, particularly NSAIDs and some antimicrobials. An appropriate and safe dental care can be provided to these patients with the working knowledge of renal disorders and related problems and in close coordination with the Nephrologists or the patients' physician.

References

1) National Kidney foundation. American Journal of Kidney disease 2002; 39 (2): S1-S266

2) Craig, R.G., Interactions between chronic renal disease and periodontal disease. Oral Dis 2008; 14: 1-7.

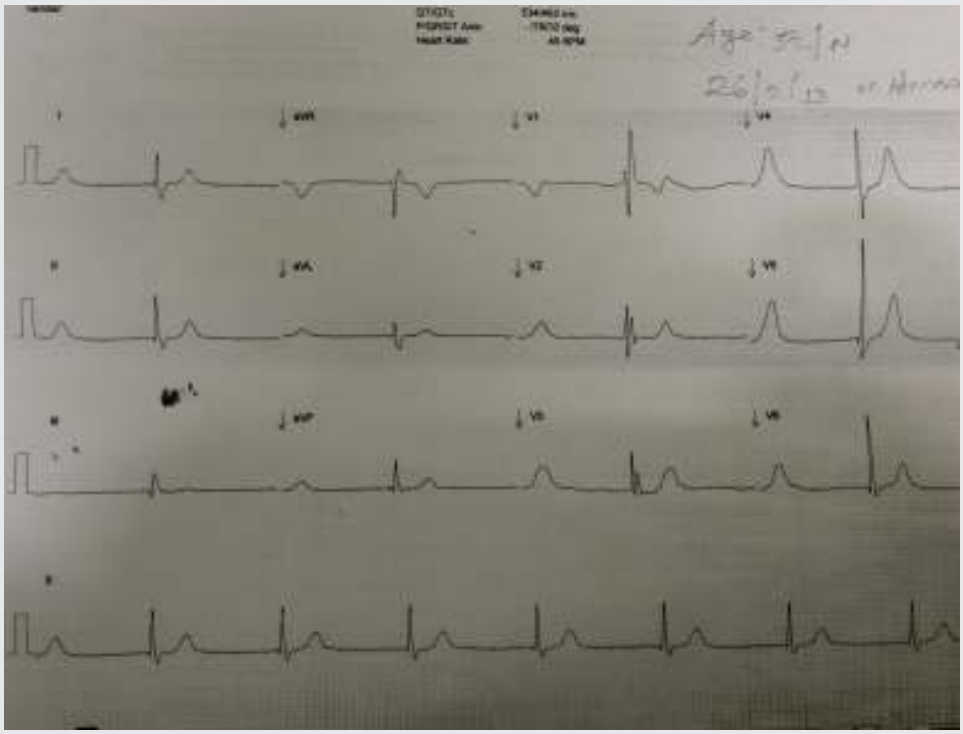
3) Kerr, A.R. Update on renal disease for the dental practitioner. Oral Surg 2001; 92: 9-16

4) Munar, M.Y., Singh, Guidelines for drug dosing regimens in chronic kidney disease. Am Fam Physician 2007; 75: 1487-1496

5) Crispian Scully. Medical problems in Dentistry. 6th edn.

Diagnose the condition

52 year male admitted with history of recurrent syncope.



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Case Report

A Case of Venous Air Embolism During Paediatric Craniotomy in Sitting Position

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Abstract

Careful positioning under anaesthesia is an important aspect of intraoperative management to minimize morbidity and mortality, particularly in patients undergoing neurosurgical procedures. Amongst the different positions used in neurosurgery, sitting position is rarely used now a days in the view of high risk of venous air embolism and hemodynamic instability. This article presents a case report of venous air embolism in a pediatric patient who underwent posterior fossa craniotomy in sitting position.

Key Words: Sitting Position, Venous Air Embolism, Posterior Fossa Craniotomy.

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Case Report

A six year old boy presented with intermittent headache of one year duration, developmental delay and diminished performance in school with recent episodes of giddiness and fall. The MRI brain revealed a quadrigeminal plate tumor causing compression of the aqueduct of sylvius with obstructive hydrocephalus. He was managed with a ventriculo-peritoneal shunt and was planned for a definitive surgical procedure for excising the tumor 3 months later. The suboccipital craniotomy and near total excision of the tumor was done in the sitting position through an infratentorial supracerebellar approach.

The patient weighed 17 Kgs and was 120cms tall. He suffered from no comorbidities and there were no signs of congenital anomalies or difficult airway. General and systemic examination revealed no abnormalities. The patient was kept fasting for an appropriate duration and was given IV atropine 0.3mg and induced with IV midazolam 0.5mg, IV fentanyl 40mcg and IV propofol 40mg. IV vecuronium 2mg was given and oro-tracheal intubation was carried out with 5.0mm sized cuffed, flexometallic ETT. In addition to two wide bore intravenous catheters, a 5Fr triple lumen central venous catheter was inserted through the right subclavian vein and an arterial line was placed in right radial artery for continuous arterial blood pressure monitoring. Anaesthesia was maintained with an intravenous infusion of propofol and inhaled isoflurane in air and oxygen. The patient was ventilated with pressure controlled IPPV and a PEEP of 6 cmH_2O.

The patient was adequately preloaded with intravenous fluids and the sitting position was gradually achieved over 10minutes to avoid hemodynamic collapse while positioning from supine to sitting. A horse shoe support was placed to support the face.

Patient in sitting position with horse shoe face support

During surgery the torcula (confluence of major cerebral venous sinuses) was accidentally opened and resulted in air entrainment. There was a sudden drop in oxygen saturation (SpO_2) to 60%, End tidal CO_2 to 16mmHg and invasive BP to 60/40 mm Hg. The heart rate remained stable throughout. The surgical area was immediately flooded with saline and packed with wet gauze swabs, FiO_2 was increased to 100% and PEEP was increased to 10 cm H_2O. Minimal amount of air was aspirated from right atrial catheter when around 80ml of blood was withdrawn. Fluid loading was done and IV ephedrine was given to stabilize the hemodynamics. SpO_2, $EtCO_2$ and IBP gradually returned to normal in about 10 minutes. The rent in the torcula was clipped and the surgery was continued in the same position. At the end of the procedure the patient was reversed, extubated uneventfully and shifted to the neurosurgical ICU for monitoring.The histopathological examination of the tumour revealed it to be a grade II glioma and the patient was referred for radiotherapy.

Discussion

The use of the sitting position in neurosurgery has decreased compared to the past. The major concern is high rate of occurrence of venous air embolism in craniotomies done in sitting position. The reported incidence of VAE as detected by Doppler sonography in adults ranges from 7 to 50%[1-3]. Harrison and colleagues reported a significantly lower incidence of VAE in the paediatric age group of 9.3%[4], much lower compared to adult age groups. There are two prospective paediatric studies in the literature on the incidence of VAE in the sitting position. Meyer and colleagues reported a 26% incidence of VAE in the sitting position using capnography, in 30 children who were not treated with lower body positive pressure (MAST) or PEEP[5]. Fuchs and colleagues studied 24 children undergoing neurosurgery in the sitting position and reported a VAE incidence of 37% as detected by Doppler[6].

VAE in sitting position

A negative venous pressure relative to atmospheric pressure is necessary for venous air entrainment to occur. In the sitting position the dural venous pressure in the torcula will be negative compared to atmospheric pressure which allows air entrainment into the venous sinuses. Though most of the institutes abandoned the use of sitting position for neurosurgical procedures, Harrison and colleagues reported a lower incidence of VAE (9.3%) and VAE associated hypotension in only 2% out of 407 patients in their 16 years experience[4]. There was no significant perioperative morbidity or mortality and their results suggest that the sitting position can be used safely for neurosurgical procedures in children.

Diagnosis of VAE

The true incidence of VAE depends on the sensitivity of detection methods used during the procedure. The clinical presentation and various detection methods are detailed nicely in a review article[7]. In addition, many cases of VAE are subclinical and hence go unreported. The two main factors determining the morbidity and mortality of VAE are the volume of air entrained and the rate of accumulation. These variables are mainly affected by the position of the patient and height of the vein with respect to the right atrium. The lethal volume of air to cause VAE has been described as between 200 and 300 ml, or 3–5 ml/kg.

Clinically VAE manifests with tachyarrythmias, right heart strain pattern as well as ST and T wave changes in ECG. Myocardial ischemia may be observed with fall in blood pressure as the cardiac output decreases. Pulmonary artery pressure and central venous pressure increases as a consequence of increased filling pressure and right heart failure. There will be a significant fall in $EtCO_2$ with fall in arterial oxygen saturation(SaO_2). Cerebral hypoperfusion may occur due to reduced cardiac output which may manifest in the postoperative period as altered sensorium. Paradoxical air embolism may occur via a patent foramen ovale, a residual defect that is present in approximately 20% of adult population.

Specific monitoring modalities in the descending order of sensitivity and specificity of VAE detection are Transesophageal Echocardiography(TEE), precordial doppler, PA catheter, $EtCO_2$, ECG and esophageal stethescope. TEE is currently the most sensitive monitoring device for VAE, detecting as little as 0.02 ml/kg of air administered by bolus injection. But it is invasive, expensive and requires expertise. The precordial Doppler is the most sensitive of the noninvasive monitors, capable of detecting as little as 0.05 ml/kg of air. This is mostly used in obese patients and its position is confirmed by a bubble test. There will be a change in the character and intensity of the emitted sound. With greater air entrainment, a more ominous "mill wheel" murmur develops, indicating cardiovascular decompensation. A pulmonary artery catheter is a relatively insensitive monitor of air entrainment (0.25 ml/kg) and too invasive and hence is restricted to those patients with significant comorbidities. The fall in $EtCO_2$ occurs with air entrainment of 0.5ml/kg. The sensitivity of the esophageal stethoscope has been shown to be very low in detecting a mill wheel murmur. Timely anticipation of VAE during critical portions of the procedure is more vital than any detection device.

Prevention of VAE

Positioning: Head-up position places the patient at risk for VAE. In such situations, the propensity of incurring a negative pressure gradient between the open venous sinuses and the right atrium can be decreased by increasing right atrial pressure via leg elevation and flexion at the knees.

During insertion of central venous catheter: Insertion or removal of central venous catheter needs a few measures to prevent VAE like occlusion of needle hub or catheter during insertion or removal, insertion during exhalation phase of breathing as deep inspiration may increase the magnitude of negative pressure within the thorax. Trendlenberg position may be used during insertion of catheter as it may keep the CVP on the higher side.

Hydration: A well-hydrated patient reduces VAE risk. The right atrial pressure is to be maintained between 10 and 15 cm H_2O.

Use of PEEP: Though controversial, PEEP is being used in many institutes as a measure to minimize the risk of VAE. In addition PEEP of above 5 cm H_2O also helps to increase oxygen saturation.

Anti shock trousers: The military antishock trousers (MAST) during surgery has been shown to increase right atrial pressure in the sitting position. The right atrial pressure can be elevated and sustained above atmospheric pressure by maintaining military antishock trouser pressure greater than 50 cm H_2O[8]. There are risks of decreasing vital capacity, hypoperfusion of intraabdominal organs, and potential compartment syndromes with the use of this equipment.

Management of VAE

High vigilance and suspicion by the anaesthesia and surgical teams along with newer monitoring devices enable early diagnosis and prompt management of VAE. Stepwise management of VAE includes prevention of further air entrainment, reduction of volume of air already entrained, improved oxygenation and prompt hemodynamic support when needed.

Prevention of further air entrainment

When VAE is suspected the surgeon needs to be warned and surgical site should be flooded immediately with saline. Air entry can be further prevented by eliminating the possible negative air pressure gradient by changing the position of the patient and adjusting the tilt of the table. Also transient jugular venous compression increases venous pressure there by preventing further air entrainment into the open dural venous sinuses. Nitrous oxide has to be discontinued as it may expand the volume of air embolus. In addition to prevention of hypoxia, institution of high flow oxygen minimizes the size of air embolus.

Durant maneuver

Embolic obstruction in the right side of the heart by air embolus can be relieved either by placing the patient in a partial left lateral decubitus position (Durant maneuver)or by simply placing the patient in the Trendelenburg position.

Aspiration of air from right atrium

Central venous catheter is advisable to be placed in all such cases where there is higher chance of VAE instead of emergent catheter insertion for air aspiration during an acute setting of VAE-induced hemodynamic compromise. Central venous catheter is positioned with the tip 2 cm distal to the superior vena caval–right atrial junction[9]. Though success rate is very less and variable this procedure is life saving in cases of massive air embolism.

Hemodynamic support

Hemodynamic instability is an indication of massive air embolism which needs prompt action. The increase in right ventricular afterload because of VAE leads to acute right heart failure followed by decrease in left ventricular outflow. Inotropic support will correct hypotension and better optimize the myocardial perfusion.

CPR

Chest compressions are proved to mechanically force the air out of the pulmonary outflow tract in to the smaller pulmonary vessels, thus improving forward blood flow. Cardio pulmonary resuscitation with defibrillator may be needed in massive VAE.

HBOT

Hyperbaric oxygen therapy (HBOT) is believed to be beneficial due to a reduction in the size of the air bubbles secondary to accelerated nitrogen resorption. Another advantage of HBO therapy is the increased oxygen content of the blood. The HBO therapy is appropriate for paradoxical cerebral air embolism when it can be done within 6 hours from its occurance[10].

Summary

VAE is a silent but dangerous and life threatening condition which needs prompt attention. Planning the appropriate level of monitoring in procedures with high risk of VAE and prompt stepwise management are key to patient safety. Appropriate level of PEEP, intravenous fluid loading, immediate recognition of rent in the dural sinus by the surgeon and the evidence of VAE in the monitor, flooding of the surgical site with saline and application of saline soaked gauzes, prompt aspiration from right atrial catheter and suturing of the rent in the dural venous sinus are the steps done in this patient which probably has reduced the severity of VAE and prevented major hemodynamic compromise.

References

1) Papadopoulos G, Kuhly P, Brock M, et al. Venous and paradoxical air embolism in sitting position. A prospective study. ActaNeurochir 1994;126:140-3

2) Black S, Ockert DB, Oliver WC, Jr, Cucchiara RK. Outcome following posterior fossa craniectomy in patients in the sitting or horizontal positions. Anaesthesiology 1988;69:49-56

3) Young ML, Smith DS, Murtagh F, Vasquez A, Leritt J. Comparison of surgical and anaesthetic complications in neurosurgical patients experiencing venous air embolism in the sitting position. Neurosurgery 1986;18:157-61

4) Harrison EA, Mackersie A, McEwan A, Facer E. The sitting position for neurosurgery in children: a review of 16 years experience. British Journal of Anaesthesia 2002; 88(1): 12-17

5) Meyer PG, Cuttaree H, Charron B, Jarreau, Perie AC. Prevention of venous air embolism in paediatric neurosurgical procedures performed in sitting position by combined use of MAST suit and PEEP. British Journal of Anaesthesia 1994; 73 :795-800

6) Fuchs G, Schwarz G, Stein J, Kaltenbock F, Baumgartner A, Oberbauer RW. Doppler color-flow imaging: screening of patent foramen ovale in children scheduled for neurosurgery in sitting position, J NeurosurgAnaesthesiol 1998; 10:5-9

7) Mirski MA, Lele AV, Fitzsimmons L , Toung TJK. Diagnosis and treatment of Vascular Air Embolism. Anesthesiology 2007; 106:164–77

8) Hanna PG, Gravenstein N, Pashayan AG. In vitro comparison of central venous catheters for aspiration of venous air embolism: Effect of catheter type, catheter tip position, and cardiac inclination. J ClinAnesth 1991; 3:90–4

9) Meyer PG, Cuttaree H, Charron B, Jarreau MM, Peri AC, Sainte-Rose C. Prevention of venous air embolism in paediatric neurosurgical procedures performed in the sitting position by combined use of MAST suit and PEEP. Br J Anaesth 1994; 73:795–800

10) Blanc P, Boussuges A, Henriette K, Sainty JM, Deleflie M: Iatrogenic cerebral air embolism: Importance of an early hyperbaric oxygenation. Intensive Care Med 2002; 28: 559–63

Answer to : **Diagnose the condition**

ECG shows narrow QRS complex with a ventricular rate of 45/min without a preceding P wave.But at the end of QRs complex there is a sharp deflection suggestive of retrograde P wave from AV node.

Possibilities are Sinoatrial nodal arrest or sinus exit block. TYPES OF SA NODAL DYSFUNCTION — What we call the sinoatrial (SA) node actually represents the integrated activity of pacemaker cells, sometimes called P cells in a compact region at the junction of the high right atrium and the superior vena cava. Perinodal cells, sometimes called transitional or (T) cells, transmit the electrical impulse from the SA node to the right atrium. Thus, SA nodal dysfunction can result from abnormalities in impulse generation by the P cells or in conduction across the T cells.

SA nodal pauses and arrest may result from abnormalities in impulse generation by the P cells. SA nodal exit block may be due to abnormalities in conduction across the T cells.

The mass of the SA node is too small to create an electrical signal that can be routinely recorded on the surface ECG. As a result, we generally infer SA nodal activity from the ECG appearance of the response to that activity: atrial activation as manifested by the P wave. Patient needs pacemaker (DDDR).

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Case Report

Ocular Thelaziasis in a 4 Months old Girl Child

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Abstract

Background: Worm infestations of the eye are rare situations. Among those, ocular Thelaziasis is very uncommon. Case characteristics: 4 months old-girl presented with redness, watering and irritation in the left eye for 2weeks. The Thelazia were present in the conjunctival sac. Intervention/outcome: All worms were removed; Framycetin ointment was applied. The child was asymptomatic within 10 days. Message: Awareness and early detection prevents complications.

Key Words: Ocular thelaziasis, Conjunctival sac, Animal host.

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Introduction

Worm infestations of the eye are rare. The commonest infestation mentioned in the literature is Ocular Filariasis, caused by *Loa loa.* Other worms may also inhabitate the eye, eg. Thelazia, which usually produces conjunctival infestation. Thelazia is a genus of nematode worms which are inhabitants of the eyes of dogs, cats, rabbits, camels and rarely, humans[1]. They are often called "oriental eyeworms," as they are seen in countries of Asia. Infestation with Thelazia species is called as "Thelaziasis". In the hosts they are found in the eyelids, tear glands, conjunctiva and vitreous cavity of the eyeball[1]. If this is not diagnosed early and treated it may lead to chronic conjunctivitis, scarring, keratitis, corneal ulcer and rarely intraocular problems[2]. This report is published because of its rarity and also to spread awareness among practitioners.

Case report

At the foothills of Adalur(near Oddanchatram), a 4 month old-girl was brought to our clinic by her mother with the history of itching, redness, watering and mucoid discharge from the left eye for 2weeks. There was no history of fever.

Child was exclusively breast fed and was weighing 5 kg. Left eye examination revealed mucous discharge and lacrimation with redness all over the conjunctiva indicating conjunctivitis. On careful examination, four tiny thread like glistening worms were seen [fig 1]. All the worms were seen moving very fast over the conjunctiva. On eversion of the upper eye lid, two motile worms were seen in the upper part of the fornix. Right eye examination did not reveal any worms and was normal. There was a history of street dogs visiting this family for food. Systemic examination was normal. Blood counts were normal.

Fig 1 - Thelazia worms in the eye

With the help of the ophthalmologist, 4% Xylocaine drops were instilled. The upper eyelid was double everted with a lid retractor; all the six worms were removed with suture tying forceps [fig2].

Fig 2 - Thelazia after removal

Extracted worms were preserved. Apart from conjunctivitis there was no ulceration in the conjunctiva. Intraocular structures and fundus were normal. Framycetin ointment was applied. Promethazine syrup was given. Antinematodal drugs are not indicated for local infestations hence not used. At one month follow up, the child had recovered.

The extracted worms were sent to the regional parasitology laboratory and their study revealed that the worms were white thread like structures, measuring 12-13 mm in length and 0.4-0.5 mm in width and had transverse striations [fig 2]. The head bore four pairs of papillae. The posterior end of the worm carried many pairs of papillae and spicules and was therefore reported under genus- Thelaziidae.

Discussion

Thelazia are not human parasites. They are transmitted from animals to humans through intermediate hosts, mainly Dipteran flies *(Musca autumnalis, Musca domestica, Fannia species, etc)*. The sheathed larvae released by the female worms reach the tears of the infected animal host and are ingested by the flies that feed on the tears. Inside the flies, these hatch, cross the gut wall and migrate to various tissues and develop into infectious larvae and migrate to mouth parts of flies. When these flies feed on tears of humans, they transmit the larvae into the conjunctival sac and become adult worms in 3 to 9 weeks, which may live for 1 year or longer[2].

Though travel to mountainous region has been implicated as a risk factor in some of the reports, cases have been reported in which this history was not found. Therefore it seems that vector and reservoir may be present in plains itself. This relation of vector and reservoir in plains needs further epidemiological study[3].

Thelaziasis in Indian States

There are a few cases of Thelazia infestation among humans reported from India[3]. Probably, the first case of *Thelazia callipaeda* infection was reported from Salem District, India, in 1948[3]. Subsequently, four cases were reported by various authors from Manipur, Assam, and Himachal Pradesh[3]. All these reports are of *Thelazia callipaeda* infestation except the report by Mahanta et al, 2000, in a 13 year old girl, where the case was reported as Thelazia species but the worm isolated was an immature male for which species differentiation could not be done[3]. Therefore, it may be speculated that more cases of Thelazia infestation may be present in Assam, particularly in Dibrugarh district, which may not have been recorded. On many occasions, the patients do not seek medical treatment because of the spontaneous exit of the worm and cure without specific treatment[3]. Not only India but other countries too have reported cases of infestation by Thelazia. Several studies found that up to 30-50% of cattle can be affected by Thelazia species in UK, Italy, Canada and parts of USA. Dogs showed similar infection rates in several Southern European countries[2]. In 2007, there was an interesting case report of vitreous infestation and retinal detachment in Canada[4].

Thelazia damages the tissues of the eye, especially the conjunctiva which becomes scarified, fibrous and provoke excessive secretion of lacrimal fluid[5]. Some hosts experience very severe pain due to active movement of the worms within the eye. In the same eye both adult male and female worms were found previously. This suggests that Thelazia can complete their life cycle in man, the accidental host, as well[5].

Out of ten known species of Thelazia, there are nearly 15 reports of the incidence of *T.callipaeda* in man and less than a dozen reports about *T.californiensis*, a closely allied species[6]. It is more common in animals hence it is definitely a zoonotic disease and man becomes the occasional host. Ocular Thelaziasis was reported in a chronic bedridden, mentally ill, diabetic patient and in a patient with senile dementia[6]. As per Y. Koyama, A.Ohira, T.Kono, T.Yoneyama, and K.Shiwaku, two to five thelazial worms were removed from the conjunctival sac per patient[6]. In our case, we removed six worms from the conjunctival sac.

According to the study by Otranto, D. and M. Dutto (2008), only unilateral ocular thelazial infestation were noted in their cases[7]. We observed the same in our case. A follow up after six months revealed that both eyes were normal.

Key message/Inference

This interesting case was diagnosed early and treated. Full recovery was attained in a short period. But Thelaziasis is a rarely diagnosed disease. In some places of rural India where there is a high infestation rate among animals, awareness has to be raised among paediatricians and general practitioners for early diagnosis. If not treated early, it can lead to scarring and further complications of the eye. Hygienic techniques like hand washing and various fly control measures can help in preventing the disease.

References

1) Isabel Fuentes,Isaias Montes,Jose M.Saugar,Stefania Latrofa,Teresa Garate and Domenico Otranto. Thelaziasis in humans ,a zoonotic infection. Emerging Infectious Disease 2012;18:2073-2075

2) Junquera.P. Thelazia spp parasitic Eyeworms of Dogs, Cats, Cattle,Sheep, Goats and other livestock;Biology prevention and control., Update Oct-2013: parisitipedia.net.

3) Nath R, Narain K, Saikia L, Pujari BS, Thakuria B, Mahanta J. Ocular thelaziasis in Assam: A report of two cases. Indian J Pathol Microbiol [serial online] 2008. Available from: www.ijpmonline.org/text.asp?2008/51/1/146/40430

4) Xue, C., N. Tian, and Z. Huang. Thelazia callipaeda in human vitreous. Canadian Journal of Ophthalmology 2007; 42(6):884-885.

5) Joseph,A.,Ocular Thelaziasis. Indian J Ophthalmol 1985;33:113-4

6) Koyama, Y., A. Ohira, T. Kono, T.Yoneyama, and K.Shiwaku. Five cases of thelaziasis. British Journal of Ophthalmology 2000;84:439-442.

7) Otranto, D. and M. Dutto. Human thelaziasis, Europe. Emerging Infectious Diseases 2008;14(4):647-649.

Killer Diet!

Low-carb diets like Atkins' have emphasized high intake of animal protein and fat. While they lead to successful weight reduction, they also increase serum cholesterol, thus increasing the risk of heart disease. Now a study published in BMJOpen (Jenkins DJA et al, BMJOpen 2014;4:e003505) claims that a low-carb vegan diet overcomes known drawbacks of those earlier diets. Dubbed "Eco-Atkins" diet, it helps not only in reducing your bulk but also in reducing the risk of heart disease by 10% over a period of 10 years. Principal investigator Jenkins claims that "they killed two birds with one stone — or, rather, with one diet". It combines the cholesterol reducing effect of vegan diet with weight reducing effect of low-carb diet.

- Dr. K. Ramesh Rao

Case Report

Papillary Cystadenoma of Minor Salivary Gland

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Abstract

Papillary Cystadenoma is a well-circumscribed, benign tumor that originates from the salivary glands, with the cystic cavities showing intraluminal papillary projections. Papillary tumors of the minor salivary glands are quite rare. Most of the lesions described in the literature under the heading 'papillary cystadenoma' histologically resemble an adenolymphoma without the lymphoid component.

Here we report a case of Papillary cystadenoma of minor salivary gland with special emphasis on the histomorphological features and differential diagnosis of this tumor.

Key Words: Papillary Cystadenoma, Palate, Benign Salivary Neoplasm.

Chettinad Health City Medical Journal 2014; 3(1): 18 - 21

Introduction

Papillary cystadenoma of salivary glands is a rare benign neoplasm. It constituted only 2% to 4.7%, respectively, of all minor salivary gland neoplasms, and 4% to 8.1% respectively, of all benign epithelial minor salivary gland neoplasms[1,2] . This lesion has a tendency to recur if not appropriately excised[1]. Papillary cystadenomas of the oral region are reported in literature[1,2,3,4,] however, case reports of Papillary Cystadenoma arising from a minor salivary gland of palate are even rare[5,6]. Characteristic histological features usually aid in diagnosis of salivary gland lesions. However, diagnosis of salivary gland pathology is not easy. Clinical and histological differential diagnoses have to take into account to support a diagnosis of Papillary cystadenoma.

Case Report

A 54-year-old man presented with an asymptomatic mass of the hard palate that was present for 3 years. Apart from being a known diabetic, his medical, family, dental history and review of systems were not significant. There was no history of nasal obstructive symptoms, discharge or pain in relation to the maxillary sinus areas.

Intraoral examination revealed a solitary, sessile, well-circumscribed, solid, round mass of about 4-cm in diameter (Fig 1) that was slow-growing. The mucosa overlying the mass showed no changes in colour. The surface of the swelling was smooth. There was no history of trauma, bleeding, discomfort from the swelling or pain during eating. The inspectatory findings were confirmed on palpation and the swelling was firm in consistency, non-fluctuant, non-compressible and non-pulsative. Mobility of the adjacent teeth could not be demonstrated. No abnormalities were detected extraorally. No neck masses were palpated, and no synchronous pathology was observed in the oropharyngeal region. A provisional clinical diagnosis of Pleomorphic adenoma was made.

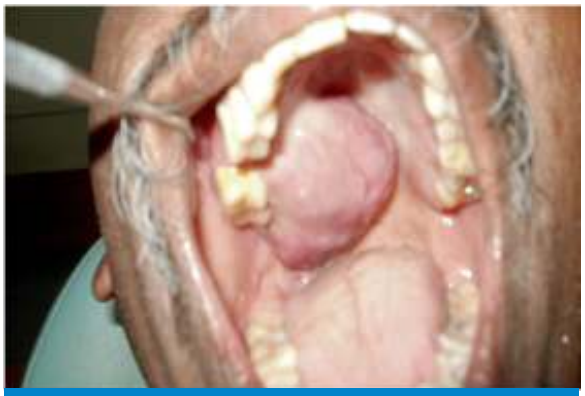

Fig. 1: 4-cm-diameter solitary, sessile, well-circumscribed, solid, round mass on the palate.

Investigations

Laboratory investigations, carried out as a routine preoperative procedure did not yield any remarkable findings. The swelling in the palate was close to the maxillary antrum. Hence a CT scan which is a superior imaging modality for delineating any bone involvement was chosen for radiological evaluation. CT scan revealed a well defined soft tissue swelling of the palate

with small extension into antrum but without erosion of antral floor or bony involvement (Fig. 2&3). Incisional biopsy was done under local anesthesia under the clinical suspicion of pleomorphic adenoma.

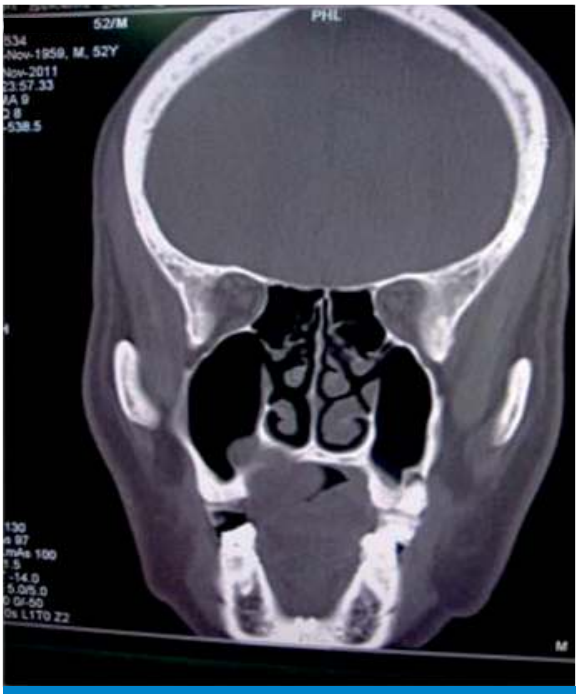

Fig. 2: A well defined soft tissue swelling of the palate with small extension into antrum but without erosion of antral floor or bony involvement

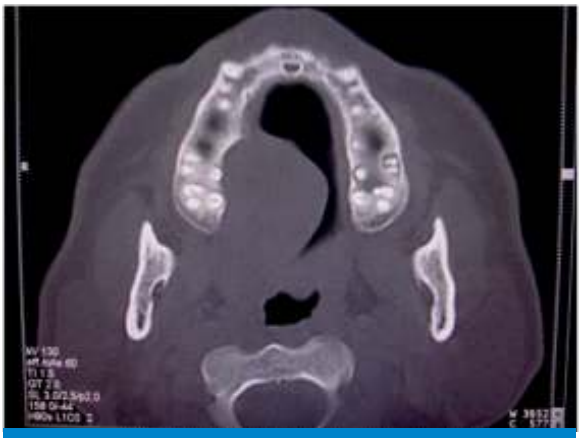

Fig. 3: A well defined soft tissue swelling of the palate with small extension into antrum but without erosion of antral floor or bony involvement

The histologic examination showed the tumor mass to be encapsulated by thick fibrous connective tissue and arranged in the form of lobules, sheets and ductal pattern. The mass was also composed of numerous cystic spaces lined by epithelium which are thrown into papillary projections and in few areas they were surrounded by thickened basement membrane. The lining epithelium comprised of cuboidal ductal cells with vesicular nuclei and showed no atypia. Thin fibrous connective tissue core admixed with few areas of haemorrhage and hyalinizations were seen. Final diagnosis was confirmative of Papillary cystadenoma of the minor salivary gland. (Fig 4, 5, 6).

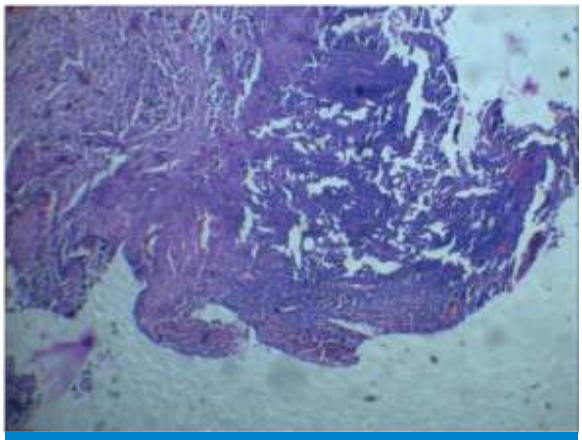

Fig. 4: The cystic space showing multiple papillary projections supported by fibrous connective tissue (H&E x4).

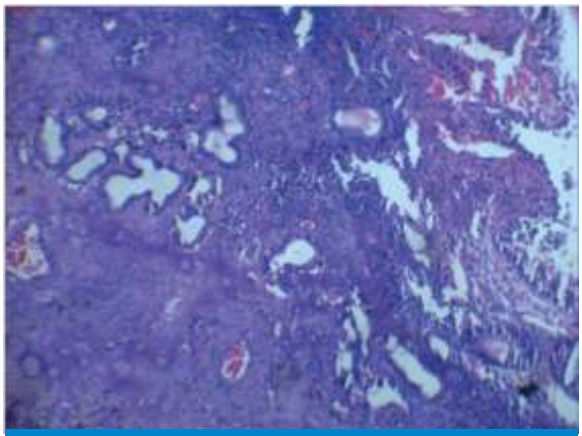

Fig. 5: The papillary projections are lined with cuboidal to columnar cells with ductal proliferation in the center of the lesion (H&E x4).

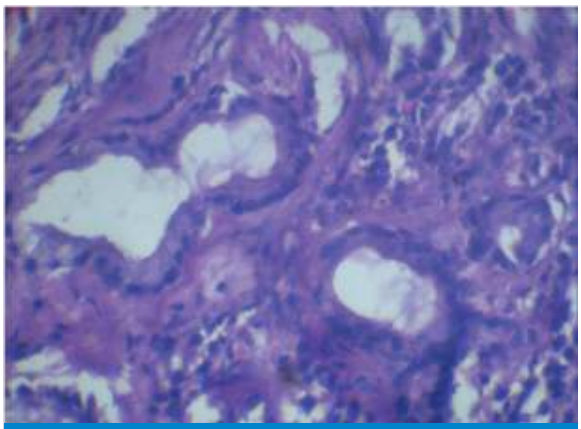

Fig. 6: The ducts comprised of cuboidal cells and partly by one to two layers of flattened cells with no cellular atypia. (H&E x40).

Differential diagnosis

Pleomorphic adenoma, Warthin's tumor, intraductal papilloma, canalicular adenoma, polymorphous low-grade adenocarcinoma, low-grade mucoepidermoid carcinoma, and the papillary cystic variant of acinic cell carcinoma were considered.

Treatment

A total excision of the tumour was planned. Under general anaesthesia with nasotracheal intubation the procedure was performed uneventfully. A clear acrylic surgical obturator, fabricated on a cast made prior to surgery, was given.

Outcome and follow-up

Postoperative period was uneventful. The patient was stable and afebrile. The patient was followed up for ten months and there was no evidence of recurrence.

Discussion

The Papillary cystadenoma (PC) is described as a cystic adenoma consisting of cystic spaces filled with papillary projections[7] , arising from undifferentiated epithelium of the intercalated duct of the glands[1] particularly the minor salivary glands. "A tumor contains multiple papillary projections and numerous types of epithelial lining cells with close resemblance to Warthin tumor and does not show any lymphoid elements" was the definition given by World Health Organization (WHO) for PC[8]. In this sense, we believe that salivary glands tumors are difficult to diagnose or interpret because there are many possible patterns of presentation. Tumors of minor salivary gland origin account for less than 25% of all salivary gland neoplasm[9] . In addition; Papillary cystadenoma of the minor salivary gland is rare[5].

The Papillary cystadenoma appears to occur more frequently in women, older than 50 years of age, with several in their seventies[10]. The most common sites are the palate and buccal mucosa, however, tumors in the lip and tongue also have been reported[11]. In our case, the tumor occurred in the palate of a 54-year-old man.

Lim et al[12] provided a cytological description of smears prepared from fine-needle aspiration of Papillary cystadenoma. The cytology could direct only to an interim diagnosis which is not definitive[13] . The ultimate histopathological diagnosis of this rare minor salivary gland neoplasm required the elimination of similar benign tumors such as Warthin's tumor, canalicular adenoma, intraductal papilloma, and malignant tumors such as low-grade mucoepidermoid carcinoma, cystadenocarcinoma, polymorphous low-grade adenocarcinoma, and papillary cystic variant of acinic cell carcinoma.

To rule out Warthin's tumor, we must check for presence of lymphoid aggregates containing germinal center, and a double-row epithelium with inner low cuboidal cell and outer tall columnar cells[8]. These histological features were not evident in our case. Canalicular adenomas also show large cystic spaces containing papillary proliferations. But the epithelium usually presents as a single-layered cord or columnar or cuboidal cells with deeply stained basophilic nuclei. The connective tissue stroma is loose in nature with prominent vascularity[8]. Intraductal papillomas are benign salivary gland tumors which are usually unicystic containing intraluminal proliferations[8]. These incongruous features ruled out canalicular adenoma and intraductal papilloma. However in our case, solid areas (usually limited in extent) and cystic areas were evident. The papillae lined by cuboidal to columnar cells usually two layers thick were seen projecting into the cystic areas.

Low-grade mucoepidermoid carcinoma shows prominent cyst formation and relatively a high noncystic epithelial proliferations[13]. The cystic papillary projections are irregular and complex similar to that seen in intraductal papilloma. In addition to the above features low-grade mucoepidermoid carcinoma exhibits minimal cellular atypia with a mixture of epidermoid, mucous, and intermediate cells which were not apparent in the present case. Cystadenocarcinoma, polymorphous low-grade adenocarcinoma, and papillary cystic variant of acinic cell carcinoma were eliminated based on the solid growth pattern in certain areas, the invasive pattern, the degree of cytological atypia, destruction of the glandular architecture, as well as invasion into the adjacent tissues like adipose, muscle, or bone tissues[14]. None of these features was observed in the present case.

Oncocytic change in Papillary cystadenoma can be focal or marked. When histology showed a unilocular cystic lesion with multiple papillary fronds lined with oncocytic cells and focal metaplastic squamous cells Papillary oncocytic cystadenoma variant can be considered[15]. But our case did not show any oncocytic cell changes.

A final diagnosis of Papillary cystadenoma was arrived based on the insight of the pathologist. Most recent report of a case involving cytological analysis and review of the literature, reported that in the authors' best knowledge, theirs was only the 12th case of this tumor seen in the palate[12]. Nevertheless, clinically and histologically, Papillary cystadenoma displays a benign behaviour with rare recurrence.

Conclusion

Papillary Cystadenoma is a benign tumor originating from the salivary glands, with the cystic cavities containing intraluminal papillary projections. Papillary Cystadenoma arising from a minor salivary gland is rare. Conservative surgical removal is the treatment of choice. This lesion has a tendency to recur if not appropriately excised. Based on both macroscopic and microscopic findings dentist must be familiar to diagnose the salivary gland neoplasm of accessory glands.

References

1) Alexis JB, Dembrow V. Papillary cystadenoma of a minor salivary gland. J Oral Maxillofac Surg 1995; 53: 70-2.

2) Waldron CA, El-Mofty SK, Gnepp DR. Tumors of the intraoral minor salivary glands: a demographic and histologic study of 426 cases. Oral Surg Oral Med Oral Pathol 1988; 66: 323-33.

3) Akin RK, Kreller AJ, Walters PJ. Papillary cystadenoma of the lower lip - report of a case. J Oral Surg 1973; 31: 858-60.

4) Cathoun NR, Cerine FC, Mathews MJ. Papillary cystadenoma of the upper lip. Oral Surg 1966; 21: 782-5.

5) Tsurumi K, Kamiya H, Yokoi M, Kameyama Y. Papillary oncocytic cystadenoma of palatal minor salivary gland: a case report. J Oral Maxillofac Surg 2003; 61: 631-3.

6) Mahler V, Schell H. Papillary cystadenoma- a rare tumor of the minor salivary glands. Eur J Dermatol. 1999; 5: 387-9.

7) Kameyama Y, Okada Y, Takehana S, Mizohata M, Nishio S, Enomoto M. Papillary cystadenoma. Int J Oral Surg 1985; 14:556-9.

8) Ellis GL, Auclair PL, Gnepp DR. Surgical Pathology of the Salivary Glands. Saunders WB; 1991.

9) Stathopoulos P, Gagari E. Papillary cystadenoma of the lower lip exhibiting ciliated pseudostratified columnar epithelium: report of a bizarre case and review of the literature. J Oral Maxillofac Surg 2012; 30:357.

10) Collins EM. Papillary cystadenoma of accessory salivary gland. Am J Surg 1958; 96:749-50.

11) Guccion J. G. Papillary cystadenoma of the palate: a case report and ultrastructural study. J Oral Maxillofac Surg 1997; 55: 759-64.

12) Lim CS, Ngu I, Collins AP, McKellar GM. Papillary cystadenoma of a minor salivary gland: report of a case involving cytological analysis and review of the literature. Oral Surg Oral Med Oral Pathol Oral Radiol Endod.2008; 105:28-33.

13) Sanjay Gupta, Pushpa Sodhani, Shyama Jain, Nita Khurana, Prem Narayan Agarwal. Oncocytic papillary cystadenoma of parotid gland: A diagnostic challenge on fine-needle aspiration cytology Diagnostic Cytopathology 2011; 39:627-630.

14) Ananthaneni A, Kashyap B, Prasad VR, Srinivas V. Cystadenoma: A perplexing entity with subtle literature. J Dr NTR Univ Health Sci 2012; 1:179-81.

15) Zhang S, Bao R, Abreo F. Papillary oncocytic cystadenoma of the parotid glands: a report of 2 cases with varied cytologic features. Acta Cytol. 2009; 53:445-8.

Not that sterile!

Until now, it was believed that placenta was a sterile organ supplying the much needed oxygen and nutrients to the foetus. That belief is no longer tenable if the results of a new study published in Science Translational Medicine (Aagaard, K. et al. Science Transl. Med. 6, 237ra65, 2014) are to be accepted. In that study, the investigators analysed 320 placentas for the presence of bacteria by shotgun metagenomic sequencing. The researchers found small number of diverse bacteria including *Escherichia coli, Prevotella tannerae and Neisseria*. The latter two are normally found in mouth. The microbiome in placenta closely resembled the one found in normal oral cavity. This might explain the well-known link between the periodontal disease in mother and pre-term birth. This study establishes that even in normal pregnancy, there is a specific bacterial community within the placenta. Further study is required to understand the role of placental microbial community in pre-term birth.

- Dr. K. Ramesh Rao

Case Report

Seizure Disorders in Pregnancy

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Abstract

Generally seizures occurring in pregnancy are thought to be due to eclampsia. We analyzed patients who were pregnant or in puerperium and presented to our hospital with convulsions, from the years 2007 to 2013. In this period, there were 4315 deliveries in our hospital. We found that 18 patients had convulsions complicating pregnancy & puerperium, an incidence of 0.417%. Of these, 12 were patients had with eclampsia [incidence of 0.27%] and 6 patients had non-eclamptic seizures, with an incidence of 0.139 %. Of these 6 patients, 2 had posterior reversible encephalopathy syndrome. The other 4 cases of non-eclamptic seizures in pregnancy were due to cortical venous thrombosis, subarachnoid hemorrhage & neurocysticercosis. None of these patients had a history of epilepsy. We are presenting these cases to highlight that several other conditions apart from eclampsia, need to be considered in a person without epilepsy presenting with convulsions during pregnancy.

Key Words: Seizure disorders in pregnancy, Cortical venous thrombosis, Subarachnoid hemorrhage, neurocysticercosis

Chettinad Health City Medical Journal 2014; 3(1): 22 - 25

Introduction

Eclampsia is the occurrence of convulsions or coma with hypertension, proteinuria and/or pedal edema between 20 weeks of gestation and 48hrs postpartum. Atypical cases are those that develop at less than 20 weeks of gestation and after 48 hours postpartum and that have some of the signs and symptoms of preeclampsia-eclampsia without the usual hypertension or proteinuria[1]. There are many causes for seizures in pregnancy other than eclampsia, like cerebral infarction, hemorrhage, due to malformations, hypertensive encephalopathy, cerebral venous thrombosis, cerebral malaria, meningitis, intra cranial tumors, metabolic diseases, posterior reversible encephalopathy syndrome, thrombophilia, thrombotic thrombocytopenic purpura[2] etc.,We present 4 such cases of non-eclamptic seizures in pregnancy due to cortical venous thrombosis, subarachnoid hemorrhage & neurocysticercosis.

Case1: Neurocysticercosis

A 29 year old gravida2 para1 live1 presented with history of convulsions at 9 weeks of amenorrhea. She had 1 convulsion at home and 1 at the local hospital. She was given phenytoin sodium at a local hospital and then referred to our hospital. She had caesarean for her previous pregnancy 1 year three months back due to pre-eclampsia. When the patient presented to us, she was drowsy, not oriented to time and place, responding to painful stimuli. Blood pressure on admission was 140/80 mm Hg and pulse rate was 102 bpm. She was afebrile. Cardiovascular system and respiratory system were found to be normal.

Investigations revealed a urine pregnancy test which was weakly positive. Except for an elevation in total count to 16700cells/cmm, uric acid level of 10.8 mg/dl and 1+ albumin in urine, rest of the blood investigations was within normal limits. Ultrasound pelvis showed a single live intra-uterine gestation corresponding to 8 weeks 6 days;MRI showed right frontal granuloma with edema (Neurocysticercosis){Fig.1-4}.

In view of the diagnosis, patient requested a medical termination of pregnancy (patient was counseled on alternative modes of management), which was performed with Mifepristone 200 mg followed by Misoprostol 600 mcg vaginally. She was started on Tablet Albendazole & IV dexamethasone for 3 days followed by Tablet Prednisolone 8 mg for 2weeks. She was discharged and on follow up no further convulsions were reported.

Complicating factors in this case: [1] Previous history of preeclampsia - there is 25% chance of pre eclampsia to recur in subsequent pregnancies (Dutta)[3]. [2] Urine albumin + 1 [3] Raised total count of 16700 [4] Serum uric acid 10.8mg/dl [5] Limitation on imaging procedures due to pregnancy.

Discussion

In the 2 other reported cases (Singhal et al.,) also the urine albumin was raised to 1+4. MRI has again proven itself to be an invaluable diagnostic tool in other reported cases[4,5].

Case2: Sub Arachnoid hemorrhage

25 year old Primigravida, post IUI conception with twin gestation at 31 weeks +3 days presented with preterm labour pains. Patient was conscious and oriented. Blood pressure on admission was 110/60 mm Hg and pulse rate was 76 beats/ min. Cardiovascular system and respiratory system were found to be normal, per abdomen- over distended uterus with multiple fetal parts felt, both fetal heart rates were good, per vaginal examination- no draining / bleeding per vaginum.

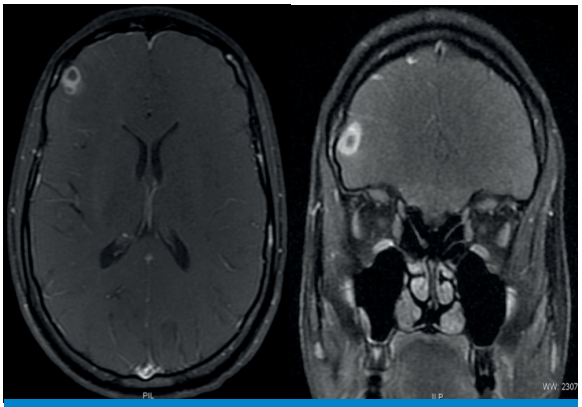

Fig 1 & 2: Contrast T1 Coronal & Contrast T1 Axial : Showing ring enhancing conglomerate lesions in the right frontal lobe.

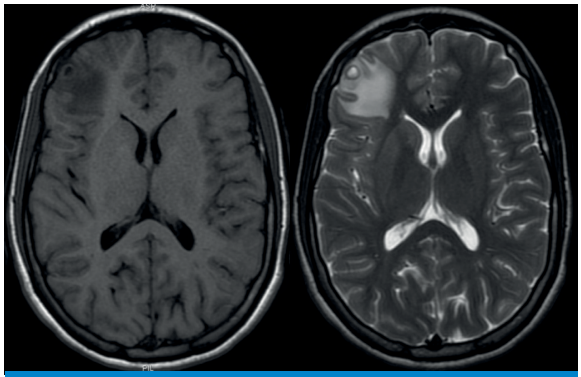

Fig 3 & 4 - T1Weighted &T2 Weighted images: Showing focal lesion with surrounding edema in right frontal lobe in grey-white matter junction.

She was admitted and as steroid prophylaxis was already given before admission, tocolytics were started. The next day she went in for preterm premature rupture of membranes. In view of extreme preterm premature rupture of membranes, patient was taken up for emergency Lower segment caesarean section and Twin A was a girl baby weighing 1.440kg with an Apgar score of 5/10, 8/10, O positive blood group. Twin B was also a girl baby weighing 1.505 kg with an Apgar score of8/10 ,8/10, B negative blood group. There was atonic postpartum hemorrhage which was managed medically and 1 unit of blood was transfused. Anti D was given. Patient developed fever of 101 F after 12 hours postoperatively & was treated with paracetamol. After 16 hours post delivery, patient had 1 episode of tonic clonic convulsions with a blood pressure of 150/84 mm Hg and Pritchards regime (magnesium sulphate regime) was started. Patient was also started on antibiotics. Fundus examination was found to be normal. Blood investigations were within normal limits. Neurophysician advised for a MRI brain / MRV to rule out cortical vein thrombosis.MRI showed intracerebral hemorrhage in left basal ganglia, sub arachnoid hemorrhage in left parietal and bilateral occipital regions. Patient was initially started on IV. Fosphenytoin & Nimodipine. Subsequently, phenytoin and sodium valproate were given orally. CT brain showed resolving subarachnoid hemorrhage. She developed diabetes insipidus which resolved spontaneously. She was discharged on post operative day 29 and advised to follow up with neurophysician.

Complicating factors: [1] history of postoperative fever

Case 3: Cortical venous thrombosis

A 23 year old gravida2 para1 live1 with previous lower segment caesarean section for oligohydramnios and cephalopelvic disproportion, was admitted at 38 weeks 5 days for safe confinement.

Clinical and biochemical examination of the patient were normal. Patient developed labor pains and was taken up for an emergency repeat lower segment caesarean section. She delivered a girl baby weighing 3.355 kg with an Apgar score of 9/10. On the 5thpost operative day, patient suddenly had one episode of generalized tonic clonic convulsions with a BP of 150/100 mm Hg, and was treated with IV Phenytoin. She had 3 more episodes of generalized tonic clonic convulsions and was given loading dose of IV Phenytoin and was shifted to ICU and intubated. CT brain revealed Right frontal hypodensity with small area of hyperintensity. Patient was diagnosed to have cortical vein thrombosis and was put on Intravenous heparin, dexamethasone, mannitol, torsemide, levetiracetam, sodium Valproate, and midazolam. MRI showed features suggestive of cortical venous thrombosis with acute hemorrhagic infarct in left frontal lobe. Patient subsequently improved and was discharged.

Case 4: Cortical venous thrombosis

26 year old female was brought in by her relatives with history of unresponsiveness for duration of one hour. Patient had delivered a full term girl baby through normal vaginal delivery at a local primary health centre 15 days ago, following which she had persistent vomiting & abdominal pain. She also had intermittent fever for the past 15 days. Patient developed numbness of right upper and lower limbs after admission along with 1 episode of generalized tonic clonic convulsions.

Patient was unconscious, pulse rate was 82bpm, blood pressure on admission was 110/60 mm Hg. Cardiovascular and respiratory systems were found to be normal. Per abdomen was soft. Both pupils were equal and reacting to light. There was right facial lag, catatonia of left upper limb, paucity of movements in right upper & lower limbs on painful stimuli and bilateral plantar flexor. All deep tendon reflexes were present in upper limb and brisk in lower limbs.

Blood work up and USG Doppler to rule out deep vein thrombosis did not reveal anything abnormal. CT brain showed cerebral vein thrombosis with hypointensities in left temporal and right frontal regions probably due to Thrombosis. MRI brain showed features suggestive of cortical venous sinuses thrombosis.

Patient was admitted in the ICU and was started on Intravenous Heparin, Dexamethasone, Mannitol, Ceftriaxone, Levetiracetam and Phenytoin. Then Inj.Heparin was changed to Inj.Enoxaparin. Patient progressively deteriorated and expired 5 days after admission. The cause of death was cortical venous sinuses thrombosis with malignant intracranial hypertension with severe brainstem dysfunction.

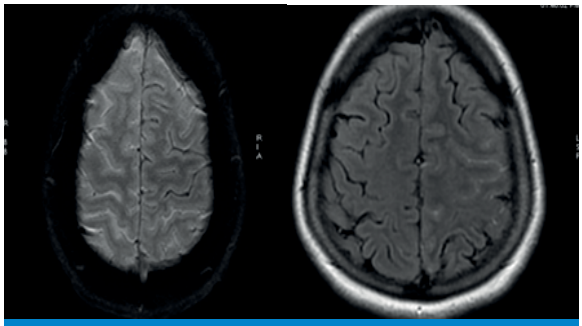

Fig 5 & 6 - T2 FLAIR & GRE images:
Showing linear hyper intensities noted on T2 FLAIR image with GRE blooming in the left parietal region, suggestive of subarachnoid hemorrhage.

Complicating factors: [1] history of postoperative fever

Discussion

This article highlights the fact that all convulsions in pregnancy are not due to eclampsia. We found that we had 18 cases of convulsions complicating pregnancy & puerperium giving us an incidence of 0.417%. Of these 12 were cases of eclampsia [an incidence of 0.28 %] and 6 were cases of non-eclamptic seizures [an incidence of 0.14 %]. Of these 6 patients, 2 had posterior reversible encephalopathy syndrome[6,7].

Table - 1

	No. of cases	Incidence
All convulsions	18	0.417
Eclampsia	12	0.28
Non eclamptic convulsions	6	0.14

Fig 7 & 8 T2 FLAIR & GRE images:
Showing mixed intense area noted in left frontal lobe in T2flair, blooming noted in left frontal lobe in GRE.

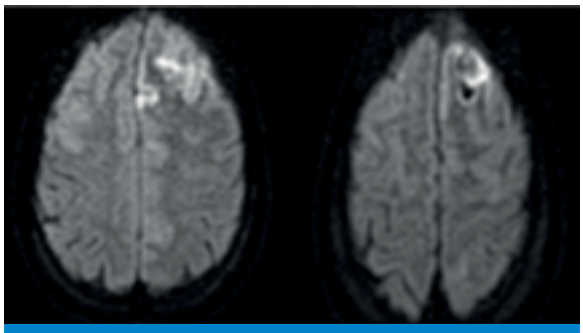

Fig 9 & 10 - DWI images:
Showing diffusion restriction in the left frontal lobe

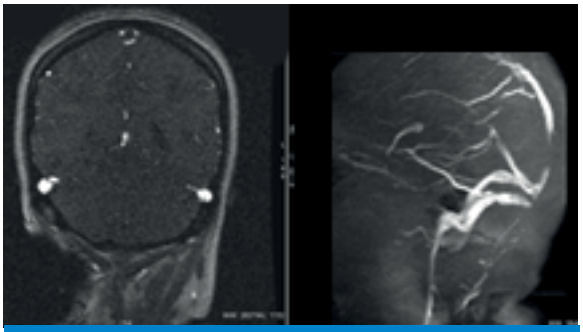

Fig 11 & 12 MRV :
Showing thrombus/ no flow in superior sagittal sinus

The differential diagnosis that should be considered include:

[1] Epilepsy: incidence is around 1 in 200 pregnancies. Usually previous history of epilepsy can be elicited.

[2] Infections – encephalitis & meningitis – fever is usually present, increased total counts are seen. Neurocysticercosis & tuberculoma are other infections that usually present as a space occupying lesion. Neurocysticercosis is due to the cysts of Taenia solium the pork tapeworm[8]. Infection happens when humans consume the ova from exogenous sources or through self infection by the fecal-oral route.

These then are digested in the stomach and release oncospheres which penetrate the intestinal wall and reach the blood stream. These oncospheres develop into cysticerci in any organ. In countries where it is endemic, cysticercosis may affect 2-4% of the populations. Convulsions in pregnancy have different consequences than in the non-pregnant. The hypoxia and acidosis caused by the convulsions, although well tolerated by the mother, can be fatal to the fetus[5].

The treatment of choice for neurocysticercosis during pregnancy is Albendazole and Prednisolone. If the patient has an intraventricular cyst, then post delivery shunting is advisable[3].

[3] Stroke – either hemorrhagic or ischemic. Ischemic strokes are caused due to cerebral vessel thrombosis or cerebral embolism. These include cortical venous thrombosis.

Hemorrhagic strokes are due to either intracerebral hemorrhage or subarachnoid hemorrhage. In pregnancy the intracerebral haemorrhage is usually associated with hypertension superimposed on pre-eclampsia or occasionally pure pre-eclampsia. Intracerebral haemorrhage has a higher mortality rate than subarachnoid haemorrhage because of its location. Subarachnoid haemorrhage is bleeding into subarachnoid space, the area between the subarachnoid membranes and pia mater surrounding the brain.

Causes: Berry aneurysms, arterio- venous malformations, infections, coagulation disorders, angiopathies, venous thrombosis, drug abuse (cocaine), tumours and trauma.

Subarachnoid haemorrhage occurs at a frequency of 6 in 1, 00, 000 pregnancies. The incidence does not differ from the general non-obstetrical population but the mortality during pregnancy can be as high as 35%. Idiopathic subarachnoid haemorrhage constitutes about 15-30% of sub arachnoid hemorrhage.

The classical signs and symptoms are:

1. Thunderclap headache,
2. Fever (around 102.2 degree F),
3. Vomiting,
4. Altered consciousness,
5. Papilloedema, 6. Neck stiffness,
7. Seizures (1 in 14),
8. Terson's syndrome (subhyaloid haemorrhage).

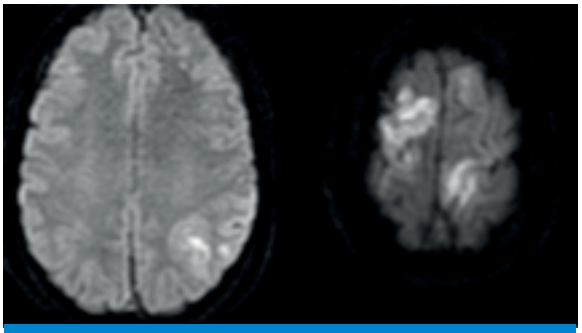

Fig 13 & 14 DWI images:
Showing multiple acute infarcts in fronto-parietal region

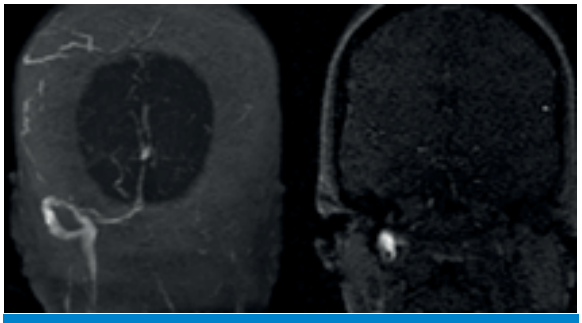

Fig 15 & 16 MRV:
left transverse sinus and superior sagittal sinus are not visualized. Right transverse sinus and sigmoid sinus are thinned out.

[4] Posterior reversible encephalopathy syndrome (PRES) - clinical features include headache, nausea, vomiting, seizures, visual disturbances and altered sensorium. PRES is due to failure of cerebral auto regulation and endothelial dysfunction. It is essentially a clinico-radiological diagnosis[2]. In PRES, the MRI images show hyper intense lesions in the cerebral white matter mainly in the parieto-occipital region. Occasionally the lesions involve the grey matter[6].

Cortical venous thrombosis is a rare disorder affecting 5/1000000. The prevalence of cortical venous thrombosis in the Indian population is about 4.5 / 1000 obstetric admissions[6]. Our incidence is 0.46/1000. Similarly the case fatality rate is less than 10%[9].

Acknowledgements

We wish to thank our Dean Prof.Ravindran for his support and encouragement. We express our gratitude towards Dr.Subramanian, Consultant Neurophysician as well as the department of radiology for their valuable inputs. We also are grateful to the Medical Records Department for their patient cooperation and for providing us with the material required for this paper.

References

1) Sibai BM, Stella CL, Diagnosis and management of atypical preeclampsia-eclampsia, AmJ Obstet Gynecol 2009; 200:481.e1-481.e7

2) Mustafa Albayrak, İsmail Özdemir, Yavuz Demiraran, Süber Dikici, Atypical preeclampsia and eclampsia: report of four cases and review of the literature in J Turkish-German Gynecol Assoc 2010; 11: 115-7

3) D.C.Dutta, Hypertensive disorders in pregnancy, Textbook of Obstetrics, 7th edition 2014: 219-40

4) Singhal et al.: Neurocysticercosis as an important differential of seizures in pregnancy: two case reports. Journal of Medical Case Reports 2011; 5:206.

5) Gowri.V,Jacob.P.C,Jain.R,Sawhney.K,"Neurocystic ercosis in pregnancy" Neurosciences 2005; Vol.10 (2): 183-185

6) Srinija.P., Abubacker Sulaiman., Anoop Sreevalsan, Somasundaram, Vasantha N.Subbiah. "Posterior reversible encephalopathy syndrome "Chettinad Health City Medical Journal 2013; 2(2): 65-68.

7) Kadkol.R, Godbole.R.R, ante partum eclampsia with posterior reversible encephalopathy syndrome, Journal of Obstetrics and Gynecology Societies of India 2012; 62 (s1): s27-s28

8) Suarez, Victor R.,Thomas A. Iannucci. Neurocysticercosis in pregnancy: a case initially diagnosed as eclampsia. Obstetrics & Gynecology 93.5, Part 2 1999: 816-818.

9) Kakade.A.S & Kulkarni.Y.S "Cerebral venous thrombosis in pregnancy" Bombay Hospital Journal, 2011; Vol53 Special issue

Case Report

Giant Dumb Bell Trigeminal Schwannoma

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Abstract

Trigeminal schwannomas account for less than 8% of intracranial schwannomas and less than 0.4% of all intracranial tumors. They originate within the ganglion, nerve root, or 1 of the 3 divisions of the trigeminal nerve. About 50% of these tumors are limited to the middle fossa, while 30% extend into the posterior fossa and 20% are dumbbell-shaped and extend into both fossae. Dumb bell schwannomas pose a great surgical challenge in removing completely. Here we present such an interesting case.

Key Words: Trigeminal-Dumb bell-Retro sigmoid-Sub temporal

Chettinad Health City Medical Journal 2014; 3(1): 26 - 28

Case Report

A 40 year old lady presented with history of dull persistent headache with right facial pain and numbness for 2 months duration. Patient also complained of giddiness and unsteadiness while walking for 1 month duration. On examination patient had normal higher mental function. Patient had right V1 V2 distribution diminished sensation with right partial Trigeminal motor involvement. Patient also had Right Grade 2 Facial Nerve involvement along with right cerebellar signs and cerebellar type nystagmus. No lower cranial nerve involvement and pyramidal tract involvement seen. MRI Brain with contrast showed Large Dumb bell shaped T1 Hypointense and T2 Hyperintense lesion arising in the middle cranial fossa at Meckel's cave extending into the posterior fossa via tentorial hiatus and occupying the right CP angle region, twisting and displacing the Brainstem and cerebellum (Fig.1). Anteriorly, the lesion extended upto superior orbital fissure. The lesion was well enhancing with contrast. Provisional diagnosis of Trigeminal Schwannoma TYPE C(Samii et al Classification)[1] considered. Since the posterior fossa component of the lesion was fairly big and cannot be removed through the Sub temporal approach, the tumor resection was planned in 2 stages. Trans petrosal approach was not considered because the patient's hearing was well preserved.

In stage 1 procedure the patient was placed in Park Bench position and through a Right retro sigmoid sub occipital approach the posterior fossa opened and CSF was let out, cerebellum became lax. There was a firm well encapsulated highly vascular lesion was seen projecting via the hiatus and pressing on the VII-VIII cranial nerve component. Careful arachnoid dissection and tumor debulking was done. Capsule was dissected meticulously under microscope from the surrounding Cranial nerves, vessels, cerebellum and brainstem. The whole tumor was removed upto tentorial hiatus in this stage. Post operatively patient had partial Facial Nerve palsy and left Hemiparesis grade 4. Post op CT scan showed no residual lesion at posterior fossa and there was a small bleed in right half of brainstem. Patient hemiparesis recovered over 4 weeks.

In stage 2, procedure was performed after 4 weeks. Through a Right Sub temporal Extradural approach the middle cranial fossa part of the tumor was removed in total. There was a bony erosion at the medial part of Petrous bone through which the tumor was protruding into the posterior fossa. Post operative period uneventful. Post operative scan showed no residual lesion (Fig 2,3). At 4 weeks follow up patient was walking without support with residual Facial Nerve palsy which is also recovering. At 3 months follow up patient had minimal facial numbness and no Hemiparesis. Follow up Contrast MRI showed no residual lesion (Fig 4).

Discussion

The trigeminal nerve emerges from the ventrolateral surface of the pons and runs anteriorly 1-2 cm through the cerebellopontine cistern to reach the petrous apex. Vascular structures such as the petrosal vein and the superior cerebellar artery lie close to the trigeminal nerve. Over the petrous apex, 7 mm of distance from the medial lip of the internal acoustic meatus, the Gasserian ganglion is enveloped by a dural deflection forming the Meckel's cave, laterally to the cavernous sinus and the carotid artery. As it leaves the Meckel cave, the trigeminal nerve is divided into 3 branches: the ophthalmic (V1), maxillary (V2), and mandibular (V3) branches. These 3 nerves run under the middle fossa dura mater and leave the temporal bone through the lateral wall of the cavernous sinus (for V1), foramen

The trigeminal nerve can also be surgically classified into 3 segments: cisternal, from the brainstem to the petrous apex; intracranial-extradural, from the Meckel cave to the foramina; and extracranial (V1, V2, and V3).Functionally, the trigeminal nerve has 2 portions: the "pars compacta," which constitutes the triangular portion and comprises the primary afferent fibers that are responsible for the special sensibility of the face; and the motor root, which carries the branchiomotor fibers to the muscles of mastication. The motor root runs practically separated from the "pars compacta" but together with the cranial portion of the nerve. At the level of the Meckel cave, it is oriented medially and leaves the skull together with the mandibular nerve.

The intracranial-extradural portions of V2 and V3 are surgically identified using the foramen spinosum as an anatomical landmark, which is located at the sphenoid bone and contains the middle meningeal artery. The foramina ovale and rotundum are located 2-5 mm superoanteriorly and 10-12 mm superomedially to the foramen spinosum, respectively.

Schwannomas originating from cranial nerves are usually benign, isolated, and slow growing. They may occur in multiple sites when associated with NF2. Schwannomas arising from the trigeminal nerves are the second most common type of intracranial schwannomas, representing 0.8-8% of these tumors. Trigeminal schwannomas tend to occur in middle-aged patients; the highest incidences are between the ages of 38 and 40 years, and are more common in women. Patients with TS frequently complain of trigeminal nerve-related symptoms, but they may also be asymptomatic. The clinical symptoms in these patients include trigeminal hypesthesia, facial pain, headaches, hearing impairment, seizures, diplopia, ataxia, and hemiparesis and increased ICP with papilledema.

Samii et al, classified the tumor extension into 4 categories based on radiological findings: Type A, intracranial tumor predominantly in the middle fossa; Type B, intracranial tumor predominantly in the posterior fossa; Type C, intracranial dumbbell-shaped tumor in the middle and posterior fossa; and Type D, extracranial tumor with intracranial extensions[1].

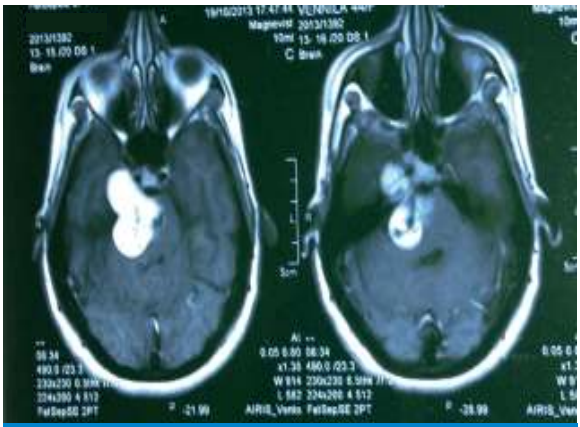

Fig 1: Contrast MRI Brain showing well contrast enhancing dumb bell shaped giant lesion arising from middle cranial fossa extending into posterior cranial fossa.

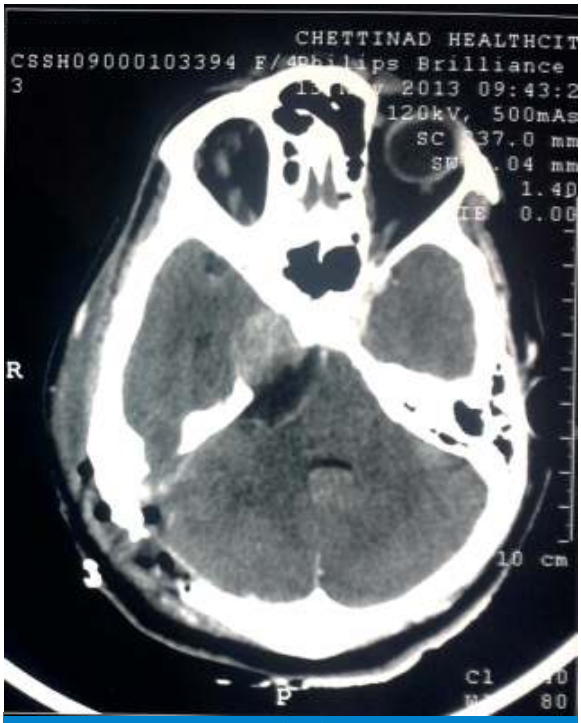

Fig 2: Post op Contrast CT after first stage showing complete excision of posterior fossa lesion and the remaining middle cranial fossa part

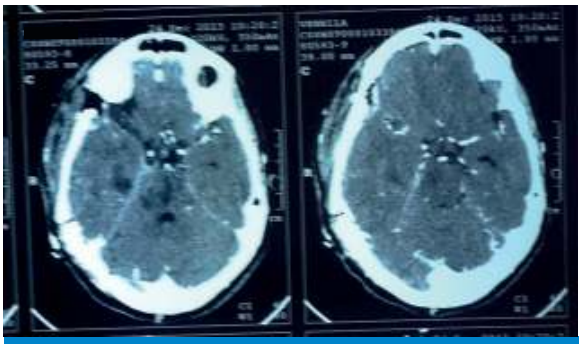

Fig 3: Immediate post op CT after second stage showing no residual lesion

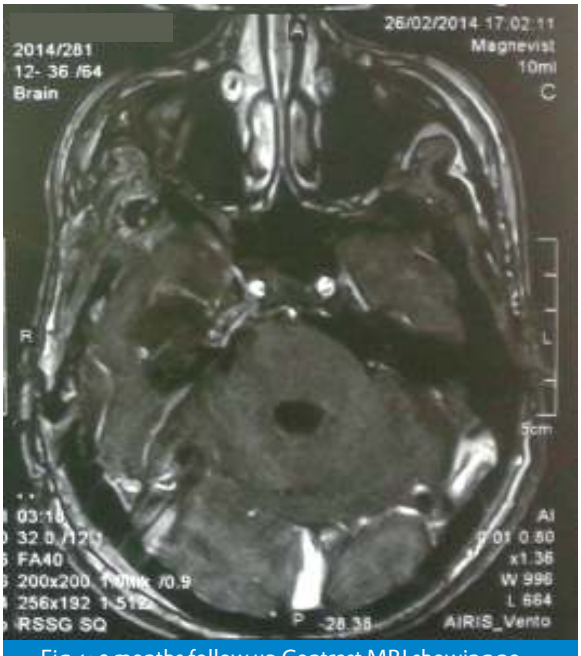

Fig 4: 2 months follow up Contrast MRI showing no residual lesion

Management strategy for TSs involves clinical observation followed by MR imaging follow-up for incidental tumors, surgical removal, and, alternatively, radiotherapy or radiosurgery. Complete or near-total surgical removal can be achieved in > 70% of the patients by means of skull base approaches and microsurgical dissection[2,3,4,5]. Involvement of the cavernous sinus is one cause of subtotal resection. In most cases, a clear plane of cleavage between the tumor capsule and the cavernous sinus structures can be found, allowing complete dissection and total resection. In the modern neurosurgical era, recurrence of TS is rare and the outcome is usually favorable; the most frequent symptom after surgery is trigeminal hypoesthesia, which is transient in most cases. Facial pain may persist after surgery, but most patients report improvement or total relief during follow-up. Diplopia, CSF leakage, meningitis, and hydrocephalus have been also described as possible complications. Most new cranial nerve deficits present resolution within 4-6 months.

Although good results have been reported with radiosurgery, this technique is reserved for small, Non resectable, and residual tumors within the cavernous sinus. Long-term follow-up of patients treated with this method is still needed to evaluate the exact role of radiosurgery in the late control of these lesions. It is evident, however, that no patient will ever be cured of this benign tumor with radiotherapy or radiosurgery[6,7,8].

Conclusion

Management of giant trigeminal schwannomas occupying multiple compartments is a challenging one. Since it is a benign tumor complete surgical excision should be done. Removing in single approach depends on the extent of the lesion and the neurological deficit.

References

1) Samii M, Migliori MM, Tatagiba M, Babu R: Surgical treatment of trigeminal schwannomas. J Neurosurg 1995; 82:711-718

2) Trigeminal neurinomas extending into multiple fossae: surgical methods and review of the literature:KKazunari Yoshida, M.D., and Takeshi Kawase, M.D..Department of Neurosurgery, School of Medicine, Keio University, Tokyo, Japan

3) Al-Mefty O, Ayoubi S, Gaber E. J. Trigeminal schwannomas: removal of dumbbell-shaped tumors through the expanded Meckel cave and outcomes of cranial nerve function. Neurosurg. 2002 Mar;96(3):453-63.

4) Youssef S, Kim EY, Aziz KM, Hemida S, Keller JT, van Loveren HR. The subtemporal interdural approach to dumbbell-shaped trigeminal schwannomas: cadaveric prosection. Neurosurgery. 2006 Oct;59(4 Suppl 2):ONS270-7; discussion ONS277-8.

5) Yoshida K, Kawase T: Trigeminal neurinomas extending into multiple fossae: surgical methods and review of the literature. J Neurosurg 1999; 91:202-211

6) Hamm KD, Gross MW, Fahrig A, Surber G, Henzel M, Kleinert G, et al: Stereotactic radiotherapy for the treatment of nonacoustic schwannomas. Neurosurgery 2008; 62:29-36

7) Hasegawa T, Kida Y, Yoshimoto M, Koike J: Trigeminal schwannomas: results of Gamma Knife surgery in 37 cases. J Neurosurg 2007; 106:18-23

8) Pan L, Wang EM, Zhang N, Zhou LF, Wang BJ, Dong YF, et al: Long-term results of Leksell gamma knife surgery for trigeminal schwannomas. J Neurosurg 2005; 102:220-224

Case Report

Kearns – Sayre Syndrome

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Abstract

The Kearns-Sayre syndrome is a rare genetic disorder caused by mitochondrial myopathy due to mutations in mitochondrial DNA and typicallydevelops before the age of twenty. Clinical triad of Kearns-Sayre syndrome are chronic Progressive External Ophthalmoplegia (CPEO), salt and pepper like Pigmentary Retinopathy and Cardiac blocks. KSS prognosis is related to the number of tissues affected and the severity of the alterations. In this article we report a patient who presented with clinical features suggestive of Kearns-Sayre syndrome.

Key Words: Mitochondrial Myopathy, CPEO, Pigmentary Retinopathy and Cardiac blocks

Chettinad Health City Medical Journal 2014; 3(1): 29 - 31

Introduction

Kearns-Sayre syndrome is a rare neuromuscular disorder first described by Thomas P. Kearns and George P. Sayre in 1958. Incidence is 3/100000 live births and is a rare genetic disorder caused by mitochondrial myopathy due to mutations in mitochondrial DNA and typically develops before the age of twenty. Clinical triad of Kearns-Sayre syndrome were Chronic Progressive External Ophthalmoplegia (CPEO), salt and pepper like Pigmentary Retinopathy and Cardiac blocks.

Case Report

19 year old male came to ophthalmology outpatient department with complaints of drooping of eye lids and difficulty in moving both eyes for the past one year, six episodes of syncope in past five months duration.There was no history of diplopia, ataxia and deafness.On examination both eyes vision was 6/60 with pin hole improvement to 6/24. Both eyes lids showed severe ptosis with poor Levetor Palpebrae Superioris and restricted extraocular movements suggestive of Chronic Progressive External Ophthalmoplegia (CPEO) (Fig 1). Conjuntiva, Cornea, Iris, Lens were normal. Intraocular pressure was within normal limits. Fundus showed pigmentary retinopathy in macula (Fig 2). Electroretinogram showed reduced photopic and normal scotopic response (Fig 3). On auscultation pansystolic murmur (2/6) was noted. Electrocardiogram showed third degree atrioventricular block with an atrial rate of 100 per minute and a ventricular rate of 37 per minute (Fig 4). Echocardiogram shows a dilated left ventricle with an ejection fraction rate of 63%. Patient has CPEO, Pigmentary retinopathy and Cardiac blocks, so we came to the diagnosis of Kearns- Sayre Syndrome.

Fig 1 : A - shows bilateral severe ptosis and B – shows external ophthalmoplegia

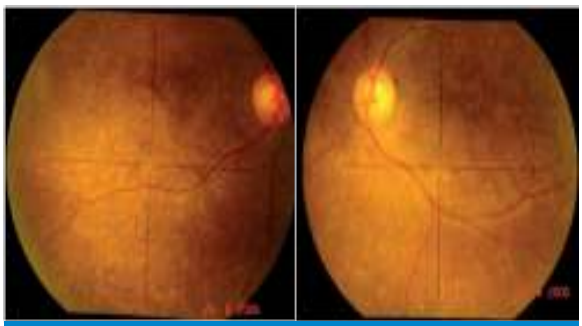

Fig 2 : Both eyes showed pigmentary retinopathy in posterior pole

Discussion

Kearns-Sayre syndrome, a rare neuromuscular disorder was first described by Thomas P. Kearns and George P. Sayre in 1958.Incidence is 1-3/100000 live births[1,2]. The Kearns-Sayre syndrome is a genetic disorder caused by mitochondrial myopathy due to mutations in mitochondrial DNA involved in oxidative phosphorylation for energy production.

Mitochondrial DNA contains many genes for normal function but deletion removes 4,997 nucleotides, which includes twelve mitochondrial genes in Kearns – Sayre syndrome. Deletions of mitochondrial DNA result in impairment of oxidative phosphorylation and a decrease in cellular energy production. Regardless of which genes are deleted, all steps of oxidative phosphorylation are affected. Tissues with high energy demand such as muscle and nervous system are particularly vulnerable to mitochondrial dysfunction, a consequence of deletions, rearrangements or other mutations in mitochondrial DNA[3,4,5]. Triad of Kearns-Sayre syndrome are Chronic Progressive External Ophthalmoplegia (CPEO), salt and pepper like Pigmentary Retinopathy and Cardiac blocks. Ptosis is the first sign in Kearns-Sayre syndrome. Other systemic involvements are deafness, ataxia, syncope, renal failure, seizure, dementia, short stature, hypocalcemia and diabetes[6,7,8,9]. The cardiac manifestations of Kearns- Sayre Syndrome are the most important aspects of the disease for determining the prognosis. Manifestations of cardiac disease occur in 57% of patients with Kearns-Sayre Syndrome, including syncopal attacks, heart failure and cardiac arrest[10,11,12]. Kearns-Sayre Syndrome is diagnosed by extra ocular muscle biopsy which shows the ragged-red cells (red fibers torn) due to intramuscular accumulation of abnormal mitochondria and it is specific for the diagnosis of mitochondrial myopathies[6,7,8]. Increased amount of protein (>1g/l) in cerebrospinal fluids in CSF analys is also specific for Kearns-Sayre syndrome[6,7]. There is no specific treatment for Kearns-Sayre syndrome. Co enzyme Q10 was tried in certain myopathy cases. Cardiac blocks are managed with cardiac pacemakers and ptosis corrected by crutch glasses (Fig 5).

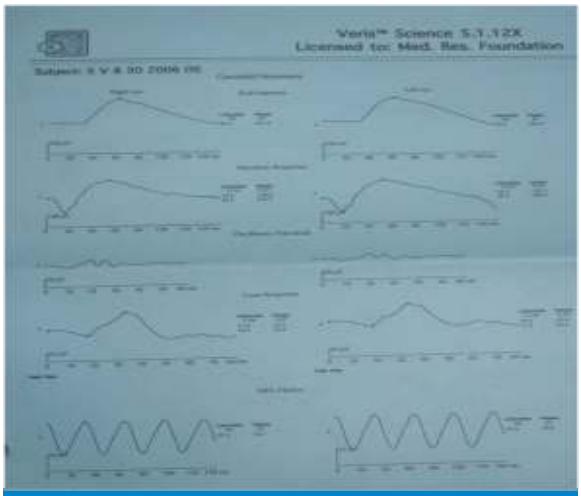

Fig 3 : Electroretinogram showed reduced scotopic and normal photopic response

Conclusions

Awareness of the nature of components of the syndrome led us to early recognition of the systemic complications and plan appropriate referral and management. KSS prognosis is related to the number of tissues affected and the severity of the alterations. The disturbances in the cardiac conduction system are responsible for high morbidity and mortality of the

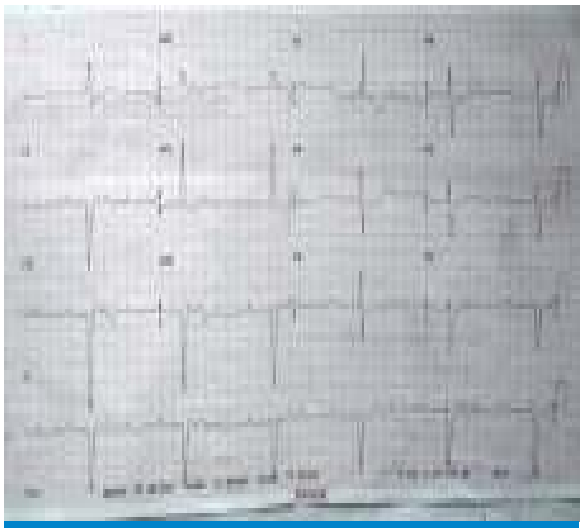

Fig 4 : ECG shows third degree atrio - ventricular block

Fig 5 : Bilateral ptosis corrected by crutch glasses

References

1) Kearns TP, Sayre GP. Retinitis pigmentosa, external ophthalmoplegiaand complete heart block: unusual syndromewith histologic study in one of two cases. Arch Ophthalmol 1958;60:280-289.

2) Nasseh IE, Tengan CH, Kiyomoto BH, Gabbai AA. Doenças mitocondriais. Rev Neurociências 2001;9(2):60-69.

3) Gerbitz KD obermeir –kusserB .ZEIRS Z mitochondrial myopathies divergence of genetic deletions biochemical defects and genetic syndromes J Neurol 1990;273-5:10

4) ZevianiM, MoraesCT, Di Mauro S.Deletions of mitochondrial DNA in aernes-sayresyndrome.Neurology 1998: 1525-32

5) BrockingtonM, AlsanjariN, Sweeney MG, Kaernes-sayre syndrome associated with mitochondrial DNA deletionor duplication, a molecular genetic and pathological study. J NeuroalSci 1995; 131: 78-87

6) Jack j Kanski Brad Bowling Clinical Ophthalmology : Seventh edition; A systematic approach; Chronic Progressive External Ophthalmoplegia: 853-854

7) American Academy of Ophthalmology; Retina and VitreousSection - 12 ; Kearns- Sayre Syndrome; 2011-2012 : 275-276

8) Albert Jakobie's Principles and Practice of Ophthalmology ; Third edition ; Retina and Vitreous ; Kearns- Sayre Syndrome: 33-99

9) Myron YANOFF and Jays DUKER Ophthalmology third edition; Retina and Vitreous; Kearns- Sayre Syndrome: 10-32

10) Young TJ, Shah AK, Lee MH, Hayes DL: Kearns Sayre Syndrome: A case report and reviewof cardiovascular complications. Pacing Clinical Electrophysiol. 2005;28:454-457

11) Schwatzkoff BB, Frenzel H, Losse B, Borgreffe M, Toyka KV, et al.: Heart involvement inProgressive external ophthalmoplegia (Kearns Sayre syndrome) Electrophysiologic,hemodynamic and morphologic findings. Journal of Cardiology. 1986;75:161-169

12) Sachdev P, Elliot PM, McKenna WJ:Cardiovascular complications of neuromusculardisorders. Curr Treatment Options Cardiovasc Med 2002;4:171-179

Diabetes is after women's heart!

In one of the largest studies of its kind published in Diabetologia (Diabetologia, May 2014 DOI: 10.1007/s00125-014-3260-6), a metanalysis & systematic review was done on the data obtained from more than 850,000 subjects over a period of 50 years with particular reference to relationship between diabetes and heart disease. It was found that diabetic women have three times greater risk of developing coronary heart disease (CHD) than their non-diabetic counterparts; in diabetic men, the risk of CHD is two-times higher than in non-diabetic men. Taken overall, women have 44% increased risk of CHD compared to diabetic men. If these findings are confirmed, screening women for pre-diabetes and a more stringent follow-up of diabetic women is necessary to prevent CHD in them.

- Dr. K. Ramesh Rao

Class Room

Study Design - A Pragmatic approach

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Abstract

Research, in simpler terms, refers to a quest for knowledge. It can also be defined as a search for pertinent information on any given topic, in a scientific and systematic way. Clinical research broadly falls into two categories based on the assignment of exposures by the investigator – experimental and observational. Experimental trials can be further subdivided into randomized and non-randomized trials; observational studies can be analytical or descriptive. The main feature of an analytical study is the presence of a comparison (control) group. Also, cohort studies, a part of analytical studies, are useful in following up of a study from the time of exposure to outcome. On the contrary, case control studies work in retrospect, i.e from outcome to exposure. Other studies like cross-sectional studies measure both the exposure and outcome at any given point and descriptive studies like case reports have no control group.

Key Words: Study design, Observational study, Experimental study, Case control, Cross sectional, Cohort.

Chettinad Health City Medical Journal 2014; 3(1): 32 - 34

Introduction

Research can be defined as a systematic investigation of any particular question to help derive new conclusions and thereby establish new facts. It involves the discovery of new knowledge and the interpretation and revision of current knowledge. The process involves asking questions thereby collating and integrating current knowledge on the topic and then designing a method to collect information for the research question; and finally deriving new conclusions from the evidence.

In an epidemiological research, the primary step is defining the hypothesis that is to be tested. This includes a clear-cut definition of the exposure(s) and outcome(s) that are under study. The next step is to decide the appropriate study design for the particular study hypothesis. This article emphasize on the various types of study designs and its implications, in order to help the beginners have a brief knowledge before getting into research work.

Study Design

Usually, the design of a study holds more significance than the analysis derived out of it. In that, a poorly designed study may never be retrieved while a poorly analyzed study always has hope for reanalysis. Therefore, it is of vital importance to give utmost consideration to the design of the study as that will govern the analysis of the data. In most of the medical studies, there are 2 main parameters - input and output. An input is an intervention or exposure to a potentially toxic compound and an output is the measure of health that is supposed to be affected by the intervention. Studies are to be categorized with reference to the time sequence in which both the parameters are studied. Clinical research has two large kingdoms: experimental and observational research. This is based on a simple question, whether the investigator assigned the exposure (e.g., treatments) or the investigator has just observed the usual clinical practice. Hence the study design can be classified as in figure 1.

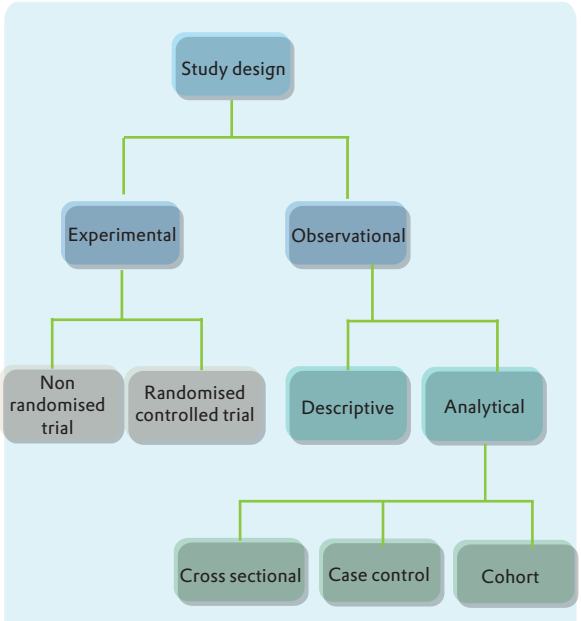

Fig 1: Classification of types of clinical Research

Experimental Study

Experimental study is the one in which an intervention is made by the investigator during the study to find the outcome of the intervention. For example, a litter of rats may be divided into two groups- intervention and control group. The rats for the intervention group are randomly selected and exposed to a supposed carcinogenic agent. After exposure, the frequency of cancer development is recorded in each group. Clinical trials of experimental nature can be further divided into randomized and non-randomized clinical trials.

Non randomized controlled trials: These are study designs in which the participants are assigned to the intervention in a non-random manner. In these trials the alternatives are defined and managed by the investigator.

Randomized controlled trial: This study design though simple, is one of the most powerful tool of research. In a randomized controlled trial the participants are randomly selected and subjected to the clinical intervention[1]. Usually, the term 'intervention' refers to treatment, but it can also be used in a broader sense so as to include any clinical management that is offered to study its effect on the health of the participants. As the name suggests, in a randomized clinical trial, the participants are subjected to the intervention in a purely random manner, or as the popular phrase goes 'by the play of chance'[2]. The likelihood of bias in determining the outcome is reduced in this type of study design. It also precludes selection bias when implemented well. A uniform diagnostic criteria is often featured in clinical trials, and further blinding of the study helps reduce the information bias. This study design is unique as it eliminates confounding bias, whether known or unknown and also is bound to be statistically efficient. Randomized controlled trials are particularly useful for examining low to moderate effects, if properly designed and implemented as they are likely to be free of bias.

Observational Study

The objective of this study is to illustrate the cause-and-effect relationships wherein controlled experimentation cannot be performed[3]. Observational study can also be referred to as natural experiments or quasi experiments. Though different terminologies are used, the theme shared among them is common wherein the strengths of an experiment are reproduced as much as possible, in the earlier stages of designing itself. Based on the presence or absence of a comparison group an observational study can be sub-classified into analytical and descriptive studies.

Descriptive Study

Descriptive studies form the bottom of the research hierarchy, and do not involve a comparison group. This study essentially describes the frequency, natural history and possible determinants of a disease[4-6]. The results of such a study explain the frequency of people developing the disease over time along with the characteristics of the disease and the people affected by it and finally, hypotheses are generated to determine the cause. More rigorous research can then be conducted on these hypotheses through analytical studies and randomized controlled trials. An example of descriptive studies is case report/series.

Analytical studies are those in which a comparison or control group is involved. In such a study, it is imperative to identify the temporal direction of the trial, which can be any one of the following :-

- If both the exposure and outcome are determined at any one point, it is a cross-sectional study.
- If the study begins with an exposure followed by observation for a few years to determine the outcome it becomes a cohort study.
- If the study begins with an outcome and the exposure is identified in retrospect, it is a case-control study.

Cross sectional Study

This study is done in order to examine the presence or absence of a disease and an exposure at a particular time, thereby focusing on prevalence and not incidence. A drawback of this study is that the temporal relation between the outcome and exposure might be unclear as both are ascertained at the same time. A cross-sectional study is also called a frequency survey or a prevalence study[7].

Cohort Study

Cohort studies begin from exposure and proceed to outcome and are therefore easier to understand than case-control studies. Here, two groups are identified- one with an exposure of interest and another without. These groups are then followed up in time to determine the outcome. If a higher incidence of outcome is developed by the exposed group than the unexposed then it would be inferred that increased risk of outcome is due to exposure. The advantage of a cohort study is that it is possible to calculate true incidence rates, the relative risks as well as associated attributable risks[2]. However, this research design may not be suitable for study of rare event(s) that take years to develop, as the yield of results will be slow and therefore highly expensive.

Case control Study

As mentioned earlier, case control studies work retrospectively, starting with outcome and then identifying the exposures that could have resulted in the outcome. As this tangent of thought is not intuitive for all clinicians, it is widely misunderstood. This study too involves two groups – outcome group and control group. Through means of chart reviews and interviews, the prevalence(or amount) of exposure to a risk factor is assessed. If the prevalence is higher among the outcome group than the control, then exposure is associated with an increased risk of outcome. Unlike cohort studies, a case control study is especially suitable for rare outcomes or diseases that take a longer time to develop like cardiovascular disease and cancer. Also, they require lesser time and effort and not as expensive

as cohort studies[2]. However before beginning the study it is imperative to keep in mind that the criteria or characteristics of both the groups(outcome & control) are similar except for the outcome in question. Many studies have been ruined due to inappropriate control groups. Additionally, if the studies rely on memory, then recall bias (better recollection of exposures among the cases than among the controls) would be high. A major drawback a case control study is that incidence rates, relative risks or attributable risks cannot be calculated as the study lacks denominators[2].

Conclusion

The core importance of a research work is to know what type of study design needs to be implemented, along with the practical feasibility, required information, estimated duration of the study and the total cost. Each study design has its own limitations and strengths. Choosing a proper study design to carry out legitimate research work is a critical step and is a paramount of importance. A good study design will acknowledge all parameters that spell the success of the study without any bias.

References

1) Jadad AR. Randomised controlled trials: a user's guide. 1998; BMJ Books, London, England

2) David A Grimes, Kenneth F Schulz. An overview of clinical research: the lay of the land. The Lancet 2002; 359: 57–61

3) Paul R. Rosenbaum. Observational Study: Encyclopedia of Statistics in Behavioral Science, ISBN-13: 978-0-470-86080-9 ISBN-10: 0-470-86080-4, Volume 3: pp. 1451–1462.

4) Hennekens CH, Buring JE. Epidemiology in medicine. 1987; Boston: Little, Brown and Company.

5) Kelsey JL, Whittemore AS, Evans AS, Thompson WD. Methods in observational epidemiology, 2nd edn. , 1996; New York: Oxford University Press.

6) Feinstein AR. Clinical epidemiology: the architecture of clinical research. 1985; Philadelphia: WB Saunders Company.

7) Last JM, ed. A dictionary of epidemiology, 2nd edn. 1988; New York: Oxford University Press.

Rhythm and diet to keep the bowel quiet

Circadian rhythm coded by circadian clock genes imposes a 24 hour cycle (including sleep) in all animals. This rhythm gets disrupted in various professionals (doctors, nurses, other shift workers etc.) and travellers (jet lag). Do such disruptions affect health? In a new controlled experimental study published in PLOS ONE (Circadian Disorganization Alters Intestinal Microbiota. PLoS ONE, 2014; 9 (5): e97500 DOI:10.1371/journal.pone.0097500), the investigators disrupted the circadian rhythm in a group of mice and fed them with a diet rich in fat and sugars. This resulted in altered intestinal microbiota with a significant increase in pro-inflammatory organisms. Disruption of circadian rhythm alone was insufficient. It required the assistance of a second environmental insult (in this case, high fat/sugar diet) to produce the effect. This may play a role in the pathogenesis of inflammatory bowel disease and colonic cancer. Including prebiotics or probiotics in the diet and maintaining a fairly good schedule might help to avert these diseases.

- Dr. K. Ramesh Rao

From the Pages of History

ABOUT THE BABINSKI SIGN

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Chettinad Health City Medical Journal 2014; 3(1): 35

Joseph F.F. Babinski

Joseph Babinski, who was associated with Charcot in Paris, in 1896, while working on clinical signs to differentiate organic from nonorganic diseases, described the extensor response of the toes in a short presentation at the Société de Biologie meeting, emphasizing the sign to organic disorders of the central nervous system.

The salient features of this presentation were:

- The sign occurred in cases of hemi- or monoplegia of organic central nervous system origin.
- To a painful, pricking stimulus on the sole of the foot: (1) The healthy side showed flexion of thigh, leg, foot, and toes; (2) The paralyzed side showed flexion of thigh, leg, foot, but the toes extended.
- The sign occurred as early as a few days after the onset of weakness.
- The sign persisted in the context of chronic weakness *(vide infra)*

Babinski's Original Presentation

(translated from "Sur le réflexe cutané plantaire dans certaines affections organiques du système nerveux central. C R Soc Biol 1896;48:207-208") **"On the Plantar Cutaneous Reflex Seen in Certain Organic Disorders of the Central Nervous System,"**
by J. Babinski.

"In a certain number of cases of hemi- or crural mono-plegia due to lesions of the central nervous system, I have observed an abnormality in the cutaneous plantar reflex herein described. On the healthy side, pricking the plantar surface causes on the healthy side a normal flexion of the thigh, the leg, foot, and the toes at the metatarsal joint. On the paralyzed side, similar stimulation causes flexion of the thigh, leg and foot, but the toes, instead of flexing, develop an extension movement at the metatarsal joint.

I have seen this phenomenon in cases of new-onset hemiplegia within the first few days of weakness as well in late cases of several months duration; I have noticed it among patients unable to move their toes voluntarily as well as in patients who can move their toes, but in this latter case, the sign is not always present.

In cases of paraplegia due to a structural lesion of the spinal cord, I have also seen toe extension after pricking the plantar surface of the foot, but in such cases, the sign is less marked.

In summary, the reflex movement that follows pricking of the plantar surface of the foot from an organic lesion of the central nervous system can vary not only in its intensity, but also its character".

Later, in the same year, Babinski noted that stroking or tickling the sole of the foot elicited the same response. In later publications, he emphasized that the sign correlated with pyramidal tract disease and could be seen with cortical, subcortical, or spinal cord lesions. In 1903, Babinski further expanded his description to not only the extensor toe sign but also the fanning or abduction of the toes. This sign became so popular that a cartoonist drew a portrait of Babinski for the popular tabloid Chanteclair, where both elements of his observation were captured with the combined imagery of the toes and a fan. The extensor response of the toes was described as the "phenomena des orteils" and the fanning of the toes was described as the "signe de l'eventail".

Though the toe extensor response was noted by many earlier, including Wernicke in a patient with hemiplegia, Stumpell in a case of amyotrophic lateral sclerosis, Remak in a case of transverse myelitis, this response was attributed to a vague spinal reflex. It was Babinski who attributed the extensor toe response to the pyramidal tract lesions and he is justifiably credited for the same. Collier in 1899 made the first English publication on this topic and he used the English term extensor response. Babinski was more acclaimed internationally than in France itself and was made honorary member of American Neurological Association and elected to the Royal Medical Society of London and was even nominated for the Nobel Prize.

References

1. Goetz CG. History of the Extensor Plantar Response: Babinski and Chaddock Signs. Semin Neurol. 2002;22(4). http://www.medscape.com/viewarticle/447785_1

2. Campbell WW. Pathologic reflexes. In: DeJong's The Neurological Examination. Ed. Campbell WW. Lippincott Williams & Wilkins. 2013. p. 585

Instruction to Authors

Chettinad Health City Medical Journal 2014; 3(1): 36 - 37

Chettinad Health City is a peer-reviewed general medical journal published four times a year by Chettinad Academy of Research and Education with the objective of providing an outlet for the following types of scientific communications:

- Reports of original research;
- Interesting case studies;
- Reviews;
- Short communications (research notes).

Besides these, the journal will also carry regular sections like latest medical news, correspondence, classroom, clinical quiz, student seminars, interviews etc. The journal is not restricted to in-house contributions and welcomes scientific communications from other Institutions in India and abroad. However, the journal strongly discourages duplication of data already published in other journals (even when certain cosmetic changes/additions are made). Besides, serialisation of the articles by the same author is not encouraged. Manuscripts must be solely the work of the author(s) stated, must not have been previously published elsewhere, and must not be under consideration by another journal. The journal prioritises reports of original research that are likely to change clinical practice or thinking about a disease. All papers submitted to the journal are subject to peer review process. All accepted papers will be appropriately edited before publication.

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All manuscripts submitted for publication to the CHCMJ should include the following:

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A covering letter should explain why the paper should be published and identify one of the authors as the corresponding author. The corresponding author (or coauthor designee) will serve on behalf of all coauthors as the primary correspondent with the editorial office during the submission and review process. If the manuscript is accepted, the corresponding author will review an edited typescript and proof, and will be identified as the corresponding author in the published article. The corresponding author is responsible for ensuring that the Acknowledgment section of the manuscript is complete.

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Manuscripts (including correspondence letters) should be submitted by e-mail/ CD/DVD as a MS Word document in addition to a hard copy. The hard copies should be typed/printed in one and half space on one side of a good quality A4 bond paper (21.0 x 29.7 cms). Pages should be numbered consecutively. Typescript should be sent to the Editor, CHCMJ. Authors are advised to see a recent issue of the journal to get familiar with the format adopted on various elements of a paper.

Formatting

All research papers (basic science, clinical trials etc.) should :-

(1) Be not more than 3000 words with 30 references

(2) Include the elements arranged in the following order:- Title; Name(s) of the author(s); Department(s) and Institution(s); Abstract; Key words; Introduction; Material & Methods; Results; Discussion; Acknowledgement; and References. Abstract, Tables and legends for Figures should be typed on separate sheets and not in continuation of the main text.

(3) The Title of the article should be short, continuous (broken or hyphenated titles are not acceptable) and yet sufficiently descriptive and informative so as to be useful in indexing and information retrieval. A short running title not exceeding 6-7 words may also be provided.

(4) The Abstract (semistructured summary), with five paragraphs (Background, Methods, Findings, Interpretation), not exceeding 300 words. It should only highlight the principal findings and conclusions so that it can be used by abstracting services without modification. Conclusions and recommendations not found in the text of the articles should not be inserted in the Abstract. A set of suitable key words arranged alphabetically may be provided.

(5) The Introduction should be brief and state precisely the scope of the paper. Review of the literature should be restricted to reasons for undertaking the present study and provide only the most essential background.

(6) In Material & Methods, the nomenclature, the source of material and equipment used, with the manufacturers' details in parenthesis, should be clearly mentioned. The procedures adopted should be explicitly stated to enable other workers to reproduce the results, if necessary. New methods may be described in sufficient detail, indicating their limitations. Established methods can be just mentioned with authentic references and if there are significant deviations, reasons for adopting them should be given. While reporting experiments on human subjects and animals, the ICMR's Ethical guidelines for biomedical research on human subjects (2000) should be adhered to. Similarly, for experiments on laboratory animals the guidelines of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) should be followed. The drugs and chemicals used should be precisely identified, including generic name(s), dosage(s) and route(s) of administration. The statistical

analysis done and statistical significance of the findings when appropriate should be mentioned. Unless absolutely necessary for a clear understanding of the article, detailed description of statistical treatment may be avoided. Articles based heavily on statistical considerations, however, need to give details particularly when new or uncommon methods are employed. Standard and routine statistical methods employed need to give only authentic references.

(7) In Results, only such data as are essential for understanding the discussion and main conclusions emerging from the study should be included. The data should be arranged in unified and coherent sequence so that the report develops clearly and logically. Data presented in tables and figures should not be repeated in the text. The same data should not be presented both in tabular and graphic forms. Interpretation of the data should be taken up only under the Discussion and not under Results.

(8) The Discussion should deal with the interpretation of results without repeating information already presented under Results. It should relate new findings to the known ones and include logical deductions. It should also mention any weaknesses of the study. The conclusions can be linked with the goals of the study but unqualified statements and conclusions not completely supported by the data should be avoided. Claiming of priority on work that is ongoing should also be avoided. All hypotheses should, if warranted, clearly be identified as such; recommendations may be included as part of the Discussion, only when considered absolutely necessary and relevant.

(9) Acknowledgment should be brief and made for specific scientific/technical assistance and financial support only and not for providing routine departmental facilities and encouragement or for help in the preparation of the manuscripts (including typing or secretarial assistance).The corresponding author must obtain written permission from each person named in the Acknowledgment section and must be willing to provide the editors with copies of these permissions if requested to do so. The corresponding author must sign the Acknowledgment statement part of the Authorship Form confirming that all persons who have contributed substantially but who are not authors are identified in the Acknowledgment section and that written permission from each person acknowledged has been obtained.

(10) The total number of References should normally be restricted to a maximum of 30. References to literature cited should be numbered consecutively and placed at the end of the manuscript. In the text they should be indicated as superscript at the end of the line. As far as possible mentioning names of author(s) under references should be avoided in text. The titles of the journals should be abbreviated according to the style used by the Index Medicus.

The references should be in Vancouver style—e.g.,

- Smith A, Jones, B, Clements S. Clinical transplantation of tissue-engineered airway. Lancet 2008; 372: 1201–09.
- Hourigan P. Ankle injuries. In: Chan D, ed. Sports medicine. London: Elsevier, 2008: 230–47.

(11) All image formats (jpeg, tiff, gif) are acceptable; jpeg is most suitable

(12) Case reports should present a diagnostic conundrum, and explain how it was solved. Case reports should

- not be more than 1000 words with 10 references
- Include the clinical presentation, history, examination, investigations, management, outcome and comments/discussion.

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