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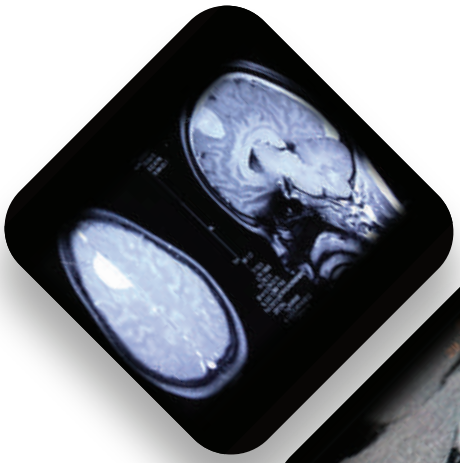

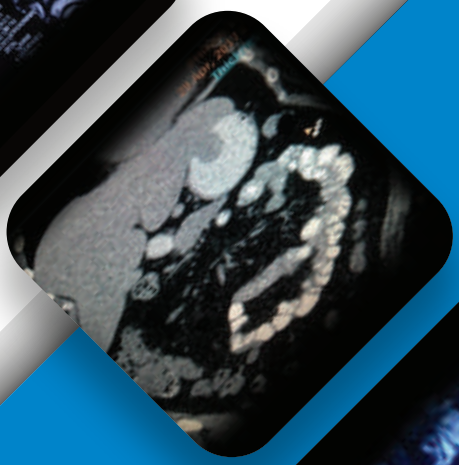

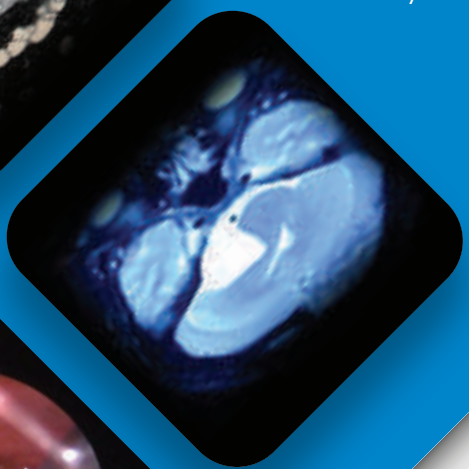

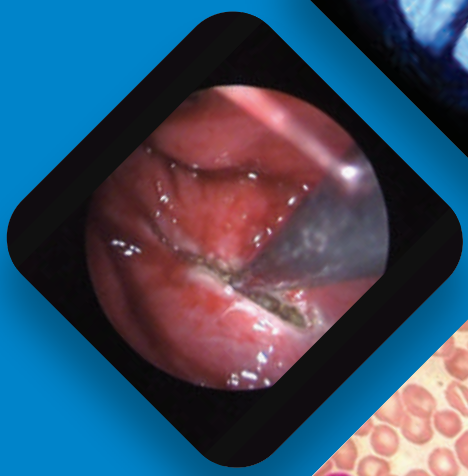

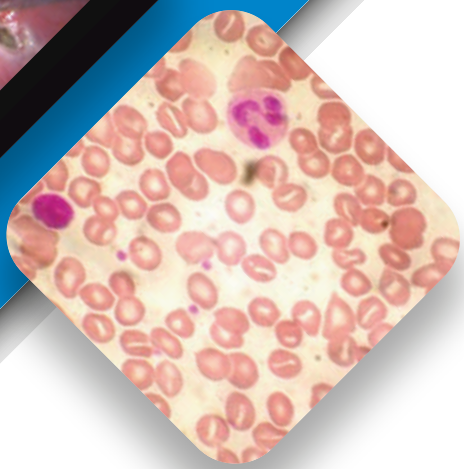

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Chettinad Health City

MEDICAL JOURNAL

Contents

Editorial

Greetings from the Editorial team of Chettinad Health City Medical Journal!

We take immense pleasure in bringing out this first issue of the 6th Volume.

We would like to take this opportunity to thank all the authors and reviewers who have supported the Journal. This issue of the Chettinad Health City Medical Journal carries two original articles, three case reports, one review article and one classroom article. A number of Interns and Post-graduates are contributing and in-turn getting benefitted by learning the valuable skill early in their medical career.

Case Reports are valuable in medical literature and have spawned new techniques and thoughts in medicine. A prime example is the case report by Bentall and de Bono of a surgical technique[1]. The Eponymous Bentall-de Bono surgery is widely practiced now.

A good case report should :-

- Recognize or describe a new disease/procedure/surgery
- Recognize rare manifestation of a disease or modifications of existing procedures/ surgeries
- Elucidate new mechanisms of disease
- Describe new adverse or beneficial effects of drugs and treatments
- Education and audit

This issue deals with a wide spectrum of topics from various specialities. The original article by Dr.Puvithra asks interesting questions on pregnancy complications associated with Polycystic ovarian syndrome. The review article on sepsis and septic shock will be of interest to the large population of clinicians, teachers and students.

Zika virus disease has been gradually taking centre stage, though the disease has been prevalent since the 1960s. The classroom article is a timely reminder to all clinicians to this emerging wide-spread disease, at a time when cases are being reported in India.

The journal rounds off with informative articles from the speciality of Otorhinolaryngology and case reports.

1) Bentall H, De Bono A. A technique for complete replacement of the ascending aorta. Thorax. 1968;23(4):338-9

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Commentary

Etiology of Endometriosis – Simplified

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Chettinad Health City Medical Journal 2017; 6(1): 2 - 3

Introduction

Endometriosis is an estrogen dependent condition commonly seen in women of reproductive age group and most often these women present with infertility and pelvic pain / dysmenorrhea. It is not clear whether endometriosis is the cause of infertility/ pelvic pain/ dysmenorrhea or it is just an associated condition. In the reproductive age group women, the incidence of endometriosis is 10 – 11%[1] whereas the incidence is more than 30%[1] in infertile population. The common sites of endometriosis are ovaries, fallopian tubes, posterior wall of the uterus, cul-de-sac, broad ligament, round ligament. Extra pelvic sites are intestines, urinary bladder, ureters, lungs, extremities, skin, and central nervous system. Ovaries are being the commonest site of endometriosis[2].

Hypothesis

Various theories have been proposed to explain the etiopathogenesis of endometriosis like retrograde menstruation, coelomic metaplasia, induction theory, lymphovascular, oxidative stress and inflammation, immune dysfunction, apoptosis suppression, genetic and stem cell theory. Do we really need these many theories, when one theory alone can explain the etiology of Endometriosis? Having too many theories may complicate the understanding of the pathophysiology and the management of the disease.

Our hypothesis

To say "Menstruation causes Endometriosis" may be stating the obvious. Retrograde menstruation theory alone can explain the etiology of endometriosis.

Retrograde menstruation theory is also called as implantation theory was proposed by John A. Sampson in 1927. It is retrograde flow of endometrial cells into the peritoneal cavity via the fallopian tubes. These endometrial cells adhere to the ovary or peritoneal cavity, implant, grow and bleed over the course of menstrual cycle. It has been documented by laparoscopy during perimenstrual phase that 76%-90%[3] of the women have retrograde menstruation. Probably all women with patent tubes may have retrograde menstruation. The most common location of endometriosis is on the posterior aspect of the uterus and towards left side of the pelvis. In congenital Mullerian anomaly like imperforate hymen and cervical stenosis, there are increased chances of retrograde menstruation and there by increased risk for developing endometriosis[4].The incidence of endometriosis is increased in women with an early menarche, frequent menstrual cycles or women with menorrhagia. There are increased chances of these women being exposed to retrograde menstruation. This retrograde menstrual blood in the peritoneal cavity gets absorbed by lymphatic system, it drains into the venous drainage, through which it spreads to the distant sites. This explains the etiology of extra pelvic endometriosis. There are only few articles on proven (Histopathological) premenarchal endometriosis without obstructive Mullerian anomaly[5]. Neonatal uterine bleeding in the immediate post natal period occurring due to withdrawal of maternal estrogen may be the source for endometrial cells in pre-pubertal endometriosis[6]. Endometriosis in post menopausal (without HRT) is rare and the incidence is only 2.2 %[7]. The author stated that all these patients were obese and signs of increased estrogen activity would have caused peripheral conversion of androgen into estrogen. These excessive estrogen has caused reactivation of the pre existing endometriotic lesions. Hence, the triggering factor in pre pubertal endometriosis may also be due to the conversion of androgen into estrogen secreted from the peripheral adipose tissue in obese children. The incidence of endometriosis in multiparous women is also relatively low i.e. 3.7 %[8]. In these women, Pregnancy ameliorates endometriosis.

Conclusion

When there is continuous periodic constant menstruation, there are increased chances of endometriosis. The frequent occurrence of menstruation, longer duration of menstruation and excessive menstruation may overwhelm the defense mechanism in some women. The failure of defense mechanisms, may lead to implantation of endometrial cells, further growth and bleed over the course of menstrual cycle leading to endometriosis.

Acknowledgements

We thank the faculty of the Department of Andrology & Reproductive Medicine for their support through important discussions and valuable comments on this topic.

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Original Article

Pregnancy Complications - Consequence of Polycystic Ovary Syndrome or Body Mass Index?

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Chettinad Health City Medical Journal 2017; 6(1): 04 - 08

Abstract

Hyperinsulinemia and hyperandrogenemia are the hormonal changes which are linked to the pregnancy complications seen in women with Polycystic Ovary Syndrome (PCOS).

Aim : This study was done to determine the complications that can occur in pregnant women with polycystic ovary syndrome, and to ascertain whether the complications are related to PCOS per se or the Body Mass Index (BMI) of the women.

Materials and Methods : Data was collected from case records. Study group had women with PCOS, selected according to Rotterdam criteria and control group had women with unexplained infertility, with women in both groups achieving pregnancy either spontaneously, following ovulation induction (OI) with timed intercourse or controlled ovarian hyperstimulation (COH) with Intrauterine insemination (IUI).

Study design : A retrospective study. **Study duration**: Women who attended the clinic between January 2009 – Dec 2014, **Study Setting** : Department of Reproductive Medicine and Andrology, Chettinad Super Speciality Hospital, Chennai.

Results : There were 110 women in the study group and 64 women in the control group. The age and BMI of women in both groups were comparable. The incidence of miscarriage, congenital anomalies, preterm delivery, operative delivery and neonatal complications were similar in both groups. Incidence of Gestational Diabetes mellitus (GDM) was significantly higher in women with PCOS (22.6%), and there was an upward trend with increasing BMI. There was also an increased incidence of Large for gestational age babies in women with PCOS, but there was no statistical significance.

Conclusion : Unlike previous publications, our study revealed no significant increase in pregnancy and neonatal complications in women with PCOS, except for Gestational diabetes, the incidence of which was related to BMI. Therefore, we suggest that PCOS and the pregnancy complications are a consequence of increasing BMI, and that PCOS may not be incriminated as the independent cause for these complications.

Key Words: Polycystic ovary syndrome, PCOS, Hyperinsulinemia, Hyperandrogenemia, Pregnancy complications, Gestational diabetes mellitus, Neonatal complications.

Introduction

Polycystic ovary syndrome (PCOS) is the commonest ovulatory disorder accounting for 60-85% of anovulatory patients[1] and the commonest endocrinopathy in women of reproductive age group[2].

Most women with polycystic ovary syndrome have oligo-ovulation rather than anovulation, ie; they present with irregular cycles and very few have total absence of menstruation. Therefore, the chances of spontaneous conception in women with PCOS is slightly higher when compared to other causes of infertility. Moreover, simpler treatment modalities like ovulation induction provide better success rates in women with just PCOS as the cause for infertility[3]. These have resulted in an increasing prevalence of pregnant women with PCOS.

The altered hormonal milieu of PCOS, like hyperinsulinemia and hyperandrogenemia have been implicated in the pathogenesis of pregnancy complications like gestational diabetes, gestational hypertension and preterm birth. These hormonal changes, followed by development of PCOS are the consequence of excess adipose tissue and not vice versa. Earlier, obesity was being considered as the major cause for PCOS[4], but a retrospective study done in our department showed that, among the women diagnosed with PCOS, 32% had a normal body mass index (BMI)[5]. Obesity has also been proven to be an independent risk factor for pregnancy complications[6].

Aim

To determine the complications that can occur in pregnant women with polycystic ovary syndrome, and to ascertain whether the complications are related to PCOS per se or the BMI of the women.

Materials and methods

Study design : A retrospective study.

Study group : Women who attended the clinic between January 2009 – Dec 2014, and achieved pregnancy either spontaneously, following ovulation induction (OI) with timed intercourse or controlled ovarian hyperstimulation (COH) with Intrauterine insemination (IUI).

Study Setting : Department of Reproductive Medicine and Andrology, Chettinad Super Speciality Hospital, Chennai.

The study group had women with PCOS, who fulfilled the Rotterdam criteria[7] and the control group had women with Unexplained infertility, who were regularly ovulating, had patent fallopian tubes and male partner's sperm parameters were normal.

The case records of the women who attended the clinic and became pregnant either spontaneously, following ovulation induction (OI) with timed intercourse, or Controlled Ovarian Hyperstimulation (COH) with Intrauterine insemination (IUI), were reviewed for treatment details. The department conducts a yearly follow-up programme for the mothers who underwent infertility treatment and for children born after infertility treatment. During this evaluation, a detailed antenatal history is obtained and recorded. Those patients who did not attend the evaluation session were contacted through phone to obtain a detailed antenatal history.

Inclusion criteria

- Age - 20-35 years
- Primary and secondary infertility

Exclusion criteria

- Other causes of anovulation like hypothyroidism and hyperprolactinemia
- Other causes for recurrent miscarriages like uterine anomalies, Antiphospholipid antibody syndrome
- Pre-existing Impaired glucose tolerance (IGT) or Diabetes mellitus (DM)
- Concurrent treatment with Metformin
- Recent ovarian surgeries like laparoscopic ovarian drilling
- Multiple gestation
- Ongoing pregnancy
- Associated Male factor
- ART pregnancies
- History could not be elicited

Primary outcome

- Live birth
- Miscarriage
- Termination of pregnancy for anomalies
- Gestational age at delivery (term/preterm)

Secondary outcome

- Mode of delivery (Vaginal delivery/Cesarean section)
- Ectopic pregnancy
- Antenatal morbidities
- Neonatal outcome

Statistical analysis

The association between factors were calculated using Odd's ratio. Significance calculated using Chi square and Student t- test. P value - <0.05 was considered significant.

Results

The number of patients included in each arm is mentioned in Table 1.

Group	Number of women
Study group (PCOS)	110
Control group (Unexplained Infertility)	64

Table 1 - Number of women

Characteristics	PCOS	Unexplained
Mean Age (years)	26.87	27.77
Mean BMI (kg/m^2)	24.94	24.49

Table 2 - Basal characteristics of study participants

The mean age and Body mass index (BMI) of the participants were comparable in both groups, as shown in Table 2, and most of the women in both groups belonged to the category of Normal BMI.

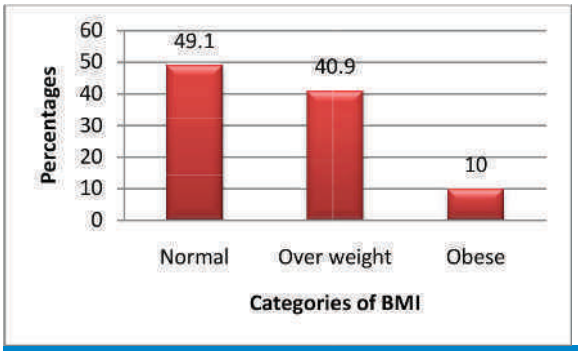

Fig 1 : BMI distribution in PCOS group

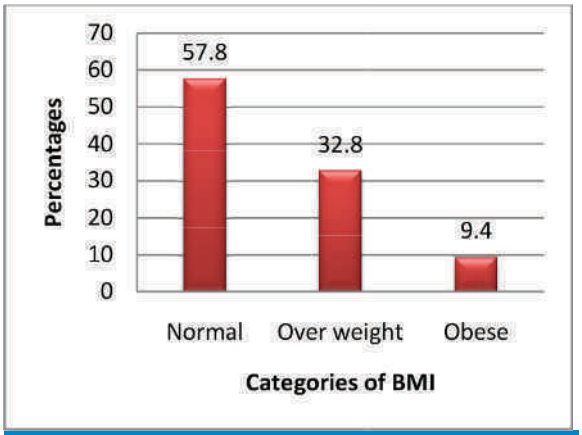

Fig 2 : BMI distribution in Unexplained infertility group

The BMI categorization was done according to the WHO classification of BMI. Normal BMI- 18.5 - 24.9 kg/m2, Overweight - 25 - 29.9 kg/m2, Obese - >30 kg/m2.

	PCOS (n=110)		Unexplained (n=64)		
	Number	Percentage	Number	Percentage	p value
Live birth	84	76.4	48	75.0	0.83
Miscarriage	22	20.0	10	15.6	0.64
Ectopic	2	1.8	5	7.8	0.07
Anomalies	2	1.8	1	1.6	0.9

Table 3 - Outcome of pregnancy

The pregnancy outcome in the groups are shown in Table 3. There was no significant difference in the outcome in both groups. Though there was no statistical significance, the incidence of ectopic pregnancy was higher in the Unexplained infertility group (1.8% vs 7.8%), which could probably be due to a subtle tubal factor in the patients.

Table 4 shows that there is no difference in the mode of delivery among the live births in the two groups.

Mode of delivery	Groups		Odds ratio	Chi square	P-value	95% CI	
	PCOS (n=84)	Unexplained (n=48)				Lower	Upper
LSCS	54 (64.3%)	29 (60.4%)	1.179	0.196	0.658	0.568	2.449
Vaginal	30 (35.7%)	19 (39.6%)					

Table 4 - Comparison between mode of delivery

Though the number of preterm deliveries were higher in the PCOS group, as shown in Fig 3, there was no significant difference. [OR 1.83 (95% CI 0.5565-6.0392), p value – 0.3190].

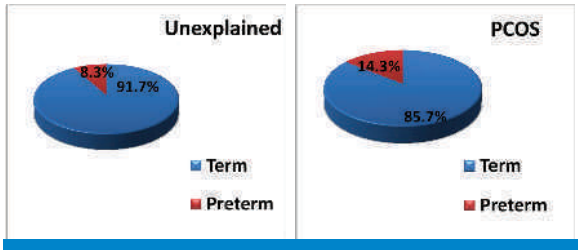

Fig 3 : Gestational age at delivery

The pregnancy morbidities as shown in Table 5, were calculated only in women whose pregnancies resulted in live birth. Except for the incidence of gestational diabetes, the other pregnancy morbidities were not significantly higher in women with PCOS. Among the pregnancies that crossed viability, 22.6% of the women had developed gestational diabetes (GDM) and were started on Insulin therapy at around 5 months of gestation. In women with unexplained infertility, none developed GDM. In the PCOS group, 2 women had gestational hypertension (GHTN), whereas none had GHTN in the unexplained infertility group. Due to small numbers, the significance of GHTN cannot be explained in this study. The other antenatal complications like prelabour rupture of membranes (PROM), polyhydramnios, oligohydramnios and Fetal growth restriction (FGR), were similar in both the groups.

	PCOS (live birth, n = 84)		Unexplained (live birth, n= 48)		
	Number	Percentage	Number	Percentage	p value
GDM	19	22.6	0	0	0.02
GHTN	2	2.4	0	0	0.49
PROM	7	8.3	2	4.2	0.37
FGR	1	1.2	1	2.1	0.69
Oligohydramnios	4	4.8	3	6.2	0.71
Polyhydramnios	1	1.2	0	0	0.73

Table 5 - Antenatal complications

As per the study objective, in order to ascertain whether it is PCOS or obesity which is responsible for the increased incidence of GDM in the PCOS group, the women were classified according to the WHO classification for BMI. The distribution of BMI in women with GDM is shown in Fig 4.

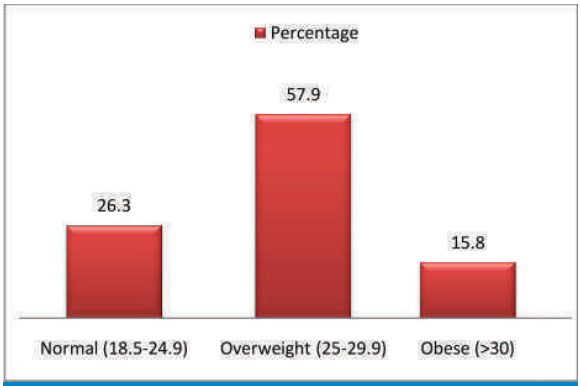

Fig 4 : Pre-pregnancy BMI distribution of women with GDM

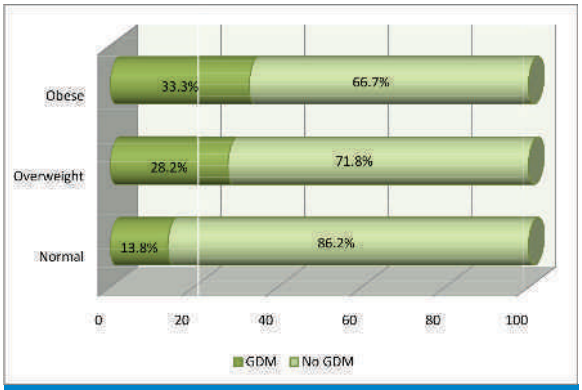

Fig 5 : Incidence of GDM in relation to pre-pregnancy BMI in women with PCOS

Among the women with GDM, 26.3% had normal BMI, 57.9% were overweight and 15.8% were obese, thereby interpreting that the number of obese patients were comparatively lesser. As seen in Fig 5, when the incidence of GDM was calculated in all women with PCOS, in relation to the pre-pregnancy BMI, 13.8% of women with normal BMI, 28.2% of overweight women and 33.3% of obese women had developed GDM. Therefore it is obvious that there was an increasing tendency for developing GDM as the pre-pregnancy BMI increased.

There was no significant difference in the neonatal outcome in both groups(Table 7). Neonatal intensive care unit (NICU) admission rates were higher in neonates of women with PCOS , but the numbers were not statistically significant. NICU admission was primarily for preterm care or for observation of the neonate in view of GDM in the mother. Among the babies born to women with PCOS and gestational diabetes, 3 babies developed hypoglycemia for which they required NICU admission and glucose infusion.

Though not statistically significant, there was an increased incidence of large for gestational age (LGA) babies in the PCOS group. Among the mothers who gave birth to LGA babies, only one mother had GDM. It was assessed if there is a correlation between the mother's BMI and the increased birth weight of babies. As seen in the Fig 6, all mothers with LGA babies were non-obese, and more than half of them were of normal built, suggesting that it could be due to the metabolic and hormonal changes in mothers with PCOS. We may not be able to arrive at a conclusion in view of numbers.

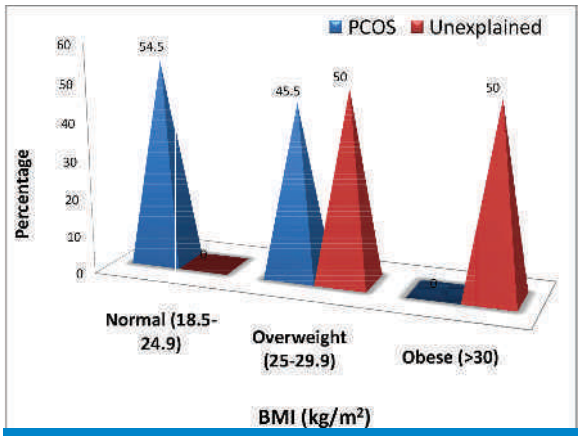

Fig 6 : BMI distribution of mothers of LGA babies

Discussion

Boomsma et al (2006) conducted a meta-analysis of the pregnancy outcome with PCOS, and found a higher risk of developing GDM, pre-eclampsia and preterm birth[8]. There was also a significantly higher perinatal mortality and NICU admissions in these patients. Most of the studies included in the meta-analysis did not take into account the BMI of the patients, which would be a direct confounding factor. In this study, the study and the control group were age- and BMI-matched.

	PCOS (live birth = 84)		Unexplained (n=48)		
	Number	Percentage	Number	Percentage	p value
NICU	21	25	7	14.6	0.16
Physiological jaundice	4	4.8	3	6.2	0.71
Preterm care	5	5.9	2	4.2	0.97
Respiratory distress	3	3.6	1	2.1	0.63
Hypoglycemia	3	3.6	0	0	0.34
Infection	1	1.2	0	0	0.45
Single umbilical artery	1	1.2	0	0	0.45
Observation	5	5.9	1	2.1	0.55
Large for gestational age	11	13.1	2	4.2	0.17

Table 6 - Neonatal outcome

The live birth rate, miscarriage rate and the incidence of preterm delivery, operative delivery and congenital anomalies was similar in both groups. Incidence of GDM was significantly higher in women with PCOS (22.6%), and it was also seen that among all women with PCOS, higher the BMI, higher was the probability of developing GDM. With this observation, we comprehend that, PCOS may not be the cause for GDM, but both PCOS and GDM are the consequence of increasing BMI. A study done in Jammu and Kashmir, India, showed similar results, but the number of PCOS women included were lesser than our study[9].

Studies have quoted a threefold increase in the incidence of neonatal hypoglycemia is babies born to women with PCOS[10]. In our study, the neonatal outcome was similar in both the groups, except for the incidence of hypoglycemia. Among the 19 babies born to GDM mothers, 3 babies developed neonatal hypoglycemia for which they required intravenous glucose infusion. Preterm babies and babies born to GDM mothers required neonatal intensive care monitoring.

Conclusion

Women with PCOS are generally said to have a greater tendency to develop pregnancy and long term health complications[8]. This conclusion was derived from studies, in which the comparison was not done with age and BMI matched controls. PCOS was thus thought to be 'the cause' for these complications. According to our study, in women with similar BMI, there was no difference in the incidence of any pregnancy complication in PCOS women. The incidence of gestational diabetes also increased with increasing BMI. Therefore, we suggest that PCOS may not be the independent or primary cause for the pregnancy complications or metabolic diseases like coronary artery disease, cerebrovascular disease and uterine malignancies. There may be a common factor like the BMI or weight gain which is involved in the pathogenesis of all these events.

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Original Article

Transoral Approach To CV Junction - Odontoidectomy - Case Series

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Chettinad Health City Medical Journal 2017; 6(1): 09 - 12

Abstract

BACKGROUND: The endoscopic transoral approach offers a risk-free access to midline and ventral lesions of the craniovertebral junction. Benefits of this approach include 1) Direct exposure to ventral lesions (bony pathology, granulation tissue etc) possible through this route alone; 2) Avascular plane of dissection through median pharyngeal raphe and clivus; 3) Less injury to brainstem structures as head is kept in an extended position.

METHODS: Endoscopic transoral approach (ventral route) was used to decompress the craniovertebral junction lesions. The odontoid process was drilled, to remove compression on the spinal cord. Stabilization of the cervical vertebra was done with occipitocervical fusion in the following week.

RESULTS: Cervicomedullary junction decompression through transoral odontoidectomy was done successfully in 7 patients from February 2013 to June 2014 with minimal or no complications. On a 1-2 year follow-up, there was no evidence of CVJ instability and patients had improvement of neurological function.

CONCLUSION: The endoscopic transoral odontoidectomy is a better surgical technique for ventral lesion of the craniovertebral junction.

Key Words: CV Junction, Odontoid, Endoscopic Trans Oral

Introduction

The CVJ is an area which encompasses the occiput, axis, atlas, and supporting ligaments[1]. It accounts for approximately 25% of the vertical height of the entire cervical spine. Surgical exposure of the region around the foramen magnum and the first two cervical vertebrae is necessary for lesions that threaten loss of stability and spinal cord compression, especially by dens.The endoscopic transoral approach provides a direct route ventral lesions of the craniovertebral junction [2-6]. Removal of the lesion may be combined with stabilisation procedure in a second sitting. In other cases clinical symptoms may require a posterior fusion to be performed first followed later by an ablative procedure.

Materials and Methods

Patients: The following seven patients were operated in our department from Feb 2013 to June 2014:

- Case 1- 16 years male with weakness of all 4 limbs with power 2/5 in all 4 limbs due to CV junction anomaly.
- Case 2- 24 years male with weakness of all 4 limbs with power 2/5 in upper limbs and power 1/5 in lower limbs diagnosed as a case of granulomatous lesion of odontoid.
- Case 3-32 years male with weakness of all 4 limbs due to granulomatous lesion of odontoid
- Case 4- 53 years male with weakness of all 4 limbs due to odontoid compressing the cord.
- Case 5-54 year male with weakness of all 4 limbs due to odontoid compressing the spinal cord.

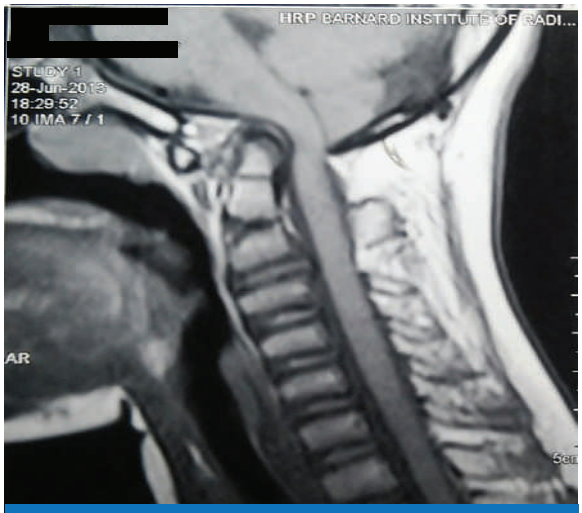

Fig 1 : MRI showing enlarged odontoid compressing the spinal cord

- Case 6 - 14 years female with paresis of all 4 limbs with power 4/ 5 in all 4 limbs diagnosed as granulomatous lesion of odontoid.
- Case 7 – 35 years female with paresis of all 4 limbs due to rheumatoid arthritis involving cervical spine.

Plain radiographs and dynamic polytomography formed the preliminary imaging[6]. For an accurate visualization of the lesion, computerized tomography (CT) with 3D reconstruction and magnetic resonance imaging (MRI)were taken(Fig 1).

Surgical technique

Patients were put under general anesthesia through orotracheal intubation. With the surgeon on the right side of the patient, endotracheal tube was fixed in the left. Using 0 degree Hopkins rod Telescope posterior pharyngeal wall was split open through a linear midline incision (Fig 2) extending from the upper border of the first cervical vertebra to the lower border of the second cervical vertebra, ligaments split in midline and longitudinal muscles retracted laterally, arch of atlas identified and drilled out exposing the underlying odontoid process (Fig 3).

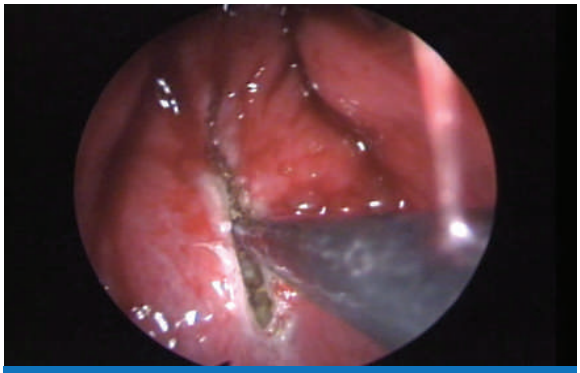

Fig 2 : Posterior Phryngeal Wall Spilt Incision Made

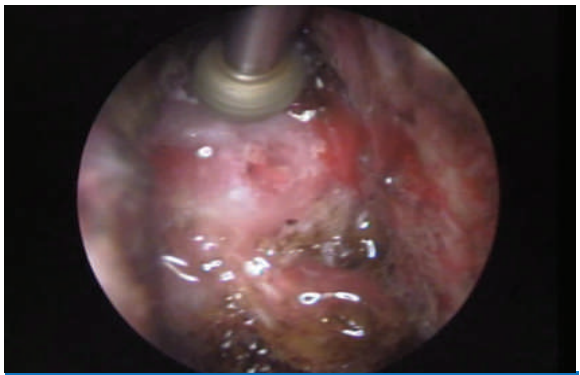

Fig 3 : Showing Arch Of Atlas Being Drilled

The odontoid process compressing the spinal cord was freed from the surrounding soft tissue attachments and drilled out by diamond burr leaving a thin plate of bone overlying the thinned out cruciate ligament and spinal dura. The residual egg shelled thin odontoid process was dissected from the spinal dura (Fig 4) till dural pulsations were encountered.

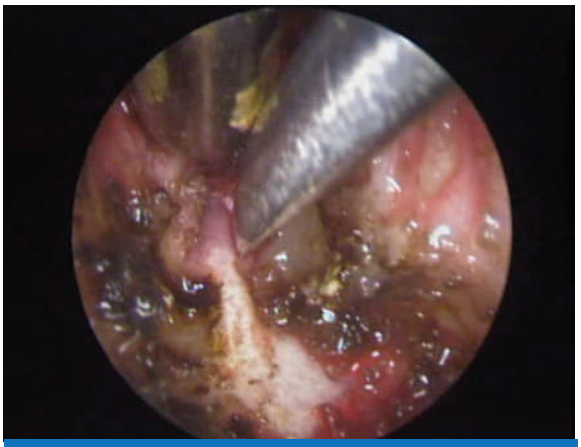

Fig 4 : Showing Showing Delineation of Odontoid Process

Patients were put on nasogastric tube feeding for one week. Stabilization of the cervical vertebra was done with occipitocervical fusion in the following week.

Results

Cervicomedullary junction decompression through transoral odontoidectomy was done successfully in 7 patients. None needed tracheostomy or gastrostomy tube placement in the post operative course. From the first week itself, patients were started on liquid diet and later to regular diet. There were no postoperative complications like velopharyngeal insufficiency, cerebrospinal fluid leakage, infection, or meningitis. All 7 patients underwent posterior stabilisation after odontoidectomy. On a 1-2 year follow-up, there was no evidence of CVJ instability. Patients with power 2/5 improved to 4/5 and patients with preoperative power more than 3/5 almost had near normal neurological function post operatively.

Discussion

Patients presenting with irreducible AAD with or without basilar invagination can be surgically managed by anterior or posterior approach. Posterior approach [7-10] has become obsolete because of the increased risk of complications. Commonly performed anterior approaches are transoral and transnasal. Occasionally, transcervical excision of the odontoid process, with anterior release and anterior fusion[11, 12] or anterior release and posterior fusion[13] has been done. Initially transoral odontoidectomy was done with the help of microscope. The procedure required palatal splitting for better exposure and so the incidences of complications were high. In our study, endoscopic transoral excision of the odontoid proved to be a safer and more effective approach. We have achieved excellent decompression with odontoidectomy and resection of C2 base and clivus in all patients.

As compared to the microsurgical technique, Pillai et al[14] reported better surgical exposure in the posterior pharyngeal wall and clivusregion by the endoscopic technique. Mazhar Husain et al[15] were also able to achieve good decompression in their patients. Palatal splitting that is needed in the microsurgical technique (especially in basilar invasion) was avoided in all our patients. Similar results have been reported before[16].

Compared to the microscopic excision which requires a 2.5 to 3cm mouth opening, this procedure was done with just a 1.5cm gap. Surgery could be performed in an extended or flexed neck position. We encountered intra- operative difficulty in dural closure and post operative dysphagia for up to 2 to 3 weeks. Even with risk of contamination by oral bacterial flora, there was not any incidence of infection. The endoscopic transnasal approach to CVJ lesions also reveals a comparable result in safety and efficacy[17-20] with added advantage of early oral feeding, avoidance of palatal splitting, less occurrence of tongue edema and infection. Its drawback lies in the difficulty in excision of lesions in lower body of C2[21]. The choice between transoral and transnasal approach was decided by the radiological line drawn along the floor of palate to the posterior pharynx (nasopalatal line). This serves as the reference point to assess the location of the lesion. Lesion high above the nasopalatine line can be easily accessed by endoscopic transnasal approach. Lesion just above the nasopalatine line can be dealt by both transoral and transnasal approach[22,23]. Whereas, lesions below the reference line is safely approached transorally. The transoraland transnasal approaches do have their own restraints. Patients may need an additional posterior approach for atlantoaxial fusion[11]. Endoscopic transcervical single - stage anterior release, reduction, and posterior fixation (with video guidance) were found to be effective [11, 24]. An artificial atlanto-odontoid joint could be implanted, which provides stability and preserves rotatory movements after odontoid resection[25]. A single - stage transoral procedure using atlantoaxial reduction plate for fixed AAD avoids the need for resection of dens and clivus or a posterior fusion process.

Meticulous preoperative assessment of the airway and pulmonary status was done for all patients. In those with unstable spine, awake intubation was performed to prevent injury to the spinal cord. We did immediate extubation after surgery for all except in those who had difficult airway or post - operative tongue / pharyngeal edema. In the latter, ET was kept for a few more days.

As with pre-operative respiratory function, the status post surgery should also be monitored[26]. We have observed that there is more deterioration of pulmonary reserve (Functional vital capacity, forced expiratory flow etc)in the AAD group than in patients undergoing surgery for compressive cervical lesions.

Conclusion

The endoscopic transoral odontoidectony is a better surgical technique for ventral lesion of the craniovertebral junction. It provides a direct visualization of the lesion which is further improved with angled endoscopes. It carries the distinct advantages of a safe and complete decompression of the lesion with minimal mouth opening and avoidance of palatal splitting. Complications like meningitis or velopharyngeal insufficiency is negligible. Occipitocervical fusion and tracheostomy is seldom needed in this approach.

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Original Article

Prediction of Intra Operative Tumor Consistency and Histopathological Subtype with Preoperative MR Imaging in Intracranial Meningiomas – A Prospective Analysis

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Abstract

Aim : To establish the correlation between Magnetic Resonance Imaging (MRI) characteristics and intra-operative consistency of meningiomas and establish the correlation between MRI characteristics and histological subtype of meningiomas.

Materials and Methods : This is a prospective analytical study. All the cases of intracranial meningiomas diagnosed and operated at the Department of Neurosurgery, Chettinad Hospital and Research Institute, Chennai during the 2 year period Jan 2014 to Dec 2015, totally 25 patients were included in the study. Patient clinical details including history and examination findings were noted. The MRI findings including T1 and T2 image characteristics of the tumors were recorded and graded preoperatively based on the previous studies as mentioned below. Intraoperative consistency of the tumor was also noted and histopathological type of the tumor was also recorded. Patient clinical details including history and examination findings were noted. The MRI findings including T1 and T2 image characteristics of the tumor were recorded and graded preoperatively based on the previous studies as mentioned below. Intraoperative consistency of the tumor was also noted and histopathological type of the tumor was also recorded.

Results : Preoperative prediction of the tumor consistency from the MRI correlated with the actual intra-operative consistency in 64% of cases and preoperative prediction of the pathological type from the MRI correlated with actual histopathological report in 36% of cases.

Conclusion : MRI is useful in prediction of intra-operative consistency of meningioma to a larger extent but a prediction of histopathological subtypes on the basis of MRI has not been possible to similar degree possibly because of varying number of subtypes.

Key Words: Meningioma, Consistency, MRI contrast.

Introduction

Harvey Cushing coined the term "Meningioma" in 1922. Meningioma is a dural based tumor that arises from arachnoid cap cells. The incidence is approximately 2.3 per 100,000 for benign meningiomas and 0.17 per 100000 for malignant meningiomas[1]. The principle treatment remains surgical resection with external beam radiotherapy, radiosurgery, arterial embolization and chemotherapy as an adjunct therapy when necessary[2].

The surgical resection remains the mainstay of treatment for meningiomas. The tumor consistency, vascularity, peri tumoral oedema, bone invasion, etc. play important role in planning the surgery. The consistency of the meningioma may be soft, firm or combination of both. In earlier days predicting the intra-operative consistency and histological type of the meningioma were difficult. But, with the advent of Computed tomography (CT) and Magnetic Resonance Imaging (MRI), several papers have reported the correlation between the imaging characteristics, tumor consistency and histological type of meningiomas.

Aim and Objectives

The aims of this study include the following:

1. The correlation between MRI characteristics and intra-operative consistency of meningiomas.
2. The correlation between MRI characteristics and histological subtype of meningiomas.

Materials and Methods

This is a prospective analytical study. All the cases of intracranial meningiomas diagnosed and operated at the Department of Neurosurgery, Chettinad Hospital and Research Institute, Chennai during the 2 years period were included in the study.

The patient details of the individual were entered in a detailed proforma. Patient clinical details including history and examination findings were noted. The MRI findings including T1 and T2 image characteristics of the tumor were recorded and graded preoperatively based on the previous studies as mentioned below. Intraoperative consistency of the tumor was also noted and histopathological type of the tumor was also recorded.

Patient clinical details including history and examination findings were noted. The MRI findings including T1 and T2 image characteristics of the tumor were recorded and graded preoperatively based on the previous studies[3] as mentioned below. Intraoperative consistency of the tumor was also noted and histopathological type of the tumor was also recorded. MRI findings were grouped into three to correlate with consistency (Table 1) as follows.

Group 1	Soft (T1-hypo-intense and T2-hyper-intense).
Group2	Intermediate consistency(T1-iso-intense, T2- iso to hyper-intense).
Group3	Firm (T1-hyper-intense and T2- hypo-intense).

Table 1 : MRI Grouping of Meningiomas

This was used to predict the tumor consistency preoperatively and the preoperative prediction was correlated with actual intraoperative consistency of the tumor.

Intraoperative consistency grading was made based on the 5 point scale described by Zada et al (2013)[4] (Table 2)

Grade-1	Extremely soft tumor, internal debulking with suction only.
Grade-2	Soft tumor, internal debulking mostly with suction and remaining fibrous strands resected with easily foldable capsule.
Grade-3	Average consistency, tumor cannot be freely suctioned and requires mechanical debulking and the capsule then folds with relative ease.
Grade-4	Firm tumor, high degree of mechanical debulking required and capsule remains difficult to fold.
Grade-5	Extremely firm-calcified tumor, approaches density of bone and capsule does not fold.

Table 2 - Intraoperative Grading of Meningiomas as described by Zada et al (2013)[4]

For convenience, the five point scale (Zada, 2013)[4] was divided into three groups:

Group I: Zada grade - 1 and grade - 2.
Group II: Zada grade - 3.
Group III: Zada grade - 4 and grade -5.

Similarly MRI and histopathology prediction was made based on the T2 image characteristics (Table 3), and for the purpose of study histopathology was divided into four groups.

Group I	Iso-intense (transitional and meningothelial subtypes).
Group II	Hypo-intense (fibroblastic and psammomatous subtypes).
Group III	Hyper-intense (angioblastic subtypes).
Group IV	Other histopathological subtypes.

Table 3 - T_2 Characteristics of Meningiomas on MRI and their histopathology prediction

Descriptive analysis of base line characteristics of the study population, location of tumor and grading and type of meningioma both before and after surgery was done. Frequencies and percentage was used for categorical variables. Mean and standard deviations were used for quantitative variables. The correlation between the preoperative and post-operative grading was done by cross tabulation. Percentage agreement was calculated by totaling the proportion of concordant pairs in cross tabulation. Kappa statistic and p-value was computed to assess the statistical significance of the agreement between pre and post-operative grading and type of tumor. IBM SPSS version 21 was used for statistical analysis.

Observations & Results

A total of 25 participants were included in the final analysis. The minimum age of the study participants was 23 years and the maximum age was 60 years, with a mean of 43.20 years (SD 9.58). (Table 4 & Figure 1)

Parameter	Mean	Median	95% CI		Standard Deviation	Minimum	Maximum
			Lower	Upper			
AGE (In years)	43.20	41.00	39.24	47.16	9.587	23	60

Table 4 - Age distribution of study population (n=25)

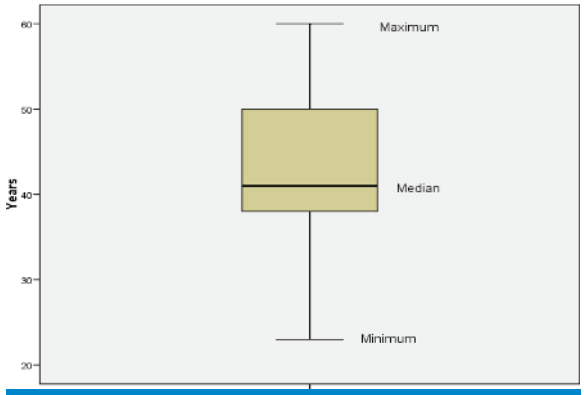

Fig 1 : Box and whisker plot showing age distribution of study population

Out of 25 study participants, 20(80%) were females and only 5 (20%) participants were males.

Gender	Frequency	Percentage
Female	20	80.0
Male	5	20.0
	25	100.0

Table 5 - Gender distribution of study population:

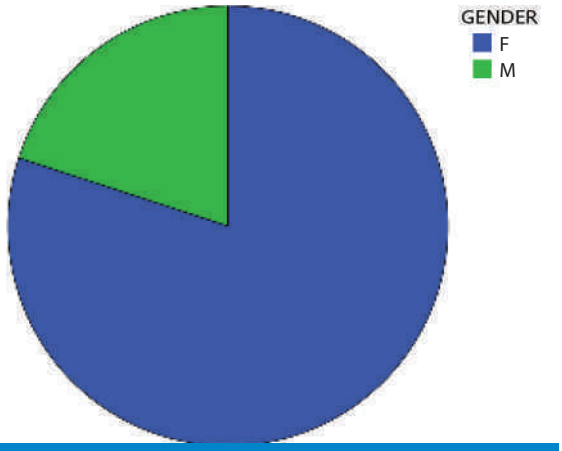

Fig 2 : Gender distribution of study population (N=25)

Location	Frequency	Percentage
Convexity	7	28.0
Sphenoid wing	6	24.0
Parasagittal	4	16.0
Falcine meningioma	3	12.0
Intraventricular	2	8.0
Basal meningiomas	1	4.0
cerebellopontine angle	1	4.0
Suprasellar	1	4.0
Total	25	100.0

Table 6 - Location of the tumor in study population

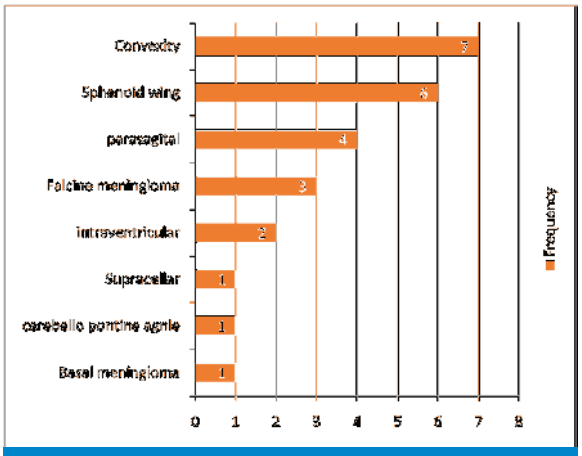

Fig 3 : Location of tumor in study population.

In the study, the most common location of the tumor was convexity (28%) followed by sphenoid wing (24%), parasagital (16%), falcine(12%), intraventricular (8%),basal meningioma, cerebellopontine angle and suprasellar meningioma (4%)[5], as shown in Table 6 and Figure 3.

MRI T_1 intensity	Frequency	Percentage
Isointense	18	72.0
Hypointense	7	18.0
Hyperintense	0	0.0
Total	25	100.0

Table 7 - MRI T_1 intensity for tumor grading.

T_1 MRI characteristics showed iso-intensity in 18 cases (72%), hypo-intensity in 7 cases (18%) (Table 7).

MRI T_2 intensity	Frequency	Percentage
Isointense	6	24.0
Hypointense	8	32.0
Hyperintense	11	44.0
Total	25	100.0

Table 8 - MRI T_2 intensity for tumor grading.

T_2 MRI intensity showed hyper-intensity in 11 cases (44%), hypo-intensity in 8 cases (32%) and iso-intensity in 6 cases (24%) (Table 8).

	Frequency	Percentage
Group I	11	44.0
Group II	7	28.0
Group III	7	28.0
Total	25	100.0

Table 9 - Pre-operative consistency grading of the tumor

In this study, most of the tumors were group I (44%) and group II and group III were 28% each (Table 9) in the preoperative assessment. The actual intraoperative grades were 44% group I, and 36% in group II and 20%

	Frequency	Percentage
Group I	11	44.0
Group II	9	36.0
Group III	5	20.0
Total	25	100.0

Table 10 - Intra operative consistency grading of the tumor

in group III (Table 10). In our study most of the tumors were in the group I (soft).

	Frequency	Percentage
Group I	8	32.0
Group II	6	24.0
Group III	11	44.0
Group IV	0	0.0
Total	25	100.0

Table 11 - Pre-operative pathological type.

	Frequency	Percentage
Group I	18	72.0
Group II	2	8.0
Group III	2	8.0
Group IV	3	12.0
Total	25	100.0

Table 12 - Post-operative pathological type.

The predicted histopathological subtypes of meningiomas in the basis of MRI finding were as follows : group I: 8 cases (32%), group II: 6 cases (24%) and group III: 11 cases (44%) (Table 11). The actual histopathological subtypes were as follows : group I: 18 cases (72%), group II: 2 cases (8%), group III: 2 cases (8%) and group IV: 3 cases (12%) (Table 12).

Preoperative and the intra-operative grades of the tumor correlated perfectly in the 16 out of 25 cases. The kappa scoring for the consistency grading was calculated to be 0.446 and the p-value was 0.002 with percentage agreement of 64%. Based on the kappa statistic value there is a moderate agreement.

Pre-operative grading	Intra operative grading			Percentage agreement	Kappa statistic	P-value
	Group I	Group II	Group III			
Group I	8 72.7%	3 33.3%	0 0.0%	64%	0.446	0.002
Group II	2 18.2%	4 44.4%	1 20.0%			
Group III	1 9.1%	2 22.2%	4 80.0%			

Table 13 - Correlation between pre and intraoperative consistency grading.

Pre-operative grading	Intra operative grading			Percentage agreement	Kappa statistic	P-value
	Group I	Group II	Group III			
Group I	8 72.7%	3 33.3%	0 0.0%	64%	0.446	0.002
Group II	2 18.2%	4 44.4%	1 20.0%			
Group III	1 9.1%	2 22.2%	4 80.0%			

Table 14 - Correlation between pre and post-operative histopathological subtype.

The correlation between the pre and postoperative histopathological subtypes showed a kappa score of 0.105 with p-value of 0.239 and percentage of agreement is 36%. The magnitude of inter user agreement on the basis of kappa statistics was only a slight agreement

Illustrative Cases

CASE 1: Anterior 1/3 rd falcine meningioma (Fig 4,5,6)

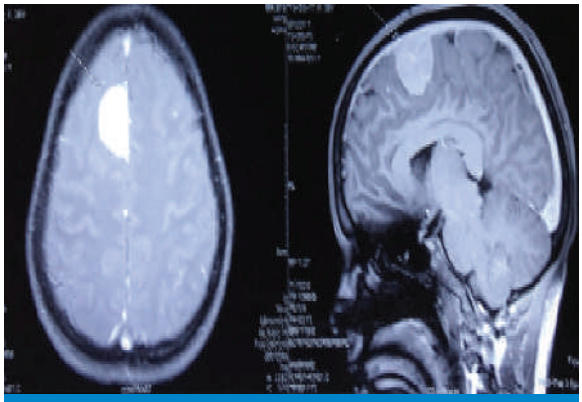

Fig 4 : Preoperative MRI of a middle 1/3rd falcine meningioma with a preoperative consistency of group-II (intermediate consistency).

Fig 5 : Completely excised falcine meningioma specimen with Intraoperative consistency of group-I (soft).

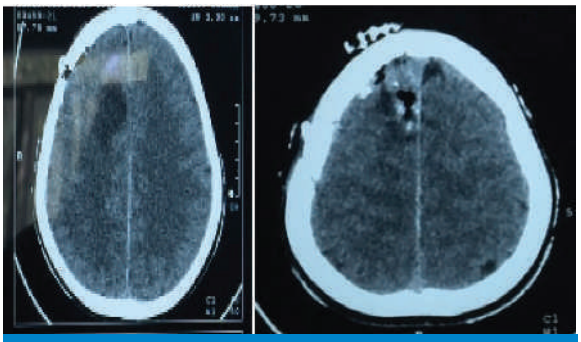

Fig 6 : Post-operative CT brain of anterior falcine meningioma showing complete excision of the tumor with post-op changes.

CASE 2: Case of left parietal convexity meningioma (Fig 7,8,9).

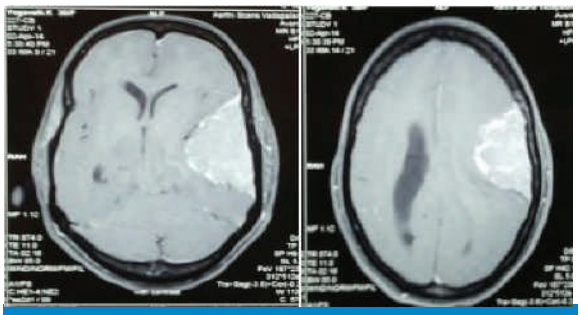

Fig 7 : Pre-operative MRI showing left parietal convexity meningioma with Preoperative consistency of group-I (soft).

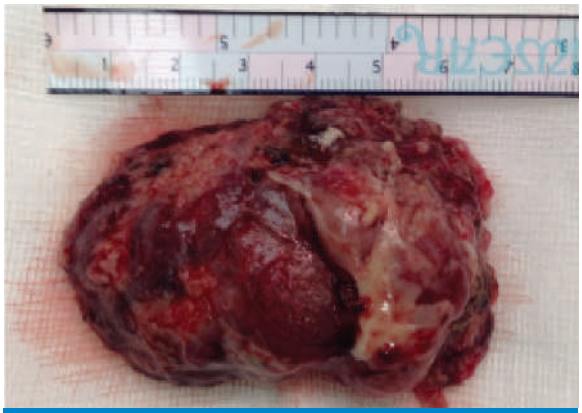

Fig 8 : Image showing the completely excised convexity meningioma.Intraoperative consistency of group-II (intermediate consistency).

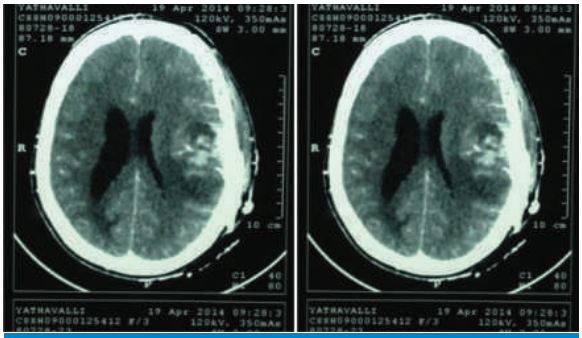

Fig 9 : Post-operative CT brain(contrast) showing post-operative changes with tumor bed hematoma and no residual tumor.

Twenty five operated cases of intracranial meningiomas have been analyzed in this study and correlation has been made between MRI appearance and intra-operative consistency and MRI and the histopathological subtypes. An attempt also made to correlate predicted consistency on the basis of MRI and actual intra-operative consistency and to correlate predicted histopathological subtypes based on the MRI and actual histopathological sub types. In the present study, T_2 hyper-intensity and T_1 hypo-intensity correlated with soft meningiomas, T_1 iso-intensity and T_2 iso to hyper-intensity correlated with intermediate consistency meningiomas, T_1 hyper-intensity and T_2 hypo-intensity correlated with firm meningiomas. Correlation of the image characteristics with various grades of the tumor was similar to previous similar studies. The following results have been derived from this study:

1. T_1 and T_2 weighted MRI were the sequences used in this study T_1-hypo-intensity and T_2-hyper-intensity correlated with soft tumor, T_1-hyper-intensity and T_2-hypo-intensity correlated with firm tumor.
2. T_2-hypo-intensity correlated with fibrous and psammomatous subtypes, T_2-hyperintensity correlated with angioblastic tumors and T_2-iso-intensity correlated with transitional and meningothelial subtypes.
3. Preoperative prediction of the tumor consistency from the MRI correlated with the actual intra-operative consistency in 64% of cases.
4. Preoperative prediction of the pathological type from the MRI correlated with actual histopathological report in 36% of cases.

Discussion

Prior information about the meningioma consistency and histopathological subtypes help in planning surgery and further follow-up. Some of the important factors that affect the decision making in surgical approach and resection of the tumors are tumor size, growth patterns, and invasion of the neurovascular structures and the consistency of the tumor. Many authors have reported that consistency is also a major limiting factor in the surgeon's ability to achieve complete resection of intracranial meningiomas. Little et al (2005)[6] reported in their series of petroclival meningiomas that risk of cranial nerve deficits increased with a multitude of factors, one being a tumor with fibrous consistency. The grading system as proposed by Zada et al (2013) for intra-operative consistency is easy to use method for the assessment of the intra-operative tumor consistency. Over the past few decades the tumor consistency has become an important variable of meningioma surgery as evolving minimally invasive options exist for removing a variety of skull base tumors. The ability to accurately predict the consistency of meningioma preoperatively based on MRI findings helps in selection of appropriate surgical approach and also provides more information regarding the requirement for a staged resection or additional challenges related to consistency.

of skull base tumors. The ability to accurately predict the consistency of meningioma preoperatively based on MRI findings helps in selection of appropriate surgical approach and also provides more information regarding the requirement for a staged resection or additional challenges related to consistency.

Hoover et al (2011)[7] in his series of 101 meningiomas, found that 50 meningiomas were soft and 51 meningiomas were firm. The association of T2 hypo-intensity with firmness and T_2 hyper-intensity with softness were statistically significant in his study and overall sensitivities for detecting soft and firm consistency were 90% and 56% respectively.

Kashimura et al (2007)[8] predicted the tumor consistency using fractional anisotropy (FA) value calculated from the preoperative MR diffusion tensor imaging found that FA values of hard tumors were higher than those of the soft tumors and concluded that FA value was significant predictor of tumor consistency.

In the present study, T_2 hyper-intensity and T_1 hypo-intensity correlated with soft meningiomas, T_1 iso-intensity and T_2 iso to hyper-intensity correlated with intermediate consistency meningiomas, T_1 hyper-intensity and T_2 hypo-intensity correlated with firm meningiomas.Correlation of the image characteristics with various grades of the tumor was similar to previous similar studies.

In our series we analyzed the correlation between the T_2 MRI intensity and the histopathology of the tumor. Maiuri et al (1999)[9] in her study of 35 cases of intracranial meningiomas to determine the intraoperative consistency found that meningiomas T_2 hyper-intense were soft and more frequently of angioblastic or syncytial subtypes, tumors that are T_2 hypo-intense or hypo-isointense were mostly of fibroblastic or transitional subtypes. In their series, meningiomas that are T_2 hypointense were mainly fibroblastic, T_2 hyper-intense were mainly syncytial, angioblastic and party transitional and T_2 iso-intense meningiomas were mainly transitional and partly fibroblastic and syncytial. In her study Maiuri et alconsidered the correlation of MR appearance with other pathologic findings. The cellularity of the tumor seems to be one of the main factors that determine the different signal intensity of various subtypes. Indeed, fibroblastic meningiomas which are mainly hypo-iso-intense have a lesser cell density; on other hand, syncytial and angioblastic meningiomas which are mainly hyper-intense on T_2 have a higher cellular density. However when the relationship between the cellularity and the signal intensity is analyzed in each single subtype, the correlation is weak and probably not significant. The vascularity of meningiomas seems to be well correlated with the MR appearance. In Maiuri et al and Chen et al[10] studies, hyper-intensity on T_2 weighted images predicted microscopical hypervascularity. Angioblastic meningiomas were almost always hyperintense on T_2 weighted images.

Somaya et al (1995)[11] studied the T_2 intensity of 40 patients and correlated with histological sub types; the mean signal intensity scores on T_2 of the fibrous type of meningiomas were lower than those of other sub types and they concluded that meningiomas hypointense on T_2 are composed primarily of fibrous elements.

In the present series, the preoperative prediction of histological subtypes was correct only in 36% of cases. The transitional, meningothelial, fibroblastic, psammomatous and angioblastic subtypes were predicted more easily than other subtypes.

T_2 weighted MRI sequence were useful in prediction of consistency and histological subtypes than T_1 weighted sequence.

The limitations of this study are relatively small sample of cases and less histological subtypes of meningiomas treated. Similar study involving larger number of cases and more varieties of histological subtypes will help to clarify the position better. This is the first time such a study has been conducted in Indian population.

We propose to continue this study on a larger number of cases of meningioma.

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Review Article

Management of Sepsis and Septic Shock

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Abstract

Management of sepsis and septic shock has been greatly evolved since the initial publications of Surviving Sepsis Campaign (SSC) guidelines in 2004. But still these conditions are associated with high mortality in patients admitted to the hospital as well as to the intensive care unit. From time to time experts have gathered information and new evidences for the betterment of care of these patients as well as to decrease the high rate of mortality associated with sepsis and septic shock. The guidelines have been revised in 2008 and 2012. The recent guideline, which is published in 2016 have taken into consideration of the best available evidences for the management of sepsis and septic shock till date. While they have incorporated few evidence based recommendation, definitions and newer modalities of assessment for the management of sepsis and septic shock; at the same time they have revised the previous recommendations based on the recently published evidences against these recommendations. Overall these guidelines will greatly help all the physicians involved in the care of sepsis and septic shock patients and will help in improving the outcome of these patients. Till new evidences are available, these recommendations will guide physicians taking their best clinical decision for the management of sepsis and septic shock.

Key Words: Sepsis, septic shock, Sequential Organ Failure Assessment (SOFA) score, resuscitation, screening, antimicrobial therapy, fluid therapy.

Review

Despite remarkable advancement in the understanding of sepsis patho-biology, it still remains as one of the leading cause of inhospital mortality. Its management has evolved greatly since the initial publications of Surviving Sepsis Campaign (SSC) guidelines in 2004[1]. The guidelines are revised in 2008, 2012 and 2016.Here is the latest recommendation for the management of severe sepsis and septic shock, which is based on the 2016 SSC guidelines[2].

The recent definition of sepsis as defined by The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) has defined sepsis as change in Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score (≥2) or presence of two of the three criterion qSOFA (Quick SOFA; Altered mental status, RR >22/min, SBP <100mmHg) score in the background of infection.[3] The task force has also defined septic shock as sepsis with persistent hypotension requiring vasopressors to maintain a mean arterial pressure (MAP) of ≥ 65mmHg and having a serum lactate level >2 mmol/L (18mg/dL) despite adequate volume resuscitation. It will enable clinicians to immediately start the management of patients with sepsis even before admission to the intensive care unit (ICU).

Initial Resuscitation

Once a patient is identified with severe sepsis the guidelines recommend initiation of the treatment and resuscitation as it is a medical emergency; and it should not be delayed pending the ICU admission. Over the last one decade these measures were based on the early goal-directed therapy (EGDT) protocol, whose credibility has been questioned in view of recently published 3 trials namely ProCESS trial, ARISE trial and ProMISE trial[4-7]. These trials have failed to show any significant mortality benefit associated with protocolized goal directed therapy compared to the standard of care protocol. But these findings could be attributed to the significant improvement in the standard of care practices which have practically incorporated the elements of EGDT over the last decade in the management of severe sepsis patient due to better sensitization. During the first 3 hours, atleast 30ml/kg of IV crystalloid fluid should be given for hypo perfusion due to sepsis and additional fluid administration should be guided based on repeated assessment of hemodynamic status. During further evaluation of shock, cardiac function should be evaluated and if available dynamic hemodynamic variables should be used to assess fluid responsiveness. The guideline strongly recommends maintaining a MAP of 65mmHg in patients with septic shock requiring vasopressors. The resuscitation should be guided with the measurement of serum lactate level as it is a marker for tissue perfusion.

Screening for Sepsis and diagnosis

A hospital performance improvement program for sepsis should be in place. It will help in screening and early identification of high risk patients. Early identification of sepsis focus will lead to early institution of treatment protocol and will improve the patient outcome[8]. The time gap between sepsis identification

and initiation of treatment is vital to the patient survival[9]. With widespread use of ultrasound by the Emergency medicine department and ICU, it is a valuable tool for the immediate screening of the patient with severe sepsis. It will be a useful tool for initial noninvasive evaluation of sepsis focus identification. For the identification of the causative organisms, at least two sets of blood cultures (both aerobic and anaerobic bottles) should be obtained before starting antimicrobial therapy. Of the two samples, at least one should be drawn percutaneously and the other one from the vascular access device, unless the device was recently (< 48 hours) inserted. The volume of blood drawn with the culture tube should be ≥ 10 mL[10]. Samples can be refrigerated or frozen if processing cannot be performed immediately. For identification of systemic fungal infection rapid diagnostic methods such as the use of 1, 3 β-d-glucan assays, mannan and anti-mannan antibody assays will be helpful.

Antimicrobial Therapy

Effective antimicrobials should be administered within 1 hour of sepsis identification. Each hour of delay in septic shock patient is associated with significantly increased mortality. Most studies support giving antibiotics to septic shock patient without any delay[8, 11]. The empiric antibiotics will include one or more drugs that have broad spectrum activity covering suspected pathogens. Also they should able to achieve adequate therapeutic concentration at presumed site of suspected infection. Empiric antifungal therapy should be considered where invasive fungal infection is suspected. The choice of antibiotic should be guided by the local prevalence patterns of bacterial pathogens and susceptibility data. Daily reassessment of the antibiotic regimen should be done by the clinician and due consideration should be given for potential de-escalation of the drug, once the causative organism is identified or if there is failure of any response to the treatment regimen. The empiric coverage should be narrowed once the causative pathogen is identified or if there is adequate clinical recovery. It will prevent development of resistance as well as reduce both toxicity and cost. Bio marker such as low procalcitonin level may be used to assist the clinician in making the decision regarding the discontinuation of the empiric antibiotics in patients who have no subsequent evidence of infection[12, 13]. The guideline recommends against the use of prophylactic antimicrobial therapy in patients with severe inflammatory states of noninfectious origin (e.g., severe pancreatitis, burn injury). Appropriate antibiotic dosage should be used according to both pharmacokinetic and pharmacodynamics of the drug.

Combination empiric antibiotic should used only for patients with septic shock aiming at the most likely pathogen. It strongly recommends against the use of combination therapy for the routine treatment of patients with neutropenic sepsis or bacteremia. An infectious disease consultation should be taken wherever multidrug resistance pathogen is suspected. Combination antimicrobial therapy should be used for streptococcal toxic shock syndrome with penicillin and clindamycin. For Pseudomonas aeruginosa bacteremia associated with respiratory failure and septic shock, a combination therapy with an extended spectrum beta-lactam and either an aminoglycoside or a fluoroquinolone is necessary[14,15]. Similarly, for Streptococcus pneumonia infections a more complex combination of beta-lactam and a macrolide is required. However the combination therapy should not be given for more than 3 to 5 days. The duration of antibiotic therapy should not be more than 7 to 10 days unless clinically indicated. Longer duration of treatment is required in patients with slow response, those with undrainable foci of infection, bacteremia with Staphylococcus aureus; some fungal and viral infections, or immunologic deficiencies, including neutropenia. Those patiets who have suspected associated viral infection empiric antiviral treatment should be initiated.

Source Control and infection prevention

Emergent source control should be done with specific anatomical diagnosis of infection like necrotizing soft tissue infection, peritonitis, cholangitis andintestinal infarction. An intervention should be undertaken for source control within the first 12 hours after the diagnosis, except in case of infected peri-pancreatic necrosis. For infected peri-pancreatic necrosis the definitive intervention should be delayed until an adequate demarcation of viable and nonviable tissues has occurred[16]. For the purpose of source control the least invasive physical insult will be preferred[17]. If any intravascular access device is suspected as the source of infection then it should be removed promptly after establishing other site for vascular acess[18, 19].

Selective oral decontamination (SOD) and selective digestive decontamination (SDD) should be used to reduce the incidence of ventilator-associated pneumonia (VAP). Also oral chlorhexidine gluconate (CHG) should be used for oropharyngeal decontamination to reduce the risk of VAP in ICU patients with severe sepsis.

Fluid Therapy

A fluid challenge technique should be always used where fluid administration continues. The fluid resuscitation of severe sepsis and septic shock should be done with crystalloid. Either balanced crystalloids or saline can be used for this purpose. When patients requires substantial amount of crystalloids, then albumin can be added with crystalloids for fluid resuscitation. Hydroxyethyl starches(HES) must be best avoided for fluid resuscitation of severe sepsis and septic Shock. This recommendation is based on the findings of the results of the VISEP, CRYSTMAS, 6S, and CHEST trials[20-23]. Those who require substantial amounts of crystalloids should be resuscitated with the use of albumin, as albumin administration is safe and equally effective as 0.9% saline[24]. Patients with sepsis-induced tissue hypoperfusion with suspicion of hypovolemia should be given an initial fluid challenge to achieve a minimum of 30 mL/kg of crystalloids. It has suggested the use of crystalloids over gelatins while resuscitating patients with sepsis or septic shock. During ongoing fluid administration hemodynamic improvement should be assessed using dynamic parameters of fluid responsiveness. These techniques include passive leg raises, fluid challenges against stroke volume measurements, systolic pressure variation,

and stroke volume variation. Echocardiography also can be used as bed side tool to assess the volume status and fluid responsiveness.

Vasoactive medications

Vasopressors to be started early to maintain a MAP of 65 mmHg and norepinephrine is recommended as the first-choice of vasopressor[25]. Norepinephrine is more potent as well as more effective at reversing hypotension in patientswith septic shock as compared to dopamine. Dopamine causes more tachycardia and is also more arrhythmogenic than norepinephrine[26]. When an additional agent is required to maintain the target MAP then either vasopressin (up to 0.03 U/min) or epinephrine should be added to norepinephrine. Vasopressin levels have been found to be low in patients with septic shock[27]. Vasopressin (up to 0.03 U/min) can be added to norepinephrine to raise the MAP or to decrease the norepinephrine dosage. However, low-dose vasopressin is not recommended as the single initial vasopressor for the treatment of sepsis-induced hypotension[28]. Use of dopamine as an alternative vasopressor agent to norepinephrine is reserved only for highly selected patients (eg, patients with low risk of tachyarrhythmias and absolute or relative bradycardia). Phenylephrine is not recommended for the treatment of patients with septic shock. Also low dose dopamine should not be used for renal protection[29,30]. All patients who require vasopressor therapy should be placed with an arterial catheter, as estimation of BP using cuff will be mostly inaccurate during shock. Patients with myocardial dysfunction as evidenced by low cardiac output or with ongoing signs of hypoperfusion, despite adequate intravascular fluid loading and adequate use of vasopressor agents, should be given trial with dobutamine infusion. Any predetermined cardiac output goal should not be targeted during its use.

Corticosteroids

The guideline recommends against the use of intravenous hydrocortisone for the treatment of adult septic shock patients if adequate fluid resuscitation and vasopressor therapy are able to restore hemodynamic stability. If patient has persistent hypotension despite all the measures then add intravenous hydrocortisone alone at a dose of 200 mg per day[31]. A continuous infusion is preferred over its bolus administration to avoid hyperglycemia and hypernatremia. Clinicians should taper the patient from steroid therapy when vasopressors are no longer required. The guidelines recommended against the use of corticosteroids in the treatment of sepsis when there is no shock.

Blood and blood products

Red blood cell should be transfused only when the hemoglobin concentration decreases to < 7.0 g/dLin adults except in patients with myocardial ischemia, severe hypoxemia or acute hemorrhage[32]. Erythropoietin should not be used for the treatment of anemia associated with severe sepsis. Fresh frozen plasma should not be used to correct laboratory clotting abnormalities in the absence of bleeding[33, 34]. It can be transfused prior to any planned invasive procedures. For platelets, it should be administered prophylactically when counts are ≤ 10,000/mm3 (10×10^9/L) in the absence of apparent bleeding. If the patient has a significant risk of bleeding then platelet should be transfused when counts are ≤ 20,000/mm^3 (20×10^9/L). Higher platelet counts (≥ 50,000/mm3 [50×10^9/L]) are required for active bleeding, surgery, or invasive procedures. Intravenous immunoglobulins should not be used in adult patients with sepsis or septic shock.

Anticoagulants and blood purification

While the guidelines recommends against the administration of antithrombin; there is no recommendation for the use of thrombomodulin or heparin for the treatment of sepsis or septic shock. The guideline made no recommendation for the use of blood purification techniques such as high-volume hemofiltration and hemoadsorption (or hemoperfusion).

Mechanical Ventilation

Clinicians should use lung protective ventilation strategy with a target tidal volume of 6 mL/kg predicted body weight in patients with sepsis induced acute respiratory distress syndrome (ARDS). Plateau pressures should be measured in these patients and the initial upper limit goal should be ≤ 30 cm H2O[35, 36]. PEEP should be applied to avoid alveolar collapse at end expiration. Strategies based on higher levels of PEEP should be used for patients with sepsis-induced moderate to severe ARDS[37]. Recruitment maneuvers should be used in sepsis patients with severe refractory hypoxemia due to ARDS. Ventilation strategy with positioning should be considered in sepsis-induced ARDS patients with a PaO_2/FiO_2 ratio ≤ 100 mm Hg wherever feasible[38]. The guideline strongly recommends against the use of high-frequency oscillatory ventilation (HFOV) in adult patients with sepsis-induced ARDS.

Patients who are on mechanical ventilation should be be maintained with the head of the bed elevated between 30 and 45 degrees to limit aspiration risk and to prevent the development of VAP[39]. A specific weaning protocol should be in place for patients on mechanical ventilation. Patients will undergo spontaneous breathing trials regularly to evaluate the ability to discontinue mechanical ventilation and if the spontaneous breathing trial is successful, extubation should be considered. Guidelines recommended against the routine use of the pulmonary artery catheter for patients with sepsis-induced ARDS[40,41]. A conservative fluid strategy is recommended for patients with established sepsis-induced ARDS who do not have evidence of tissue hypoperfusion. In the absence of bronchospasm, β2-agonists should not be used for the treatment of patients with sepsis-induced ARDS[42, 43]. The guideline made no recommendation regarding the use of NIV for patients with sepsis induced ARDS.

Sedation, Analgesia, and Neuromuscular Blockade in Sepsis

Sedation should be minimized in mechanically ventilated sepsis patients, targeting specific titration end points, so as to reduce the duration of mechanical ventilation and ICU and hospital lengths of stay[44-46]. Neuromuscular blocking agents (NMBAs) must be avoided if possible in septic patients without ARDS due to the risk of prolonged neuromuscular blockade following their discontinuation. If NMBAs must be used then depth of blockade should be monitored using train-of-four. A short course of an NMBA (≤ 48 hours) can be used for patients with early, sepsis-induced ARDS and PaO_2/FiO_2< 150 mm Hg.

Glucose Control

Guideline recommends a protocolized approach to blood glucose management in ICU patients with severe sepsis. Insulin should be started when two consecutive blood glucose levels are > 180 mg/dL[47,48]. Blood glucose values should be monitored every 1 to 2 hrs until glucose values and insulin infusion rates are stable, after that it should be monitored every 4 hours. The point-of care capillary blood glucose testing should be interpreted with caution, as it may not accurately estimate arterial blood or plasma glucose values[49]. If patient has arterial catheter than arterial blood should be used for point of care testing of blood glucose. The target upper blood glucose level should be ≤180 mg/dL and hypoglycemia should be avoided[47].

Renal Replacement Therapy (RRT) and bicarbonate therapy

Both continuous renal replacement therapy (CRRT) and intermittent HD are equivalent in achieving short term survival rate in patients with severe sepsis and AKI[50]. Those patients who are hemodynamically unstable, CRRT will facilitate management of fluid balance. RRT should not be used without absolute indication for dialysis. Sodium bicarbonate therapy should not be used to improve hemodynamics or reducing vasopressor requirements in patients who has hypoperfusion-induced lactic acidemia with pH ≥ 7.15[51, 52]. Bicarbonate will lead to sodium and fluid overload, an increase in lactate and PCO_2, and a decrease in the serum ionized calcium.

Deep Vein Thrombosis Prophylaxis

Patients admitted to the ICU have significant risk for developing deep vein thrombosis (DVT)[53]. Patients with severe sepsis should receive daily pharmaco-prophylaxis against venous thromboembolism (VTE). This should be done with daily subcutaneous low-molecular weight heparin (LMWH). If the creatinine clearance of the patient is < 30 mL/min, then dalteparin or UFH should be used. Patients with severe sepsis should be treated with combined pharmacologic therapy and intermittent pneumatic compression devices[54, 55]. Those patients who have contraindication to heparin use (eg, thrombocytopenia, severe coagulopathy, active bleeding, and recent intracerebral hemorrhage) should not receive pharmaco-prophylaxis. They should receive mechanical prophylactic treatment, such as graduated compression stockings or intermittent compression devices unless contraindicated[56-58].

Stress Ulcer Prophylaxis

The risk factor for GI bleeding includes coagulopathy, mechanical ventilation for at least 48 hours and possibly hypotension. Stress ulcer prophylaxis should be given with either proton pump inhibitor or Histamine-2 receptor antagonists (H2RAs)to patients with severe sepsis/septic shock who have bleeding risk factors[59-61]. Those patients who do not have any risk factors should not receive any stress ulcer prophylaxis.

Nutrition

Nutrition should be started within the first 48 hours after a diagnosis of severe sepsis/septic shock. Oral or enteral feedings should be started rather than either complete fasting or administration of only intravenous glucose. Mandatory full caloric feeding should be avoided in the first week of illness, rather a low-dose feeding (eg, up to 500 kcal per day), should be started and advanced gradually as tolerated by the patient[62, 63]. Intravenous glucose and enteral nutrition should be started rather than total parenteral nutrition (TPN) alone or parenteral nutrition in conjunction with enteral feeding in the first 7 days after a diagnosis of severe sepsis/septic shock. The guideline suggests the use of either early trophic/hypocaloric; which can be increased according to patient tolerance or early full enteral feeding in critically ill patients with sepsis or septic shock. While the guideline suggested against the routine monitoring of gastric residual volumes, the same can be measured in patients with feeding intolerance and those patients who are at high risk for aspiration. For patients with feeding intolerance prokinetic agents should be used. Also post-pyloric feeding tube should be placed for patients with feeding intolerance and those who are at high risk for aspiration.

No specific immune modulating supplementation should be added to the nutrition[64]. It has recommended against the use of omega-3 fatty acids as an immune supplement to the feed.The guideline strongly recommended against the use of IV selenium and glutamine, while suggested against the use of arginine to treat sepsis and septic shock. The guideline has no recommendation for the use of carnitine for sepsis and septic shock.

Setting Goals of Care

The goals of care and prognosis of the patient should be discussed with patients and families. Appropriate palliative care principles and end-of-life care planning should be considered where applicable. These goals of care should be addressed within 72 hours of ICU admission.

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Case Report

A Rare Combination of Stomatocytosis with Abnormal Blood Lipids and Gilbert's Syndrome

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Chettinad Health City Medical Journal 2017; 6(1): 27 - 29

Abstract

Stomatocytosis is a rare hemolytic disorder occurring due to abnormal lipid bilayer of RBC membrane. In a suspected hemolytic disorder, unconjugated hyperbilirubinemia out of proportion to drop in hemoglobin suggests a probable underlying Bilirubin uptake/ metabolism problem in liver. Gilbert's syndrome is the commonest among them. Though genetic testing can be used to confirm it, it is generally a clinical diagnosis in a patient with indirect hyperbilirunemia and normal liver and hematological tests. Single dose Rifampicin test may be used for confirming the diagnosis. Association of abnormal serum lipids and RBC lipids have been found in Abetalipoproteinemia in which Acanthocytes (spur cells) are seen. Here we present a 25 years male who had abnormally low serum lipid levels and stomatocytes presenting as hemolytic jaundice.

Key Words: Stomatocytosis, Stomatocytes, Hemolysis, Hyperbilirubinemia, Gilbert's syndrome, Peripheral smear, Lipids

Introduction

Red Blood Cell (RBC) membrane is made of lipid bilayer, cytoskeletal proteins and carbohydrates. Abnormalities in the lipid bilayer cause alteration in RBC shape, fluidity and in its permeability to water and ions. Lipid bilayer is made of cholesterol and phospholipid in nearly equal proportions. Abnormalities in inner lipid layer produces stomatocytes while outer lipid layer produces Acanthocytes (spur cells) and Echinocytes (burr cells)[1]. Stomatocytes are RBCs having a large wide central pallor resembling a transverse-slit or stoma. Acanthocytes are seen in patients with Abetalipoproteinemia, characterised by absent apo B lipoproteins and in patients with severe liver disease[1].

Case Report

A 25 year old male presented with recurrent episodes of jaundice for past 6 years. He remembers a history of anemia with Hemoglobin around 9gm % in childhood. There was no history of high colored urine, clay colored stools or pruritus. There was no family history of recurrent anemia or jaundice. On examination, he had no pallor; Icterus was present and no pedal edema. He had no hemolytic facies. Vitals were stable. Respiratory and cardiovascular system examination was normal. Abdomen examination showed no organomegaly, but Traube's space was obliterated.

Investigations

The below mentioned investigations were done. Hemoglobin(Hb) – 12.8gm/dl, Mean Corpuscular Volume (MCV) – 92.3fl, Mean Corpuscular Hemo globin (MCH) – 30.2pg/cell, Mean Corpuscular Hemoglobin Concentration (MCHC) – 32.7gm/dl, Red cell distribution width (RDW) – 14.8%, Total count (TC) 7200 cells per cu mm, Differential Count (DC) – Polymorphs - 67%, Lymphocytes- 27%, Eosinophils- 3%, Monocytes - 3%.

Peripheral Smear showed normocytic normochromic RBCs with multiple Stomatocytes (more than 40% of RBCs), as shown in Fig 1.

Liver function tests (LFT) -
Total Serum Bilirubin - 4.3 mg/dl, Direct Bilirubin - 0.13 mg/dl, SGPT - 35 IU, SGOT - 47 IU, SAP - 134 IU, GGT - 23 IU, Total protein – 7.8 g/dl, Serum Albumin – 4.4 g/dl, Globulin – 3.4 g/dl. Reticulocyte Count – 3.8, Reticulocyte Index - 3.2, LDH – 436, Serum Uric

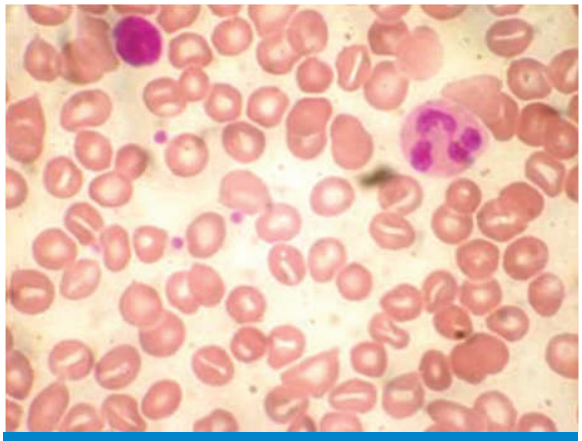

Fig 1 : Peripheral smear picture showing stomatocytes

acid – 7.8 mg/dl, Serum Haptoglobin – 0.171g/dl (0.3-2g/dl), Osmotic Fragility Test – normal, Coomb's test – negative, Hb electrophoresis – normal with HbF oncentration – 0.5%, HbA2 Concentration – 2.6%.

USG Abdomen showed Moderate splenomegaly, no gallbladder calculi. Blood group A positive.

HBsAg, Anti HCV and HIV were Negative.

Lipid Profile - Total cholesterol -20 mg/dl, HDL - 0 mg/dl, TGL - 115mg/dl. Measured LDL level -21 mg/dl.
Apo lipoprotein levels - Apo A - 20.1 mg/dl (110-205mg/dl), Apo B - 39.9 mg/dl (55- 140 mg/dl). Lipid Electrophoresis - showed a faint band in VLDL area, no bands in any other area

Serum Bilirubin pre & post oral intake of 900 mg of Rifampicin

- Pre rifampicin - Total -3.4mg/dl, direct -0.16 mg/dl
- Post rifampicin - Total - 6.6mg/dl, direct - 0.64 mg/dl

Discussion

Recurrent jaundice from childhood due to unconjugated hyperbilirubinemia can be due to hemolytic jaundice or congenital hyperbilirubinemias. Gilbert's syndrome, common among the congenital indirect hyperbilirubinemia is a benign autosomal dominant condition occurring due to defect in uptake and conjugation of indirect bilirubin. Serum bilirubin always remains around 3mg/dl and commonly does not exceed 4 mg/dl unless there is a stressful state like fasting, intercurrent illness or if there is a hemolytic disorder in addition[2]. Bilirubin elevation more than 1.5 mg/dl from the baseline, 4- 6 hours after administration of 900 mg of Rifampicin can be used as a diagnostic test for Gilbert's Syndrome[3]. On the other hand, Crigler - Najjar is a more serious disease having a much higher bilirubin levels which manifests as kernicterus in childhood.

In our patient, serum bilirubin was usually around 4 mg/dl and it increased from 3.4 to 6.6mg/dl, 6 hours after a single oral dose of 900 mg of Rifampicin suggesting the diagnosis of Gilbert's Syndrome.

Our patient also had evidence for hemolytic jaundice in the form of mild anemia, splenomegaly, elevated reticulocyte index, LDH and uric acid, reduced Haptoglobin and peripheral smear showing plenty of Stomatocytes.

A Bilirubin of 4.3mg/dL in a patient with Hb of 12.8g/dL suggested jaundice out of proportion to anemia. This suggested a combination of hemolytic jaundice due to stomatocytosis along with an underlying Gilbert's syndrome

Other causes of stomatocytosis like Rh null phenotype, RBCs with no Rh Ag namely (D,d,C,c,E,e)was ruled out[4]. Our patient had "A" positive blood group.

Another striking abnormality he had was grossly low lipid values. He had very low cholesterol levels -Total cholesterol -20 mg/dl, HDL - 0 mg/dl, TGL - 115 mg/dl. His measured LDL was 21. Such low lipid levels occur with rare inherited conditions like Abetalipoproteinemia, familial hypobetalipoproteinemia and familial combined hypolipidemia[5]. Among these low lipid conditions, RBC membrane defect namely Acanthocytes are described, as in Abetalipoproteinemia and Familial Hypobetalipoproteinemia. But Stomatocytes have not been described in such conditions.

Stomatocytosis have been described with absent and low HDL conditions like Tangier's Disease and Lecithin Cholesterol Acyl Transferase (LCAT) deficiency[6,7]. These low HDL conditions are associated with deposition of cholesterol in various tissues like liver, spleen, tonsils etc. But these conditions have normal VLDL and LDL levels.

Lipid electrophoresis of our patient showed absent chylomicron band, a faint VLDL band, absent HDL band, absent LDL band and absent Lipoprotein (a) band and his apo protein levels namely Apo A and Apo B levels were low.

Such a combination of absent HDL and low/ absent LDL occurs in a condition called Familial Combined Hypolipidemia. This disorder occurs due to mutation in Angiopoietin like Protein 3 gene (ANGPTL3) causing deficiency of this protein. This leads to increased activation of lipoprotein lipase and endothelial lipase causing increased catabolism of VLDL and HDL respectively causing decreased levels of LDL and HDL[5].

Lipid abnormalities in our patient suggest that he has Combined Hypolipidemia. But there is no literature stating an association between combined hypolipidemia and stomatocytosis. Probably the absent HDL in this condition can cause stomatocytosis. We could not screen his other family members.

Further studies are needed to find out the clear association between low serum lipids, LDL/HDL and RBC membrane defects.

Conclusion

Low lipid levels are associated with RBC membrane defects. Acanthocytes occur with Abetalipoproteinemia, a condition with low chylomicrons, low VLDL and low LDL. Stomatocytes occur with low HDL conditions. Lowering lipids to very low levels with statins or the newer PCSK 9 inhibitors might have effects on RBC membrane and also in other lipid structures. Further studies are needed to confirm the findings.

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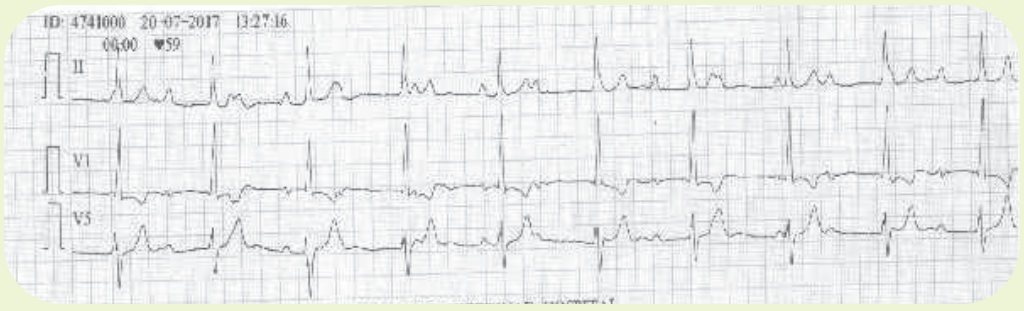
INTERESTING ECG

15 year old asymptomatic boy with the following ECG



- Dr.G.Ashok, Consultant Cardiologist, CSSH.

Answer in page : 45

Case Report

Unusual Presentation of Gastric Neuroendocrine Tumour

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Abstract

Gastric neuroendocrine tumors (NETs) develop from neuroendocrine cells. Gastric NETs are usually discovered as submucosal lesions during upper gastrointestinal endoscopy. NETs are graded into 3 types based on mitosis and Ki-67 index. We describe a case of upper GastroIntestinal Bleeding which was diagnosed to be a well differentiated type III neuroendocrine tumor of the stomach.

Key Words: Neuroendocrine tumor, GI bleeding, Endoscopy

Introduction

Neuroendocrine tumours previously mentioned as NETs are now described collectively under a term called Gastroenteropancreatic Neuroendocrine tumours (GEPNETs). They originate in the enterochromaffin cells located in the gastrointestinal (GI) tract. NETs are subdivided into foregut (gastric, duodenal and pancreatic) midgut (jejunal, ileal, cecal) and hindgut (distal colic and rectal)[1] Most common site of origin is ileum, followed by the rectum and the appendix[2,3]. Recent accepted nomenclature is by primary tumour site not by embryologic origin.

Gastric neuroendocrine tumours comprise less than 1% of all gastric tumours [4]. Depending on clinical presentation and histological findings, three types exist. Type I is associated with enterochromaffin like (ECL) cells hyperplasia, hypergastrinemia, achlorhydria and chronic atrophic gastritis with or without pernicious anemia[5] Type II is associated with Zollinger-Ellison syndrome (ZES) and multiple endocrine neoplasia (MEN-1) syndrome. Type III tumors are large, solitary, sporadic and invasive in nature[5].

They are usually asymptomatic or present with various upper abdominal symptoms of pain abdomen, bleeding and anemia. We describe a case of a large type III neuroendocrine tumor of the stomach.

Case Report

A 39 year old female presented with moderate hematemesis followed by malena and generalized weakness. There was no previous history of blood vomiting, pain abdomen or distension. On physical examination she was obese with BMI of 48kg/m^2 and mild pallor was present, Vitals were normal. Laboratory findings reveal Hemoglobin of 8.6 gm/dl, otherwise normal.

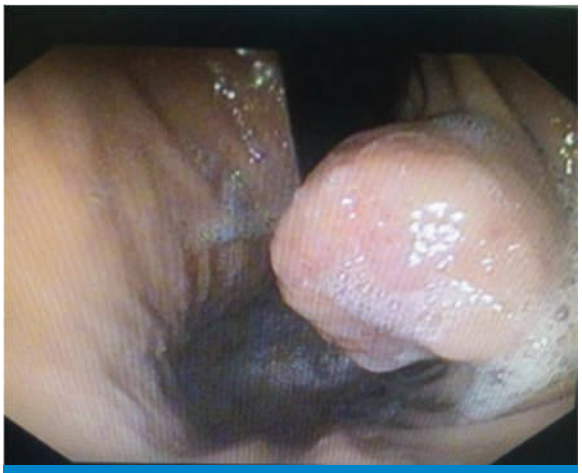

Fig 1 : Upper GI endoscopy

Upper GI endoscopy (Fig 1) showed a (2 cm x 3 cm), globular, submucosal lesion with blood spot, 5cm below the esophago gastric junction in proximal body, along the greater curve. A possibility of Bleeding gastrointestinal stromal tumor (GIST) was kept and Endoscopic Ultrasound (EUS) was planned.

EUS(Fig 2) done with radial array echo endoscope showed a Single large mass lesion of 2.5 x 2.2cm in anterior wall along greater curve in proximal stomach with surface ulceration and no active bleeding, it appeared to be arising from submucosal layer and able to delineate the third and fourth layer clearly, hence the diagnosis of neuroendocrine tumour of stomach was made.

CT abdomen (Fig 3) showed no evidence of regional lymphadenopathy or distant organ metastasis. Patient did not depict any clinical evidence of carcinoid syndrome.

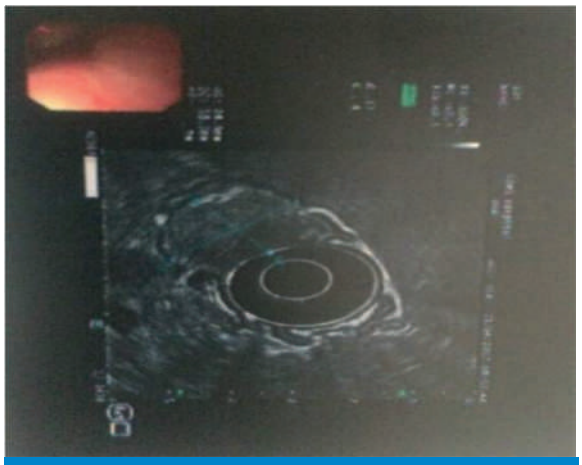

Fig 2 : EUS image

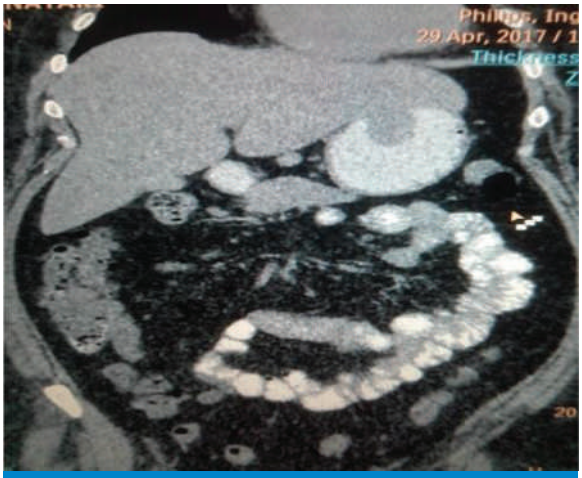

Fig 3 : A well defined endophytic, isodense, enhancing lesion seen in fundus.

After careful evaluation, patient was referred to surgeon and planned for surgery. An open surgery with partial gastrectomy was done and a segment measuring 6x 3 cm was sent as gross specimen (Fig 4).

Negative margins were confirmed by frozen section. Cut surface showed a lobular mass measuring 3x2x2 cm with mucosal ulcerations. Resected margins were free of tumor cells with no vascular and perineural invasion.

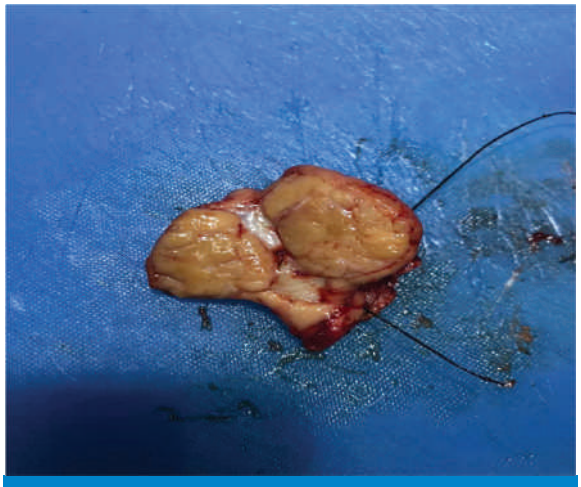

Fig 4 : Gross specimen

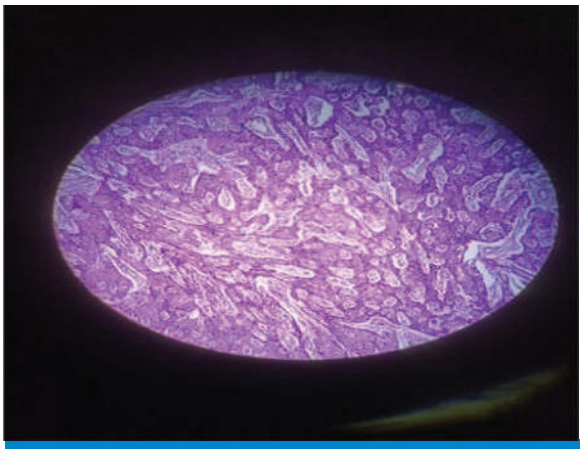

Fig 5 : Nests, trabaculae, ribbons of large Neuroendocrine cells

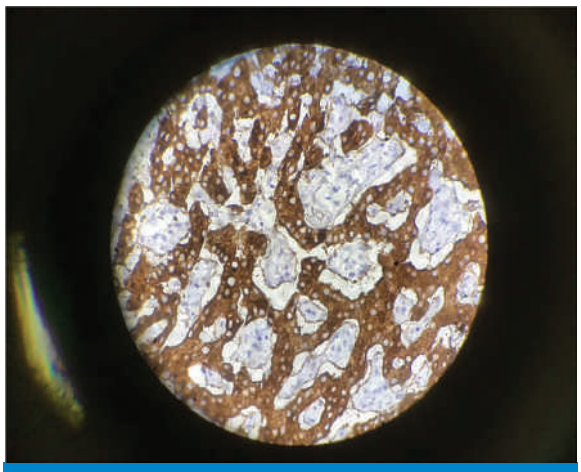

Fig 6 : Synaptophysin and Chromogranin shows bright membranous positivity

Histopathology of the mass showed a well differentiated gastric neuroendocrine tumor (Fig 5), invading muscularis propria which stained positive for synaptophysin and chromogranin A (Fig 6) with background chronic gastritis.

A diagnosis of large solitary type III gastric carcinoid with low grade malignant potential of Grade–G1(Mitosis < 2 /10 hpf, Ki 67 <= 2%) as per modified WHO grading system and TNM Stage of T2 was made. Patient remained stable in post operative period and advised to follow up with 68Ga-DOTATATE PET/CT after six months[6].

Discussion

NETs are explained by two major classifications, the WHO and American Joint Committee on Cancer. The 2010 WHO classification is based on number of mitosis and the Ki67 index shown in Table 1. The 2009 American Joint Committee on Cancer/Union for International Cancer Control(AJCC/UICC) classification system uses tumor invasion, number of lymph nodes affected and metastases (TNM).

Due to increase in screening endoscopies, incidence has increased[7] to 1–2 cases per 100,000 population per year with a female predominance.

WHO(2010)and ENETS Nomenclature	GRADE	Mitotic Count	Ki – 67 Index (%)	Cell Type
NET	G1	<2mitosis/10HPF	<2	--
NET	G2	2-20 mitosis/10HPF	3-20	--
Neuroendocrine carcinoma (NEC)	G3	>20 Mitosis/10HPF	>20	Large v/s small cell

Ref : ENETS - European Neuroendocrine Tumour Society

Table 1 - WHO classification of NETS

In type I GNETs, atrophic gastritis because of autoimmune etiology or related to H.pylori causes destruction of parietal cells, responsible for hypergastrinemia[8]. Type 1 tumors are multifocal, having size less than 2 cm, located in fundus or body.

Patients with gastric NET suspicion should be evaluated with serum chromogranin A level and gastrin levels to rule out hyper-gastrinemia. On endoscopy gastric NETs are found incidentally when dyspeptic symptoms or anemia are evaluated. Biopsies of normal appearing mucosa also helps to rule out atrophic gastritis. To assess depth in lesions of more than 2 cm Endoscopic ultrasound (EUS) should be done[9]. An Octreotide scan and FDG-PET scan are still more sensitive when symptoms of carcinoid syndrome are present.

It is important to consider Gastric NETs while evaluating any gastric polyp. Gastric NETs may present with Gastro-intestinal bleeding and anemia. The early diagnosis of these rare tumors makes a difference if they are having high malignant tendency.

Grade determines the prognosis. NET G1 is having good prognosis with high 5 year survival. NET G2 is aggressive but favourable prognosis. NET G3 are already invasive at initial diagnosis. The overall 5 year survival for all gastric NETs is 49%.

In Neuroendocrine carcinoma (NEC) prognosis is poor as malignant potential is high. NET less then 1cm can be removed by endoscopic means, However risk of recurrence exists. NEC requires extensive surgery[10]. Liver metastasis requires treatment with somatostatin analogues, hepatic artery embolisation, radiotherapy or chemoembolisation. The adjuvant chemotherapy for NEC is cisplatinum based chemotherapy[11].

Our patient, had no distant metastasis and was treated with partial gastrectomy, although theoretical risk of recurrence still exists. This case is reported for its rarity of the site and unusual presentation.

Conclusion

Treatment of GEPNETs includes team-based approach, using multiple tools to improve outcomes.

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Case Report

An Unusual Cause of Hemifacial Spasm

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Abstract

Hemifacial spasm is a hyperactive rhizopathy of the seventh cranial nerve. It is usually ascribed to vascular compression of the facial nerve at the root exit zone. Tumors, vascular malformations are unusual causes of hemifacial spasms. We report one young adult presenting with hemifacial spasms as a sole manifestation. On imaging it was found to be having large cerebellopontine angle epidermoid cyst and was managed surgically.He had good relief of hemifacial spasms after surgery. Hemifacial spasms as a sole presentation of cerebellopontine angle epidermoid cyst is relatively rare. Only few cases are reported in the literature.Patients with hemifacial spasms should have imaging to exclude structural causes at the cerebellopontine angle and brainstem.

Key Words: Hemifacial Spasm, Cerebellopontine Angle Tumour, Epidermoid Cyst

Introduction

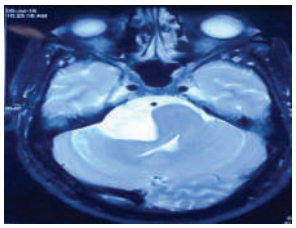
Hemifacial Spasm is the most common hyperactive cranial rhizopathy characterized by involuntary contractions of the muscles (spasms) on one side of the face (hemifacial). It is generally the result of vascular loop compression of the facial nerve at its root exit zone from the brainstem. It may also be associated with other organic lesions like tumors, aneurysms, vertebral artery dolichoectasia, cerebral infarctions, multiple sclerosis plaques, etc. Although the occurrence of tumor compression causing hemifacial spasms was recognized, cerebellopontine angle epidermoid cysts have rarely been described[1,2]. Herein, we report one such case with a cerebellopontine angle epidermoid cyst having hemifacial spasms as the sole presenting complaint.

Case report

A 28-year male was admitted to the hospital with the complaint of intermittent twitching of the muscles on the right side of his face. These involuntary spasms occurred repetitively within 1-2 hrs intervals for a day. The spasms were also observed during physical examination. There was no alteration of consciousness or associated involuntary movements of any other body parts of his body during the spasms. He had no history of convulsion, neurotrauma or developmental delay in childhood. There was no family history of neurological disease. The neurological examination was normal.

Magnetic resonance imaging (MRI) of the brain was requested. It revealed a well-demarcated cyst [hypointense on T1-weighted imaging and hyperintense on T2-weighted imaging] in the right cerebellopontine cistern. To differentiate between epidermoid cyst and arachnoid cyst, diffusion-weighted imaging (DWI) was done. It was hyperintense on DWI. (Fig 1).

DWI



T2W

MRAngiogram

Fig 1 : Evaluation by different imaging modalities

The results of the laboratory tests including hemogram, biochemical tests were normal. The patient was informed about his disease and advised to have neurosurgery treatment option. He was operated with the retrosigmoid (lateral suboccipital) approach in neurosurgery department. The diagnosis was also confirmed histologically. Hemifacial spasm completely disappeared after the surgery.

Discussion

Hemifacial Spasms is a hyperactive rhizopathy of the seventh cranial nerve. Hemifacial Spasms are frequently caused by vascular compression at the root exit zone of the facial nerve. Besides compressive neurovascular structures, it can also be caused by other organic lesions like tumors. The incidence of tumor - related Hemifacial Spasms is very low (0.3–2.5%)[1,3-5]. The main tumors found in cistern of the cerebellopontine angle are vestibular schwannomas, meningiomas, and epidermoid cysts. The epidermoids represent 0.2-1.8% of all primary intracranial tumors, and approximately 5% of all masses encountered in cerebellopontine angle[6].

Typical MRI appearance of an epidermoid tumor is hypo to slight hyperintense on T1W images, iso to hyperintense on T2W images, and hyperintense on DWI.[7,8] Arachnoid cysts appear as hypointense on T1W images and hyperintense on T2W images. However, DWI is an important technique to differentiate epidermoid cysts and arachnoid cysts. In case of an arachnoid cyst, DWI reveals a hypointense lesion, which is isointense to CSF. However, epidermoid cysts appear hyperintense on DWI as in our case[8]. It is due to T2 shine -through which refers to high signal on DWI that is not due to restricted diffusion, but rather to high T2 signal which shines through to the DWI and because of long T2 decay time.

Clinicians need to be aware that patients with Hemifacial Spasm should be scanned for brainstem lesions. MRI studies are essential to detect the vascular structures running adjacent to the root exit zone that might distort the facial nerve and compress the brain stem around the root exit zone, and to exclude other organic causes like tumors, Multiple Sclerosis plaques or cystic lesions. As in our case, an epidermoid cyst in cerebellopontine cistern, compressing the pons, which contains the nuclei and root exit zone of the facial nerve, may present with Hemifacial Spasms as the sole symptom.

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Classroom Article

Zika Virus-An Emerging Viral Illness and Congenital Zika Virus Syndrome

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Abstract

Zika viral infection is an emerging viral infectious disease. Most of the cases are asymptomatic, a few may present as a very severe illness, rarely leading to death. The common presentation is a febrile illness with rash, myalgia, arthralgia, conjuctivitis and headache. Congenital Zika virus syndrome produces a wide range of Central Nervous System and ocular abnormalities in newborn. Studies have also suggested a strong association between Zika virus infection and Guillain-Barre' syndrome. Primary route of spread is by the bite of Aedes mosquito and vertical transmission. It can also spread by sexual route and blood transfusion. Diagnosis is by RNA-Nucleic acid testing (RNA-NAT) and RT-PCR. Like other Flaviviral illnesses (Dengue, Yellow fever and Chikungunya), there is no specific treatment for Zika viral illness other than symptomatic treatment. So prevention is the main modality stressed.

Key Words: Zika Virus, mode of transmission, clinical features, congenital Zika virus syndrome, Flaviviral infections, diagnosis, prevention.

Introduction

There are several emerging viral and other infectious diseases, one among them being Zika viral disease (ZVD) which has recently come into the limelight because of its association with increased number of cases of microcephaly in babies born to mothers infected with Zika virus during pregnancy in Brazil in 2015. However, Zika virus has been in existence since 1947 and is named after the Ugandan forest where it was first isolated. There have been 4 cases of Zika virus reported in India since 2016, and considering the fact that the vector for Zika virus (Aedes aegypti and Aedes albopictus) is plentiful in India, it is a ticking time bomb waiting to explode any time into an epidemic. The purpose of this review article is to spread awareness regarding Zika virus infection, clinical features, diagnosis and prevention.

Biology

Zika virus belongs to the flavivirus family and is similar to dengue virus, yellow fever virus, Japanese encephalitis virus and West Nile virus. It is an enveloped virus with an icosahedral core and single stranded positive sense RNA (Fig 1). Like other flaviviruses, it has a nucleocapsid of 25-30nm diameter, encased by a lipid bilayer which has envelope proteins E and M. The overall virion is 50nm in diameter[1]. There are seven non structural proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B, NS5) and three structural proteins (envelope protein, premembrane protein and capsid protein) which help in attachment.

Phylogenetic analysis has revealed two lineages of Zika virus[2]:

1. Asian strain(further classified into Malaysian and Micronesian strains)
2. African strain(further classified into Nigerian cluster MR766 and prototype cluster isolated in Uganda)

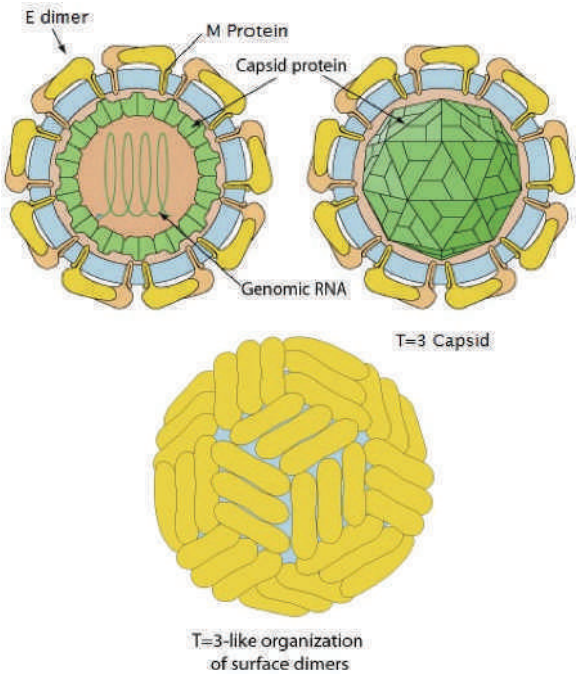

Fig 1 : Structure of Zika virus

Source: www.laboratoryinfo.com

Mode off Transmission:

1. Mosquito bite[3]
   This is the primary mode of spread by Aedes(A.aegypti and A.albopictus). Aedes mosquitos are aggressive feeders and primarily bite during the day time, but can also however bite during the night time.These mosquitos lay eggs in domestic water collections like coconut shells, pots, flower vases, tyres, etc. Aedes albopictus is slowly replacing Aedes aegypti in urban areas, and has a longer life span of about 10 weeks.

2. Vertical transmission[3]:
   Pregnant mother can transfer the virus to the fetus, if infection is acquired during the antenatal as well as during the perinatal period.Though there are no reports of transmission through breast feeding, Zika virus has been isolated in breast milk, and hence there is a risk of transmission through breast feeding. In a study of three Zika virus infected mothers, Zika virus was demonstrated in the breast milk and blood of all three mothers. Of the three newborns, two had confirmed Zika virus infection. Due to the variable incubation period of Zika virus, antepartum and intrapartum transmission could not be ruled out in these cases[4].

3. Sexual transmission[3]:
   Few studies have shown the presence of Zika virus in the seminal fluid[5]. Another study has demonstrated prolonged presence of Zika virus RNA in the semen, even 62 days(maximum of 180 days) after the onset of symptoms[6].

4. Blood transfusion[3]:
   Though there are no such confirmed cases in USA, multiple reports are there in Brazil. There are two reported cases of transmission of Zika virus by platelet transfusion[7]. Centre for disease control USA have mandated screening for Zika virus in blood donors from August 2016. So far 40 were found to be positive.

5. Laboratory and healthcare setting exposure[3]:
   Samples from persons with suspected Zika virus infection should be handled with Biosafety level 2 precautions.

Clinical Features:

The clinical features are almost indistinguishable from other viral illnesses in the flavivirus grouplike dengue and chikungunya.However the presentation is mild in most of the cases. Incubation period ranges from three days to two weeks. Most of the cases (80%) are mild or asymptomatic and hence go unnoticed[8].

(i) Clinical features are:

1. Rash is the most common presentation(82.1%)[9]
   It is usually a maculopapular rash involving the facial region and upper limbs (95%),torso (93%), lower limbs(86%). There is also associated itching (82%) which is usually intense. Infrequently the palms (30%) and soles (13%) are involved[10].

2. Febrile illness is seen in75% of cases[9]
   In contrast to other flaviviral illnesses, Zika virus usually causes a mild fever. Rarely, it can cause a high grade fever.

3. Arthralgia is seen in 61.9%[9].
   This commonly involves the wrist, ankle and the small joints of the hand and foot. Involvement of larger joints like elbow, knee are rare. Unlike Chikungunya, joint pain usually recovers.

4. Oedema has been noted in 39.6%[9].

5. Myalgia (32.1%) and back pain (1.5%)[9].

6. Conjuctivitis (50.7%)[9].

7. Headache (24.6%), retro orbital pain(17.1%) and dizziness(4.5%)[9].

8. GIT manifestations[9] noted are Abdominal pain (6%), Vomiting (3.7%), Diarrhea (2.2%).

9. Constitutional symptoms such as Fatigue (12.7%), anorexia(3%) has been documented[9].

10. Other less common presentations are Sore throat (3.7%), Cough (1.5%), Lymphadenopathy (5.2%) and Aphthous ulcers (2.2%)[9].

11. Neurological manifestations:

(i) Guillain-Barre syndrome: In a study among 42 patients diagnosed to have GBS, 98% had anti-zika virus IgG or IgM. Neurological symptoms started within 6 days from the onset of infection[11]. The short interval between the onset of Zika viral illness and the onset of GBS suggests a parainfectious pattern rather than the classical post infectious pattern[12] (Fig.2). The possible reasons for this is not exactly known, but can be due to[13]:

   (a) Zika virus triggers an immune molecular mimicry against neural antigens before the onset of clinical symptoms

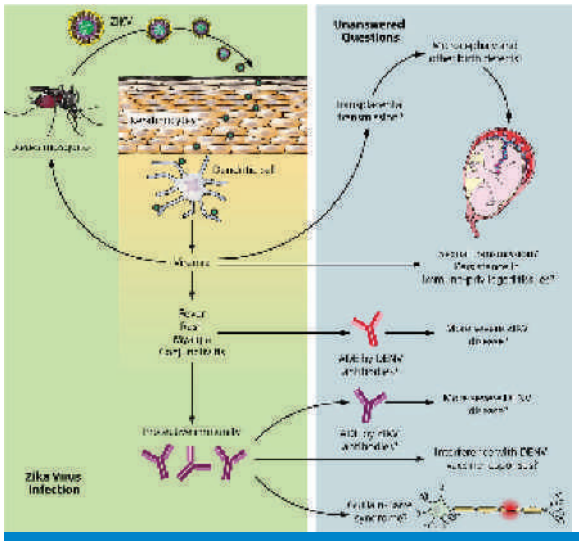

Fig 2 : Pathogenesis of Zika Viral Disease

Source: www.jvi.asm.org

(b) Through mechanisms unrelated to molecular mimicry
(c) Direct viral neural damage/invasion
(d) Production of a hyperimmune response

(ii) Other neuro manifestations are acute myelitis presenting with Hemiparesis and sensory abnormalities(parasthesias), 7 days after onset of infection[14].

(iii)Meningo-encephalitis is seen rarely[15].

(iv)Auditory disturbances observed are bilateral metallic sound and a small delay between sound and perception of the sound[16].

12. Rare presentations:

(i) Prostatic infection presenting as pain over the perineal region, UTI like symptoms and hematospermia[17].

(ii) Bleeding manifestations (Gingival bleeds, hematuria and hematospermia). However the incidence of bleeding is lower compared to Dengue and Chikungunya[18].

13. Zika Viral Deaths:

(a) There is a reported case of death following Zika virus infection in a 15 year old girl with sickle cell disease (Hb SC). The patient developed an acute febrile illness with myalgia, arthralgia, retro-orbital pain, abdominal pain and jaundice. She was provisionally diagnosed with Dengue. The patient's condition then deteriorated with deepening of jaundice, ARDS, severe hypoxemia and bleeding diathesis (prolonged PT and aPTT; patient had hemothorax). The patient was positive for Zika virus by RT-PCR[19].

(b) Another case of Zika virus related death was in USA, a 73 year old man being treated for prostatic cancer(otherwise in good health). He then developed a serious febrile illness and passed away soon after. There was history of travel to Mexico one week before the illness. He was found to be positive for Zika virus(same strain as that circulating in Mexico). The man had a previous history of dengue. This could possibly explain the severity of Zika virus disease in this patient (due to antibody-dependent enhancement/ADE)[20].

(c) Another death was reported from Peurto Rico, in a 70 year old man, the cause being immune thrombocytopenic purpura[21].

14. Some studies have shown cardiovascular manifestations in Zika viral infection in the form of serious rhythm abnormalities (Ventricular arrhythmias, atrial fibrillation and atrial tachycardia) and sometimes even cardiac failure[22].

From 2016 to 2017 there have been 4 laboratory confirmed cases of Zika virus infection in India. 3 cases were from Ahmedabad, Gujarat[23]. The most recent case was from Krishnagiri district in Tamil Nadu[24]. Since there is no significant travel history in these cases, the source of infection could probably be due to an already circulating strain of virus in India. The only evidence for the existence of the virus in India is the detection of antibodies against Zika virus, most prevalent in Bharuch district (of the then Bombay state), Gujarat and Nagpur[25].

Case 1: (November 2016) 34 year old female who had delivered a normal child, developed a low grade fever during the post natal period. There was no significant travel history or history of fever during pregnancy.

Case 2: (January 2017) During a routine antenatal clinic surveillance at BJ medical college, Gujarat, a sample from a 22 year old female at 37th week of gestation was found to be positive for Zika virus.

Case 3: (February 2017) During an acute febrile illness(AFI) surveillance at BJ medical college, Gujarat a sample from a 64 year old male who had complaints of fever for 8 days turned up to be positive for Zika virus.

Case 4: (July 2017) The patient was a 27 year old male who complained of fever, headache, redness of eyes, photophobia and photophobia. RT-PCR done in Manipal Centre for Virus Research was positive. Subsequent tests at the National Institute of Virology, Pune found the urine positive for Zika virus.

IMPORTANT DIFFERENCES BETWEEN THE FLAVIVIRAL INFECTIONS[26] (number of plus denotes how common or how severe the particular manifestation is)

(a) Zika Virus:
1. Rash: +++
2. Fever: either absent or mild in nature
3. Itching: +++
4. Joint pain: +
5. Myalgia: +
6. Conjuctivitis: +++
7. Headache: +
8. Bleeding manifestations: Very rare
9. Shock: Very rare
10. Leucopenia and/or thrombocytopenia: very rare
11. Recovery: 4-7 days
12. **Antenatal and Perinatal infection: Congenital Zika Virus Syndrome**

(b) Dengue Virus:
1. Rash: +
2. Fever: Moderately high fever lasting for 4-7 days
3. Itching: +
4. Joint pain: +
5. Myalgia: ++
6. Conjuctivitis: Very rare
7. Headache: ++
8. Bleeding manifestations: ++
9. Shock: +/-
10. Leucopenia and/or thrombocytopenia: +++
11. Recovery: 6-7 days
12. Antenatal and Perinatal infection: No fetal anomalies

(c) Chikungunya:
1. Rash: ++

2. Fever: High grade lasting for 2-3 days
3. Itching: +
4. Joint pain: +++
5. Myalgia: +
6. Conjuctivitis: +/-
7. Headache: +
8. Bleeding manifestations: +/-
9. Shock: Very rare
10. Leucopenia and/or thrombocytopenia: +
11. Recovery: within 7 days
12. Antenatal and Perinatal infection: No fetal anomalies

Congenital Zika Virus Syndrome (CZS)

Zika virus can cause a variety of congenital conditions (congenital Zika virus syndrome) when the mother had acquired infection during the antenatal period. Though many of the congenital abnormalities in congenital Zika virus syndrome are also seen in other congenital infections, there are 5 unique manifestations which are characteristic to Congenital Zika virus infection[27]:

(1) Microcephaly with a partly collapsed skull.
(2) Cerebral cortex thinning/atrophy with sub cortical calcifications.
(3) Retinal abnormalities: scarring of macula and pigmentary retinal mottling.
(4) Basal ganglia involvement presenting as increased muscle tone and other extra pyramidal manifestation
(5) Congenital contractures and CTEV.

1. Cranial Abnormalities[27]

Severe microcephaly is most common.From 19th may, 2016 there have been 1384 confirmed and 3332 suspected microcephaly cases caused due to Zika virus in Brazil and 88545 suspected and 31616 confirmed Zika virus infections, suggesting the rate of microcephaly to the total number of Zika virus infected cases to be around 1%-4%.Other anomalies seen are Cranio facial disproportion (95.8%), Biparietal depression (83.3%), Prominent occiput (75%). Excess nuchal skin in 47.9% of cases[28]. Zika virus is also associated with fetal brain disruption sequence(FBDS), where there is collapse of the cranial bones secondary to decreased brain volume and intra cranial pressure. Though FBDS is not exclusive to Zika virus, it has rarely been seen before[29]. CNS abnormalities noted are Cerebral cortex thinning Enlarged ventricles and Intracranial calcification[30]. The intracranial calcifications are strikingly similar to that seen in congenital cytomegalovirus(CMV) infection. However, the location of the calcifications in both differ. It is periventricular in CMV and subcortical in Congenital Zika virus infection. Corpus callosum abnormalities, Cerebellar abnormalities(especially involving the vermal region) also have been observed[31].

2. Ocular Anomalies[29]

- Microphthalmia
- Cataract
- Coloboma
- Chorioretinal atrophy
- Focal pigmentary mottling
- Optic nerve hypoplasia/atrophy

3. Congenital Contractures

May manifest as Congenital tallipes equinovarus or arthrogryposis multiplex congenital. 3 large case series describing microcephaly due to congenital Zika virus syndrome have shown incidence of isolated club foot to be 3.8-14% and arthrogryposis to be 5.7-11%[29].

4. Neurological Sequelae Observed are:[29]

- Motor dysfunction
- Cognitive disabilities
- Extrapyramidal manifestations: Increased muscle tone, tremors, irritability, posturing[32].
- Seizures
- Visual and/or hearing defects.

Diagnosis[33]

1. RNA-NAT(nucleic acid testing)-Confirmatory test:
- This should be done on serum/urine sample within the first 14 days of symptom onset.
- Though a positive result is almost confirmatory of Zika virus infection, a negative result does not rule out infection and serum should be subjected to serological testing (IgM antibody testing).

2. RT-PCR
- Though the FDA has not approved this test, it has authorized its use under an Emergency use authorization (EUA).

3. Zika MAC ELISA
- This is used to detect IgM antibodies in the serum.
- However this test is not specific due to cross reaction with other flaviviruses like dengue and chikungunya.

4. Diagnosis of congenital Zika virus infection[34]

Laboratory testing for congenital Zika virus infection is recommended in cases where Zika virus infection is suspected in the mother. rRT- PCR testing is done on the serum and urine of the infant, and IgM antibodies should be concurrently tested on serum by IgM ELISA. Testing should be done within a period of 2 days. If CSF sample is available, rt-PCR and IgM ELISA tests can be performed on the CSF sample. Testing on cord blood sample is not desirable as the sample might be contaminated with maternal blood, yielding false positive results. A positive rt-PCR test for Zika virus is more predictive than a positive IgM ELISA test. Infants diagnosed with congenital Zika virus infection should be assessed periodically for the development of ocular, auditory, cognitive, behavioural and musculoskeletal problems and treated accordingly.

Prevention

1. Control of mosquitos:
Antilarval measures:

a) Environmental control: Elimination of mosquito breeding places/source reduction such as elimination of domestic/artificial collections of water.

b) Chemical methods[35]:
Larvicides used: Bacterial larvicides (Bacillus thuringiensisisraelensis), Chlorpyrifos, Fenthion, Temephos.

c) Biological control[36]:
The use of larvivorous fish like: Gambusia, Lebistes, Aphanius, Danio, Rasbora, Anabas, etc.

Anti-Adult measures[35]:

a) Residual sprays:
Indoor residual spraying (IRS): Long acting insecticides are sprayed on the walls and roofs of houses to kill mosquitos that rest on these surfaces.

Insecticides used: DDT, Malathion, Fenitrothion, Propoxur, Pirimiphos-methyl, Bendiocarb

b) Space spraying:

The usual recommendation for space spraying is in cases of emergency like an epidemic or an impending epidemic. The aim of space spraying is a quick and mass destruction of the adult mosquito population to reduce the intensity of transmission.

Insecticides used: Deltamethrin (ultra low volume liquid/emulsion), Lambda-cyhalothrin (emulsifiable concentrate), Malathion (emulsion and ultra low volume liquid)

c) Long-lasting insecticidal nets[35]:
DawaPlus 2.0 (Deltamethrin coated on polyester), Duranet (Alpha-cypermethrin incorporated into polyethylene), Olyset Net (Permethrin incorporated into polyethylene)

2. Prevention of sexual transmission for those travelling to an area with risk of Zika virus[37]:

a) Only the male partner travelling to an area with risk of Zikavirus:Sexual abstinence or use of condoms for a period not less than 6 months, irrespective of whether the person has symptoms of Zika viral disease or not.

b) Only the female partner travels to an area with risk of Zika virus: Sexual abstinence or use of condoms for a period not less than 8 weeks, irrespective of whether the person has symptoms of Zika viral disease or not.

c) If both the male and female partner travel to an area of risk of Zika virus: Sexual abstinence or use of condoms for a period not less than 6 months, irrespective of the whether either of them have symptoms or not.

3. Prevention of transmission through blood products[38]:
As per FDA recommendations, blood donors should be considered ineligible if they have any of the following risk factors:

a) Medical diagnosis of Zika virus infection in the past 6 months.

b) Residence in, or travel to, an area with active Zika virus transmission within the past 6 months.

c) Sex within the past 6 months with a male who is known to have either one of the above risk factors mentioned above.

If blood products are to be transfused, testing for Zika virus must be done when the blood product is being used for pregnant women, to prevent CZS.

4. Vaccine: Zika virus vaccine is under development. Animal studies have shown very promising results (almost 100% efficacy)[39]. Currently human trials are being conducted.

Treatment[40]

Like other viral illnesses like dengue and chikungunya, there is no specific treatment for Zika viral disease.
Treatment is mainly symptomatic:
Plenty of oral fluids to avoid dehydration
Bed rest
Paracetamol is the preferred drug of choice for reduced fever and pain since other NSAIDS have a risk of precipitating bleeding (unless dengue is ruled out)

Conclusion

Zika viral disease is an emerging viral disease that has the potential to increase in number in the coming years. Since 4 cases have already been reported in India, and the vector Aedes aegypti is in abundance, Zika virus should be considered in the differential diagnosis of viral illness. Samples negative for Dengue and Chikungunya in suspected Zika viral illness should be sent for further analysis for detecting Zika virus in order to assess the true magnitude of the disease in the country. A large percentage of the infections are asymptomatic, however severe disease and very rarely death have been reported. Congenital Zika viral disease can cause a wide spectrum of fetal anomalies. The virus can be transmitted by routes other than mosquito bites and vertical transmission, like sexual transmission and blood transfusion. Since treatment is mainly symptomatic, prevention is of prime importance.

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Peace of Mind

Chronic Non Specific Pain - An Old Father's Letter to His Young Daughter with Non Specific Chronic Pain

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Chettinad Health City Medical Journal 2017; 6(1): 42

I am glad to note that all your results are normal and you have no apparent major health problem. Of course I acknowledge that you continue to have pain but please feel relieved that there is no cause for concern or alarm. I am also very happy to note that you have a very healthy lifestyle.

The greatest asset/crown is our body - no matter how unsatisfied we are with it. Our knowledge, intellect, wisdom are jewels in the crown. We inherit these from our parents/ grandparents. You must have inherited it from your grandmothers.

After 47 years in the field of medicine, I strongly feel that there is no perfect body, knowledge, intellect or wisdom. We all have our short comings, both physical and intellectual. I was 18 years when I started having severe , excruciating abdominal pain. It was wrongly diagnosed as amoebiasis initially but subsequently diagnosed as renal/ureteric colic. One Senior Professor even remarked that it is like cancer; keeps recurring. I have had countless attacks of ureteric colic since then, for the past 35 years. Only in the last 10 years, I have not had an attack of ureteric colic, thanks to Amma (mother). I had Lithotripsy and started taking plenty of fluids. Lithotripsy crushed the stone and probably also my pancreas. I ended up with impaired glucose tolerance/prediabetes/diabetes. There is a price we pay for everything in life, except of course, " Father's Love ". I have had allergic rhinitis all my life; keep sneezing several times in the morning or at other times, several times in the day. Doctors advised me anti histaminic (allergic) drugs or steroid sniff. By breathing exercises I have it now mostly under control.

You may recollect Paatti's (grandmother's) leg problem. She had it since she was 25 years old but continued all her activities and learned to live a full life with it. She was advised surgery by several doctors; had steroid injection in her leg; the pain continued. She managed to avoid all surgeries and had a full and satisfying life.

Our body is Nature's/God's/Parent's gift to us. It is a machine and there are trillions of cells, innumerable tissues, 206 bones, so many joints, fascia, cartilage, ligaments, etc. Some pain somewhere in the body at some time or several times or daily is certainly not a pleasant thing. Persistent pain is certainly most annoying but if it is not progressive, debilitating or disabling, it should not cause us any disturbance. We must first exclude any of the major causes for the problem. If there is no discernible cause for the problem, we have to learn to cope up with it and carry on with life. Of course we need to periodically recheck to confirm that there is no major problem cropping up.

Modern medicine is neither modern nor often evidence based. Some doctors are good at giving new names/ syndromes without adequate evidence. Musculoskeletal disorders are mostly due to undue stress and strain, improper position, nutritional deficiency or over exertion. We are all not the same. If I were to run because Hussain Bolt runs, I would end up with huge problems. Healthy life style can help relieve many of these problems. I overplayed shuttle cock and landed with Plantar Fasciitis and Calcaneal bursitis forcing me to go on a wheel chair and walker for several days. I have had back ache for the last several decades. Annoying but not disabling. I often get relief by back exercises and massage.

Physiotherapy and massage, hot fomentation, cold compress help to relieve pain in many musculoskeletal disorders. Since we are reasonably sure that there is no major health problem, I think you should focus on physiotherapy. Physiotherapist may be a good choice to consult and also consider Bio-feedback to reassure yourself that there is nothing wrong with you.

In conclusion, all of us are made differently. Even identical twins are not identical. In your own language - "methylation is different even in identical twins". Therefore it is inappropriate to say that we are not like other 26 year olds. Since comparisons are odious and lead us nowhere. We must be happy that we are better off than most of the 26 year olds. Following is a Thamizh poem.

அரிது அரிது மானிடராதல் அரிது
மானிடராயினும் கூன் குருடு செவிடு பேடு நீங்கிப் பிறத்தல் அரிது
கூன் குருடு செவிடு பேடு நீங்கிப் பிறந்த காலையும்
ஞானமும் கல்வியும் நயத்தலரிது
ஞானமும் கல்வியும் நயந்த காலையும்
தானமும் தவமும் தான் செய்தல் அரிது

(Being born as a human is most venerable,
Even revered is, to be born without being dumb, deaf, humpback or blind
Even if born without disabilities, it is rarer
To have knowledge and education
Even if one has good knowledge and education, it is rarer
To be benevolent and do penance)

- Avvaiyar

We are all fortunate to be what we are. Of course, we all aspire for better health, more money, more name and fame and more of everything. There is nothing wrong about that. However we also have to accept limitations posed by Nature and the circumstances and accept and enjoy our body and our life. Our greatest possession is our body. We must learn to respect and enjoy it with all its limitations.

உள்ளம் பெருங்கோயில் ஊனுடம்பு ஆலயம்
(The heart is a great temple and the fleshy body the shrine)

- Thirumular

Therefore my dear Rasathi - Please get over your sickness and be your normal VIBRANT self. You are the apple of our eyes.

- (Identity withheld)

Instruction to Authors

Chettinad Health City Medical Journal 2017; 6(1): 43 - 45

The following are the uniform requirements for manuscripts submitted to the Chettinad Health City Medical Journal, which are in accordance with "Uniform requirements for Manuscripts submitted to Biomedical Journal" developed by International Committee of Medical Journal Editors (October 2001).

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The submitted manuscripts are taken up for review for possible publication assuming that they have not been simultaneously submitted or already accepted or published elsewhere. The initial review is conducted by the Editors. Manuscripts lacking significant originality, important message and those with serious flaws are rejected. The unaccepted manuscripts will not be returned. The other manuscripts are sent to two or more experts in the field for review and they are blinded for the identity of the contributors. The reviewers' comments and acceptance or rejection of the manuscript will be informed to the contributors in 8 to 10 weeks. The accepted articles will be copy edited for format, spelling, grammar, punctuation, etc.

Types of Manuscripts and word limits

Original articles: This includes case series, randomised control trials, interventional studies, studies involving screening and diagnostic procedures, studies of outcome analysis, studies involving cost-effective analysis and surveys with high response rate. Word limit is 2500 excluding references and abstract.

Review articles: This includes systematic critical assessment of literature and other data sources. Word limit is 3000 excluding references and abstract.

Case reports: This includes report of new cases, very rare cases and very interesting cases. There should not be just reporting of cases; but their clinical significance or implications should be emphasized. Word limit is 1000 excluding references and abstract; with up to 10 references.

Letter to the Editor: This includes short decisive observations, including brief reporting of rare and interesting cases. Word limit is 400 with up to 4 references.

Other Sections: Include Editorials, Perspective articles,History articles, Class room articles, which are by invitation from the Chief Editor.

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Authorship criteria

Authorship should be based on substantial contributions to:

1) to concept and design or data acquisition or data analysis and data interpretation;

2) preparation of manuscript, critical revision and contribution to the intellectual content;

3) final approval of the manuscript version to be published.

Mere fund acquisition for the study or data collection or general supervision of the research project do not qualify for authorship.

All the authors must have contributed substantially to the work and must be able to take responsibility of the respective portions of their contributions.

The authors should be named in the order of their relative contribution towards the study or the manuscript writing. This order cannot be changed after submission of the manuscript without the written consent from all the authors.

Number of authors

1) Original papers: Maximum of six from a single institution.

2) Case reports and review articles: Maximum of four.

3) Images and letter to editor: Maximum of three.
There must be a written justification if the number of authors exceeds these limits.

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The manuscript enclosed with covering letter and contributors' form signed by all the authors with the photographs, should be sent as a soft copy to the Chief Editor. However, the authors are encouraged to send the manuscripts along with the above enclosures as E-mail attachment to the Chief Editor. The covering letter must include the undertaking that the manuscript has not been simultaneously submitted/ accepted/ published elsewhere. Conflict of interest if any in the form of financial or other relationship also should be disclosed. Copies of any permission to reproduce already published material including illustrations or photographs and consent for publication of identifiable material should be sent along with the manuscript.

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Font style and size: Time New Roman Size 12 for the text and 14 for the titles.

Double spacing without justifying.

The language and spelling style should be American English.

Pages should be numbered serially starting from the Title Page.

Title Page

This should contain:

- Title of the article (which should be short, relevant to the manuscript and informative)
- Type of the article (Original paper/review article/case report, etc.)
- Running title (short title) with less than 50 characters
- Names of authors (Name followed by initials/Last name, First name and initials of middle name) with the highest academic degree. Prefixes like Dr, Prof, etc. are avoided.
- The name of the department(s) and institution(s) where the work has been carried out.
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- This should carry the full title of the manuscript and abstract.
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Manuscript Pages:

Introduction

This should state the purpose of the study/article and the basis and rationale for the study.

Methods

- This should state nature of study - observational/ experimental/trial, etc.,whether prospective/ retrospective.
- Selection of the subjects (patient/experimental animals) including controls.
- Details of the methods, apparatus (with the manufacturers name and address) and procedures.
- References should be quoted for established methods including statistical methods.
- New or less known methods should be described in detail with the rationale and limitations
- Generic names of drugs and chemicals used, including dose, route of administration should be stated.
- Randomized control trials should give the details of the protocol, methods of randomization, conceal men of allocation to treatment group and the method of blinding/masking as per the CONSORT statement (Moher D, Schulz KF, Altman DG: The CONSORT Statement: Revised Recommendations for Improving the Quality of Reports of Parallel-Group. Randomized Trials. Ann Intern Med. 2001;134:657-662, also available at http://www.consort- statement.org).
- Reports of human studies should state that the procedures in accordance with the ethical standards of the responsible Institutional/Regional Ethical Committee on human studies and with the Helsinki Declaration, 1975 revised in 2000 (http://www.wma.net/e/policy/17-c_e.html). Patients' identity including name, initials, hospital number,etc. shall not be disclosed.
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Results

The results are shown in sequence in the form of text, tables/illustrations, wherever required.

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Only important observations are summarized/ emphasized.

Discussion

- New and important aspects of the study and the conclusions drawn from them and the implications for the future research are stated.
- There shall not be any repetition of the statements and data from the introduction and results section.
- The observations and conclusions of this study are compared and related to the other similar or relevant studies.
- False and unsubstantiated claims on cost or economic benefits shall be avoided.
- New hypotheses drawn from the study shall be stated and labeled as such, if required.

Acknowledgements

This shall be in the last page of the manuscript.

This may include:

1) General support from faculty that need acknowl- edging, not amounting to authorship.
2) Technical help
3) Financial and material support with the actual naure of support.

References

- Numbering is done consecutively in the text (not in alphabetical order)
- The references are identified in the text, tables and legends by Arabic numerals in superscript.
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- Tables shall be self-explanatory and shall not be repeated in text.
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ECG showing

Atrial rate of 100, Ventricular rate of 60 per minute.

AV dissociation, Narrow complex QRS

PP interval enclosing QRS is shorter than the one without QRS suggestive of CHB – with supra hisian escape rhythm with Ventriculophasic sinus arrhythmia

- Dr.G.Ashok, Consultant Cardiologist, CSSH.

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