

Original Article

Sneddon-Wilkinson Disease in Three Different Ages – A Case Series and Review of Literature

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Abstract

Subcorneal pustular dermatosis is a rare, chronic, relapsing neutrophilic dermatosis characterized by typical clinical pattern of eruption with multiple sterile, flaccid pustules, vesiculopustules or bullae commonly arising in females with a predisposition to the flexural sites. Its characteristic histopathology reveals subcorneal neutrophilic infiltrate. Here we report a case series of three patients of different age groups -15 year old male, 23 year old female and a 45 year old female who came with the complaints of sudden onset of discrete, flaccid pustules over the body. Most of them showed hypopyon formation. Patients were otherwise healthy and asymptomatic.

Histopathology was done from an intact pustule which revealed subcorneal split with neutrophilic infiltrate. Immunofluorescence was negative.

Key Words: SCPD, Subcorneal pustular dermatosis, sterile pustules

Introduction

Subcorneal pustular dermatosis (SCPD) is a neutrophilic dermatosis characterized by acute onset of symmetrical, flaccid, sterile, pea sized pustules occurring in crops with a predilection to the flexural sites of the body. Classical lesions show positive "hypopyon sign" that is the collection of pus in the lower half of the bulla. Histopathological presence of subcorneal neutrophilic deposition is characteristic of SCPD. It is a rare dermatosis with only 200 cases being reported so far.¹

Case History

Case number 1

A 15 year old male came with complaints of sudden onset of pustules over both axilla, chest and abdomen for past 2 weeks. Patient was treated earlier (after the onset of pustules as impetigo with cephalosporins for 5 days) but found no improvement and continued to develop new lesions. Patient was otherwise healthy and asymptomatic. Cutaneous examination showed multiple tiny pustules arising over the normal skin seen over the anterior aspect of chest, abdomen and both axilla. Axilla showed coalescing / circinate pattern with few lesions showed crusting. Hypopyon sign was positive in few lesions [figure 1].



Figure 1 : Shows tiny 0.5-1cm discrete pustules over the axilla and chest with some of them coalescing to form circinate pattern in the axilla

Case number 2

A 23 year old female came with sudden onset of generalised tiny pustular eruptions over the body involving abdomen, groins, thighs, legs and submammary region and for past 2 weeks [figure 2]. Patient was otherwise asymptomatic.



Figure 2 : shows multiple tiny erythematous papulovesicles and pustules over the anterior aspect of legs

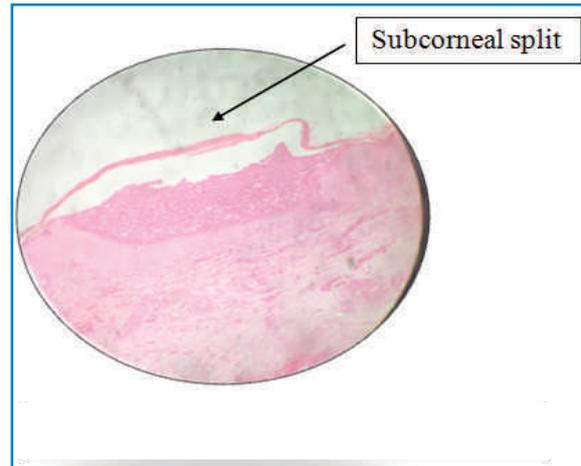


Figure 4: Histopathology Showing Subcorneal Split

Case number 3 :

A 45 year old female came with the complaints of sudden onset of asymptomatic tiny discrete pustules with some of them showing hypopyon sign over the both submammary region for the past 10 days [figure 3]. some of the lesions ruptured to form erosions with collarette scales. Patient was otherwise asymptomatic.

There was no history of drug intake / fever/topical application/occlusiveclothing/oral ulcers / athralgia / co-morbidities like diabetes or hypertension. Mucosa / scalp and nails were normal in all 3 cases. Based on the clinical findings, a differential diagnosis of impetigo, candidiasis, subcorneal pustular dermatosis, pustular psoriasis , pemphigus foliaceus, were considered. All necessary blood investigations like complete blood count was normal, HIV and VDRL, RA factor were non reactive. Gram stain, culture and KOH was negative. Tzanck smear showed abundant neutrophils. Histopathology showed subcorneal split with neutrophilic microabscess [figure 4,5].

Direct Immunofluorescence was negative. The investigations for paraproteinemia were not done as the patients were asymptomatic. Based on the above findings a diagnosis of subcorneal pustular dermatosis was made. All patients were treated with Dapsone 100mg per day. There was complete resolution of skin lesions in case 1 at the end of 2 months and in case 3 at the end of 3 months whereas patient in case 2 lost follow up.

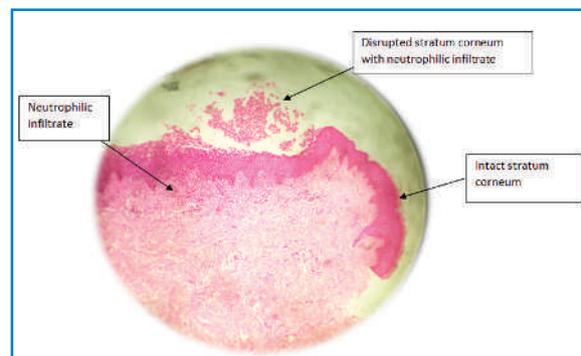


Figure 5: Histopathology showing disrupted stratum corneum with neutrophilic infiltrate

Discussion

It is eponymously known as Sneddon-Wilkinson disease as it was 1st described as a case series in 6 patients by Ian Sneddon and Darrell Wilkinson in the year 1956.² It is commonly seen in elderly females. The most common age group of presentation is 40-60 years. Though rare, SCPD can occur at any age group as seen in our cases. Occurrence of children and adolescents is extremely rare with only 20 cases being reported in literature.³

The exact pathogenesis of SCPD is unknown. Recent studies suggest that the hyperactivation of neutrophils in SCPD might be due to the chemotactic effect overproduction of TNF- α as is evidenced by the presence of increased levels of TNF- α in the blister fluid and serum of the patient with SCPD.⁴ TNF- α inhibitor like infliximab produces rapid therapeutic response in a recalcitrant and severe case of SCPD but the response was temporary.^{5,6} Adalimumab also produced similar effects.⁷ It is a non antibody mediated mechanism since no antibodies are being demonstrated against desmogleins 1 and 3 and immunofluorescence study being negative.⁸

SCPD typically presents with pea sized, sterile, symmetrical pustules or vesiculopustules which may be discrete, or in groups or might coalesce to form large bulla. They may arise from a normal looking skin or over an erythematous base. Most of them show positive hypopyon sign or Meniscus sign with half clear and half pustular (lower half) lesions. This is classical of SCPD but can also be seen in secondarily infected vesicubullous disorders like pemphigus, bullous pemphigoid, and linear IgA dermatosis.⁹



Figure 3 : Shows discrete tiny pustules arising over the submammary region with some of them showing hypopyon sign and on rupturing forms erosions with collarette of scales

The blisters are flaccid(subcorneal level) and rupture to form scaly or crusted lesions presenting in an arcuate or annular fashion. They usually heal with mild hyperpigmentation. Common sites of predilection include intertriginous areas like axilla, groins, submammary and inframammary region and can also involve trunk and extremities¹⁰. Mucosa and scalp are spared and involvement of palms and soles is extremely rare.¹¹

Patients are usually asymptomatic and healthy. It is a benign disorder with recurrence and remissions. Prognosis is usually good as it does not have systemic involvement in most of the cases but there are reports of its association with SLE, thymoma,¹¹ IgA gammopathy,¹² pyoderma gangrenosum,¹³ Crohn’s disease,¹⁴ Sjogren's syndrome,¹⁵ rheumatoid arthritis,¹⁶ non-hodgkins lymphoma.¹⁷ Systemic involvement has a poorer prognosis.

Differential diagnosis of SCPD [Table 1] include pustular psoriasis, acute generalized exanthematous pustulosis, dermatitis herpetiformis , pemphigus foliaceus , IgA pemphigus , impetigo , bullous dermatophytosis.

DIFFERENTIAL DIAGNOSIS	DIFFERENTIATING POINTS
PEMPHIGUS FOLIACEOUS ^{18, 19}	<ul style="list-style-type: none"> Occurs in seborrhoeic areas of body Cornflake like crusting Mucosal involvement may be seen Nikolsky sign is positive Histopathology: acantholysis in the upper epidermis(subcorneal or granular layer) DIF : IgG deposition in intercellular spaces of upper epidermis
DERMATITIS HERPETIFORMIS ²⁰	<ul style="list-style-type: none"> Intensely pruritic papulovesicles , vesicles or urticarial lesions involving the extensor surfaces of the body Histopathology: subepidermal blister with neutrophilic microabscess especially over the tips of dermal papilla Immunofluorescence: granular IgA/C3 deposition in papillary dermis Association of bowel disturbances in the form of Ulcerative colitis or Crohn’s disease Gluten sensitive dermopathy
IGA PEMPHIGUS ²¹	<ul style="list-style-type: none"> Vesiculopustules commonly seen over flexures that spreads to other sites(like trunk and extremities) histopathology: intraepidermal split(SCPD type- subcorneal level and IEN type –commonly lower epidermis) with mild acantholysis and neutrophilic deposition DIF – fishnet pattern with IgA deposition at intercellular region(SCPD Type – upper epidermis and IEN type – lower or entire epidermis)
AGEP ²²	<ul style="list-style-type: none"> Mainly preceded drug intake(90%) or viral infection Tiny non-follicular, sterile sheets of pustules on an erythematous base usually associated with fever , leukocytosis or eosinophilia Common sites - flexures. Spontaneous resolution on withdrawal of etiological agent Histopathology- shows the presence of the intracorneal, subcorneal, or intraepidermal pustules with spongiosis and perivascular infiltrates containing neutrophils and eosinophils, edema of papillary dermis. In some cases, necrotic keratinocytes and leukocytoclastic vasculitis may also be found. Immunoflorescence is negative ,absence of tortuous dilated vessels
PUSTULAR PSORIASIS ²³	<ul style="list-style-type: none"> Tiny sterile pustules on an erythematous base either arising de novo or over psoriatic lesions.Pustules coalesce to form lakes of pus. Systemic symptoms include fever, chills, malaise, anorexia, nausea, and severe pain. Other findings include subungual pustules and geographic tongue. Triggers include – stress ,drugs like NSAIDs ,corticosteroids, etc and pregnancy , infections ,. Laboratory abnormalities like – leukocytosis , elevated ESR , hypocalcemia Histopathology: parakeratosis , hypogranulosis , irregular acanthosis with suprapapillary thinning , elongation of rete ridges , Munro’s microabscess ,large subcorneal multilocular spongiform pustules of kogoj(large when compared to plaque psoriasis) , dilated tortuous blood vessels in dermal papillae and perivascular lymphocytic infiltrate in upper dermis. Not all typical features of psoriasis may be present in pustular psoriasis as the migration of polymorphs is too rapid for the features to develop. Immunofluorescence – negative

IMPETIGO ²⁴	<ul style="list-style-type: none"> Caused by Staphylococcus aureus and streptococci Common in school children Common over perinasal region and legs Honey coloured crusting Excellent response to antibiotics Gram stain or culture – to demonstrate the organism
BULLOUS DERMATOPHYTOSIS ²⁵	<ul style="list-style-type: none"> Usually following topical steroid use for long duration KOH or culture – to demonstrate organism HPE- PAS/GMS stain Immunofluorescence –negative
CANDIDIASIS ²⁶	<ul style="list-style-type: none"> Common in immunocompromised patients Occlusion and sweat favour its growth(common in flexures) KOH mount –pseudohyphae , hyphae and budding yeast cells HPE-GMS/PAS stain shows fungal elements Immunofluorescence - negative
SWEET'S SYNDROME ²⁷	<ul style="list-style-type: none"> Classical sweet's syndrome is characterized by fever, neutrophilia,tender erythematous skin lesions(papules, nodules and plaques) and a diffuse infiltrate consisting predominantly of mature neutrophils that are typically located in the upper dermis(can be confirmed with criteria for diagnosis) Pustular variant appears on an erythematous base studded with pustules Pathergy test may be positive

Table 1: Differential diagnosis of SCPD

Drug of choice is Dapsone usually 100mg/day. But the use of dapsone is limited in many cases by dapsone hypersensitivity syndrome , anemia and methemoglobinemia. The other drugs which can be used include colchicines,²⁸ acitretin,²⁹ Phototherapy, corticosteroids ,infliximab, and adalimumab, etanercept³⁰ steroids, pentoxifylline,³¹ maxacalcitol³²

AUTHORS	YEAR	AGE	SEX	CASE DESCRIPTION	ASSOCIATIONS	TREATMENT
Ferrillo M, Villani A, Fabbrocini G, Mascolo M, Megna M, Costa C, Napolitano M ³³	2018	34 years	Female	Pustules over the abdomen , gluteal region ,elbows and extremities for past 2 years	Pyoderma gangrenosum	Dapsone 100mg/day for 20 months
Márcio Martins Lobo Jardim, Ticiano Andrade Castelo Branco Diniz ,Thaís Amaral Carneiro Cunha ,Neusa Yurico Sakai Valente ³⁴	2018	15 years	Female	Pustular lesions over trunk , upper and lower limb with temporary remissions with hyperpigmentation was seen for past 4 years	-	Dapsone 100mg/day that was tapered to 50mg/day for 3 months
Fatemeh Mokhtari , Nazila Poostiyan ³⁵	2018	37 years	Female	Recurrent pustules over trunk and extremities for 2 weeks	Scleroderma	Topical steroids , burrows solution(patient refused to take oral dapsone)
Kundak S, Bağ Ö, Gülez N, Ergin M ³⁶	2017	5 years	Female	Recurrent pustules over axillae, inguinal folds, upper and lower limbs, and pubis, and neck, upper back for past 7 months	Elevated IgA without gammopathy CD19+ B cell deficiency	IVIg and dapsone 1mg/kg
Wargo JJ, Adams M, Trevino J ³⁷	2017	56 years	Female	Patient developed vesicles and vesiculopustules over the body for a duration of 1 week .similar episodes were seen 2 months back	Ulcerative colitis , episcleritis	Dapsone

Kretschmer L, Maul J, -T, Hofer T, Navarini A 38	2017	29 years	Female	pustules over trunk , flexures and face for 3 weeks	-	Patient was treated with single dose of 350 mg of infliximab which was shifted to a maintenance therapy of dapsone which lead to drop in hemoglobin and was again started on infliximab maintenance.
Bohelay, G. , Duong, T. , Ortonne, N. , Chosidow, O. and Valeyrie- Allanore, L. ³⁹	2015	Early 20's	Male	Macular erythema followed by non follicular pustules	Mycoplasma pneumonia	Topical steroids
Sanjana Iyengar BA, Cindy J Chambers MPH, Shurong Chang, Maxwell A Fung , Victoria R Sharon. ⁴⁰	2015	17 years	Male	Pruritic bright erythematous patches with few pustules seen over flexural areas of the upper extremities and flank and collarettes of scale on the scalp	Coccidioides immitis	managed with fluconazole for Coccidioidomycosis
Massimiliano Scalvenzi, Franco Palmisano, Maria Carmela Annunziata, Ernesto Mezza ⁴¹	2013	7 years	Male	Flaccid pustules with annular , circinate pattern seen over face trunk , extremities	Atopic dermatitis	Dapsone 1mg/kg/day for 4 weeks followed by alternate day dosing
Jayakar Thomas and K. Parimalam	2012	-	Female	Papules, pustules and scaling over the axilla. Recurrences were seen in summer for past 2 years	-	Dapsone 100mg/day
Elise I Brantley, Pranav Sheth ⁴²	2009	37 years	Female	Vesicles/pustules over the chest, back, abdomen, and thigh for one-year duration involving the abdomen, back, and thighs	Rheumatoid arthritis, scleroderma	Dapsone 50 mg a day with prednisone 2.5 mg for 2 weeks. There was a flare after 2 months that was managed with Dapsone 100 mg daily

Table 2: Interesting case reports of SCPD in the recent years.

Conclusion

Pustular disorders are one of the common skin conditions encountered in a day to day practice. It can be divided into generalized pustular eruptions and localized pustular eruptions. Not all the pustules are of infective cause. Classically SCPD presents with sterile pea sized pustules in flexures in healthy adults , hypopyon sign and histopathology of subcorneal neutrophilic pustule with recurrence and remissions. High index of suspicion is required to diagnose this rare disorder as most of the cases are being misdiagnosed and treated as pyoderma as was seen with our case (case 1).

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திருக்குறள் 948 / Thirukkural 948:



நோய்நாடி நோய்முதல் நாடி அதுதணிக்கும்
வாய்நாடி வாய்ப்பச் செயல்.

நோய் இன்னதென்று ஆராய்ந்து, நோயின் காரணம் ஆராய்ந்து, அதைத்
தணிக்கும் வழியையும் ஆராய்ந்து உடலுக்கு பொருந்தும் படியாகச்
செய்யவேண்டும்.

Physician should make proper diagnosis, investigate the etiology/cause and then proceed the appropriate treatment.