Journal of the Postgraduate Institute of Medicine 2023; 10(1): E200 1-6

http://doi.org/10.4038/jpgim.8382

Case Report

Systemic lupus erythematosus presenting as Sweet syndrome: A case report

Sulakshi Rajasuriya, M I Mujaheith

Colombo South Teaching Hospital, Sri Lanka.

Key words: **Sweet syndrome, SLE, male, diagnostic criteria**

Corresponding Author: Sulakshi Rajasuriya, E-mail:<rajasuriyasulakshi@gmail.com >https://orcid.org/0000-0002-1842-3496

Received: 23 Apr 2021, accepted revised version: 19 Oct 2022 Published: 16 Jan 2023

Competing Interests: Authors have declared that no competing interests exist

Introduction

Dr Robert Douglas Sweet described acute febrile neutrophilic dermatosis or Sweet syndrome (SS) in 1964 [1]. The aetiology of SS might be post-infectious, post- inflammatory, malignancy associated, drug induced or idiopathic [2]. A literature review reveals several cases of SS occurring in patients with already diagnosed systemic lupus erythematosus (SLE). However, SS as the first presentation of SLE is reported infrequently and even scarcer is this manifestation noted in males. We present a previously healthy 50-year-old male who was diagnosed as SS and on further evaluation found to have concomitant SLE. His cutaneous manifestations responded completely to prednisolone. However, he needed long term hydroxychloroquine for the management and prevention of further relapses of SLE.

Case Report

A 50-year-old, previously unscreened, Sri Lankan male presented with high grade, intermittent fever of 5 days duration with inflammatory type pain involving bilateral knee and ankle joints. Concomitant to the fever, he had developed a non-itchy, tender rash involving the neck, trunk and limbs accompanied by bilateral gritty red eyes and painless oral ulcers. There were no other autoimmune symptoms. He did not complain of anorexia or loss of weight, but a dry cough and sore throat was associated. Examination revealed a well-built, ill-looking man with bilateral conjunctival suffusion. He was haemodynamically stable with no pallor or icterus. Erythematous tender plaques and nodules were noted, with some targetoid lesions with pseudovesiculation and mamillated edges, involving his face, neck, trunk and upper limbs with relative sparing of the lower half of the body. There were multiple

shallow ulcers involving the palate and lips but no anogenital ulceration. Bilateral knee and ankle joints were tender but there were no effusions and the small joints were spared. Examination of the respiratory and cardiovascular systems was unremarkable with no hepato-splenomegaly or lymphadenopathy.

On investigation, his full blood count revealed a persistent leucocytosis with a neutrophil predominance above 70%. The erythrocyte sedimentation rate (ESR) was persistently above 100mm/hr and he had a high CRP. Liver function tests were deranged with AST and ALT above 5 times the upper limit of normal and an elevated gamma-GT and ALP. Total protein and albumin and globulin fractions were normal, as were the renal functions and urine analysis. Chest X-ray was normal. He had sterile blood, sputum and urine cultures and mycoplasma IgM/IgG antibodies and melioidosis antibodies were undetected. Tuberculosis screening was negative as was screening for hepatitis B, C, Epstein Barr and cytomegalovirus. VDRL was non-reactive and retroviral screening negative. The COVID rapid antigen and ~~the~~ PCR were negative. The MAT for antibodies to Leptospira and PCR were negative as was antibody to scrub typhus.

The patient was started on intravenous broad-spectrum antibiotics, empirically and a skin biopsy revealed sheets of neutrophils and nuclear dust in the dermis with peri adnexal and perivascular accentuation with no fibrinoid vascular changes or thrombosis. With these findings our patient fulfilled the 2 major criteria for the diagnosis of SS and fulfilled the minor criteria with fever, high ESR and neutrophilia. The patient was started on oral prednisolone 1mg/kg/day and exhibited a dramatic clinical improvement, but his ESR remained persistently elevated although the CRP gradually dropped.

The other investigations were directed towards finding the cause for the SS. Even though there was a probable viral respiratory tract infection, we were reluctant to attribute SS purely to it due to the persistently high ESR. The normal ultrasonography and contrast CT (chest-abdomen-pelvis) ruled out occult malignancies and the blood picture showed no evidence of haematological malignancies with a negative myeloma screen. Colonoscopy failed to reveal any evidence of inflammatory bowel disease and 2D ECHO was normal. In the presence of a persistently elevated ESR, oral ulcers and joint symptoms, ANA was done which was positive with a titre of 1/2560 with low C3 and C4 levels. However rheumatoid factor, ds-DNA and anti-sm antibodies were negative as well as the extended nuclear antigen panel. On evaluation of his abnormal liver functions, we were confounded by the abnormalities induced by SS itself. Therefore, an ultrasound guided liver biopsy was done to exclude any underlying pathology and it revealed acute on chronic hepatitis with mild interface hepatitis involving neutrophils, lymphocytes and plasma cells. There was no bile duct injury with florid duct lesions nor periportal sclerosing lesions. With these findings the criteria for autoimmune hepatitis was not met.

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Entry criteria for SLE diagnosis was fulfilled with the positive ANA and combined with fever, oral ulcers, joint involvement and hypocomplimentaemia, a diagnosis of SLE presenting as Sweet Syndrome was made probably precipitated by a viral respiratory tract infection. The patient was started on high dose oral prednisolone for induction of remission and the skin rash as well as the haematological and liver enzyme elevation gradually improved. Hydroxychloroquine was started and he was discharged with a tapering off regime of prednisolone. He presented after several months with recurrence of oral ulcers and joint symptoms and an ESR above 100 with no evidence of any other organ involvement and was managed with a course of oral steroids. Currently he remains well on HCQ with no further episodes of flares for the last 1 year.

Discussion

Acute febrile neutrophilic dermatosis was described by Dr. Robert Douglas Sweet in a disease defining article published in the British Journal of Dermatology [1]. The initial diagnostic criteria were proposed by Su and Liu in 1986 and were later modified by von den Driesch in 1994 [3,4]. Currently, SS is classified under neutrophilic dermatoses which are a spectrum of diseases including pyoderma gangrenosum and subcorneal pustular dermatosis [5,6]. The diagnostic criteria include two major and four minor criteria and both major and two of the four minor criteria have to be present to diagnose the disease.

The major criteria are:

1. Abrupt onset of painful erythematous plaques or nodules
2. Histopathological evidence of dense neutrophilic infiltrate.

The minor criteria are:

1. Pyrexia>38^0 C
2. Association with underlying infection, autoimmune disease, malignancy or vaccination
3. Excellent response to treatment with systemic corticosteroids or potassium Iodide
4. Elevated inflammatory markers or leukocytosis of >8000/cmm with more than 70% neutrophils.

SS has been described in several clinical settings, the classical or idiopathic form, the malignancy associated form and the drug induced form [2]. Classical SS is commonly described in women and may occur secondary to infection, inflammatory bowel disorders, vaccines or pregnancy [7,8]. It has been commonly reported secondary to upper respiratory tract infections and gastroenteritis [2].

Malignancy associated SS most commonly occurs secondary to haematological malignancies, particularly acute myeloid leukaemia [2]. Among the solid tumours, breast cancers and tumours of the genitourinary and gastrointestinal tract are most common, with adenocarcinomas being more frequently associated [9,10]. SS has been reported with

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autoimmune disorders such as rheumatoid arthritis [11] and autoimmune hepatitis [12,13]. Reported cases of SS as the initial manifestation of SLE are exceedingly rare. To our knowledge, this is the first case of SLE presenting as SS reported in Sri Lanka.

Our patient fulfilled the criteria for SS and the challenge was to identify the underlying cause. ANA positivity and hypocomplimentaemia along with his clinical symptoms confirmed the diagnosis of SLE. Evaluation for autoimmune hepatitis was done but the liver biopsy was not suggestive with a negative serology. The interpretation was difficult as the extra-cutaneous manifestations of SS confused the clinical picture.

The pathogenesis of SS is thought to be multifactorial. The exact mechanism is unknown but it is postulated to be due to a hypersensitivity reaction in response to an exogenous or endogenous allergen which activates a cascade of cytokines leading to neutrophil activation and infiltration and a T cell mediated response [14,15]. Granulocyte colony stimulating factor, granulocyte macrophage colony stimulating factor, interferon gamma and interleukin 1, 3, 6 and 8 are thought to be the potential mediators of the syndrome [14,16]. This would explain why GCSF is the most common drug associated with drug induced SS [7,8]. Even in malignancy associated SS, elevated levels of GCSF with these interleukins have been demonstrated [14].

Extra-cutaneous manifestations of SS have been described involving almost all the organs of the body. With relevance to our case, hepatic involvement is reported to manifest as a non-specific elevation of liver enzymes with GGT being more affected [17]. Our patient revealed a similar pattern of liver function abnormalities. The tender, erythematous skin lesions are the sine qua non for diagnosing SS. They are usually asymmetrically distributed with the face and proximal limbs being more affected [4,6]. The skin lesions of SS are also known to show pathergy and on resolution, heal without scarring [18]. Histopathologically, they will reveal a dense band like neutrophilic infiltrate in the papillary dermis without any leukocytoclastic vasculitis [19] which is what was demonstrated in our patient. Comparatively, acute cutaneous lupus will show predominantly a scattered perivascular, periadnexal and interface lymphocytic infiltration with immunofluorescence revealing granular deposits of IgM [20].

The gold standard for the treatment of SS is steroids, either systemic or, in the case of few localized lesions, intra-lesional or topical. Other first line treatments to be considered are potassium iodide and colchicine [17]. SLE with SS as the presenting feature is a rare occurrence with the first case being reported by Hou et al in 2005 [21] and the first paediatric case being reported by Burnham et al soon after [22]. Since then, several cases of SLE with SS have been reported, of which some were drug induced [23]. To our knowledge, there have been only two cases of SS as the initial presentation of SLE reported in male patients in the literature [24,25]. Though both SLE and classical SS manifest predominantly in females, this is the third such case to be reported in a male.

Conclusion

It is important to consider Sweet Syndrome in the differential diagnosis of a patient presenting with fever and rash with a predominant neutrophilia. Confirmation of the diagnosis would require a skin biopsy. If the diagnosis is confirmed, patients should always be screened for underlying malignancies and autoimmune diseases since it will markedly alter the course of treatment for the patient as well as the prognosis.

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