Panuveitis in Sweet syndrome

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Ocular manifestations of Sweet syndrome, or acute febrile neutrophilic dermatosis, are usually limited to the anterior segment. We report the case of a patient with bilateral panuveitis and retinal vasculitis associated with Sweet syndrome. A 45-year-old Asian female with an undiagnosed febrile illness with rash presented with bilateral panuveitis with haemorrhagic occlusive retinal vasculitis. Skin biopsy confirmed Sweet Syndrome. Intraocular inflammation resolved with a combination of topical and systemic corticosteroids as well as intravenous cyclophosphamide, with resulting permanent severe right visual impairment. Although an uncommon condition, Sweet syndrome should be considered in any febrile patient with skin lesions and uveitis.

Key words: Acute febrile neutrophilic dermatosis, panuveitis, retinal vasculitis, sweet syndrome, uveitis

Sweet syndrome (SS), or acute febrile neutrophilic dermatosis, is an uncommon dermatologic disorder associated with fever, neutrophilia, and painful erythematous skin papules and nodules.[1,2] We present a case of bilateral panuveitis and retinal vasculitis, which, to our knowledge, is the first reported case associated with SS in New Zealand.

SS subtypes include classical (idiopathic), malignancy-associated and drug-induced.[1,2] The incidence of ocular involvement in SS is estimated at one-third of cases, mostly anterior segment involving.[1] Posterior involvement is rare and there are only 7 such case reports in SS to date, with only three cases being panuveitis (all bilateral).[3-7] Our case was slightly unique such that there was severe inflammation in both anterior and posterior segments bilaterally.

Case Report

A 45-year-old apparently healthy Asian female presented to Ophthalmology with bilateral visual loss for a week. A week prior, she was discharged from General Medicine with an undiagnosed febrile illness with rash and temperatures above 38°C. This erythematous, tender and painful rash made of small papules, pustules and nodules joined by larger areas of swollen plaques started abruptly in her lower limbs then upper limbs, with minimal torso involvement and no oral or genital ulceration [Fig. 1a]. She had no joint pain. A skin biopsy was still pending. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were significantly elevated, with leukocytosis and neutrophils exceeding 70%. Negative tests included blood, urine, fecal and throat cultures; Hepatitis B and C, HIV, syphilis serology, HSV and VZV PCR skin swabs. Chest X-ray was normal. She received empirical IV cefuroxime and oral aciclovir.

On examination, her rash seemed to be resolving. Best corrected visual acuity (BCVA) was hand movements in the right and 20/120 in the left, while intraocular pressure was 13 mmHg in the right and 12 mmHg in the left. Conjunctival injection without lesions was noted. There was severe non-granulomatous bilateral panuveitis (3 + anterior chamber cells and flare bilaterally, bilateral posterior synechiae with diminished pupillary light reaction and impeded afferent pupillary defect assessment, no iris nodules, 3-4 + vitreous flare bilaterally) with bilateral hemorrhagic occlusive retinal vasculitis, retinitis, macular edema, without optic disc involvement [Fig. 2a and b].

A right vitreous tap was performed. She received bilateral empirical intravitreal ganciclovir 4 mg injections, intravenous aciclovir and prednisolone 1% drops. Vitreous aspirate was negative for CMV, HSV, VZV and toxoplasma. However, the sample was insufficient for microscopy and culture. 2 days later, the skin biopsy reported showing neutrophilic dermatosis without vasculitis, cementing the diagnosis of Sweet syndrome [Fig. 1b]. Other negative tests were serum CMV serology, Quantiferon TB Gold, anti-neutrophil cytoplasmic antibody, anti-nuclear antibody, angiotensin-converting enzyme, and serum hCG. Protein electrophoresis pattern and CT chest, abdomen and pelvis were normal.

The patient received three doses of 1 g intravenous methylprednisolone daily followed by oral prednisone 60 mg daily, tapered over 10 months. Under Rheumatology, she received 6 cyclophosphamide 15 mg/kg infusions spaced two weeks apart. Serial examinations and fluorescein angiograms over one year showed resolution of bilateral ocular inflammation, macular edema and perivascular leakage [Fig. 2c and d]. However right macular atrophy and neovascularization in the left superior retina [Fig. 2d] were noted, the latter currently observed. BCVA stabilized at 20/200 in the right and 20/35 in the left.

Discussion

The pathogenesis of SS remains unclear but considered to be multifactorial, and may be contributed by sepsis,

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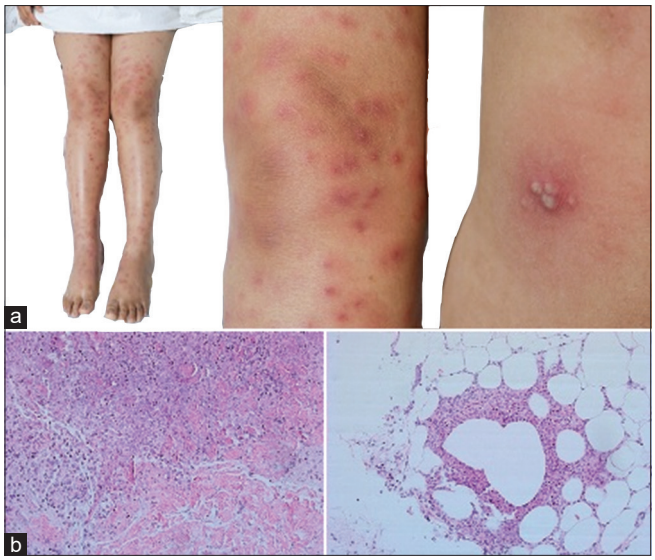

Figure 1: (a) Erythematous maculopapulopustular rash on the upper and lower limbs of our patient. (b) Photomicrograph of skin biopsy specimen showing dense dermal neutrophilic infiltration and lobular panniculitis, without vasculitis (haematoxylin-eosin, original magnification x250 and x100 respectively)

Major criteria
Abrupt onset of painful erythematous plaques or nodules, occasionally with vesicles, pustules, or blisters
Predominantly neutrophilic dermal infiltrate without leukocytoclastic vasculitis
Minor criteria
Fever >38°C
Preceded by a
Nonspecific respiratory infection
Gastrointestinal infection
Vaccination
OR associated with:
Inflammatory disease
Hemoproliferative disorder or visceral malignancy
Pregnancy
Abnormal laboratory values at presentation (three of four):
ESR >20 mm/h
Elevated CRP
Leucocytes >8,000
Neutrophils >70%
Excellent response to treatment with systemic corticosteroids or potassium iodide

Figure 3: Diagnostic criteria for classical SS as modified by von den Driesch in 1994. Both major criteria and two minor criteria are required to establish the diagnosis.[2]

hypersensitivity reaction, autoimmune process, and/or granulocyte-colony stimulating factor (G-CSF) production by cancer cells.[1]

Our case was of the classical subtype of SS, predominantly affecting women aged between 30 to 60 years, and which may be associated with an upper respiratory or gastrointestinal infection, inflammatory bowel disease or pregnancy.[1,2] The

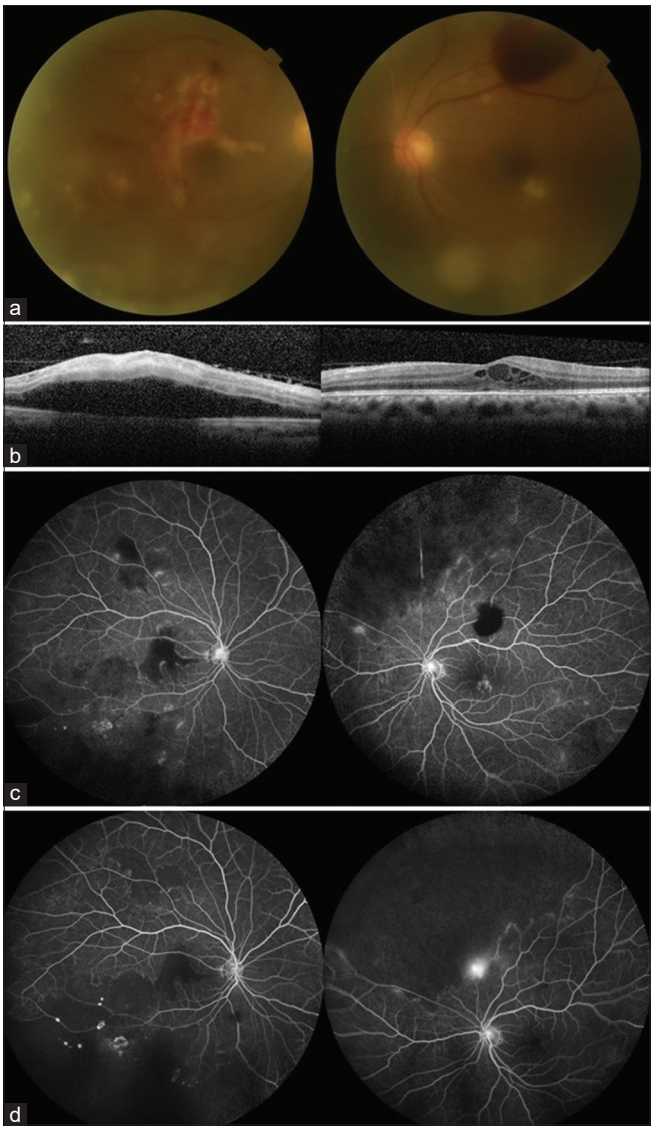

Figure 2: (a) Right and left fundus photographs showing vitritis with haemorrhagic occlusive vasculitis. (b) Right and left OCT macula showing inner retinal thickening. (c) Right and left recirculation phase angiograms one month after presentation, showing multiple areas of perivascular leakage and filling defects. (d) Right and left recirculation phase angiograms eight months after presentation, showing perivascular leakage resolution with neovascularisation at the left superior retina

onset of the malignancy-associated subtype of SS may precede or proceed the diagnosis of cancer, with some authors considering it as a manifestation of undiagnosed cancer, or a recurrence in a previously cancer-diagnosed patient. The most common associated malignancy with SS is acute myeloid leukemia, although other hematological disorders and solid tumors are also implicated.[1,2] The drug-induced subtype of SS is most commonly associated with G-CSF, although multiple other medications have also been associated with this. The simple withdrawal of the offending agent frequently improves the dermatosis.[1]

Our patient fulfilled at least 2 major and 2 minor diagnostic criteria for SS diagnosis [Fig. 3], presenting with an abrupt painful rash, skin biopsy showing dense

neutrophilic infiltration without vasculitis, pyrexia above 38°C, elevated ESR and CRP, and leukocytosis with more than 70% neutrophils.[1,2]

SS and Behcet disease can clinically overlap[4,8] and there have even been reported cases of concurrent SS and Behcet disease.[1] Behcet disease, in contrast to SS, is not usually associated with malignancy or medications, and has higher association with panuveitis.[4] Both may express human leucocyte antigen (HLA) types B51 and B54 (although the earlier is predominant in Behcet disease and the latter in SS).[3,4,8,9] Thus, diagnosis should rely on examination and biopsy of skin lesions, routine HLA-typing is not recommended. Further, our patient displayed a lack of oral and genital aphthae, negating a diagnosis of Behcet disease.[8]

Systemic corticosteroids are the therapeutic gold standard for SS,[1,2] our patient responded rapidly to this. Infective causes of ocular inflammation need to be ruled out before treatment. Steroid-sparing agents are important for frequent recurrences of inflammation and to minimise corticosteroid side effects.[1,3] The decision to use cyclophosphamide over other steroid-sparing agents was made by the rheumatologists.

Conclusion

All SS cases should be screened for malignancy, offending drugs and pregnancy in women of child-bearing age.[1-3] SS should be considered in the differential diagnosis of any febrile patient with skin lesions and uveitis.

Research Ethics

The patient gave her informed consent prior to her inclusion in the case report.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

References

1. Cohen PR. Sweet's syndrome--A comprehensive review of an acute febrile neutrophilic dermatosis. Orphanet J Rare Dis 2007;2:34.
2. von den Driesch P. Sweet's syndrome (acute febrile neutrophilic dermatosis). J Am Acad Dermatol 1994;31:535-56.
3. Lobo AM, Stacy R, Cestari D, Stone JH, Jakobiec FA, Sobrin L. Optic nerve involvement with panuveitis in Sweet syndrome. Ocul Immunol Inflamm 2011;19:167-70.
4. Matsumiya W, Kusuhara S, Yamada Y, Azumi A, Negi A. Sweet's syndrome with panuveitis resembling Behcet's disease. Jpn J Ophthalmol 2012;56:268-72.
5. Song WK, Bang D, Choi YJ, Lee SC, Oh SH. Sudden visual loss due to occlusive venous vasculitis associated with Sweet syndrome. Arch Dermatol 2009;145:216-8.
6. Sato M, Kawamura T, Hase S, Katsumata S, Oshika T. A case of bilateral retinal vasculitis associated with Sweet syndrome. Retina 2005;25:800-2.
7. Baartman B, Kosari P, Warren CC, Ali S, Jorizzo JL, Sato M, *et al.* Sight-threatening ocular manifestations of acute febrile neutrophilic dermatosis (Sweet's syndrome). Dermatology (Basel, Switzerland) 2014;228:193-7.
8. Criteria for diagnosis of Behcet's disease. International Study Group for Behcet's Disease. Lancet 1990;335:1078-80.
9. Lee MS, Barnetson RS. Sweet's syndrome associated with Behcet's disease. Australas J Dermatol 1996;37:99-101.