Malaysian Journal of Ophthalmology

© Malaysian Journal of Ophthalmology 2025; 7:1-8
Case report
https://doi.org/10.35119/myjo.v7i1.324

Is this too sweet? Orbital infiltration as the only sign of Sweet syndrome relapse

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Abstract

Background: Sweet syndrome (acute febrile neutrophilic dermatosis) is a rare dermatologic disorder with accompanying features of systemic inflammation. Ocular presentations of Sweet syndrome vary, including periorbital/orbital inflammation, dacryoadenitis, conjunctivitis, episcleritis, limbal nodules, iritis, peripheral ulcerative keratitis, and choroiditis.
Case presentation: We present a case of a relapsed Sweet syndrome manifesting only with ocular features of extraocular muscle infiltration. The patient presented only with limited extraocular movement, resulting in diplopia. He responded well to oral steroids and fully recovered after 3 months.
Conclusion: Ocular manifestation could be the only presenting sign of Sweet syndrome relapse even in the absence of other systemic manifestations and negative laboratory investigations. Therefore, a high index of clinical suspicion is necessary in order to initiate early and appropriate treatment.

Keywords: acute febrile neutrophilic dermatosis, extraocular muscles, ocular involvement,Sweet syndrome, systemic inflammation

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Infiltrasi orbit sebagai satu-satunya petunjuk kemunculan semula sindrom Sweet

Abstrak

Latar belakang: Sindrom Sweet (atau acute febrile neutrophilic dermatosis) adalah satu penyakit dermatologi yang unik dan mempunyai ciri-ciri radang di seluruh badan. Penglibatan mata dalam sindrom Sweet ini termasuklah radang di mata atau di keliling mata, dakrioadenitis, konjunktivitis, episkleritis, nodul limbus, iritis, peripheral ulcerative keratitis dan choroidits.
Pembentangan kes: Kami membentangkan satu kes sindrom Sweet yang hanya melibatkan infiltrasi otot mata sahaja. Pesakit mengalami masalah menggerakkan bola mata yang menimbulkan gejala penglihatan berganda (double vision). Dia memberi respon yang baik terhadap ubat steroid dan pulih sepenuhnya selepas tiga bulan.
Kesimpulan: Masalah melibatkan mata boleh menjadi satu-satunya tanda sindrom Sweet, tanpa manifestasi sistemik yang lain, dan dengan penyiasatan makmal yang negatif. Indeks kecurigaan klinikal yang tinggi adalah perlu untuk mengenalpasti sindrom ini dan memulakan rawatan awal yang sesuai.

Kata kunci: demam neutrofilik dermatosis akut, infiltrasi seluruh badan,otot mata, penglibatan mata, Sindrom Sweet

Introduction

Sweet syndrome is a multisystem syndrome consisting of dermatologic lesions with potential involvement of almost all the other organ systems.[2] It is a rare disorder characterized by fever and the acute onset of skin rashes, normally consisting of multiple tender plaques or nodules involving the arms, legs, trunk, face or neck.[3] It is idiopathic in the majority of affected individuals (classic Sweet syndrome). Less often, the disorder can be drug-induced or associated with an underlying malignancy.[3]

Case presentation

A 43-year-old Chinese man with underlying classic Sweet syndrome was referred by the rheumatology team for sudden onset of restriction extraocular movement in the left eye. He complained of diplopia at the extreme lateral, up, and down gazes. He denied any blurring of vision and there was no eye redness. He reported a history of fever 1 week prior to presentation. There were no other systemic manifestations such as skin rashes and joint pain.

He had been diagnosed with Sweet syndrome in 2004 after presenting with prolonged fever and migrating joint pain. He had episodic pyrexia for a month with concurrent skin rashes affecting his arms and trunk. Subsequently, he developed joint pains with no specific distribution suggestive of any form of autoimmune disease. Laboratory tests revealed high white cell count with neutrophilia (neutrophil count of 82%), raised C-reactive protein (CRP) of 35.8 mg/dL, and erythrocyte sedimentation rate (ESR) greater than 150 mm/hr. Skin biopsy was consistent with the diagnosis of Sweet syndrome. Even though he was started on oral corticosteroids, dapsone and colchicine, and followed by the second-line immunosuppressant methotrexate, he had frequent disease relapses due to non-compliance to treatment. He developed temporal lobe cerebritis and left mastoiditis in 2008 and 2010, respectively. He was diagnosed with optic neuritis diagnosed in the left eye in 2014, with full vision recovery with intravenous methylprednisolone.

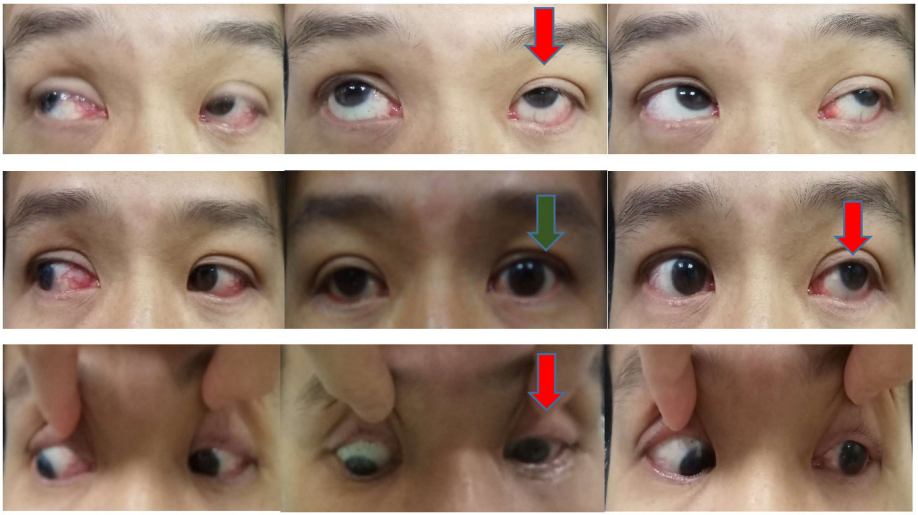

Fig. 1. Nine-gaze picture showing left hypertropia (green arrow) with limitation seen at elevation, abduction, and depression (red arrows).

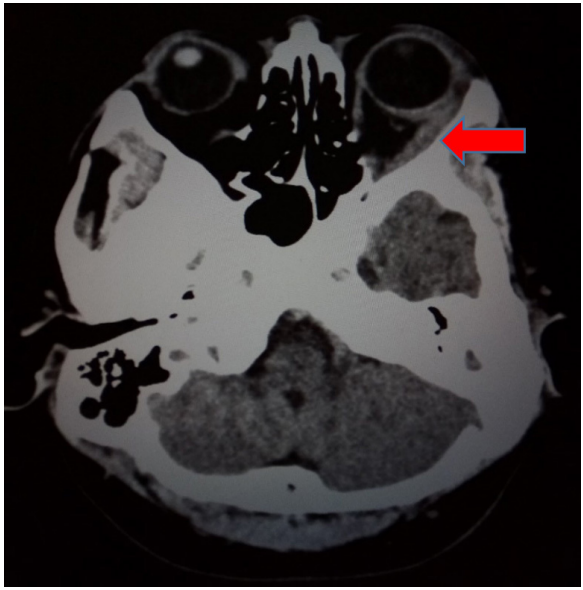

Fig. 2. Contrasted computerised tomography scan of the brain and orbit, revealing enhancing soft tissue mass in the lateral extraconal space of the left orbit with bulky left inferior and lateral recti (red arrow).

Eye examination during this presentation revealed vision of 6/6 in both eyes. The left eye showed afferent pupillary defect, abnormal colour vision, and reduced light sensitivity, all of which were similar to the episode of optic neuritis he had experienced before. The left eye was hypertropic and the movement was restricted on the lateral, up, and down gazes (Fig. 1). He reported diplopia at extreme gazes. The conjunctivas were mildly injected with otherwise normal fundus examination.

A contrasted computerised tomography scan of the brain and orbit revealed an enhancing soft tissue mass in the lateral extraconal space of the left orbit involving the lateral and inferior rectus muscles extending to the orbital apex. Both extraocular muscles were found to be bulky (Fig. 2). Laboratory investigation showed raised CRP at 1.1 mg/dL, but white cell count was normal. Other inflammatory or infectious aetiologies were ruled out through a thorough systemic review, leading to a likely diagnosis of relapsed Sweet syndrome.

A diagnosis of extraocular muscle infiltration secondary to relapsed Sweet syndrome was made and he was started on oral prednisolone 1 mg/kg/day. Oral methotrexate 7.5 mg weekly and oral folic acid 5 mg daily were commenced, and oral prednisolone dose was tapered. He fully recovered after 4 months, with no residual diplopia or extraocular movement limitation.

Discussion

Sweet syndrome was first described by Dr. Robert Douglas Sweet in 1964.[4] It is classified as a neutrophilic dermatosis, a skin disorder characterized by the accumulation of neutrophils in the dermis layer.[1] Sterile neutrophilic infiltrates may also be found in the other organs, such as lung, bone, liver, spleen, brain, and eye.[1] Infiltration of other organs can occur prior to, or after the appearance of skin lesions.[1]

There are 3 clinical types of Sweet syndrome as described by Cohen and Kurzrock: classic/idiopathic type (38–53%), malignancy-associated (25–44%), and drug-induced (4–24%).[5,6] The idiopathic type may be seen in association with infection, several inflammatory or autoimmune diseases, or even pregnancy.[5,7,8] Several malignancies have reported correlations with Sweet syndrome, including myeloproliferative disorders.[5,7,8] Drug-induced Sweet syndrome has been a well-known entity which occurs most frequently in patients receiving granulocyte colony stimulating factor, although many case reports in the literature describe occurrences with antibiotics (minocycline, ofloxacin, trimethoprim-sulfamethoxazole), as well as antiepileptics (diazepam), antihypertensives (frusemide), oral contraceptives, antipsychotics (clozapine), and retinoids.[5,7]

Sweet syndrome has a female predilection, with ages ranging from 30 to 50 years.[3] There is however no gender predominance seen in children.[3] Its pathogenesis is unknown, although Gassuddin *et al.* proposed an immunologic mechanism in which there is an imbalance between T helper cell types and cytokine secretion.[9] Hypersensitivity to eliciting bacteria, viral, or tumour antigen is another suggested theory, as it may trigger neutrophil activation and infiltration leading to Sweet syndrome.[5]

The diagnosis of Sweet syndrome is made based on a detailed history, clinical evaluation with identification of classic signs, and a variety of specialized tests.[3] The clinical and pathological diagnostic criteria have been categorized as major and minor (Table 1) and the presence of 2 major and 2 minor findings has been proposed as necessary for diagnosis.[10]

In this case, the patient had prolonged fever, skin rashes, and pain in multiple joints in his first presentation. Laboratory workout had shown raised white cell count with neutrophil predominance, raised CRP, and raised ESR. The diagnosis of Sweet syndrome was confirmed histopathologically through skin biopsy done in 2004. For this presentation, other than restricted ocular movement with preceding fever, the patient did not have any skin rash and CRP was the only raised inflammatory marker. A diagnosis of presumed relapse of Sweet syndrome was made. Infiltration of the left inferior and lateral rectus muscles on a contrasted CT scan further supported the diagnosis.

Table 1. Clinical and pathological criteria for the diagnosis of sweet syndrome

Type of criteria	Criteria
Major	Abrupt onset of tender plaques (occasionally pustules or vesicles)
	Neutrophilic infiltration of the dermis (no evidence of vasculitis)
Minor	Underlying systemic conditions: respiratory or gastrointestinal infections, vaccination, inflammatory disorders (ulcerative colitis, Crohn's disease), malignant tumours, pregnancy
	Malaise, fever
	Laboratory test results during onset (3 of the following required) • ESR > 20 mm • elevated CRP • leukocyte count > 8.0 x $l0^9$/l • differential neutrophil count > 70%
	Response to treatment with systemic corticosteroids

Modified from von den Driesch.[10] Both major and 2 minor criteria necessary for diagnosis.
CRP: C-reactive protein; ESR: erythrocyte sedimentation rate

Ocular involvement is not uncommon and has been reported in 4–72% of patients.[2,11] The most common ocular manifestations include conjunctivitis, episcleritis, keratitis, and iritis.[2,11] Recent case reports published on the subject, however, have brought about evidence of newly recognized, posterior ocular involvement presenting as vitritis and retinal vasculitis.[2]

If left untreated, Sweet syndrome lesions can remain for weeks to months. However, without any therapeutic intervention, the dermatosis-related symptoms and cutaneous lesions are usually self-limiting in the classical type.[12] Sweet syndrome is usually highly steroid-responsive in the absence of associated malignancy; therefore, systemic corticosteroids are the mainstay of therapy.[12] Our patient was started on oral prednisolone 1 mg/kg/day. In most cases, treatment with a low dose of corticosteroids is proven effective in eliminating symptoms.[3] Although corticosteroids are the mainstay of treatment, there are no standardized treatment protocols for affected individuals due to its rarity. Other first-line systemic treatments are potassium iodide and colchicine.[3,12]

Second-line agents including indomethacin, clofazimine, cyclosporin, and dapsone have been used as monotherapy in cases of recurrence after corticosteroid tapering.[12] In addition, cyclosporine and dapsone have also been used in combination with other drugs or as corticosteroid-sparing agents.[12] Our patient was started on oral methotrexate 7.5 mg once a week when oral prednisolone was tapered due to the frequent relapses. He responded well to treatment and has remained disease-free to date.

Conclusion

Ocular manifestation could be the only presenting sign of Sweet syndrome relapse in the absence of other systemic manifestations and negative laboratory tests. Therefore, a high index of clinical suspicion is necessary in order to initiate an early and appropriate treatment.

Declarations

Informed consent for publication
The patient has provided informed consent for the publication of the clinical data and images contained in this case report.

Competing interests
None to declare.

Funding
None to declare.

Acknowledgements
None to declare

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