ACITRETIN-INDUCED NECROTIZING SWEET'S SYNDROME IN A PATIENT HAVING PSORIASIS

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ABSTRACT

A 52-year-old male presented with multiple tender, plum-coloured facial plaques following the treatment with acitretin 50 mg/day for his psoriasis. The lesions subsided over 3 months. Acitretin was restarted at 20 mg/day as psoriasis flared. A week later, the patient presented with fever and a symmetrically distributed, tender, livid, hemorrhagic papulopustular eruption and large violaceous ulcerated plaques on both soles. Within a week, the patient developed abdominal pain and distension. CT scans of the abdomen showed segments of small bowel wall thickening. Chest X-ray showed consolidation and nodularity of the lung bases. Histopathology demonstrated findings consistent with a diagnosis of Sweet's syndrome. The diagnosis of drug-induced Sweet's Syndrome was established. The patient was treated with a combination of intravenous methylprednisolone and cyclophosphamide. Drug-induced SS has been reported to be associated with many drugs, especially granulocyte-monocyte-colony-stimulating-factor and all-trans-retinoic acid. Although very rare, acitretin-induced SS should be considered in a patient who develops pustulonecrotic skin lesions and systemic upset after intake of acitretin.

KEYWORDS: *Sweet's Syndrome, Psoriasis, Acitretin*

INTRODUCTION

Sweet's syndrome, also known as acute febrile neutrophilic dermatosis, is a rare inflammatory skin disorder characterized by tender, swollen, and blister-like skin plaques or nodules. Systemic symptoms, including fever and a general feeling of illness, typically accompany this condition. Notably, individuals with Sweet's syndrome often exhibit an elevated count of neutrophils, a diagnostic indicator.[1] Sweet's syndrome can be associated with various underlying conditions, including infectious agents, upper respiratory tract infections, hematological malignancies (blood-related cancers), leukaemia, and inflammatory bowel diseases like Crohn's disease or ulcerative colitis. In more severe cases, Sweet's syndrome can lead to sterile neutrophilic infiltration, which means an accumulation of neutrophils in various organs and tissues throughout the body. These affected organs and tissues may include the bones, joints, central nervous system, eyes, gastrointestinal tract, and lungs. This widespread involvement can result in a broad spectrum of symptoms. It can be diagnostically challenging because it may mimic other infectious and inflammatory conditions, such as sepsis, pneumonitis, infective endocarditis, purpura fulminans, hemorrhagic varicella, intestinal obstruction, vasculitis (including medium vessel variants and ANCA-positive types), and pityriasis lichenoides et varioliformis acuta (a specific skin condition).[1,2,3] The treatment approach for Sweet's syndrome often involves addressing the underlying cause when identified. Additionally, corticosteroids and other immunosuppressive medications are frequently used to manage the skin and systemic symptoms associated with this condition.[4] If Sweet's syndrome is suspected or concerning symptoms are present, it is essential to seek a dermatologist's or rheumatologist's expertise for proper evaluation and management. Drug-induced Sweet's Syndrome (SS) is a recognized phenomenon that can occur due to exposure to various medications.[1,5] Among the drugs implicated in triggering SS, granulocyte-monocyte-colony-stimulating factor (GM-CSF) and all-trans-retinoic acid (ATRA) are notable examples, particularly in the context of treating acute promyelocytic leukaemia (APL). In the case of APL, treatment often involves using ATRA, a form of vitamin A and a retinoid. ATRA is employed to induce differentiation of leukaemia cells, and it can be associated with SS as a potential side effect.[5,6,7] On the other hand, Isotretinoin is a medication commonly used to treat severe acne. While it is not typically associated with SS, there have been rare reports of SS occurring after initiating isotretinoin therapy in dermatological settings.[8,9,10] It's important to note that SS induced by medications, including retinoids like ATRA and Isotretinoin, is considered a rare and unusual adverse reaction. The exact mechanisms by which these drugs may trigger SS are not fully understood, and individual patient factors may influence the occurrence of SS in response to these medications. Medical professionals should be vigilant in monitoring patients receiving these medications for

the development of SS and should consider discontinuing the drug and providing appropriate treatment if SS is suspected or confirmed. As with any medication, it's crucial for healthcare providers to weigh the potential benefits and risks when prescribing these drugs and to inform patients about potential side effects, including the rare possibility of SS.

CASE

A 52-year-old male presented with multiple tenders, plum-coloured and edematous plaques on his face (Figure 1a) after starting acitretin 50 mg/day for his psoriasis. He was systemically well. The possibility of retinoid-induced Sweet's syndrome was considered, and acitretin was stopped. The patient was denied biopsy and was reluctant to start any medication for facial lesions, which subsided in 3 months, but his psoriasis flared. He was reluctant to try phototherapy or immunosuppressives and wished to restart acitretin at 20 mg/day. After a week of restarting acitretin, he presented with fever and a symmetrically distributed, tender, livid, hemorrhagic papulopustular eruption involving the face, arms, legs and lower trunk with large violaceous ulcerated plaques on both soles (Figure 1b-f). He was admitted to the hospital and empirically started on intravenous (IV) flucloxacillin and IV acyclovir after obtaining blood cultures and lesional samples for Tzanck smear and viral PCR, which turned out to be negative. Given the clinical possibility of necrotizing neutrophilic dermatoses, 30 mg/day of prednisolone was added, and a skin biopsy was obtained.

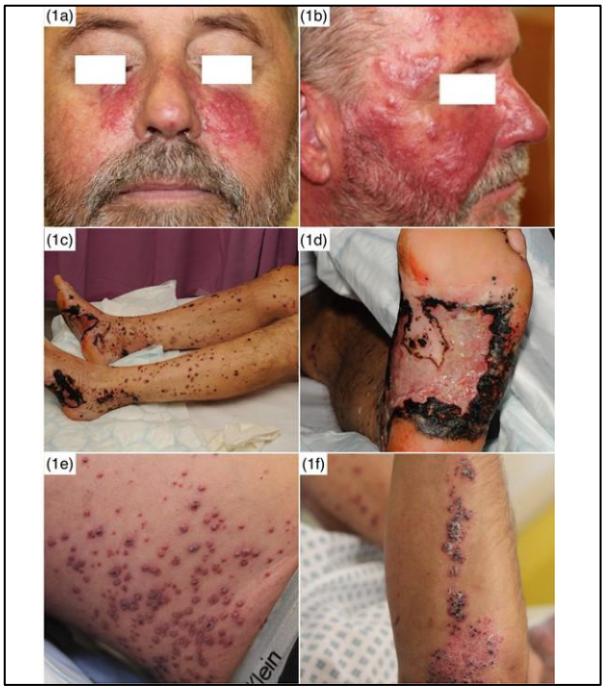

Figure 1: a) Multiple, tender, plum-coloured and edematous nodule plaques on the face after starting acitretin 50 mg/day for psoriasis. After restarting acitretin 20 mg/day, 1b) more severe eruption on face, c) tender, livid, hemorrhagic papulo-pustular eruption involving legs; d) large violaceous ulcerated plaques on sole; e) lower trunk and f) hemorrhagic lesions of Sweet's syndrome koebnerizing on psoriatic plaques on elbows.

Within a week, the patient developed abdominal pain and distension without melena or hematuria. Blood showed raised white cell count $13x10^9$/L (neutrophilia: $10.55x10^9$/L), thrombocytosis ($514x10^9$/L), high CRP 123mg/L; and normal ESR, urine sediment, stool exam and liver/ renal function tests. A full immunology screen was negative, including anti-neutrophil cytoplasmic antibodies and cryoglobulins. CT scans of the abdomen showed segments of small bowel wall thickening (Figure 2a). Chest X-ray showed consolidation and nodularity of the lung bases (Figure 2b). The patient denied further pulmonary or intestinal biopsy and angiography. Meanwhile, histopathology became available and demonstrated diffuse dermal edema and infiltration by neutrophils without evidence of fibrinoid necrosis ((Figure 2c) and negative immunofluorescence, consistent with a Sweet syndrome diagnosis. His previous facial eruption and current histopathology, systemic features, and blood investigations led to a final diagnosis of retinoid-induced necrotizing Sweet's syndrome.A combination of intravenous methylprednisolone and cyclophosphamide was started, and he experienced significant improvement in his skin lesions and pain in his abdomen within 48 hours.[7] He has switched to prednisolone 60mg daily, which was gradually tapered. He was discharged and suggested not to take acitretin or other retinoids in future for his psoriasis (Figures 2d and e). A year later, his psoriasis remains under reasonable control with methotrexate 10 mg/ week, and he has not developed any haematological malignancy or inflammatory bowel disease.

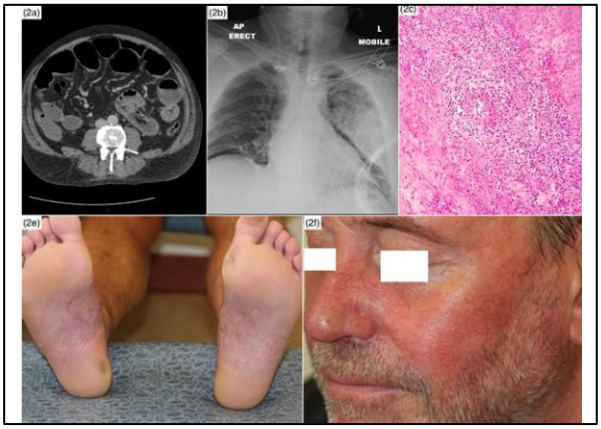

Figure 2: a) CT scans of the abdomen showing segments of small bowel wall thickening; b) Chest X-ray showing consolidation and nodularity of the lung bases; c) diffuse dermal edema and

infiltration by neutrophils without evidence of fibrinoid necrosis or vasculitis on histopathology from flank skin (H and E, 200x); d and e) resolution of lesions after withholding acitretin and initiation of methyprednisolone pulse and cyclophosphamide infusion.

DISCUSSION

Sweet's syndrome is a reactive neutrophilic dermatosis with characteristic tender edematous/ pseudovesicular cutaneous plaques in conjunction with systemic upset and blood neutrophilia in the setting of infections, haematological malignancies and inflammatory bowel disease.[8] Systemic manifestations of SS include fever and malaise; however, sterile neutrophilic infiltration of bone and joints, central nervous system, eyes, gastrointestinal tract and lungs can rarely occur, especially in necrotizing SS and in the setting of hemorrhagic and ulcerative skin lesions as seen in our patient can mimic numerous infective and inflammatory conditions including sepsis, pneumonitis, infective endocarditis, purpura fulminans, hemorrhagic varicella, intestinal obstruction, vasculitis including the medium vessel and ANCA positive variants and pityriasis lichenoid et varioliformis acute.[8-10] To our knowledge, this is the first case report of SS secondary to acitretin. Interestingly, acitretin is also the drug of choice for managing pustular psoriasis and has been reported to be effective in reactive neutrophilic dermatoses arising in people with acquired interferon-gamma deficiency. Therefore, 11 SS secondary to retinoids seems to be an idiosyncratic reaction secondary to a genetic predisposition.

CONCLUSIONS

Though very rare, retinoid-induced SS should be considered in a patient who develops pustulonecrotic skin lesions and systemic upset after intake of acitretin.

LIMITATIONS:

As in any case report, ours cannot offer causal inference nor can represent population, therefore generalization in not possible. Other limitations of this report are emphasis on the rare and selection bias.

CONFLICT OF INTEREST: None

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