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Histiocytoid Sweet Syndrome associated with anorectal lymphogranuloma venereum in a patient with HIV infection

Aws Waleed M. Al-Hayani1*, Iris Martínez Alemany1, Carlos Santonja2, Alfonso Cabello Úbeda1, Laura Prieto Pérez1, María Carmen Ceballos-Rodríguez3, Irene Carrillo Acosta1, Miguel de Górgolas Hernández-Mora1, Beatriz Álvarez1

1 Division of Infectious Diseases. Fundación Jiménez Díaz University Hospital. Universidad Autónoma de Madrid (IIS-FJD, UAM). Madrid, Spain.
2 Department of Pathology, Fundación Jiménez Díaz University Hospital. Universidad Autónoma de Madrid (IIS-FJD, UAM). Madrid, Spain.
3 Department of Dermatology, Fundación Jiménez Díaz University Hospital. Universidad Autónoma de Madrid (IIS-FJD, UAM). Madrid, Spain.

Abbreviated title: Histiocytoid Sweet Syndrome

Keywords: Sweet’s Syndrome, Histiocytoid Sweet Syndrome, Chlamydia trachomatis, lymphogranuloma venereum, HIV.

* Corresponding author:
Aws Waleed Mohammed Al-Hayani, M.D.
aws.alhayani@quironsalud.es
Division of Infectious Diseases
Fundación Jiménez Díaz, University Hospital
Avda. Reyes Católicos, 2
28040, Madrid, Spain
ABSTRACT

Sweet Syndrome (SS) belongs to a group of diseases known as neutrophilic dermatoses. An uncommon variant named Histiocytoid Sweet Syndrome (HSS) can be associated with a variety of conditions, including cancer, infections, drug toxicity and others.

Here we present an instance of HSS in an HIV-positive patient in the setting of an infectious disease.

MEDICAL IMAGERY

A 47-year-old male patient from Spain, presented with a 15-day history of painful skin lesions on the nape of his neck, forearms and hands. He also complained of rectal pain, constipation and tenesmus. He reported no fever, nausea, vomiting, abdominal pain or any other symptom. Physical examination revealed erythematous painful non-pruritic papules and plaques of 6-15mm in diameter, and some vesicle-looking lesions (Figure 1). There was no involvement of his palms, soles, or mucous membranes. The rest of the physical exam was unremarkable. He was a man who had sex with other men. His medical history was remarkable for sexually acquired stable stage-2-HIV-infection since 2009, for which he received treatment with RPV/FTC/TDF, recently switched to EVG/c/FTC/TAF due to osteopenia.

Laboratory tests revealed a normal hemogram with normal value of neutrophils and the biochemistry did not show relevant findings except for mild elevation of acute phase reactants, C-reactive protein and erythrocyte sedimentation rate. He had 468 cells/ul CD4+ T-lymphocyte count and undetectable HIV-1 RNA.
viral load (< 20 copies/mL). Under the suspicion of Sweet’s syndrome of pharmacological origin, EVG/c/FTC/TAF was discontinued and ART with RPV/FTC/TDF was then restarted. The patient also was treated with oral corticosteroids without any response. A skin biopsy was performed, and the histological study revealed interstitial dermatitis with a predominance of histiocyte-looking and occasional giant cells; many of the cells were positive for myeloperoxidase on immunohistochemical study. These findings are consistent with Histiocytoid Sweet Syndrome (HSS). (Figure 1).

An anoscopy was performed and disclosed signs of severe proctitis with ulcers and a purulent exudate (Figure 1). Consequently, the patient received empirical treatment with Ceftriaxone 250mg intramuscularly, Penicillin G benzathine 2,400,000 IU intramuscularly in a single dose and Doxycycline 100mg every 12 hours orally for 7 days. Further diagnostic results were negative for syphilis and both hepatitis B and C. The real-time multiple PCR testing performed in the anal swab was positive for Chlamydia trachomatis (CT) serotype lymphogranuloma venereum (LGV) (Allplex™ genital ulcer real-time PCR multiple assay; Seegene, South Korea). The patient was advised to extend Doxycycline treatment for 21 days, with complete resolution of the skin lesions as well as the proctitis symptoms. Other possible causes of Sweet’s Syndrome were also ruled out. A thoracoabdominopelvic CT-scan was performed in order to rule out an underlying oncological disease, showing no relevant findings. An autoimmunity panel was also carried out with negative results for ANAs, ANCA (anti-PR3 and anti-MPO), antiphospholipid antibodies, rheumatoid factor, cryoglobulins, and complement C3 and C4.
However, eighteen months later, he sought for medical advice again because of almost identical symptoms, with similar skin lesions and symptoms of proctitis. Anal swab confirmed CT reinfection and a new cycle of 3-week treatment with Doxycycline was completed with total resolution of symptoms likewise.

In conclusion, based on the clinical course and histological findings, a diagnosis of HSS associated with anorectal LGV infection was made; the patient fully recovered after properly treating the underlying CT infection. After a two-year follow-up the patient has remained asymptomatic.

DISCUSSION

Sweet Syndrome (SS) or acute febrile neutrophilic dermatosis was first described in 1964 by Dr. Robert Douglas Sweet (Sweet RD., 1964). It is a disorder of unknown etiology characterized by fever, neutrophil leukocytosis and painful skin lesions (nodules or erythematous plaques) of asymmetric distribution usually involving the face, neck, and extremities (Villarreal-Villarreal et al, 2016. Cohen, 2007). There are three categories of SS according to etiology: classic or idiopathic, malignancy-associated, and drug-induced SS (Cohen, 2007). It is more frequent in women between 30-50 years of age (Cohen, 2007. Cohen and Kurzrock, 2003). The diagnosis is usually confirmed with histological study revealing edema of the papillary dermis with an infiltrate consisting of mature neutrophils in the prototypical case (Cohen and Kurzrock, 2003. Corazza et al, 2008).

In 2005, a new histopathological variant was described: the Histiocytoid Sweet Syndrome (HSS) (Requena et al, 2005). HSS has a similar clinical course
classic SS in terms of age of onset, characteristics, and distribution of skin
lesions, but neutrophilia is infrequently present, in about 20% of patients (Peroni
et al, 2015). Histological findings are distinctive and are characterized by an
infiltrate composed of histiocyte-looking cells representing immature myeloid
cells, i.e., neutrophil precursors. Lymphocytes and eosinophils have also been
described as part of the inflammatory infiltrate (Peroni et al, 2015. Alegría-
Landa et al, 2017). HSS has been associated mainly with hematological
neoplasms (e.g., lymphomas, leukemias) (So et al, 2015), but it also has been
related to infections, autoimmune diseases, inflammatory bowel disease,
Treatment in both cases is based on the administration of corticosteroids, as
well as addressing the underlying cause, if it exists or is known.

In conclusion, HSS is a variant of the classic SS that presents similar clinical
characteristics but with different histological findings, where immature myeloid
cells predominate. It is mostly associated with hematological neoplasms and
less frequently with infectious entities. In our patient the associated condition
was anorectal lymphogranuloma venereum (LGV) infection, whose appropriate
treatment was followed by progressive remission of the skin lesions.
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CONFLICT OF INTEREST

The authors declare the following conflict of interest, financial or otherwise:

ACU reports grants and personal fees from ViiV Healthcare, personal fees from Gilead, personal fees from Janssen, personal fees from Merck, unrelated to the submitted work.

MGH reports grants and personal fees from ViiV Healthcare, personal fees from Gilead, personal fees from Janssen, unrelated to the submitted work.

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AUTHOR CONTRIBUTION

All the authors contributed to the final version of the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Verbal informed consent was obtained from the patient (registered in the patient’s electronic health record).
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Figure 1 A and B: erythematous painful papules and plaques, and some vesicle-looking lesions on the nape of his neck, forearms and hands. C: anoscopy with signs of severe proctitis with ulcers and a purulent exudate. E: immunehistochemical study for histiocyte marker CD163, showing abundant positive cells. F: immunehistochemical study for Myeloperoxidase, showing that many of the histiocyte-looking cells are positive, representing granulocyte precursors.