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HISTIOCYTOID SWEET SYNDROME IN A PATIENT WITH CRDM-TYPE MYELODYSPLASTIC SYNDROME

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Abstract: *Histiocytoid Sweet syndrome was first described in 2005 as a histological variant of acute febrile neutrophilic dermatosis. Unlike classic Sweet syndrome, the dermal inflammatory cell infiltrate in histiocytoid Sweet syndrome consists of histiocytoid cells, which are thought to be immature myeloid cells. A 69-year-old male patient with a medical history of CRDM type myelodysplastic syndrome was consulted for a tender and slightly pruritic erythematous papular rash, some lesions showing central vesiculation, disseminated to the trunk and limbs, with an onset of about 1 month. His general condition was relatively good without fever. In the context of the pre-existing haematological condition, a leukemic transformation with concomitant leukaemia cutis was suspected and a skin biopsy was performed. The histopathological examination revealed an infiltrate in the superficial dermis consisting predominantly of mononuclear cells with cytomorphological characteristics of monocyte/histiocyte, with frequent interstitially dispersed neutrophils, and perivascular immature granulocytes and lymphocytes. Immunohistochemical staining was positive for myeloperoxidase and CD68 in numerous cells in the infiltrate, establishing the diagnosis of histiocytoid Sweet syndrome.*
The histiocytoid variant of Sweet syndrome should be recognized as a distinct entity by clinicians, so Sweet syndrome should not be excluded in the absence of classic clinical and histopathological manifestations.

Key words: *Histiocytoid Sweet syndrome; myelodysplastic syndrome.*

1. Introduction

Histiocytoid Sweet syndrome (HSS) is a rare inflammatory skin condition, described by Requena in 2005 as a histopathological variant of acute febrile neutrophilic dermatosis (NSS). [1] Unlike the classic form of Sweet's syndrome, the inflammatory infiltrate in HSS consists of myeloperoxidase-positive histiocytoid cells which are thought to be immature myeloid cells. We present the case of a 69-year-old male patient diagnosed with HSS.

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2. Clinical Case

A 69-year-old male patient with a medical history of CRDM type myelodysplastic syndrome (refractory cytopenia with multilineage dysplasia) with severe macrocytic anemia and secondary thrombocytopenia under therapy with 4 mg methylprednisolone per day and epoetin alfa 40.000 U every 7 days, was consulted for a sensitive and slightly pruritic erythematous papular rash, some lesions outlining a central vesicle, disseminated to the trunk and limbs, with onset of approximately 1 month (figures 1 and 2). His general condition was relatively good without fever. In the context of the pre-existing hematological condition, a leukemic transformation with concomitant leukemia cutis was suspected and a skin biopsy was performed.

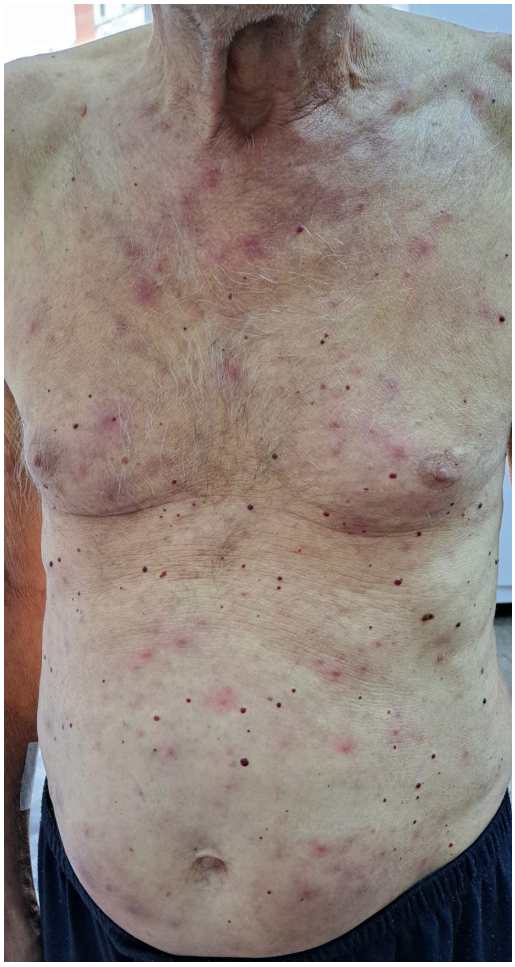

Fig. 1. *Clinical appearance - erythematous papules with central vesicle disseminated to the trunk*

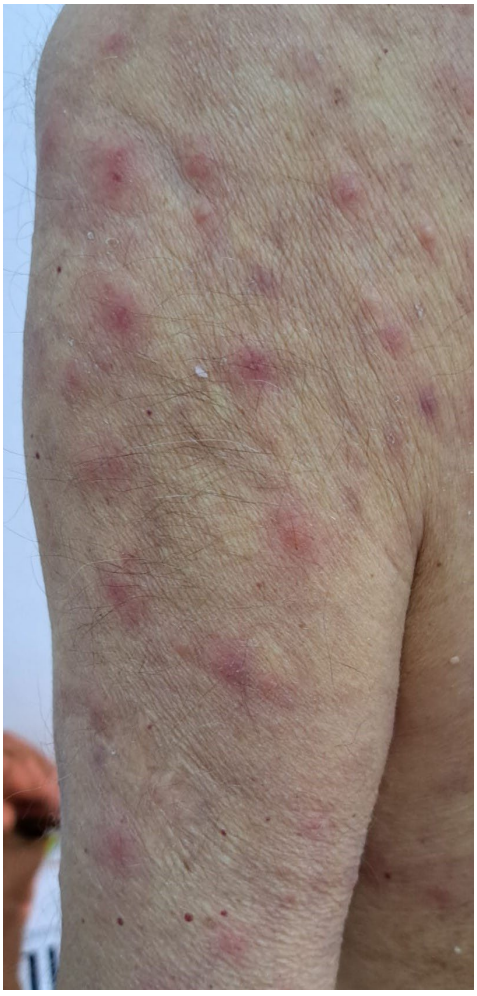

Fig. 2. *Clinical appearance - erythematous papules on the left arm*

The histopathological examination revealed an infiltrate in the superficial dermis consisting predominantly of mononuclear cells with cytomorphological characteristics of monocyte/histiocyte, with frequent interstitially dispersed neutrophils, and perivascular immature granulocytes and lymphocytes (figure 3). Immunohistochemical staining was positive for myeloperoxidase and CD68 in numerous cells in the infiltrate, establishing the diagnosis of histiocytoid Sweet syndrome (figure 4 and 5).

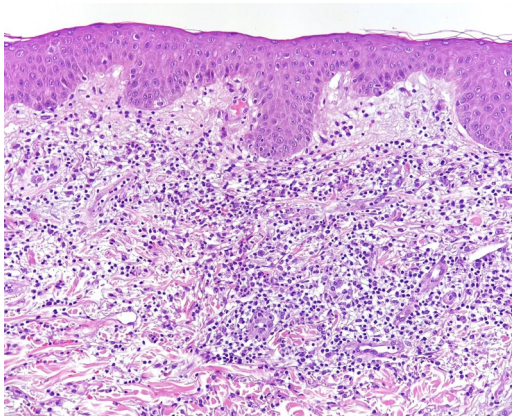

Fig. 3. *Histopathological examination - inflammatory infiltrate in the superficial dermis consisting predominantly of mononuclear cells (HE stain, x20)*

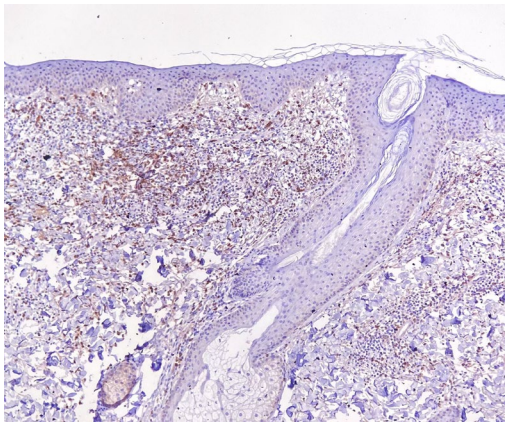

Fig. 4. *Immunohistochemical staining positive for myeloperoxidase*

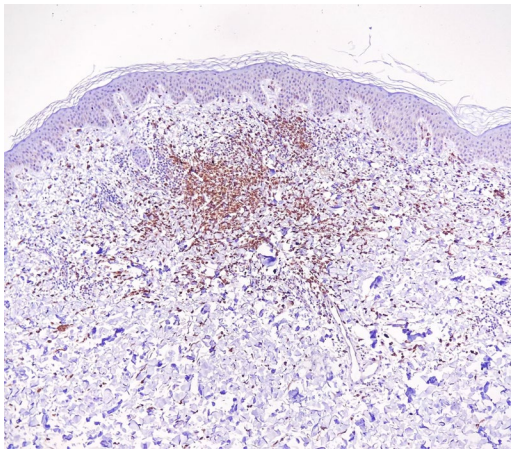

Fig. 5. *Immunohistochemical staining positive for CD68*

Laboratory investigations showed a high erythrocyte sedimentation rate (30 mm/1h), refractory moderate anemia (Hb – 8.1 g/dL, Ht – 23%) with ring sideroblasts, thrombocytopenia (65,000/mm3), leukocytes 4,110/mm3 with basophilia 5.6%, reticulocytes 3.3%, with differentiated leukocyte formula without immature myelocytes in the peripheral blood. Direct and indirect Coombs tests were negative.

Under systemic corticosteroid therapy with methylprednisolone 32 mg/day, dose progressively reduced, the evolution was towards remission of the papular eruption but followed by relapse approximately two weeks after discontinuation of treatment, requiring resumption of corticosteroid therapy.

3. Discussions

Sweet syndrome (SS) is characterized by a variety of symptoms and histological changes that include skin lesions, systemic manifestations of acute disease, and a

dermal inflammatory infiltrate with a significant neutrophilic component. SS can be divided into three forms: classic, malignancy-associated, and drug-induced. [2]

Dermal neutrophilic infiltrate without vasculitis is considered the major histological feature of NSS. However, several studies have described cases with other associated cellular components, such as lymphocytes and mononuclear cells of uncertain lineage but resembling histiocytes and showing myeloperoxidase expression. [3, 4] This histological variant was called histiocytoid SS (HSS) due to the lack of consensus on the name of this variant of SS to date. [1]

Although the clinical manifestations are largely similar to the classic form of SS, with infiltrated, painful nodules or plaques representing the most common cutaneous manifestation, cases with atypical manifestations have also been reported. Extracutaneous involvement is rare in HSS. All cases of HSS require diagnosis by histopathological examination.

From a histopathological point of view, HSS demonstrates a dense dermal inflammatory infiltrate with monocytic cells with basophilic, large, elongated, reniform nuclei and eosinophilic cytoplasm, which immunohistochemically are positive for CD15, CD 43, CD 45, CD68, MAC-386, HAM56, myeloperoxidase and lysozyme. [1] The most important differential diagnosis is leukaemia cutis, which corresponds to cutaneous infiltration with neoplastic leukocytes. Both conditions have similar immunoprofiles (immunoreactivity for lysozyme, myeloperoxidase, CD43, CD45 and CD68) and often indistinguishable cytological appearance. [1] However, based on the clinical manifestations and the absence of immature myeloid cells in the peripheral blood, the diagnosis of HSS was established in the presented case.

Unlike classic SS, HSS appears to be more frequently associated with myelodysplastic syndromes (46% vs 2.5%) and with haematological malignancies (42.5% vs 25%) [5], including lymphoid neoplasms [6,7,8]. It is unclear whether SS associated with haematological malignancies reflects a paraneoplastic manifestation or a differentiated leukaemia cutis. The myeloperoxidase-positive histiocytoid cells that are dominant in HSS can be considered immature myeloid progenitors recruited to the skin. These cells, although much less numerous, can also be identified in the infiltrates of classic SS, where mature neutrophils are the main cell type. [9]

The development of HSS does not appear to have prognostic implications in patients with an associated haematological malignancy, such as leukaemia cutis. [10] Thrombocytopenia was not associated with a higher risk of malignancy-associated HSS, as has been reported with NSS. [2]

Treatment, monitoring and possible associated diseases are the same as those described in the classic form of SS.

If HSS precedes the diagnosis of malignancy, screening for neoplasia should begin with age-appropriate screening guidelines and be based on the most commonly associated malignancies, along with ongoing monitoring of the complete blood count.

4. Conclusion

The HSS variant should be recognized as a distinct entity by clinicians, so Sweet syndrome should not be excluded in the absence of classic clinical and histopathological manifestations.

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