Caso Clínico

HISTIOCITOSE DE CÉLULAS NÃO LANGERHANS PEDIÁTRICA - UM CASO ATÍPICO

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RESUMO – **Introdução**: As histiocitoses são um grupo heterogéneo de doenças caracterizadas pela proliferação e infiltração dos tecidos por histiocitos. Durante muito tempo as histiocitoses foram conhecidas por diferentes nomes, reflectindo a falta de conhecimentos em relação à sua origem. **Caso clínico**: Uma criança aparentemente saudável de 4 meses de idade foi observada por lesão cutânea de crescimento progressivo com 1 mês de evolução. Mãe com diagnóstico de síndrome de Sjögren. Observava-se uma placa bem definida, firme, eritematosa, com 30mm diâmetro, de bordos elevados, no dorso do nariz, além de pequenas pápulas eritematosas, com 5 dias de evolução, na região malar esquerda, região torácica esquerda e braço direito. O estudo analítico mostrou anticorpos antinucleares elevados e anti-SS-A positivo. O exame histopatológico confirmou o diagnóstico de histiocitose de células não Langerhans. Surgiram progressivamente novas pápulas e placas anulares, eritematosas, dispersas pela face, tronco e membros, com resolução espontânea da lesão inicial do dorso do nariz. Cerca de 2 meses após a observação inicial, todas as lesões regrediram espontaneamente, com normalização laboratorial ao 1 ano de idade. **Conclusão**: Muitos autores acreditam que os diferentes subtipos de histiocitose representam apenas diferentes estadios da mesma doença. A imunofenotipagem da histiocitose nem sempre permite identificar o subtipo envolvido, pelo que são frequentes os casos atípicos.
PALAVRAS-CHAVE – Criança; Doenças da Pele; Histiocitose de Células Não Langerhans.

CHILDHOOD NON-LANGERHANS CELL HISTIOCYTOSIS - AN ATYPICAL CASE

ABSTRACT – ***Introduction:*** *Histiocytoses correspond to a heterogeneous group of disorders characterized by the proliferation and infiltration of histiocytes in tissues. For years, many of the histiocytoses where known by numerous names, reflecting the lack of understanding regarding their origin.* ***Case report:*** *A previously healthy, 4-month-old infant presented a cutaneous lesion of progressive growth on his nose since 1 month ago. The mother has a diagnosis of Sjögren syndrome. On examination, there was a firm well-defined erythematous plaque with 30 mm of diameter and raised edges, on the bridge of the nose. At the left cheek, left thoracic region and right arm there were also small erythematous papules with 5 days of evolution. The analytical study showed elevated antinuclear antibodies and anti-SS-A. Histopathological examination confirmed the diagnosis of non-Langerhans cells histiocytosis. Progressively, more annular erythematous papules and plaques appeared scattered over the face, trunk and limbs with spontaneous resolution of the first lesion on the nose. About 2 months after the initial evaluation, all lesions had regressed spontaneously, with normalization of analytical study at one year-old.* ***Conclusion:*** *Many authors believe that the different subtypes of histiocytosis represent only different stages of the same disease. Immunophenotyping of histiocytosis does not always identify the subtype involved, making the occurrence of atypical cases frequent.*
KEY-WORDS – *Child; Histiocytosis, Non-Langerhans-cell; Skin Diseases.*

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INTRODUCTION

Histiocytoses correspond to a heterogeneous group of disorders that is characterized by the proliferation and infiltration of histiocytes in tissues. Three histiocytes of cutaneous importance are: Langerhans cell, mononuclear cell/ macrophage, and dermal dendrocyte/dendritic cell. Dysfunction of these histiocytes has led to a group of poorly understood disorders.[1,2]

The development of immunohistochemical stains has provided insight into these conditions. It is now clear that the histiocytoses are closely related entities, with Langerhans cell histiocytosis (LCH) and non-Langerhans cells histiocytosis (non-LCH), representing the two major groups of histiocytoses.[3]

CASE REPORT

A previously healthy, 4-month-old, male infant was referred to the dermatology department due to a progressively increased cutaneous lesion on his nose since 1 month ago. The parents denied fever, anorexia and weight loss, as well as respiratory or gastrointestinal complaints. The mother has the diagnosis of Sjögren syndrome. Physical examination revealed a firm well-defined erythematous plaque with 30mm of diameter, and raised edges, on the bridge of the nose. Multiple 3 to 5 mm erythematous papules with 5 days of evolution were observed on his left cheek, left thoracic region, and right arm (Fig. 1).

The analytical study showed elevated antinuclear antibodies (ANA) (1/1280) and anti-SS-A (>240U/mL) with no other significant alterations. Microbiological study of tissues was negative for fungi, mycobacteria and parasites. Histopathological examination was performed and revealed a monomorphic infiltrate of cells throughout the dermis with irregular eosinophilic cytoplasm and hyperchromatic, sometimes indented nuclei of variable sizes. Immunohistochemical stain was positive for vimentin (+++), lysozyme (+++), CD68 (+++), CD45 (+++) and negative for S100, CD1a and CD3, suggesting the diagnosis of a non-LCH (Fig. 2).

The lesion of the nose resolved after one month of follow-up, but, progressively, more erythematous papules and annular plaques with dark red center appeared over the face, trunk and limbs (Fig. 3). A topical corticosteroid (methylprednisolone aceponate 1mg/g) was applied in the more infiltrated lesions with complete regression of all lesions 2 months after the initial evaluation (Fig. 4). A second analytical study showed a decrease of ANA (1/160) and anti-SS-A (126U/mL), with normalization at one year-old.

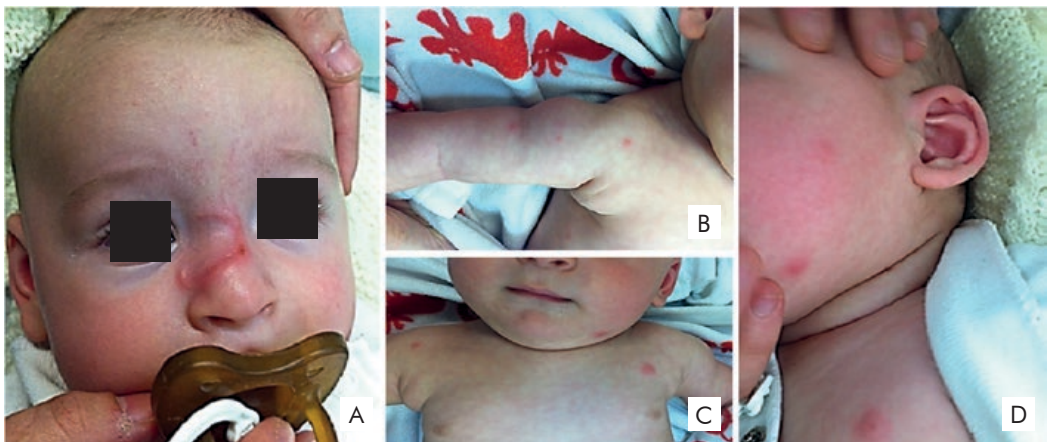

Fig 1 - Firm well-defined erythematous plaque with 30 mm of diameter and raised edges, on the brige of the nose **(A)**; Small erythematous papules on the right arm **(B)**;, left thoracic region **(C)** and left cheek **(D)**.

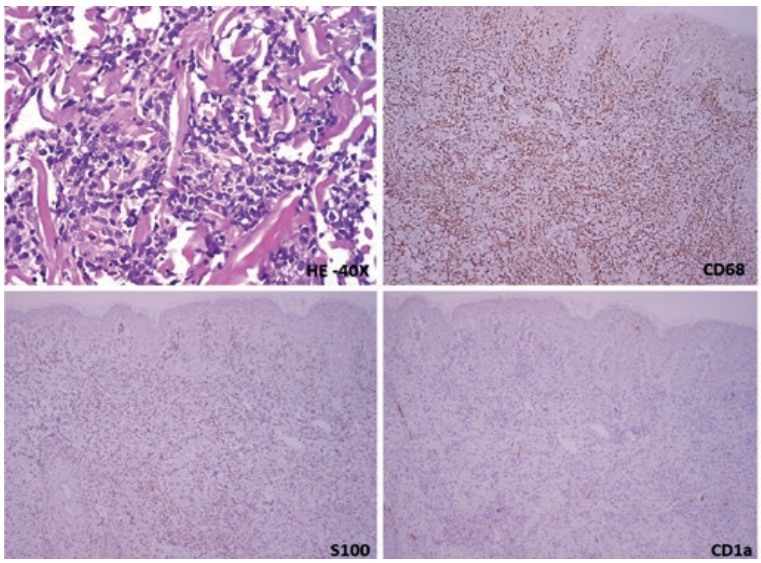

Fig 2 - Monomorphic infiltrate of cells throughout the dermis with irregular eosinophilic cytoplasm and hyperchromatic, sometimes indented nuclei of variable sizes (HE, 40x). Immunohistochemical stain positive for CD68, and negative for S100 and CD1a.

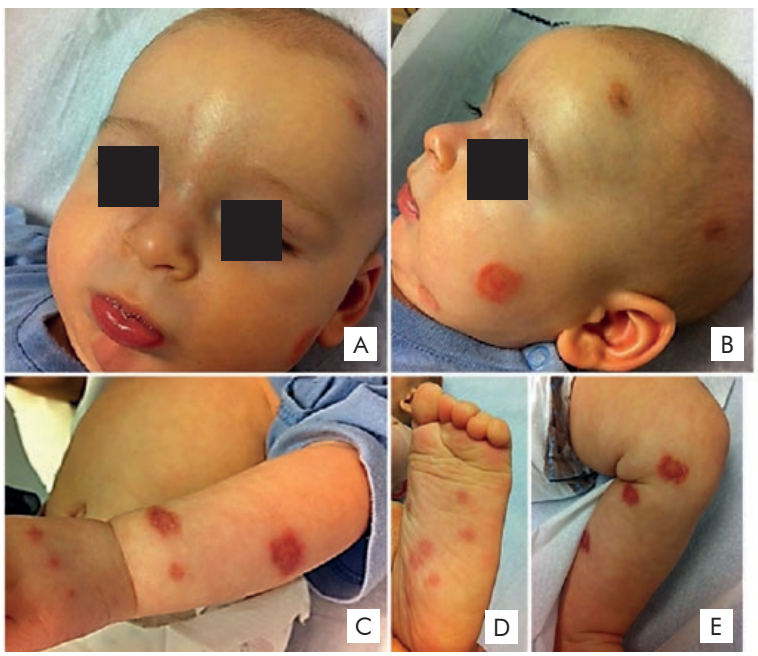

Fig 3 - After 1 month of follow-up: resolution of the nasal lesion **(A)**; annular erythematous papules and plaques with dark red center over the face **(B)**, trunk **(C)** and limbs **(D,E)**.

DISCUSSION

The results of the histopathological and immunohistochemical examination of the present case allowed the diagnosis of a non-LCH, excluding some subtypes like the indeterminate cell histiocytosis and the Rosai-Dorfman disease.[4,5] The age of onset (4 months) and the clinical features of the observed lesions (widespread erythematous papules and plaques without extra-cutaneous involvement and spontaneous resolution) are not fully characteristic of any subtype of non-LCH.

In the case of a benign cephalic histiocytosis, the lesions are usually smaller and localized (2-5 mm papules on the face and neck with residual hyperpigmentation).[6,7]

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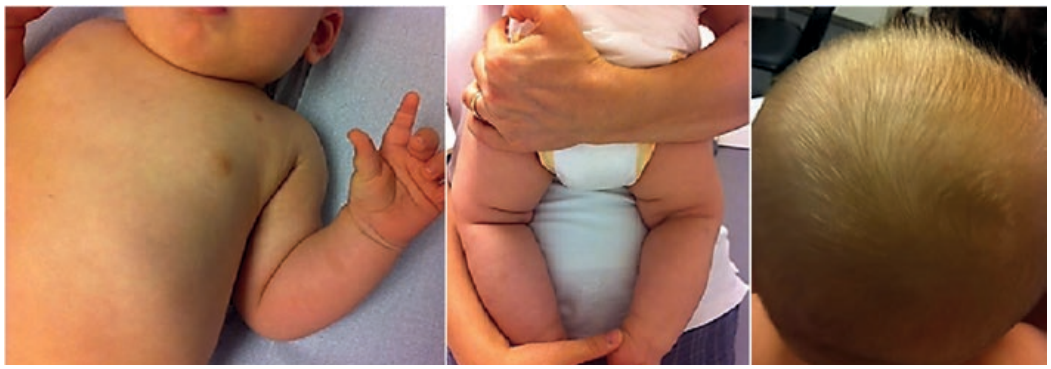

Fig 4 - After 2 months of follow-up: complete regression of all lesions.

Generalized eruptive histiocytoma is characterized by hundreds of recurrent red to brown papules, axially distributed, and adults are affected more commonly than children.[8] Juvenile xanthogranuloma is the most common histiocytic disease of childhood, with small and large nodular forms which acquire a yellow color as they mature. Foamy cells, foreign-body giant cells and Touton giant cells (histiocytes with a wreath of nuclei surrounded by foamy cytoplasm) are characteristic of xantogranuloma, but were not identified in the presented case.[9] Necrobiotic xanthogranuloma is more common in the sixth decade and frequently associated to monoclonal gammopathy. The classic lesion is an asymptomatic indurated papule, nodule or plaque with a yellow hue on the periorbital region.[10] Reticulohistiocytosis is primarily seen in adults with mucous membrane lesions, polyarthritis and histiocytes with characteristic "ground glass" appearance on histopathological examination.[11] At last, xanthoma disseminatum is classically characterized by the triad of cutaneous xanthomas, mucous membrane xanthomas, and diabetes insipidus which were not observed in the presented case.[12]

We hypothesized that elevated ANA and anti-SS-A might be the sign of an underlying auto-immune disease transmitted by his mother who suffered from Sjögren syndrome, and perhaps could be the trigger of the presented histiocytosis.

In conclusion, although widely described and classified, the pathophysiologic mechanism of histiocytosis remains unknown. Many authors believe that the different subtypes of histiocytosis represent only different stages of the same disease. Immunophenotyping of histiocytosis does not always identify the subtype involved, making the occurrence of atypical cases frequent.

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