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Multiple juvenile xanthogranulomata

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Abstract

Juvenile xanthogranuloma is the most frequent form of non-Langerhans cell histiocytosis in children. Clinically, it presents as well defined, yellowish papules that are typically located on the head, neck, upper trunk, and proximal region of the extremities. Although solitary lesions are the most common presentation, few cases of multiple juvenile xanthogranuloma have been described, more frequently associated with extracutaneous involvement. We report a 2-month-old girl with 22 cutaneous papules, clinically and histologically compatible with juvenile xanthogranulomas. Screening of visceral involvement was performed with no evidence of systemic disease. Identifying high-risk factors of systemic disease in patients with multiple juvenile xanthogranuloma is essential to perform an appropriate management of this entity.

Keywords: histiocytosis, juvenile. myelomonocytic leukemia, multiple xanthogranuloma, neurofibromatosis, systemic disease

Introduction

Juvenile xanthogranuloma (JXG) is the most frequent form of non-Langerhans cell histiocytosis, and is an uncommon, usually benign and self-limited skin disease. Although JXG is a well-known entity and is generally limited to the skin, a few cases of multiple JXG, more frequently associated with extracutaneous involvement, have been described in the literature.

Case Synopsis

A 2-month-old girl presented to the dermatology clinic for the progressive appearance, in the last month, of 22 asymptomatic skin lesions on the scalp, upper part of the trunk, and proximal region of the extremities (**Figure 1**). She had no other systemic symptoms. The skin lesions had a papular morphology and a firm consistency with a smooth, well-defined surface and a yellow-to-brown color hue. On dermoscopy, a yellow background with erythematous border, pale-yellowish globules, and fine linear vessels were observed.

Skin biopsy showed a dense cellular infiltrate in the papillary dermis composed of lymphocytes, histiocytes, and multinucleated giant cells (**Figure 2**). Immunohistochemistry was negative for S100, CD1a, and CD207, and positive for FXIIIa, CD68, lysozyme, and vimentin (**Figure 3**). According to these results, the diagnosis of multiple juvenile xanthogranuloma was made.

After consulting with the pediatricians, we jointly decided to order blood tests (complete blood count, lipid and liver profile), an abdominal ultrasound, and a neurological and ophthalmologic examination, to rule out visceral involvement. All the complementary tests were normal. The patient is continuing observation with no new associated symptoms, and with regression of some of the papules.

Case Discussion

Juvenile xanthogranuloma is the most frequent form of non-Langerhans cell histiocytosis in childhood. It is an uncommon, usually benign, asymptomatic, and self-limiting entity. Up to 85% of JXG cases present during the first year of life, although adult-onset cases have also been reported. Juvenile xanthogranuloma has a slight male predominance and there appears to be no familial association [1].

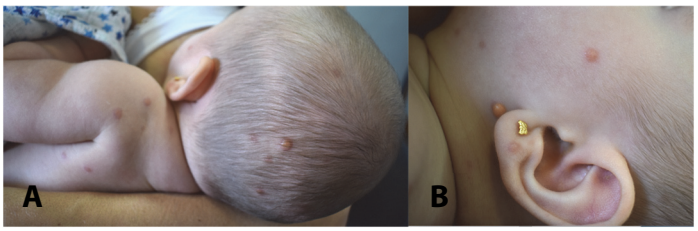

Figure 1. ***A)*** *Multiple erythematous-yellow skin lesions with papular morphology and well-defined surface on scalp, preauricular region and left shoulder.* ***B)*** *Preauricular erythematous-yellow papules.*

Its etiopathogenesis is unknown, although many authors believe that it is a reactive granulomatous histiocyte response to unknown physical or infectious stimuli, without associating alterations in lipid and glucose metabolism [2].

Clinically, it presents as well defined, solitary, or multiple lesions (2 or more), with papular or nodular

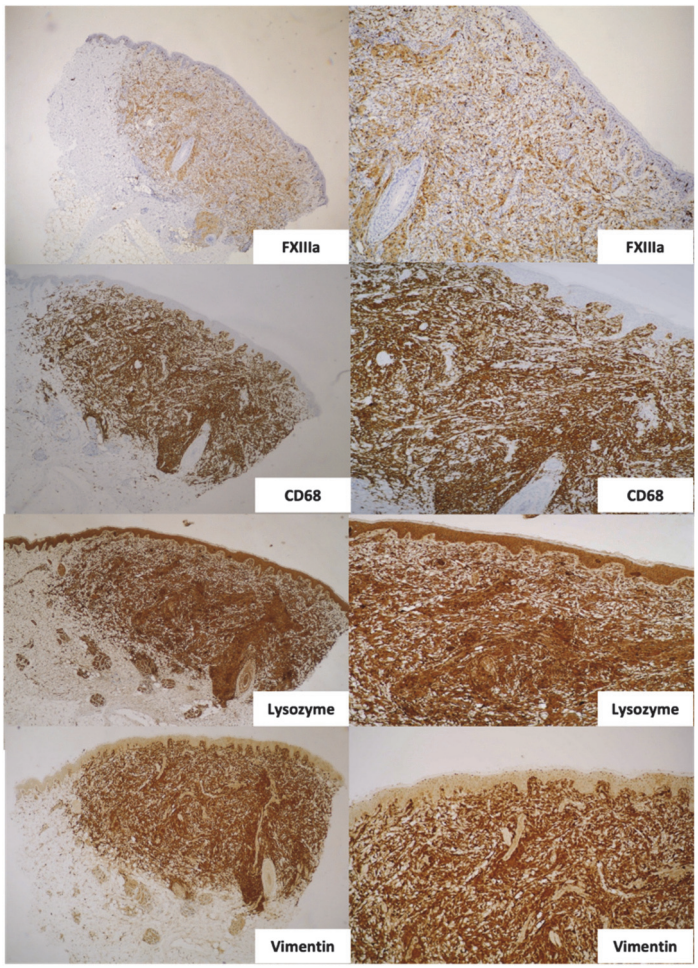

Figure 3. *Histopathological examination of a skin lesion. Immunohistochemistry staining with FXIIIa (40× and 100×), CD68 (40× and 100×), lysozyme (40× and 100×), and vimentin (40× and 100×).*

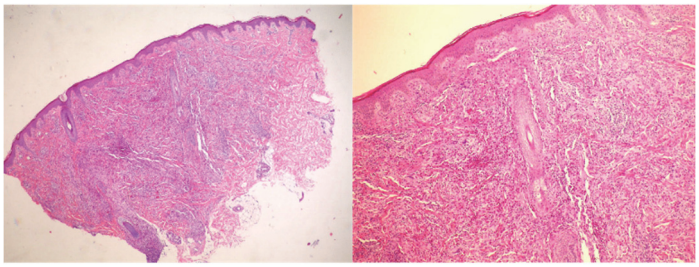

Figure 2. *Histopathological examination of a skin lesion. H&E stain showing a dense cellular infiltrate in the papillary dermis composed of lymphocytes, histiocytes and multinucleated giant cells, 40× and 100×.*

morphology, smooth surface, and reddish coloration at the beginning. There is often progressive evolution towards a yellowish-orange tone. The lesions are asymptomatic and are typically located on the head, neck, upper trunk, and proximal region of the extremities [2,3].

Diagnosis is usually clinical, but diagnostic skin biopsy is recommended in the case of multiple lesions to rule out other pathologic processes. Histology shows dense, well- demarcated dermal lymphohistiocytic infiltration interlaced with giant cells. Immunohistochemistry is positive for macrophage markers (CD68, CD163, KiM1P, anti-FXIIIa, vimentin, and anti-CD4) and negative for S100, CD1a, and CD207, consistent with Langerhans cells [3,4].

The differential diagnosis, mainly in multiple forms, includes: Langerhans cell histiocytosis, other non-Langerhans cell histiocytosis (cephalic histiocytosis, generalized eruptive histiocytoma, giant cell reticulohistiocytoma), urticaria pigmentosa, tuberous xanthomas, dermatofibroma, angiomas, nevus, molluscum contagiosum, and pyogenic granuloma [5].

Although juvenile xanthogranuloma lesions are limited to the skin and spontaneously regress in most cases, extracutaneous involvement has been described, more commonly in the multiple juvenile xanthogranuloma forms [6]. The most frequently involved organ is the eye; ocular lesions do not resolve spontaneously, unlike cutaneous lesions, and patients may develop decreased visual acuity, hyphema, or glaucoma [7,8]. This involvement has been described more often in patients with early age

of presentation (under two years), regardless of the presence or absence of skin lesions. Other organs that may be affected include the central nervous system, lungs, liver, spleen, gastrointestinal tract, bones, gonads, and kidneys. In addition, an association between juvenile xanthogranuloma, neurofibromatosis type 1, and juvenile myelomonocytic leukemia has been described, although is currently controversial [9]. The occurrence of all three entities is infrequent, but, nevertheless, the presence of JXG in neurofibromatosis type 1 patients appears to be significant, given that these patients have 20 to 30 times higher risk of developing juvenile myelomonocytic leukemia compared to neurofibromatosis type 1 patients without JXG lesions.

Considering that extracutaneous involvement is rare, there is no consensus on the need for additional tests in the absence of systemic involvement. Some authors advocate neuro-ophthalmologic evaluation and the performance of complementary tests, such as blood analysis with hemogram and liver profile. Additional imaging tests are often recommended in high-risk cases including new diagnoses, multiple skin lesions, age younger than two years, or signs and symptoms suggestive of visceral involvement [2,3,6].

Given the self-regressive nature of JXG, treatment is not usually required unless complications arising from visceral locations occur. In isolated cutaneous forms, some authors recommend annual observation to check for regression of the lesions [10].

Conclusion

Although juvenile xanthogranuloma is well-known, usually benign, and limited to the skin, a few cases of multiple JXG, more frequently associated with extracutaneous involvement, have been described. Identifying high-risk factors of systemic disease in patients with multiple JXG is essential to appropriately manage these patients.

Potential conflicts of interest

The authors declare no conflicts of interest.

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