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CASE REPORT

Juvenile Xanthogranuloma: the benignity behind an atypical lesion

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Keywords:
Xanthogranuloma, juvenile, Histiocytosis, non-Langerhans-Cell, Xanthomatosis, Tinea, Impetigo.

Abstract

Objective: To describe a rare case of Juvenile Xanthogranuloma (JXG) in an infant in order to inform more about this pathology little described in academia, thus avoiding unnecessary treatments and approaches. **Case description:** This is a 4-month-old infant with a single nodular lesion in the abdomen that has progressively evolved since birth. A crusty-looking lesion with small adjacent nodules, central ulceration and blurred borders, approximately 3 centimeters in diameter. With the diagnostic hypothesis of impetigo raised, he used topical and oral antibiotics, without success. Then, suspected of dermatophytosis, he used antifungal agents, without improvement. Due to the persistence of the lesion, an ultrasound of the lesion was requested and referred to a dermatologist. Only after the biopsy was the diagnosis of JXG confirmed. **Comments:** JXG is a rare and benign pathology, belonging to the group of non-Langerhans histiocytosis that typically appears in pediatric age. Lesions most commonly occur on the skin and have a characteristic morphology. They are usually asymptomatic and spontaneous regression is expected in approximately five years. However, the disease can lead to extracutaneous involvement and other important pathologies may be related to the condition, thus requiring an extension of workup to prevent irreversible sequelae to the patient.

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INTRODUCTION

Juvenile xanthogranuloma (JXG) is a rare histiocytic disorder of unknown etiology,[1,2,3] which affects children up to two years of age.[2] It is the most common form of non-Langerhans histiocytosis and its incidence in the population is unknown.[3] JXG manifests clinically as a reddish-yellow papule or nodule that regresses spontaneously between the ages of three and five years.[1,4] Diagnosis is based on clinical and histology findings.[3,4] However, a small proportion of patients may develop extracutaneous involvement with irreversible sequelae, if not diagnosed and treated early on.[2,3]

This case report describes the rare case of an infant with juvenile xanthogranuloma and offers information to the academic community about the diagnosis and management of a disease scarcely described in medical literature.

CASE REPORT

The patient described in this case is D.S.M., a male infant born at 29 weeks of gestation without an apparent cause, with good postnatal development. In a routine visit with a pediatrician at four months of age (corrected age of 53 weeks), a single nodular lesion was found on his right flank, with imprecise borders, a crusted appearance and a central ulceration measuring approximately 3.0 cm in its largest diameter (Figure 1, image on the left). According to his parents, the lesion had been there and grown gradually since his birth.

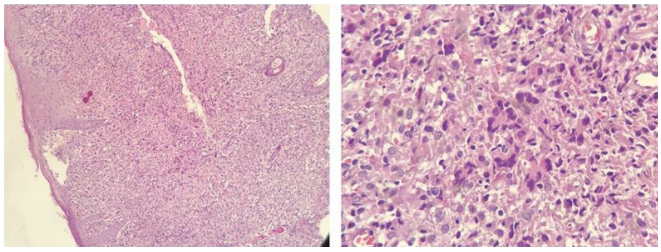
The patient was initially diagnosed with impetigo and prescribed a local topical antibiotic medication (Mupirocin). The prescription was later changed to oral cephalexin at the usual dose, but no changes were seen in the lesion. Dermatophytosis was then considered and topical antifungals were started, also without improvement. In the meantime, the lesion grew in size and developed clearer borders, with a lichenified appearance and a slightly yellowish color (Figure 1, image on the right). The infant remained asymptomatic and afebrile. He was referred to a dermatologist for further evaluation. Ultrasound scans and a biopsy of the lesion were ordered.

The ultrasonography report described it as an oval lesion in close contact with regional muscles and partially defined borders, presenting a superficial anechoic area surrounded by a hyperechoic area, without evident calcifications, measuring 3.8 x 0.5 x 2.9 cm and showing little peripheral vascularization on Doppler mode.

The core biopsy (Figure 2) showed a proliferation of histiocytic cells, some xanthomatous cells, along with some spindle-shaped cells, forming nests/bundles, coexisting with multinucleated Touton-type giant cells and inflammatory infiltrate, including lymphocytes and eosinophils, consistent with JXG.



Source: personal archive.
Figure 1. Macroscopic appearance of the lesion
Initial image of the lesion (left) and evolution of the lesion after four months (right).



Source: personal archive
Figure 2. Microscopic appearance of the lesion
Fragment of the lesion at 100x (left) and 400x magnification (right).

Investigation for extracutaneous manifestations carried out after diagnosis found no additional signs or symptoms. The infant has been asymptomatic and in good clinical condition.

DISCUSSION

Juvenile Xanthogranuloma is present at birth in 5-17% of the cases of disease or appears in the first year of life in 40-70% of the patients.[4] In children, JXG affects preferentially affects boys, with a ratio of 1.4:1.[2-5] Although the term juvenile xanthogranuloma is used, lesions may also occur in adults, mainly between the ages of 20 and 30 years, without a predilection for sex and with spontaneous regression.[5] The cause of the disease is not well defined, although some authors suggested that it occurs as a response to trauma or infection.[5]

Lesions occur most commonly on the skin and present a characteristic morphology. The clinical manifestation presents itself as a reddish or yellowish to brown papule, plaque or nodule measuring 0.5 to 2 cm.[3,6] The most commonly affected sites are the head, neck and upper part of the trunk, although lesions may occur in other parts of the body, with the exception of mucous membranes, which are rarely affected.[3,4,6] Initial lesions tend to be redder and raised, but as they mature, they become gradually more lipidized (yellowish) and flatter.[3]

Histology is characterized by a well-demarcated, dense proliferation of histiocytes in the superficial dermis, with a mixed infiltrate of mononuclear cells, multinucleated giant cells consistent or not with Touton giant cells (characterized by a ring of nuclei surrounded by a foamy cytoplasm) and spindle-shaped cells.[4,5] Touton cells are observed in 85% of the cases of JXG, and are present in the mature stages of the disease.[7] In the final stage of JXH, fibroblasts are increased

and infiltration is replaced with fibrosis.[4,7] In Langerhans cell histiocytosis (LCH) there is a predominance of CD1a +, langerin + and S100 + cells; In non-Langerhans cell histiocytosis (non-LCH), there is a predominance of histiocytes that do not fit the LCH phenotype.[3,5,6,7] JXG is the most common variant of non-LCH, and stains with the following markers: CD68 or Ki-M1P and anti F XIIIa, anti-CD4 vimentin.[3,5]

Differential diagnosis must consider other types of Langerhans and non-Langerhans cell histiocytosis, especially benign cephalic histiocytosis and generalized eruptive histiocytoma. JXG can be distinguished from Langerhans cell histiocytosis based on clinical characteristics, histopathology and immunomarkers.[8]

Skin lesions are generally asymptomatic and spontaneous regression is expected within one to five years.[2,3,5,6] Healed lesions may leave an atrophic or hyperpigmented scar.[7]

Extracutaneous involvement occurs in 5-10% of the cases, with the eye being the most commonly affected site.[4,7,9] However, the liver, lungs, spleen, lymph nodes and other organs may also be involved.[3,4,6,7] Injury to the iris is the most common complication, and cases of spontaneous intraocular hemorrhage, glaucoma and blindness have been described.[3,5,6,7] Typically, lesions appear in infants under one year of age.[5] Occurrence of hyphema, with or without increased intraocular pressure, is a common sign of JXG.[5,7] JXG must be considered in the differential diagnosis of infants with hyphema.

Juvenile xanthogranuloma may also be associated with other conditions. JXG occurs in association with neurofibromatosis type 1 (NF1) in 5-10% of the cases, and about 30% of the patients with NF1 are below the age of two years.[3,6] The association of JXG, NF1 and juvenile myelomonocytic leukemia has been described in some case reports. The association between JXG and Niemann-Pick disease, urticaria pigmentosa or cytomegalovirus infection requires further clarification.[6] Unlike other xanthomatous conditions, JXG has not been associated with other metabolic or lipid disorders.[6]

The diagnosis of JXG is based on the physical appearance of the lesions. Since they are typically benign, self-healing lesions, biopsy is needed only to confirm doubtful cases of JXG.[3,4,6] Dermoscopy is a non-invasive method that helps in the description of lesions. Examiners seek a pattern for JXG, which consists of lesions with a yellow-orange base with an erythematous halo (the setting sun sign), pale yellow clouds that correspond to dermal xanthomatous infiltrate, and arboriform vessels from the periphery to the center of the lesion.[3,10]

Due to the benign nature of the disease and its tendency for spontaneous regression, conservative treatment of the lesion is indicated.[3,6,10]

Routine ophthalmic evaluation is not recommended for patients with asymptomatic cutaneous JXG.[2,3,5,9] Asymptomatic eye involvement is rare, and patients with acute symptoms must be referred to specialized care. There are no prospective studies on the benefits of routine ophthalmic evaluation for children with cutaneous JXG.[5,9] Patients under the age of two years with multiple micronodular JXG lesions smaller than 10 mm are at higher risk of eye involvement and benefit from routine follow-up with a specialist.[9]

Patients with systemic involvement and symptoms must be evaluated individually. Treatment may include lesion excision, radiation therapy, chemotherapy, and immunosuppression.[3,6]

In general, JXG resolves spontaneously within five years[3,5,6] and does not require interventional therapy, only continued lesion monitoring.[3,6]

CONCLUSION

The literature about juvenile xanthogranuloma is limited, probably on account of the condition's benign outcomes and poor histological confirmation in suspected cases.[3] Although benign and self-limiting, JXG may occasionally cause systemic involvement, with serious but preventable sequelae. JXG may also occur in association with other conditions that require additional investigation. In such cases, it is important to recognize the associated conditions and refer patients to a specialist for better management and monitoring of the condition.

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