Case Report

Congenital Giant Juvenile Xanthogranuloma, Let It Be

Michael Carletti, DO[1]; Daniel A. Nguyen DO, PharmD[1]; Joseph S. Susa, DO[2]; Stephen E. Weis, DO[1]

Author affiliations are listed at the end of this article.

Correspondence to:
Daniel Nguyen, DO, PharmD
University of North Texas Health Science Center
855 Montgomery St.
Fort Worth, TX 76107
(daniel.nguyen@unthsc.edu)

Abstract

Description

Juvenile xanthogranuloma (JXG) is a rare type of non-Langerhans cell histiocytosis. JXGs are benign and have a self-limiting course generally lasting 6 months to 3 years, with some reported durations longer than 6 years. We present a rarer congenital giant variant, defined as lesions with a diameter larger than 2 cm. It is uncertain if the natural history of giant xanthogranulomas is similar to the usual JXG. We followed a 5-month-old patient with a 3.5 cm in diameter, histopathologically-confirmed, congenital, giant JXG located on the right side of her upper back. The patient was seen every 6 months for 2.5 years. At 1 year of age, the lesion had decreased in size, lightened in color, and was less firm. At 1.5 years old, the lesion had flattened. By 3 years old, the lesion had resolved but left a hyperpigmented patch with a scar at the punch biopsy site. Our case represents a congenital giant JXG that was biopsied to confirm the diagnosis and then monitored until resolution. This case supports the clinical course of giant JXG not being affected by the larger lesion size and that aggressive treatments or procedures are not warranted.

Keywords

juvenile xanthogranuloma; juvenile xanthogranuloma/epidemiology; skin and connective tissue diseases; non-Langerhans-cell histiocytosis; biopsy

Introduction

Juvenile xanthogranuloma (JXG) is a benign proliferative disorder of histiocytes. While rare, it is the most common type of non-Langerhans cell histiocytosis (LCH). The incidence of JXG is unknown. A survey of 117 dermatologists, with an average of 12 years of practice in pediatric disease, reported a low frequency of the disease of approximately 2 new cases yearly.[1] Among those diagnosed with JXG, some may encounter ocular complications. Of these 2371 cases of JXG, there were only 7 cases of intraocular JXG.[1] JXG usually occurs in infants and young children, typically involving the head, neck, and upper body. The disease presents as solitary or multiple red or brown papules, plaques, or nodules with a yellowish hue. Touton giant cells are a characteristic finding in histology.[2] Cutaneous lesions of JXG most often spontaneously resolve with an unremarkable course.[3] Special stains are usually only performed in atypical cases to avoid unnecessary, aggressive procedures and to rule out other tumors with a less favorable prognosis.[4,5]

There are multiple clinical variations of JXG that are even rarer. These variations have been described as keratotic, plaque-like, and giant.[6] Our case represents a congenital, giant JXG that was biopsied to confirm the diagnosis and then monitored for resolution, with only hyperpigmentation remaining. Per Ladha and Haber, there have only been 51 cases of giant JXG reported in the English literature.[7] The natural history of giant JXG is uncertain as most reported cases have not included long-term follow-up.

Case Description

Our patient presented as a 5-month-old female for evaluation of a lesion on the right side of her upper back that was present at birth

and had been growing in conjunction with the patient's normal growth development. She was born healthy, without complications, and was developing normally otherwise.

Upon examination, we discovered a firm, freely mobile 3.5 cm disc-shaped subcutaneous nodule with a yellow, peau d'orange surface, a violaceous vascular-appearing halo, and a central depression (**Figure 1**). The elevation of the lesion measured 6 mm. She was then sent for a Doppler ultrasound of the lesion to rule out a vascular component. Vascular studies confirmed a non-pulsatile lesion.

She returned to the clinic, and a 4-mm punch biopsy was performed. Histopathological studies revealed foamy histiocytes, and a few Touton giant cells were observed. Langerhans cell histiocytosis was excluded, and the diagnosis of giant JXG was confirmed through immunohistochemistry. The lesion stained positive for CD68 and factor XIIIa (**Figure 2**). At that time, we recommended no further treatment and followed the patient every 6 to 12 months.

At 1 year of age, the lesion had decreased in size, lightened in color, and was less firm. At 1.5 years old, the lesion had flattened and was an orange-red color. By 3 years old, the lesion had resolved with a remaining hyperpigmented patch and a scar at the biopsy site (**Figure 3**).

Discussion

JXG is the most common type of non-LCH. JXG usually occurs in infants and young children and typically involves the head, neck, and upper body. They present as solitary or multiple red or brown papules, plaques, or nodules with a yellowish hue.[2,8] Multiple unusual clinical variants have been described, including keratotic, plaque-like, and giant JXG. These clinical variants are histologically indistinguishable.[6] Case reports in the medical literature support a similar natural history.[9] However, there are few reports regarding the natural history of giant JXG. Giant JXGs are slightly more prevalent in males and appear within the first year of life in almost 75% of the cases, while 15% are present at birth.[2] Lesions with a diameter larger than 2 cm are classified as giant JXG.[7] In contrast, non-giant JXGs have a female predominance and are most often found on the proximal extremities or upper back.[4] The cause of JXG is unknown, but it is often considered a reactive process, with histiocytes responding to traumatic or infectious stimuli.[10]

The course of JXG in patients with skin-limited disease is typically benign and self-limited. These lesions usually regress within 6 months to 3 years without any treatment.[9] Hyperpigmentation and mild anetoderma or atrophy may be present afterward.[3] Giant JXG is a rare variant, and little is known about its natural

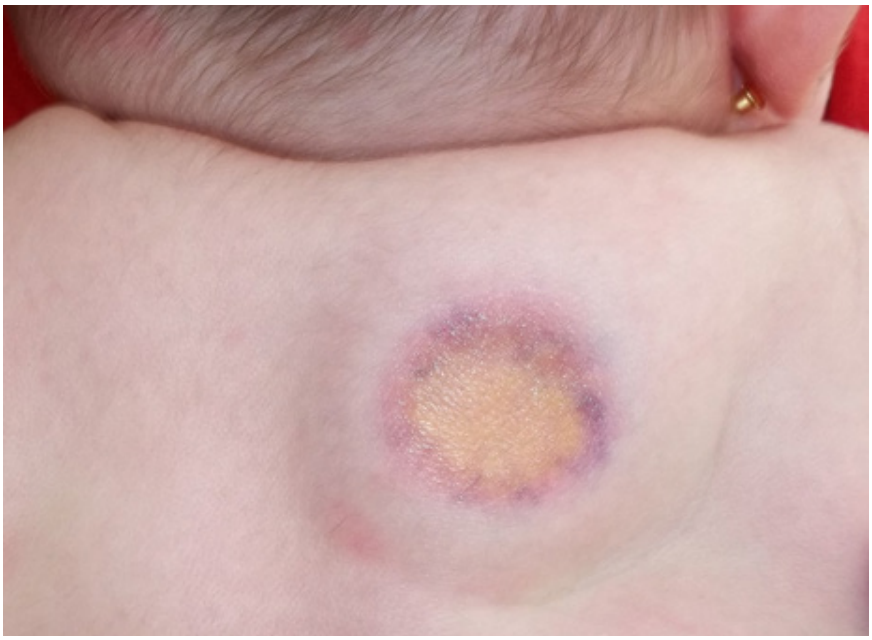

Figure 1. Congenital giant JXG is shown at initial presentation with a 3.5 cm lesion on the right upper back of a 5-month-old female.

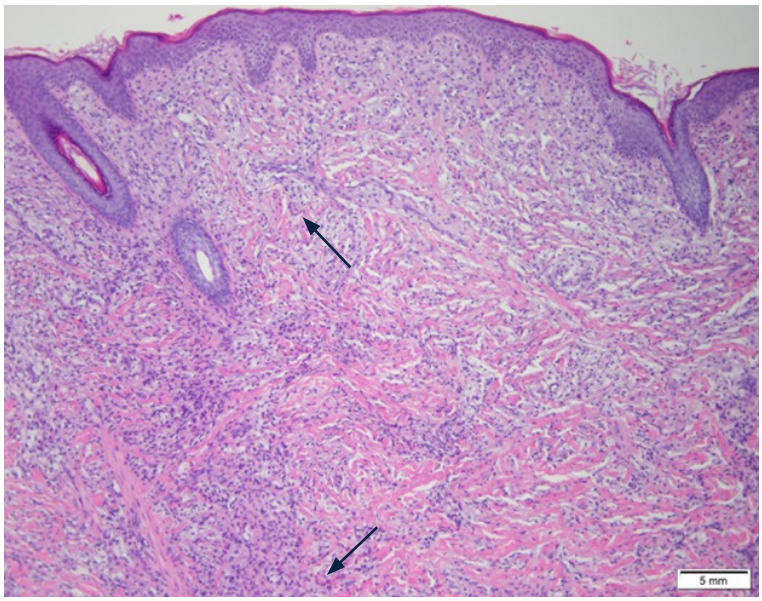

Figure 2. A biopsy shows a dermal histiocytic infiltrate. Multiple foamy (xanthomatous) histiocytes can be seen. Touton giant cells are a characteristic finding (indicated by arrows). (20x magnification)

history. In our case report, we observed the resolution of a giant JXG within 3 years. This outcome is not a universal finding, as 2 cases of giant JXG have been reported, both lasting greater than 6 years without resolution.[11,12] In one case, a 10-year-old Japanese male had JXG lesions on his arms and face since he was 6 months old. The arm lesions improved, but his facial lesions were constant and did not improve.[11] In another case, a 7-year-old Polynesian female also had JXG lesions since she was 6 months old, which had continued to evolve until she was 1 year old. Her lesions stayed constant without any resolution.[12]

No treatment is required for cutaneous JXG as the lesions are usually self-limited. Despite their anticipated spontaneous resolution, lesions are occasionally removed for cosmetic purposes or functional concerns based on their location.[2]

The pathology of JXG and its multiple variants will demonstrate a dense infiltrate of his-

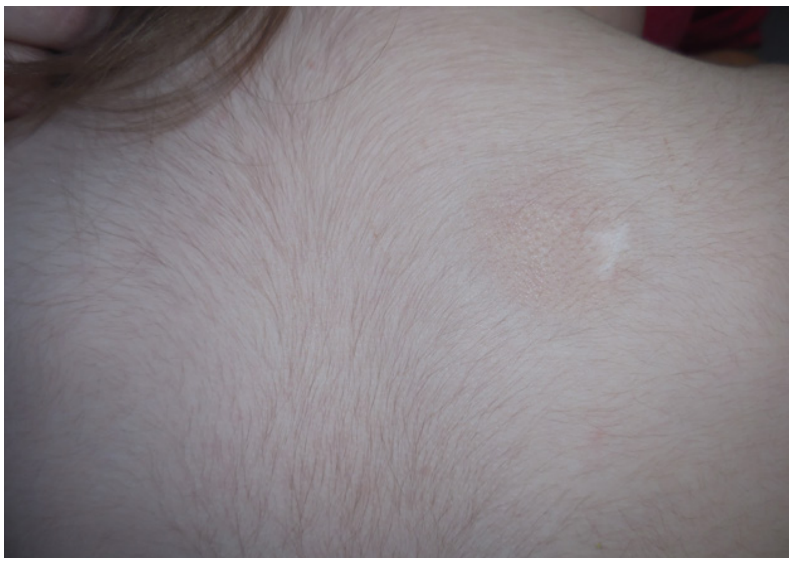

Figure 3. By the age of 3, there was resolution of the lesion with only a hyperpigmented patch remaining along with a scar at the punch biopsy site.

tiocytes, with small lesions in the superficial dermis and large lesions extending deeper into the subcutis. Evolving JXG lesions can account for variations in the histiocytes, which develop lipids in their cytoplasm as they mature and create a foamy xanthomatous appearance. Touton giant cells are a characteristic finding. However, they are not required and may be infrequent or even absent in early lesions or lesions associated with systemic disease.[2] JXG typically has eosinophils, lymphocytes, and plasma cells admixed.[13]

Immunohistochemically, JXG stain positive with non-LCH histiocyte markers such as CD68 and factor XIIIa, while CD1a and Langerin (CD207) are always negative. In contrast, LCH cells are always CD1a and CD207 positive and usually CD68 negative.[6,14] Another Langerhans group disorder, Erdheim-Chester disease (ECD), stains CD68 and CD163 positive, while CD1a stains are negative. Ultrastructural analysis by electron microscopy would show an absence of Birbeck granules in JXG and ECD but positive detection in LCH.[13]

The diagnosis may be difficult, and it is important to differentiate JXG from the other non-LCH and LCH disorders. Under the revised classification of histiocytoses and neoplasms of the macrophage-dendritic cell lineages, JXG was classified in the "C" group, also known as cutaneous and mucocutaneous diseases.[13] Histopathologic confirmation is recommended to avoid unnecessary, aggressive procedures and to rule out other tumors with a less favorable prognosis.[4] Typically, LCH tends to show more epidermotropism of Langerhans cells and lacks Touton giant cells and lipidized cells. LCH also shows characteristic "coffee bean nuclei." The grouping of clinical and histopathologic features allows for differentiation between JXG and either benign cephalic histiocytosis or generalized eruptive histiocytoma. JXG can be differentiated from LCH through immunohistochemistry.[15,16]

JXG most often occurs in the skin, but any organ can be involved. The eye is the most common site of extra-cutaneous involvement affecting the unilateral iris. Ocular involvement occurs at an incidence of 0.3-0.5% and is associated with the risk of glaucoma and subsequent blindness.[1] Routine ocular exams are controversial given the low incidence. However, they are deemed prudent in patients less than 2 years of age who have multiple skin lesions due to an increased risk of involvement.[3]

There has been an association of JXG with café-au-lait macules and juvenile myelomonocytic leukemia (JML).[2] Patients with multiple café-au-lait macules are at increased risk of neurofibromatosis Type 1 (NF1), which has also been found to have an increased risk of JML.[17] A "triple association" has been observed in patients with JXG, NF1, and JML. Patients with both JXG and NF1 have an increased risk (20-32 fold) of developing JML, with a reported observed frequency of 1/1.05 x 10^6.[15,17]

Conclusion

This case illustrates a rare giant congenital variant of a JXG, the most common type of non-LCH. Lesions larger than 2 cm are classified as giant and rarely reported. The lesions are often misdiagnosed, as a variety of clinical presentations have been described including exophytic, polypoid, atrophic plaque, mass with peripheral papules, and even ulceration. Our case report appears to show that large lesion size does not affect the generally accepted clinical course for skin-limited JXG regression. Regression typically ranges from 6 months to 3 years, though lesions persisting beyond 6 years have been reported.[4] Histopathologic confirmation is recommended to avoid unnecessary, aggressive procedures and to rule out other tumors with a less favorable prognosis. We show the importance of recommending a management plan of close monitoring and no further treatment or procedures. Our patient only had a remaining hyperpigmented patch where a congenital giant JXG once occupied the majority of the right side of her upper back.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Author Affiliations

1. University of North Texas Health Science Center/Medical City Fort Worth, Fort Worth, TX
2. Cockerell Dermatopathology, Dallas, TX

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