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MODESTUM

Case Report **OPEN ACCESS**

Juvenile xanthogranuloma: A case report and literature review

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ABSTRACT

Juvenile xanthogranuloma is a benign, self-limiting tumor that arises from histiocyte proliferation of unclear aetiology in children. Cutaneous manifestation is most common, and systemic involvement rarely occurs. Early diagnosis, on the other hand, is necessary for further evaluation in order to avoid disease complications later on. A four-month-old baby boy was referred to a dermatology clinic by the paediatric team because he had multiple skin lesions.

Multiple well-defined borders, soft, non-fluctuant yellow and reddish papules or nodules ranging in size from 2.0 to 4.0 cm, have been seen over the scalp, face, chest, upper back, and upper limbs since birth. The examination of the eyes, heart, lungs, and abdomen is unremarkable. The results of additional imaging to test for systemic involvement were negative. A skin biopsy shows dense dermal infiltration by sheets of mononuclear histiocytes, from polygonal to spindle-shaped and plump, possessed of abundant pale eosinophilic cytoplasm with indistinct cytoplasmic borders. These lesion cells are diffusely positive for CD68 and negative for CD1a and S100. The features are consistent with juvenile xanthogranuloma. Following an 11-month follow-up, the skin lesion was much flatter and softer than before.

Although systemic involvement with cutaneous juvenile xanthogranuloma is uncommon, a thorough examination is required to avoid conditions that are associated with high morbidity and mortality, such as hepatic failure, progressive central nervous system disease, and myeloid leukaemia.

Keywords: juvenile xanthogranuloma, congenital, non-langerhans cell histiocytosis

INTRODUCTION

Juvenile xanthogranuloma (JXG) is a rare skin disease. It is benign, self-healing condition characterized by solitary or numerous reddish or yellowish skin papule or nodule on the skin, most often on the head, neck, or upper trunk.

JXG belongs to the broad group of non-Langerhans cell histiocytosis and mostly affects children in their early years [1]. It is a proliferative disorder of histiocytic cells of the dermal dendrocyte phenotype. It is diagnosed clinically and confirmed by skin biopsy. JXG has a usually benign course, with spontaneous resolution after a few years. Extracutaneous or systemic forms are extremely uncommon and can cause significant morbidity.

As a result, early detection is important so that further evaluation can be performed to rule out any undiagnosed systemic manifestations. It may be confused with other rare skin conditions, including spitz nevus, solitary mastocytoma, and occasionally nevus sebaceous. Early detection is essential because treatments differ.

CASE PRESENTATION

A four-month-old baby boy was born at forty weeks and five days via spontaneous vertex delivery with a good APGAR score. He was then admitted to the newborn intensive care unit (NICU) after birth because he has multiple nodular yellowish cutaneous lesions and presumed sepsis. He was however, active and well with appropriate weight gain. He was later diagnosed with JXG with a differential diagnosis of blueberry muffin rash or subcutaneous fat necrosis. He also had glanular hypospadias and planned for surgical repair at age two years old. He is the only child in the family. Antenatally, his mother had a history of urinary of tract infection at thirty-two weeks, and had completed antibiotics and mild anemia in pregnancy. There is no rare skin disease running in the family. His immunizations were completed up to his age and his developmental milestones were appropriate for his age.

On examination, he was active, not syndromic, pink, not tachypnic, good pulse volume, no cleft lip or palate. There were multiple yellowish swellings spread around his body, including his scalp, left periorbital, neck or upper chest, bilateral upper

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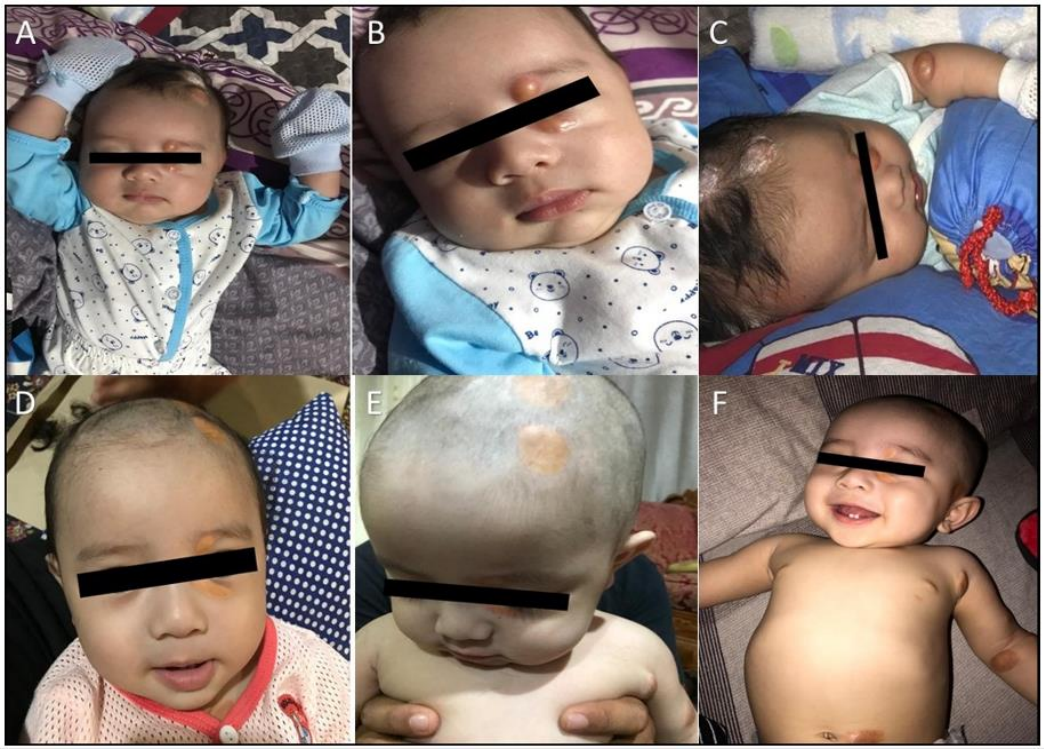

Figure 1. At four months old, A, B, and C show the lesions over the periorbital area, scalp, and forearm, while D, E, and F show the lesions at six months old

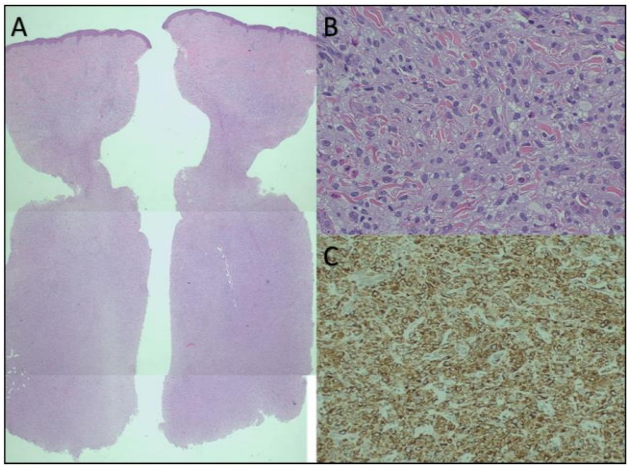

Figure 2. Tissue skin biopsy revealed (A) dermal infiltration by sheets of mononuclear histiocytes, (B) cells that were polygonal to spindle-shaped and plump, with abundant pale eosinophilic cytoplasm with indistinct cytoplasmic borders, and (C) cells are diffusely positive for CD68

limbs, back, base of the penis shaft, and left lower limb. The sizes of the lesions were ranged from 0.5 to 4.0 cm (**Figure 1**).

The lesions over the left upper limb and back were yellowish and dark purplish in color. Most of the lesions were well-defined borders, soft in inconsistency, not fluctuant, and not erythematous. The results of the lung, cardiovascular, and abdominal examinations were unremarkable. He had done an eye assessment and there was no abnormality detected.

During NICU admission, additional tests were performed, and an ultrasound scan of the cranium revealed no evidence of a gross lesion. The ultrasonography abdomen revealed mild left renal hydronephrosis, which was treated conservatively. Full blood picture was sent, and no evidence of haematological malignancy was seen. The TORCHES screening was done on both his mother and him and revealed that they were all non-reactive.

A skin biopsy was taken over the lesions on the upper back which showed dense dermal infiltration by sheets of mononuclear histiocytes. These cells are polygonal to spindle-shaped and plump, possess abundant pale eosinophilic cytoplasm with indistinct cytoplasmic borders. Mitosis is rare. Scattered foamy cells are seen, especially at the superficial dermis. Multinucleation is not obvious. Intermingled within are a few eosinophils and lymphocytes. No necrosis is present. These lesion cells are diffusely positive for CD68; negative for CD1a and S100. These finding was correlated with JXG (**Figure 2**). Following an eleven-month follow-up, the skin lesions were much flatter and softer than before, as shown in **Figure 3**.

DISCUSSION

JXG is a rare non-langerhans cell histiocytic disorder and first described in the year 1905 by Adamson as congenital xanthoma multiplex. It belongs to the heterogeneous group of histiocytic lesions with a macrophage phenotype and variable factor XIIIa and fascin reactivity. JXG is most commonly a paediatric disorder that manifests during the first two years of life [1, 2]. The estimated prevalence about one case per million children. Adult-onset JXG incidence making up only 10% of all cases. JXG was found in 129 of 24,600 paediatric tumors over the course of 35 years in a large tumor registry [3]. Males are more likely than females to develop JXG, but there are no differences in prevalence rates between men and women that have been observed for adult-onset JXG [4]. There was a low incidence of ocular and systemic manifestations in paediatric cutaneous JXG [5].

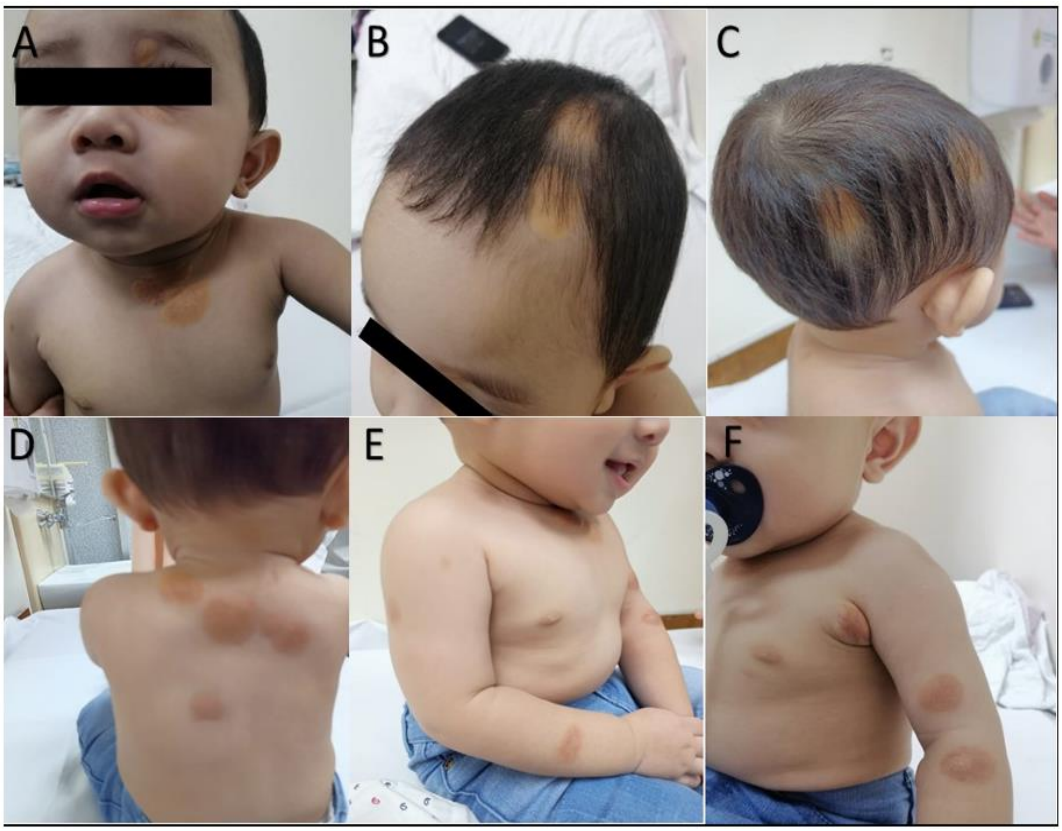

Figure 3. Follow-up at eleven months revealed a lesion over (A) the periorbital and upper chest, (B) the frontal scalp, (C) the temporal area of the scalp, (D) the upper back, (E) the left upper limb, and (F) the right upper limb and armpit

The aetiology and pathogenesis of JXG remains uncertain. The overproduction of a type of histiocyte cell used in the body's immune system in response to nonspecific tissue injury is thought to be the cause of JXG. JXG appears as a well-defined reddish or yellowish to orange papule, plaque, or nodule that is 0.5 to 2 cm in diameter with a smooth surface and firm consistency [6]. Lesions can appear anywhere on the body, although they are more prevalent on the head, neck, and upper trunk. Early lesions are typically redder and higher in elevation, but as they mature and become more lipidized, they become yellower and flatten. The lesions are usually solitary, although they can be numerous, with extracutaneous and systemic involvement. All organs and systems are susceptible. Systemic lesions may occur in the liver, lung, spleen, lymph nodes, bones, and the gastrointestinal tract [2]. JXG cases with systemic involvement is also characterized by frequent activating somatic mutations of mitogen-activated protein kinase pathway genes [7].

JXG is a clinical diagnosis that requires a skin biopsy to confirm. Classic histology of JXG shows a dense, well-demarcated, nonencapsulated lymphohistiocytic infiltrate of mononuclear cells, multinucleated giant cells with or without the features of Touton giant cells and spindle cells penetrating the dermis and subcutaneous fat [8]. The epidermis and adnexa are unaffected, though the epidermis can be thinned and, rarely, ulcerated. Touton giant cells characterized by a central wreath of nuclei and a peripheral rim of eosinophilic to foamy vacuolated cytoplasm with high lipid content.

The microscopic appearance varies according to lesion stage. Only histiocytes, or spindle-shaped fibrohistiocytic cells with lipid-free macrophages seen in early stage JXG. Touton multinucleated giant cells and vacuolated foamy macrophages, lipid-laden mononuclear cells are seen in more mature JXG in the superficial dermis [4, 8]. Immunostaining is crucial for confirming the diagnosis. JXG is positive for factor XIIIa, an interstitial dendrocyte marker, as well as CD68, CD163, CD14, and fascin. Generally, S100 and CD1a staining, the latter of which is specific for langerhans cells, both come out negative [8]. Dermoscopy revealed the "setting sun" pattern, which consists of a yellow-orange central area, a pale lesion with an erythematous halo surrounded by peripheral linear telangiectasias in mature JXG [4].

Prognosis and treatment for JXG is determined by the location of involvement. Solitary lesions are usually harmless, self-limiting and regress over time up to five years. Ocular JXG affects the iris primarily and is frequently isolated from cutaneous involvement. Therefore, routine referral to an ophthalmologist is not recommended unless patients under the age of two present with multiple micronodular (10 mm) JXG [5]. There are no prospective studies of the benefits of routine ophthalmologic evaluation for children with cutaneous JXG. Diagnostic testing, on the other hand, can be done based on the patient's clinical history.

All children with multiple cutaneous JXG lesions especially less than two years old should be screened for systemic JXG, which includes a CT or MRI of the brain, chest, and abdomen to rule out viscera-systemic involvement or the possibility of other benign tumors [9-11]. Systemic cases with histiocytes infiltrated into viscera increase morbidity and cause fatality as they are complicated by hepatic failure, severe hypercalcemia, progressive CNS disease, and myeloid leukaemia [12]. Systemic JXG involves vulnerable sites such as the brain or larynx, necessitating low-dose chemotherapy [4].

CONCLUSION

The majority of JXG patients experience benign, self-limiting symptoms that typically begin in childhood and have an unknown aetiology. Although it is a clinical diagnosis, it should still be referred to a specialist for further testing to rule out systemic involvement. Extracutaneous or systemic signs can occur in some patients, which are exceedingly rare but can result in considerable morbidity. The liver, eye spleen, lung, and central nervous system are the most prevalent and vulnerable extracutaneous site. Despite the low prevalence of systemic involvement, a thorough and comprehensive assessment is required to avoid disease complications and mortality.

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