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CLINICAL VIGNETTE

Multifocal Cutaneous-Systemic Juvenile Xanthogranuloma in an Infant: Report of a Rare Case

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Abstract

Juvenile xanthogranuloma (JXG) is a histiocytic disorder primarily occurring in childhood. Usually benign and self-limited, the most common presentation is a solitary cutaneous lesion. Extracutaneous involvement occasionally occurs with JXG. JXG with systemic involvement is rare and potentially fatal. We present an infant with multiple subcutaneous JXG and visceral involvement, who had an excellent clinical course without treatment.

Case Presentation

A 2-week-old healthy-term female neonate presented with numerous asymptomatic subcutaneous nodules. Physical examination was remarkable for 1-2cm firm, mobile, skin-colored subcutaneous nodules over the hip, chest, and scalp (Figure 1). Differential diagnosis included subcutaneous fat necrosis, neuroblastoma, leukemia cutis, and mastocytosis. A biopsy of a chest wall nodule revealed a dense histiocytic and eosinophilic infiltrate without Touton giant cells. The histiocytic cells were immunopositive for CD 163, Factor XIIIa, CD 68, and CD 14. S100 and CD1a were negative (Figure 2). The histologic findings were consistent with JXG. A CBC was within normal limits. On abdominal ultrasound, there were multiple focal lesions with targetoid appearance and vascularity noted within both lobes of the liver. The biliary system, pancreas, spleen, kidneys, and pelvis were normal. A PET-CT scan of the whole body revealed numerous subcutaneous nodules and a nodule in the liver that was FDG-avid. No treatment was initiated, and the patient was followed clinically along with serial CBCs and liver function tests. The child continued to develop scattered nodular lesions, some of which were noted to spontaneously reduce in size. Subsequent imaging studies showed no further internal organ involvement. She also developed 2 cafe-au-lait macules on her legs that remained stable with time. There was no ocular involvement on ophthalmologic examination. At 19 months of age, the child remains in good health with normal growth and development, and her JXGs are following the expected course with spontaneous involution.

Discussion

Juvenile xanthogranuloma (JXG) is the most common form of non-Langerhans cell histiocytosis. Typically affecting infants and young children, JXG may be congenital but frequently develops in the first year of life.^{1,2}

The etiology of JXG is unknown. Lesions represent proliferations of histiocytes that are believed to derive from dermal dendrocytes.³ More recently, Kraus et al.⁴ presented evidence of possible CD4+ plasmacytoid monocyte origin.

The most common site of involvement is the skin. Lesions may either be solitary or multiple, and frequently appear as firm, yellowish, tan-orange papulonodules. Although they may occur in any location on the body surface, JXG has a predilection for the head and neck, followed by the upper torso and the extremities.⁵

Rarely, extracutaneous and systemic-visceral manifestations may also occur. A solitary mass in the subcutaneous or deep soft tissue is the most common extracutaneous presentation. In two large series, this represented 5% and 4% of cases.^{6,7} The eye is the most frequently affected extracutaneous site, and ocular involvement is greatest in children less than 2 years of age and those with multiple skin lesions.⁵ Systemic-visceral disease may involve the central nervous system, intestine, heart, liver, lung, spleen, kidney, bone, and pancreas.⁶⁻⁸

Histologic findings vary depending on the age of the lesion. Early JXG shows a dense monomorphic histiocytic infiltration mimicking Langerhans cell histiocytosis (LCH). Older lesions contain foamy histiocytes with Touton giant cells. Late lesions show a prominent fibrohistiocytic proliferation.⁷ Special stains are used to differentiate JXG from LCH and non-LCH. Langerhans cells are S-100 and CD1a positive while histiocytes in JXG are strongly immunoreactive for vimentin, CD 68, and factor XIIIa.^{6,7}

Systemic JXG typically has a benign clinical course and does not require therapy. The historical treatment for JXG has been surgical excision for solitary skin lesions or observation for spontaneous regression. JXG can rarely become symptomatic and even be fatal, especially in cases with liver involvement.^{6,8} Chemotherapy regimens used to treat LCH may be effective in JXG with significant multisystem involvement.⁹

Juvenile chronic myelogenous leukemia has been found more frequently in patients with neurofibromatosis type 1 (NF1) and JXG.¹⁰⁻¹⁴ In a series by Cambiaghi et al.,¹⁰ among 14 patients under the age of 4 years who had JXG and NF1, none of the children developed hematologic malignancies during a follow-up period of 11 years. JXG occurring with six or more cafe au

laid spots more than 5 mm in diameter was a good marker for NF1 in the first few years of life.

Our patient is an infant with multifocal cutaneous-systemic JXG who exhibited a favorable clinical course with no complications. Juvenile xanthogranuloma should be considered in the differential diagnosis in a healthy young child presenting with multiple subcutaneous nodules. In cases with such presentation, we recommend determining the extent of internal organ involvement and monitoring for organ dysfunction.

Figures

Figure 1. A skin-colored subcutaneous nodule on the chest.

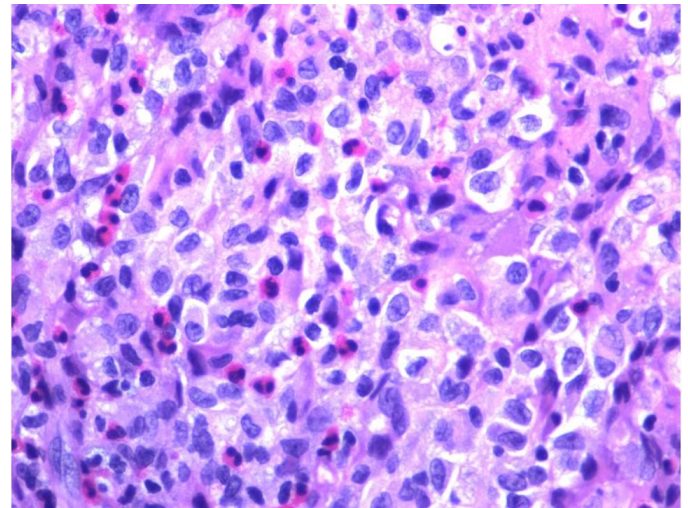
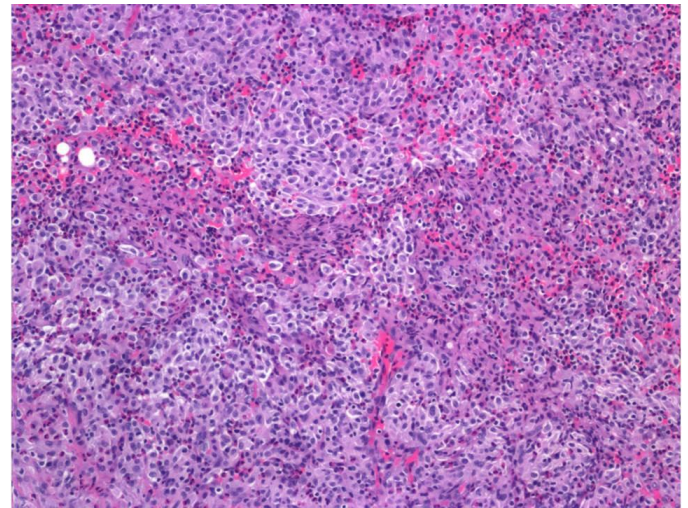
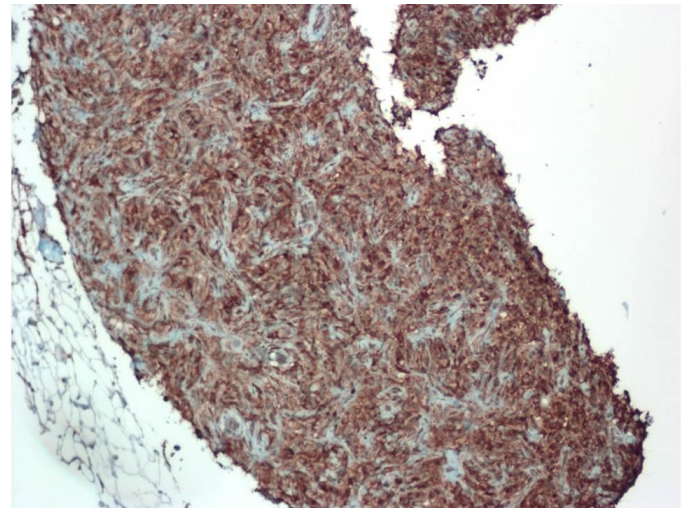
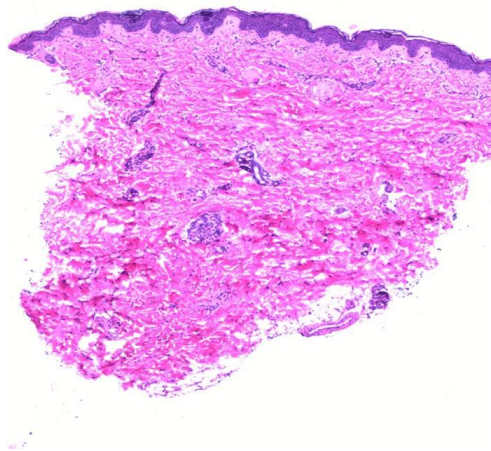
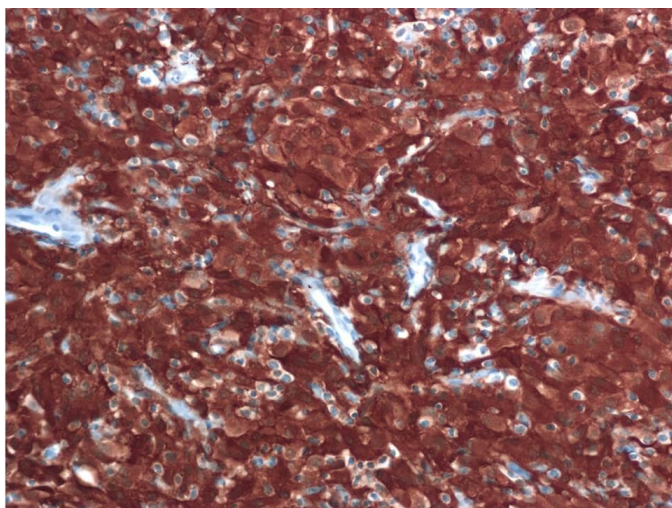


Figure 2. Histopathologic findings of a chest wall nodule seen on (A) scanning power, (B) low power magnification, (C) high power magnification. There was a dense dermal histiocytic and eosinophilic infiltrate, and (D) the histiocytes were immunopositive for CD68 and (E) Factor XIIIa. CD1a and S100 stains were negative.





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