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CASE IN POINT

PEER REVIEWED

Juvenile Xanthogranuloma: A Dome-Shaped Plaque on an Infant's Scalp

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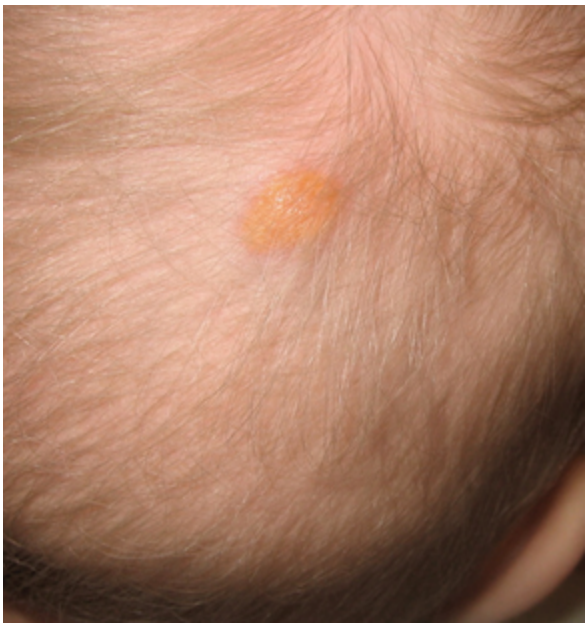
A 6-month-old Caucasian boy presented with an asymptomatic yellow-orange–colored lesion on the scalp, which was first noted at birth. The lesion was initially pink-red colored and had slowly increased in size over time. The infant was born to a 24-year-old primigravida at term following an uncomplicated pregnancy and a normal vaginal delivery. The parents were nonconsanguinous, and there was no family history of similar lesions or neurofibromatosis. The neonatal course was uneventful, and there was no history of trauma. The infant was otherwise in good health. A review of systems was unremarkable.

Physical examination revealed a solitary, well-demarcated, oval, yellow-orange–colored, dome-shaped plaque measuring 4 × 10 mm on the vertex. The lesion was purely cutaneous and not attached to any underlying structure. The rest of the examination results were unremarkable. There was no other cutaneous or systemic abnormality.

Based on the clinical appearance of the lesion (**Figure**), a diagnosis of juvenile xanthogranuloma was made. The patient's parents were reassured that the lesion was benign and that it would likely regress within a few years.



JUVENILE XANTHOGRANULOMA: AN OVERVIEW

Juvenile xanthogranuloma is a benign proliferative disorder of dendritic histiocytes that mostly affects the skin.[1] The condition was first described in 1905 by Adamson, who termed the entity "congenital xanthoma multiplex."[2] The term "juvenile xanthogranuloma" was coined by Helwig and Hackney to reflect the histologic appearance of lipid laden histiocytes and giant cells and its typical onset in childhood.[3]

Extracutaneous or systemic involvement is rare.[1] The eye is the most frequent extracutaneous site affected; the incidence of ocular involvement is estimated to be 0.3% to 0.5%.[4,5] This review will focus on cutaneous juvenile xanthogranuloma.

Epidemiology

Juvenile xanthogranuloma is the most common form of non-Langerhans cell histiocytosis.[5,6] The true incidence is not known but is likely higher than is generally appreciated. This is because of the trend of spontaneous resolution of the lesion, and because the lesion can be mistaken for other skin conditions. In the Kiel Pediatric Tumor Registry in Germany between 1965 and 2001, 129 (0.52%) of 24,600 patients were documented to have juvenile xanthogranuloma.[7] As the studied population was highly selected, the results are not generalizable. Juvenile xanthogranuloma is more commonly observed in Caucasians than in other ethnic groups,[5,8] and the disease typically affects infants and young children. Approximately 5% to 17% of juvenile xanthogranulomas occur at birth, and 40% to 70% appear during the first year of life.[1,5] Adult onset is reported infrequently.[8] In children, the male to female ratio is 1.5 to 1,[5,9] but there is no sex predilection in adults.[10-12] Most cases are sporadic.[13]

Etiopathogenesis

The exact etiopathogenesis is not known. It is believed that the condition results from a benign reactive proliferation and granulomatous reaction of dendritic histiocytes in response to an undefined stimulus.[5,8] There is a genetic predisposition, as the condition has been reported in monozygotic twins.[13]

Histopathology

Histologic findings include dense dermal infiltrate of foamy histiocytes and multinucleated cells with or without features of Touton giant cells.[1,8] Touton giant cells are characterized by a wreath of nuclei surrounded by a foamy cytoplasm and are pathognomonic of juvenile xanthogranuloma.[8] Immunohistochemistry shows that dendritic histiocytes of juvenile xanthogranuloma are positive for CD14, CD68, CD163, fascin, and factor XIIIa but are negative for CD123, CD1a, and S-100 protein.[9,10]

Clinical Manifestations

Typically, juvenile xanthogranuloma presents as a well-demarcated, dome-shaped, firm, rubbery, round-to-oval papule or nodule.[5,6,8] The size of the lesion usually ranges from 5 to 20 mm in diameter.[1,9] At first, the lesion is pink to red with a yellow tinge.[5,6] Over time, it acquires a yellow-brown or orange hue and will often flatten.[1,14] Occasionally, fine telangiectases can be seen on the surface of the lesion.[1,5,8] The lesion is usually asymptomatic[5] and is solitary in 60% to 82% of cases.[5] Sites of predilection include the head and neck, followed by the upper torso, the upper extremities, and the lower extremities.[5,8]

Atypical clinical presentations, such as generalized, lichenoid, infiltrative, keratotic, pedunculated, subcutaneous, clustered, linear, segmental, atrophic, plaque-like, horn-like, and giant variants have been reported.[5,14-19] These variants are rare and may pose a diagnostic challenge.

Diagnosis

The diagnosis is mainly clinical, based on the history (age of onset and natural history of spontaneous regression) and physical findings (color, shape, and location). The diagnosis can be aided by dermoscopy that shows the "setting sun" sign consisting of a yellow-orange central area surrounded by a peripheral pink or erythematous border with fine, branched, and/or linear vessels.[6] Additional features include "clouds" of paler yellow to orange-yellow globules that represent collections of lipid-laden histiocytes in the papillary dermis.[6] A referral to a dermatologist and/or skin biopsy for histology and immunohistochemical stains should be considered if the diagnosis is in doubt.

Differential Diagnosis

Differential diagnosis includes Langerhans cell histiocytosis, Rosai-Dorfman disease, dermatofibroma, keloid, nevus sebaceus, neurofibroma, mastocytoma, xanthoma, hemangioma, molluscum contagiosum, Spitz nevus, calcinosis cutis, pyogenic granuloma, granuloma annulare, and keratoacanthoma.[5,8,15]

Complications

Occasionally, a juvenile xanthogranuloma may ulcerate and bleed.[5,8,9] The eye is the most frequent extracutaneous site affected; ocular involvement is most common in children younger than 2 years with multiple skin lesions.[10,20] With ocular involvement, complications include spontaneous hyphema, uveitis, vitreous hemorrhage, iris heterochromia, glaucoma, cataract, and retinal detachment.[4,20]

There is a well-recognized association among juvenile xanthogranuloma, neurofibromatosis type 1, and juvenile myelomonocytic leukemia.[5,8,21] Despite the term "xantho-", the condition is not associated with hyperlipidemia or other metabolic abnormalities.[5,8]

Prognosis

In general, cutaneous lesions are self-limited and usually regress spontaneously within a few years.[1] The lesions may resolve completely or leave behind an area of residual hyperpigmentation, anetoderma, and atrophic scar.[1,5,8] Recurrence of juvenile xanthogranuloma has rarely been reported.[12]

Management

For cutaneous juvenile xanthogranuloma with onset in childhood, no treatment is necessary apart from reassurance and watchful observation. Surgical removal may be considered for cosmesis and for the purpose of obtaining a biopsy when the diagnosis is in doubt. Recurrence of the lesion after partial or complete surgical excision has rarely been reported.[22]

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