

## CASE REPORTS:

### **Juvenile xanthogranuloma: An atypical presentation in an adult**

Rachna Jagia MD, Osama Nourdeen MD, Manish Rijhwani MD

*Department of Dermatology, Farwaniya Hospital, Kuwait*

#### **INTRODUCTION**

Juvenile xanthogranuloma (JXG) is a well-recognized entity belonging to class IIa of non-Langerhan's cell histiocytosis. It is a benign cutaneous fibrohistiocytic lesion most often affecting infants and young children. Classically, it presents as solitary nodule or multiple yellowish papules with most common location on head and neck followed by upper trunk. Juvenile xanthogranuloma is rare in adults, in whom the peak incidence is in the late twenties to early thirties and most adult patients have solitary lesions.<sup>1</sup> To make a diagnosis beyond this classic description requires knowledge of the different possible clinical variants. We describe a classic case and a rather unusual clinical presentation in an adult highlighting the wide variation in presentation and importance of considering this entity in the differential diagnosis of multiple benign eruptive lesions in an adult.

#### **CASE 1**

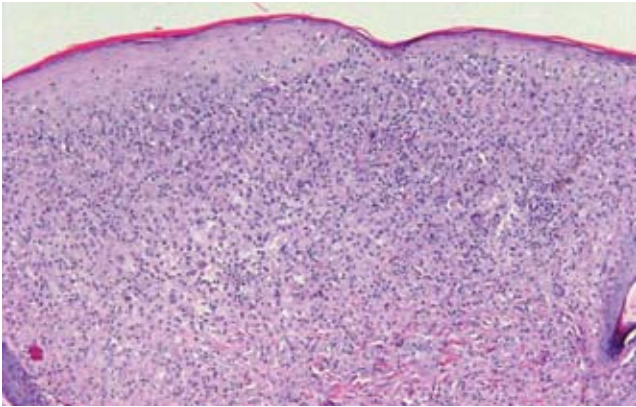
A 2 year-old girl presented with an asymptomatic solitary nodule on the scalp (Fig.1). The lesion had slowly enlarged since it was first noticed 7 months back. The child was otherwise healthy. On examination the lesion was a well circumscribed nodule, 1cm in diameter and located near the vertex of the scalp. It was yellow, shiny and firm with some evidence of telangiectasia on the surface. We kept the differential diagnosis

of giant molluscum, juvenile xanthogranuloma and nodular form of LCH. Routine investigation including complete blood count, lipid profile, liver, renal and function tests were normal. The patient under went an excision biopsy. The wound healed uneventfully leaving a minute scar. Histopathology showed upper dermal localized infiltrate. The infiltrate formed of histiocytes, lymphocytes and multinucleated giant cells (Fig.2). Some histiocytes show foamy appearance with variable sizes. Multi nucleated giant cells surrounded by foamy histiocytes and classic Touton giant cell could be appreciated. Immunocytochemical examination turned out to be positive for lysozyme, CD68, factor XIIIa and negative for S100 Protein. Based on clinical picture and biopsy the diagnosis of Juvenile xanthogranuloma (solitary nodular) was confirmed.



**Fig. 1** Scalp showing a well circumscribed yellow, shiny and firm 1 cm nodule with telangiectasias

*Correspondence: Dr. Rachna, MD, Department of Dermatology, Farwaniya Hospital, Kuwait*



**Fig. 2** Histopathology showed upper dermal localized infiltrate formed of histiocytes lymphocytes and multinucleated giant cells

## CASE 2

A 48 year-old male presented to our department with multiple disseminated cutaneous eruption that started 16 years ago on the trunk and 7 years ago on the face (Fig.3). The lesions were asymptomatic and followed a slowly progressive course. He had history of diabetes mellitus 4 years ago. The patient was otherwise healthy. General examination of all vital systems was normal. Cutaneous examination revealed numerous well-demarcated, firm, rubbery brownish yellow non-tender papulo-nodular lesions of different sizes over the face, ears, neck, front and back of the trunk (Fig.4). There were few lesions on the upper and lower extremities, predominantly over the elbows and buttocks. Examination of the mucous membranes, palms and soles was normal.

We thought of eruptive xanthoma, anthogranuloma, histiocytosis and neurofibroma as differential diagnosis and took punch biopsies from the papules on the face and the trunk. Skin biopsies (face and trunk) showed well-circumscribed exophytic nodule. The nodule was separated from the flat epidermis by clear zone formed mainly

of histiocytes with other inflammatory cells and multinucleated giant cells (Fig.5). There were numerous multinucleated giant cells with classic Touton giant cells within the infiltrate (Fig.6). Factor XIIIa was positive and S100 protein was negative on immunocytochemical examination. The diagnosis of multiple xanthogranulomas in an adult was made based on the clinical picture and histopathology. Routine investigation including complete blood count, lipid profile, liver, renal and function tests were normal. Blood sugar was 9 mmol/L. A peripheral smear examination ruled out any hematological malignancy. Radiograph of skull and chest and sonography of abdomen and pelvis were non-contributory. The patient was sent for an ophthalmologic checkup and fundoscopy, but no abnormality was detected. Looking at the benign course of disease and instances of spontaneous remission, the patient was reassured and called for regular yearly follow-up.



**Fig. 3** Numerous well-demarcated, brownish yellow papulo-nodular lesions of different sizes over the face, ears and neck

## DISCUSSION

Adamson first described this lesion in 1905 and

defined single or multiple cutaneous nodules in infancy as congenital xanthoma multiplex.<sup>2</sup> The lesions were designated nevoxanthoendothelioma by Mc Donagh in 1912.<sup>3</sup> Helwig and Macknay first coined the term juvenile xanthogranuloma in 1954,<sup>4</sup> as a benign, asymptomatic and common self-healing disorder of non-Langerhans cell histiocytosis (LCH), affecting mostly infants, children and rarely adults. Eighty per cent cases appear in the first year of life and 20-30% cases present at birth.<sup>5</sup> Lesions vary in size, but children younger than six months of age tend to present with multiple lesions with predominance in the head and neck. The male preponderance is much higher (12:1) in young infants with multiple skin lesions.<sup>6</sup>

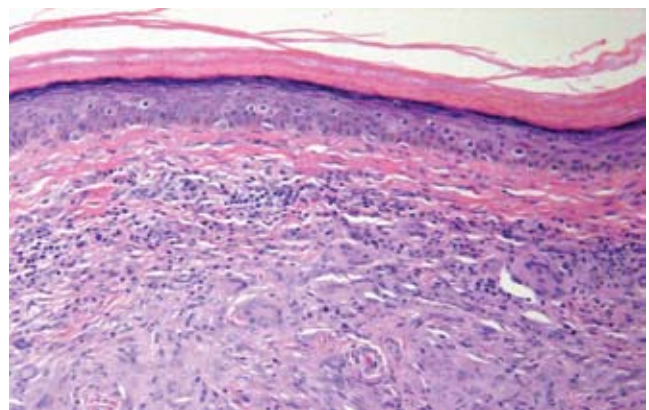
Three main clinical forms are recognized: a small nodular/papular (2-5 mm); large nodular (5-20 mm); and giant xanthogranuloma (more than 20 mm).<sup>5</sup> But unusual clinical variants like mixed form, subcutaneous form, JXG *en plaque* have been reported recently.<sup>5</sup> The clinical course tends to be benign, and lesions spontaneously regress over a period of months to years.<sup>7</sup> JXG may resolve completely or leave behind an area of residual hyperpigmentation, atrophy or anetoderma.<sup>7</sup> As previously noted, the most common areas of involvement are the head, neck and trunk, but JXG can affect almost any site of the body, including the penis, eyelid, lips, palms, soles, fingers and intraorally.<sup>7,8</sup> Intramuscular and subcutaneous JXG lesions have also been reported.<sup>8</sup> Extracutaneous sites of involvement are possible as well, including the eye, central nervous system, lung, liver and spleen.<sup>8</sup>

Histologically JXG contains a dense dermal

infiltrate of foamy histiocytes.<sup>7</sup> Other cellular infiltrates include giant cells, Touton cells, lymphocytes, neutrophils and eosinophils.<sup>7</sup> The presence of Touton cells are typical of JXG, but are not specific and may be absent.<sup>7</sup> Fibrosis may also be observed, especially in older regressing lesions.<sup>7</sup> Immunohistochemical findings are important and proliferating histiocytes are usually



**Fig. 4** Papulo-nodular lesions of different sizes over the trunk

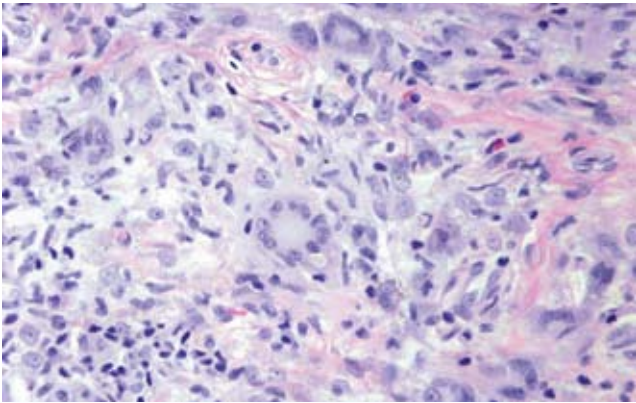


**Fig. 5** Nodule separated from the flat epidermis by clear zone formed of histiocytes, multinucleated giant cells with other inflammatory cells

negative for S-100 and CD1a and positive for HAM56 and factor XIIIa.<sup>7,8</sup>

Multiple xanthogranulomas are quite unusual in adults and that to occur in an eruptive manner is

quite rare. It is important to recognize multiple adult xanthogranulomas, because of its good prognosis and the absence of visceral involvement, therefore requiring no investigations or aggressive treatments, a very important observation made by Punithwavy *et al*<sup>9</sup> and Surajit *et al*,<sup>10</sup> in their case report of adult onset xanthogranuloma. Clinical backgrounds of patients with adult-onset xanthogranuloma are somewhat different from those of patients with juvenile xanthogranuloma, but the histological findings of both forms of the disease are identical.<sup>10</sup> Although there is benign natural history of adult onset XG, there are reports of associated hematologic malignancy



**Fig. 6** Numerous multinucleated giant cells with classic Touton giant cells within the infiltrate

and three such cases have been associated with hematological malignancy (lymphocytic leukemia and monoclonal gammopathy).<sup>5</sup>

It has been postulated that JXG represents a reactive granulomatous response of histiocytes to a yet unidentified stimulus. Evaluation for extracutaneous JXG is not indicated, unless there are symptoms or findings suggesting their presence, as they also disappear spontaneously.<sup>10</sup> Differential diagnosis includes molluscum contagiosum, cryptococcosis, benign cephalic

histiocytosis, generalized eruptive histiocytosis, xanthoma disseminatum, papular xanthoma and neurofibromas. Usually no treatment is needed as it subsides spontaneously, however in symptomatic cases chemotherapy may be needed. It is our recommendation that adult form of xanthogranuloma should always be thought of as a differential in any case of multiple eruptive disseminated papulo-nodular lesions in an adult.

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