

Case Report

Coexistence of juvenile xanthogranuloma and café-au-lait macules in a boy presented with multiple yellowish papules and brownish macules

男嬰患幼年黃色肉芽腫並偶發咖啡牛奶斑呈多發性黃色丘疹及棕色斑疹

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An eleven-month-old boy presented with increasing number of yellowish papules on scalp, trunk and limbs soon after birth. Skin biopsy revealed juvenile xanthogranuloma. He was also found to have multiple café-au-lait macules. The clinical course, complications and associations of juvenile xanthogranuloma with neurofibromatosis were discussed.

十一個月大男嬰於出生後不久在其頭皮、軀幹及四肢出現越來越多的黃色丘疹。皮膚切片活檢顯示幼年黃色肉芽腫。身上並發現多片咖啡牛奶斑。本文對幼年黃色肉芽腫的臨床表現、併發症及其相關事項予以討論。

Keywords: Café-au-lait macules, juvenile xanthogranuloma, neurofibromatosis

關鍵詞：咖啡牛奶斑，幼年黃色肉芽腫，神經纖維瘤病

Case report

An eleven-month-old boy was referred for a seven-month history of skin papules on scalp, face,

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hands and trunk. The boy was born full term with unremarkable prenatal and postnatal history. He had an elder sister who was not affected. There was no family history of inherited disease. The boy had otherwise normal developmental milestone.

The lesions were in the form of small papules of 2-3 mm in diameter initially which gradually increased in size. The first lesion was found on the right first finger web. Later, lesions began to appear on the scalp, left side of cheek, trunk and buttock. Physical examination revealed multiple papules, 3-8 mm in diameter, scattered mainly on the scalp (Figure 1), trunk and upper limbs. These papules, which were dome-shaped with smooth surface and a yellowish hue, were firm in

consistency. There was an 8 mm skin-coloured dermal papule in the right first finger web. Multiple café-au-lait macules were found on the trunk and limbs with the largest one being 1.5 cm in diameter (Figure 2). There were no other features of neurofibromatosis.

The differential diagnoses of the papular lesions were juvenile xanthogranuloma, other non-

Langerhans cell histiocytosis, Langerhans cell histiocytosis, eruptive xanthoma, sebaceous naevus, neurofibroma, cutaneous mastocytosis and molluscum contagiosum.

Skin biopsies were performed for the scalp and right finger web lesions. Both specimens showed a dense aggregate of foamy histiocytes and Touton giant cells in the dermis (Figures 3 and 4).



Figure 1. Multiple dome-shaped yellowish papules on the scalp.

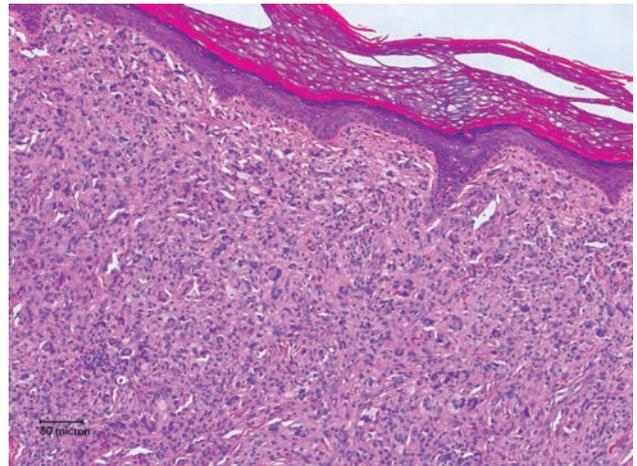


Figure 3. Note the presence of grenz zone and tumour cells with abundant pale cytoplasm mixed with scattered lymphocytes. (H&E, low power view)



Figure 2. Multiple café-au-lait macules on the back.

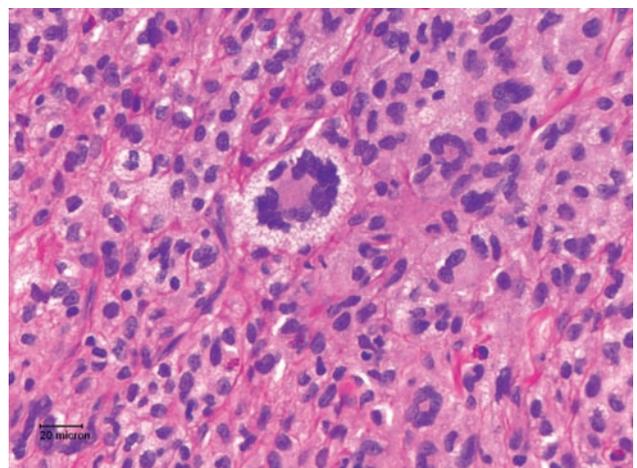


Figure 4. Classical Touton type giant cell is shown in the centre. Note the characteristic background tumour cells with abundant pale cytoplasm and folded nucleus. Eosinophils are present in the right lower field. (H&E, high power view)

The lesions were consistent with juvenile xanthogranuloma. This child was suspected to have neurofibromatosis type 1 though he had only one diagnostic feature – six or more café-au-lait macules larger than 5 mm in diameter, according to the diagnostic criteria by the National Institutes of Health Consensus Development Conference on Neurofibromatosis. The association of juvenile xanthogranuloma and neurofibromatosis will be elaborated in the discussion section.

Discussion

Juvenile xanthogranuloma (JXG) is the most common non-Langerhans cell histiocytosis. It is usually found in infants and children although many adult cases were documented. It was first reported in 1905 and the term juvenile xanthogranuloma was coined in 1954. Cutaneous JXG often presents with solitary lesion. A slight male predominance (1.5:1) was observed in children in a recent analysis.¹ Most JXG appear in the first year of life (>70%) and about 15% appear at birth.² A peak incidence in young adults in the late twenties and early thirties was observed.³ There were no familial cases reported.

There are two common clinical variants of cutaneous JXG: a micronodular form and a macronodular form.⁴ The micronodular form presents with multiple pink to red-brown papules, 2-5 mm in diameter, which rapidly become yellowish while the macronodular form presents with one or few large nodules with a size of 10-20 mm in diameter. Both presentations frequently coexist. The site of predilection is the head and neck, followed by upper torso, upper extremities and lower extremities. Unusual clinical presentations such as oral lesions, hyperkeratotic nodules, pedunculated lesions, giant tumours larger than 2 cm, lichenoid eruption and reticulated eruption had been reported.

Extracutaneous involvement was rarely reported. The most frequent and important extracutaneous

site involved was eye. The incidence of ocular involvement in patients with cutaneous JXG was estimated to be 0.3-0.4%. More than 40% of patients with eye disease had multiple skin lesions.⁵ Ocular involvement often occurs during the first two years of life.⁵ Most eye lesions involve the iris and are unilateral. Serious complications such as spontaneous hyphaema and glaucoma can cause blindness.

Other extracutaneous involvement such as lung, liver, central nervous system, kidney, heart and other visceral organs had been reported. Almost all patients with visceral tumours had multiple concurrent skin lesions that made the diagnosis of systemic lesion not difficult.

JXG had no associated metabolic disorders such as diabetes insipidus and hyperlipidaemia. JXG was found to associate with pigmentary abnormalities such as café-au-lait macules and neurofibromatosis type 1 (NF1).⁶ In addition, it is well-documented that JXG is associated with childhood leukaemia, most commonly juvenile chronic myelogenous leukaemia (JCML).⁷ Most patients had JXG noted before or at the diagnosis of JCML. The JXG is usually multiple in children presented with JCML.

There had been reports about the triple association between JXG, NF1 and JCML.^{1,8} In a recent review and analysis, the observed frequency of triple association is 30-fold to 40-fold higher than expected.¹ The risk of JCML in patients with JXG and NF1 was 20-fold to 32-fold higher than patients with NF1 alone.¹ The prevalence of a family history of NF1 was found to be higher in patients with JCML. A male predominance was also found in patients with this triple association.

The histology of JXG is characterised by a dense nonencapsulated histiocytic infiltrate in the dermis. Extension into subcutis and fascia can occur. The epidermis and adnexal structures are spared. Touton giant cell is characteristic but not

pathognomonic of JXG. The morphology of cellular infiltrate changes with evolution of the lesion. In early lesion, the histiocytes with small degree of lipidisation mixed with scanty inflammatory infiltrate. In older lesion, the histiocytes had a vacuolated foamy cytoplasm with presence of more inflammatory infiltrates. In regressing lesion, fibroblast proliferation and fibrosis were seen. Immunohistochemical staining is important to distinguish between non-Langerhans cell and Langerhans cell histiocytosis. Histiocytes of JXG are negative for CD1 α , S-100 protein and Mac-387. They are positive for HAM56, HHF35, CD68 (KP1), vimentin and factor XIIIa.

JXG is generally considered as a benign condition and no treatment is necessary. Skin lesion usually regresses within three to six years² with resulting area of hyperpigmentation or anetoderma. Recurrence had been documented after complete or incomplete excision. Extracutaneous lesions also regress. The main concern lies in the ocular lesions where risk of complications is high. Early treatment of ocular lesions is necessary to prevent complications such as glaucoma and hyphaema. Usual treatment involves using topical, systemic and intralesional steroid. Low-dose noncataractogenic radiotherapy may be used when steroid is contraindicated or non-responsive. Visceral lesions will be tackled only if vital functions are compromised.

In conclusion, JXG is a benign, self-limiting non-Langerhans cell histiocytosis. Extracutaneous involvement is rare but clinicians need to be aware

of ocular involvement as there is a high risk of complications leading to blindness. However, early referral to ophthalmologist is only necessary for those with multiple cutaneous lesions or age younger than two years. It is also advisable that an infant with JXG and café-au-lait macules suspected to have NF1 should be monitored for the development of JCML or other haematological malignancy especially if the patient is male and has a family history of NF1.

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