

Hemosiderotic Juvenile Xanthogranuloma

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Abstract: Juvenile xanthogranuloma is a non-Langerhans cell lesion mostly limited to the skin but occasionally presenting in extracutaneous locations or associated with systemic conditions. Lesions need to be distinguished mainly from dermatofibroma, xanthoma, Langerhans cell histiocytosis, or reticulohistiocytoma. Herein, we present a hemosiderotic variant of juvenile xanthogranuloma in a 12-year-old girl, which we have not found described in literature. The lesion presented at the back of the scalp as a slowly growing yellowish polypoid lesion showing occasional bleeding. The histopathological examination demonstrated a cellular infiltrate expanding the dermis, with a Grenz zone and with no remarkable changes in the overlying epidermis. The papule was made of mononucleated macrophages, many of which were xanthomatous. There were some Touton giant cells. The lesion was intermingled with a mild inflammatory infiltrate comprising lymphocytes, plasma cells, neutrophils, and some eosinophils. Many of the macrophages contained abundant cytoplasmic deposits of iron. The macrophages expressed CD68 and CD163, whereas they failed to express S100 protein, CD1a, and Langerin.

Key Words: juvenile xanthogranuloma, hemosiderotic xanthogranuloma, dermatofibroma

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INTRODUCTION

Juvenile xanthogranuloma (JXG) is a non-Langerhans cell lesion mostly limited to the skin but occasionally presenting in extracutaneous locations^{1–5} or associated with systemic conditions.^{6–11}

In the skin, JXG presents as single or multiple¹² yellowish or reddish papules or nodules (rarely plaques⁶ or large masses¹³), mainly located on the head and neck. JXG presents mainly in the first 2 decades of life,⁶ and in fact, it is very common in children.^{14,15}

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Lesions should be distinguished mainly from dermatofibroma, xanthoma, Langerhans cell histiocytosis, or reticulohistiocytoma, all of which show distinctive histopathological features.

Although some histopathological variants of JXG have been described—such as the deep form¹⁶ or the mitotically active variant^{17,18}—we present a hemosiderotic variant of JXG, which we have not found described in literature.

CASE REPORT

A 12-year-old girl was brought to the Dermatology service by her mother, complaining of a slowly growing lesion on the back of the scalp which she noticed a few months ago and was causing her significant discomfort when she combed her hair. Occasional trauma-induced bleeding was reported. Examination revealed a yellowish, pedunculated, and slightly crusted lesion measuring 5 mm in diameter. Clinically, the lesion was considered to be an epidermal nevus and curettage was undertaken. Common laboratory studies did not reveal any alteration, including lipid profile.

Histopathologically, there was a cellular infiltrate expanding the dermis, but sparing the papillary dermis and with no remarkable changes in the overlying epidermis (Fig. 1A). The papule was made of mononucleated macrophages, many of which were xanthomatous (Fig. 1B). Some of the xanthomatized cells were multinucleated, and there were some Touton giant cells (Fig. 1C). The lesion was intermingled with a mild inflammatory infiltrate made of lymphocytes, plasma cells, neutrophils, and some eosinophils (Fig. 1C). Many of the macrophages contained abundant cytoplasmic iron (Fig. 1C), stained by Perls histochemical reaction (Fig. 1D). The macrophages expressed CD68, CD4, CD31, CD45, lysozyme, and CD163, whereas they failed to express HMB45, S100 protein, CD1a, factor XIII, and Langerin. With all these histological findings, we categorized the lesion as hemosiderotic JXG.

DISCUSSION

JXG is a non-Langerhans cell lesion comprising monocyte-derived macrophages which accumulate cholesterol in their cytoplasm.¹⁹ Despite this, the condition has never been related to any metabolic disorder.

The disease occasionally involves internal organs,²⁰ mostly when it presents as multiple cutaneous nodules^{21–24} but sometimes without concomitant cutaneous involvement. Ocular involvement is one of the most common associated complications presenting as glaucoma, bleeding, or even blindness.²⁵

JXG is quite constant in its histopathological features. The amount of fibrosis can vary though, sometimes accompanied by a vague storiform pattern.¹⁷ Touton cells are a common finding in the cutaneous lesions,⁶ although they can be missing, especially in early lesions. Additional features are a chronic inflammatory infiltrate and mast cells.²⁶ Rarely,

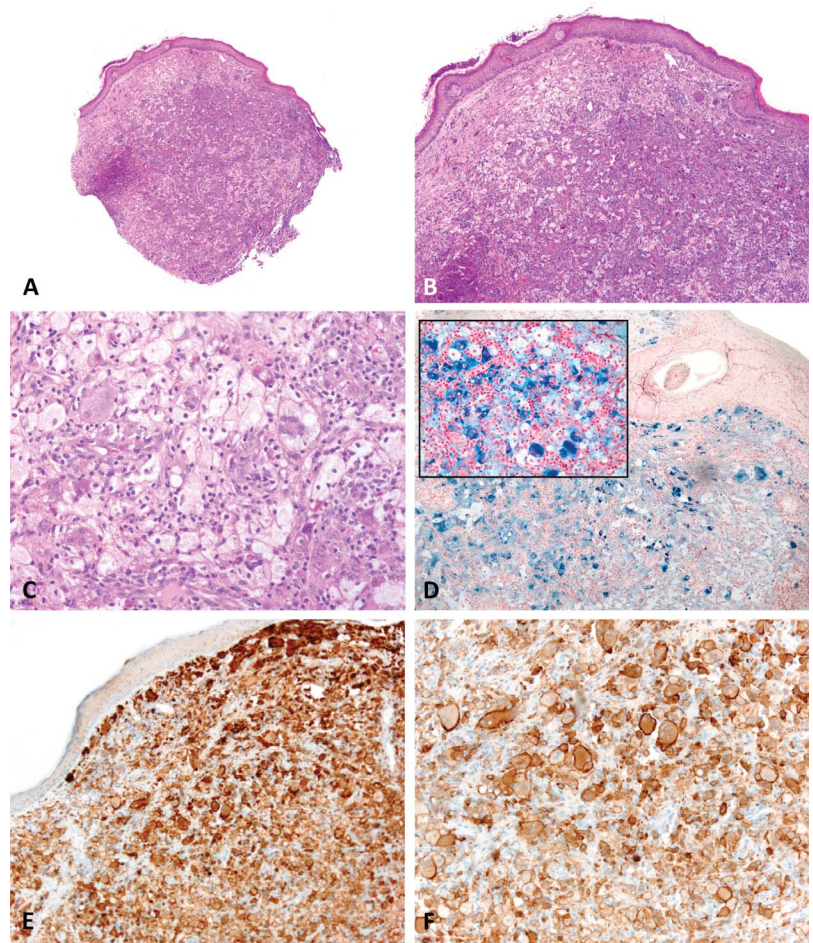


FIGURE 1. Proliferation of macrophages expanding the dermis, with a Grenz zone and with no remarkable changes in the overlying epidermis (A). The papule was made of mononucleated macrophages, many of which were xanthomatous (B). Some of the xanthomatized cells were multinucleated with some Touton giant cells (C). The lesion was intermingled with a mild inflammatory infiltrate made of lymphocytes, plasma cells, neutrophils, and some eosinophils (C). Some of the macrophages contained abundant cytoplasmic deposits of iron, a fact that was already remarkable in the hematoxylin–eosin stain (C). This, however, was most noticeable with the Perls histochemical stain (D). E and F, Immunoexpression of CD163 by the lesion.

some histopathologic variants have been described. These include the deep JXG,¹⁶ or the mitotically active variant.^{17,18}

We have found no previous cases of JXG with such a hemosiderotic change. In a study of 57 cases, Sonoda *et al* found “fine granules of iron in the tumor cells of the subepithelial region in 2 of the 15 lesions examined” with Prussian blue stain.¹⁷ A certain amount of iron deposits seems to be, in fact, something common in JXG.²⁶ However, such deposits are obviously too far from the siderotic change that we found in our case. The history of occasional bleeding in our patient is the most likely explanation for the presence of iron in the cytoplasm of the cells.

Other histopathologic diagnoses have to be considered for a lesion made of macrophages with such a prominent siderotic deposition. Dermatofibroma is one of them. In fact, there is a hemosiderotic variant (as well as a xanthomatous variant) of dermatofibroma.^{27,28} Each one representing less than 5% of dermatofibromas.²⁷ We have not found any description of a dermatofibroma combining intense hemosiderotic deposits together with widespread xanthomatous changes. Nevertheless, we do not interpret our case as a dermatofibroma: none of the main features of a dermatofibroma were evident in this lesion. There was not a remnant of storiform spindle cells. Sclerotic peripheral bundles of collagen trapped at the periphery of the lesion were not found. There

was no acanthotic hyperplastic epidermis or hyperpigmentation of the basal cell layer which is so common in dermatofibroma in contrast to JXG in which there is elongated rete ridges in a low percentage of cases.¹⁷ In addition, the presence of a more prominent inflammatory infiltrate in xanthogranuloma, which often includes eosinophils, as well as the evidence of multiple multinucleated Touton giant cells, helps to make the differential diagnosis.^{29–31}

In a very recent report, Sandell *et al*³² characterize the immunophenotype of solitary JXG with particular emphasis in the differential diagnosis with benign fibrous histiocytoma. Among the markers that were expressed by a high percentage of JXG but were negative in benign fibrous histiocytoma, the authors mentioned CD4, CD163, CD31, CD41, and lysozyme, all of which were positive in our case. Factor XIIIa (negative in our case) was expressed in 88% of their JXG.³²

The clinical data are also important in the differential diagnosis. In contrast to dermatofibroma—which is very rare in children^{27,33}—JXGs mainly present in children and they are sometimes evidenced at birth. JXG usually occurs on the head, neck and upper trunk,¹⁵ whereas dermatofibromas present predominantly on the legs and arms with very few cases on the head and neck.^{27,33} The xanthomatous variant of dermatofibroma shows even a higher tendency than other variants to present on the legs.²⁹

Langerhans cells have a very different morphology. They are either ovoid or elliptic, and they commonly show grooved, folded nuclei with inconspicuous nucleoli.³⁴ Langerhans cells do not accumulate lipids within their cytoplasm. Obviously, the immunohistochemical phenotype is crucial in identifying Langerhans cells, which express CD1a, S100 protein, and Langerin,^{35,36} all of which were negative in our case.

Xanthosiderohistiocytosis is a rare non-Langerhans cell variant of xanthoma disseminatum which presents with diffuse dark-brown infiltrations in the skin.³⁷ The clinical presentation is therefore different to our case, with multiple disseminated lesions. The individual lesions, however, are made of histiocytes, with a considerable amount of hemosiderin in their cytoplasm.

In conclusion, we present the hemosiderotic JXG as a histopathological variant not to dismiss just because of the outstanding dermal siderotic deposits.

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