Xanthomatous nevus: A potential new entity

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INTRODUCTION

Xanthomas are non-neoplastic, localized lipid deposits within the dermis and subcutis. They can present as papules, plaques, or nodules. Different clinical variants include eruptive, tuberous, tendinous, papular, plane, and verruciform xanthomas. They can occur at any age and can be idiopathic or suggest the presence of an underlying disorder of lipoprotein metabolism. The association between a xanthoma and congenital melanocytic nevus (CMN) has never been reported. Here, we present the first case and hypothesize on its etiology.

CASE REPORT

A 20-year-old girl presented with a papular lesion in her right arm emerging during childhood, with no known modification or trauma over the past years. Physical examination revealed a single, yellow, tender papule, surrounded by a pigmented melanocytic nevus, sized 0.5 × 0.7 cm (Fig 1, *A*). Dermoscopy showed a slightly atypical pigmented network with a globular pattern, centered by a distinct area with a homogeneous yellow pattern (Fig 1, *B*).

The past medical history was significant for heterozygous familial hypercholesterolemia treated with atorvastatin 10 mg per day. She was diagnosed at the age of 12 and had no previous history of xanthomas or cardiovascular disease. Despite treatment, recent cholesterol levels were elevated, with total cholesterol of 330 mg/dL, a high-density lipoprotein of 69 mg/dL, and a low-density lipoprotein of 246 mg/dL. The differential diagnosis included juvenile xanthogranuloma, xanthoma, balloon cell melanoma/nevus and, given the patient's comorbidity, lipidized fibrous histiocytoma. Histopathologic examination showed a dome-shaped lesion constituted by an intradermal nevus with a central core of medium-to-large epithelioid cells with foamy cytoplasm, without any pigment, located in the papillary dermis (Fig 2, *A-C*). Melanocytes extend around skin appendages, confirming the congenital nature of the nevus (Fig 2, *C*). Neither atypia nor mitoses were identified. The overlying epidermis was thinned, and a mild superficial perivascular lymphohistiocytic infiltrate with few reactive spindle myofibroblasts (Fig 2, *D*, *inset*) was observed at the border between the deep melanocytic component and the foamy cells. Immunohistochemical staining for CD68 and MART1 revealed a cell population consisting of both melanocytes (MART1 +) and aggregates of foamy histiocytes (CD68 +) located in the central and superficial part of the lesion. Thus, a diagnosis of congenital intradermal nevus with a superimposed xanthoma was made, confirmed also by immunohistochemical staining for MART1 and CD163 (Fig 2, *D*).

Abbreviation used:

CMN: congenital melanocytic nevus

DISCUSSION

The occurrence of 2 different lesions is known as collision tumor. Most of these cases represent a coincidence; however, certain combinations may indicate causality.[1] Diagnosis of collision lesions is challenging, especially when a pigment network raises a suspicion of malignant transformation.[2]

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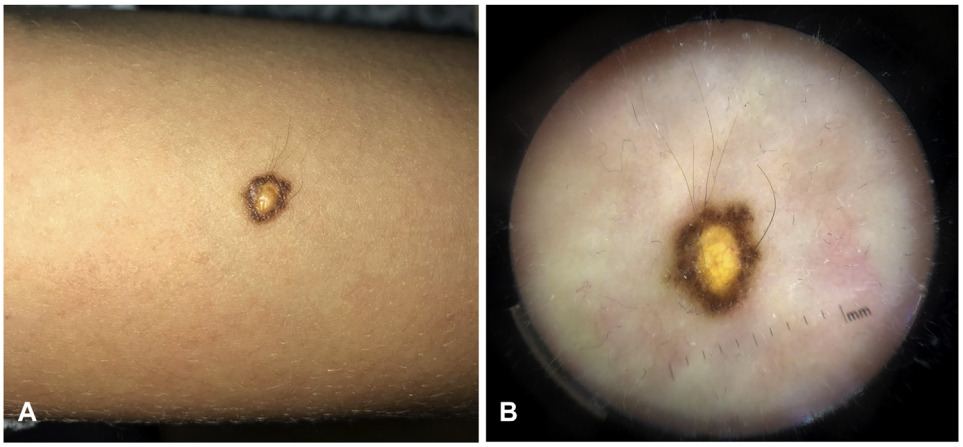

Fig 1. A, Clinical picture of the papular lesion in the right arm of the patient, showing a pigmented lesion centered with a yellowish deposit. **B,** Dermoscopy of the same lesion showing an atypical pigmented network with a globular pattern and with a homogenous yellowish area in the center.

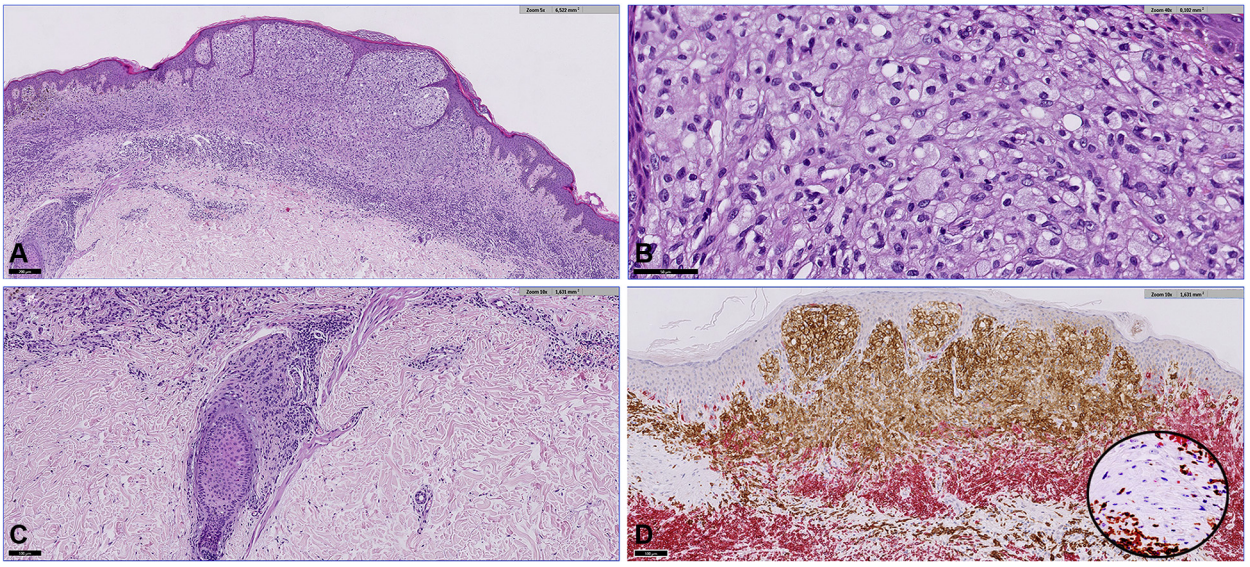

Fig 2. A, Dome-shaped lesion characterized by melanocytic nevus and foamy cells. A mild superficial perivascular lymphohistiocytic infiltrate is also observed at the edges (Hematoxylin-eosin stain; original magnification, ×5). **B,** Central area of the lesion showing medium-sized cells with large and foamy cytoplasm (Hematoxylin-eosin stain; original magnification, ×40). **C,** Congenital component of the lesion with melanocytes around a hair follicle (Hematoxylin-eosin stain; original magnification, ×10). **D,** Double immunohistochemical staining (original magnification, ×10) highlighting the histiocytic CD163 (*brown 3,3′-Diaminobenzidine*) and melanocytic MART1 (*red-magenta*) components. *Inset:* spindle myofibroblasts are interspersed at the border of the lesion.

Histopathologically, the differential diagnosis includes xanthomas, juvenile xanthogranuloma, balloon cell nevus, and lipidized fibrous histiocytoma. Skin xanthomas are characteristic of heterozygous familial hypercholesterolemia, a common, but largely underdiagnosed genetic disease, the diagnosis and optimal treatment of which during childhood are mandatory to prevent the onset of premature atherosclerotic cardiovascular disease.[3] Xanthomas are deposits of foamy macrophages with phagocytized lipid material.[4] The exact mechanism of deposition is still not well understood. A high

plasma concentration of lipids could lead to increased extravasation of lipoproteins through the vascular walls of dermal capillaries to the interstitial space,[5] where monocytes and macrophages phagocytize low-density lipoprotein aggregates and lipid complexes, forming foam cells,[5,6] which accumulate in the skin in an atherosclerosis-like process.[5] In normolipidemic patients, the expression of local tissue factors in conditions of dermal tissue alterations, such as dermatitis, tumors or scars, can lead to a xanthomatization of the cells that constitute the dermal infiltrate.[7]

The term "dystrophic xanthoma" has been proposed in the past to describe these lipid-rich foam cells that accumulate within damaged skin.[7] Furthermore, chronic inflammatory dermatoses could manifest an increase in epidermal lipids due to both tissue damage and subsequent leakage from vascular walls and lipid biosynthesis by the squamous epithelia.[8] We hypothesize that a chronic inflammatory lymphohistiocytic infiltrate, which is sometimes found in the early stages of evolving melanocytic nevus,[9] could have fostered the foamy cells deposition above the CMN, in a background of a high concentration of serum lipids. If the occurrence of a xanthomatous growth within a CMN gives rise to the clinical suspicion of malignant transformation, diagnosis is histological and confirmed by the immunophenotype, as the balloon cells stain positive for HMB-45 and MART1 and negative for CD68 and CD163.[10]

In conclusion, since xanthomas occurring in a young patient could represent an error of lipid metabolism, we suggest that the finding of a xanthomatous lesion within a CMN should prompt assessment, including family history for lipid disorders, which may allow for early diagnosis and treatment.

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Conflicts of interest

None declared.

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