Multiple Adult-Onset Xanthogranuloma: A Case Report

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ABSTRACT

Multiple adult-onset xanthogranuloma (AXG) is an unusual presentation of non-Langerhans cell histiocytoses. We have described the case of a 79-year-old patient who presented with the recent eruption of multiple cutaneous nodules over the neck, trunk and arms without any visceral involvement and the histopathological finding consistent with xanthogranuloma. Although rare, AXG remains one of the differential diagnoses of cutaneous xanthomatous disease in adults.

Keywords: Juvenile xanthogranuloma, non-Langerhans cell histiocytosis, adult-onset

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INTRODUCTION

Non-Langerhans cell histiocytosis (NLCH) represents a broad group of different disorders of proliferation of non-Langerhans cell histiocytes. The clinical spectrum of NLCH varies from benign, self-healing to systemic, progressive forms. The most common variant among those who present with a self-healing clinical pattern is juvenile xanthogranuloma (JXG). Most of the JXG cases occurred since birth or within the first year of life with typically a solitary lesion, and very rare adult cases with multiple cutaneous lesions have been reported.[1,2] Recognition of the clinical presentation with particular histological appearance and immunophenotype are required to differentiate JXG from the other diseases in its spectrum. Here, we report a case of multiple AXG without significant systemic involvement.

CASE REPORT

A 79-year-old Thai male presented with a history of gradually progressive multiple papules over his neck, trunk and extremities over a period of three months. He had hypertension and benign prostatic hypertrophy, but otherwise was in good health. Dermatological examination revealed multiple discrete shiny yellowish to erythematous dome-shaped papules on the neck, axillae, trunk, and arms. Bony prominences, palms, soles, and oral mucosa were spared (Fig 1a, 1b). Other physical examinations and review of systems were unremarkable. Laboratory investigations were within normal limits for complete blood count, blood chemistry, lipid profile and chest x-ray. Skin biopsy taken from a lesion at his right flank showed dense histiocytic cell proliferation which extended from below the overlying effaced epidermis to mid-dermis and was composed of foamy histiocytes admixed with some Touton-type multinucleated giant cells and some spindle-shaped histiocytes in slightly fibrotic stroma. There were chronic inflammatory cells, mostly lymphocytes, dispersed throughout the lesion. The subcutaneous tissue was unremarkable (Fig 2a, 2b). Immunohistochemically, the tumor cells were strongly marked with CD68 and were negative for S-100 and CD1a. Therefore, the diagnosis was made as multiple adult-onset xanthogranuloma (AXG). The patient was scheduled for serial follow up for systemic involvement. None of the specific treatments was initiated due to the benign course of the disease and lack of satisfactory treatment options.

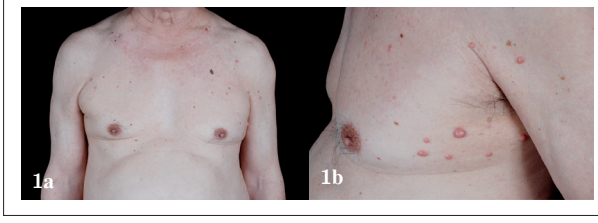

Fig 1a, 1b. Multiple yellowish to erythematous dome-shaped papules on neck, axillae, trunk, and arms.

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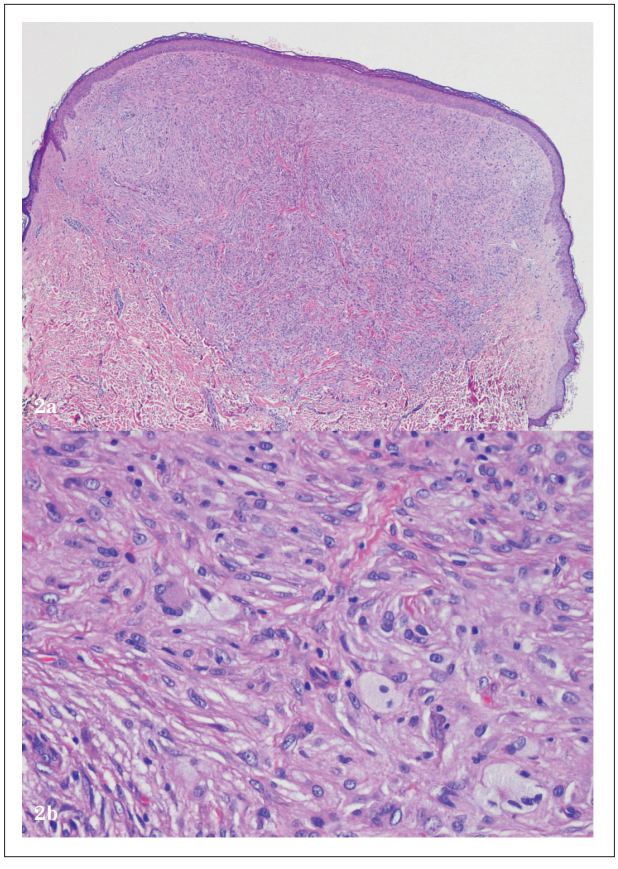

Fig 2a (H&E, x40), 2b (H&E, x400). A circumscribed tumor with proliferation of foamy histiocytes, multinucleated Touton giant cells, some spindle-shaped histiocytes and lymphocytes.

DISCUSSION

Multiple adult-onset xanthogranuloma (AXG) is a rare entity with an indolent clinical course and a good prognosis without visceral involvement.[1,2] AXG shows histological and immunohistochemical features similar to those seen in juvenile xanthogranuloma (JXG). Unlike other cutaneous xanthomatous diseases, dyslipidemia, paraproteinemia, or other metabolic conditions are uncommonly related to both JXG and AXG.[1,2]

According to the WHO 2008 classification of histiocytic and dendritic cell neoplasms, disseminated juvenile xanthogranuloma (JXG) has been proposed as a new entity of histiocytic dendritic cell neoplasms among others including histiocytic sarcoma, tumors derived from Langerhans cells, interdigitating dendritic cell sarcoma, follicular dendritic cell sarcoma, and other rare dendritic cell tumors.[3] Clinical course, histology, and laboratory profiles are necessary for differentiating among those subtypes. Our patient had clinical, histology and laboratory findings which were mostly supportive of AXG. Almost 80% of xanthogranuloma present within the first year of life, and about 20% of cases present at birth. Xanthogranuloma in adults usually have a solitary lesion while multiple eruptive type has been described as a rare manifestation.[4] The etiology of AXG and JXG has not yet been confirmed. Some authors postulated a hypothesis that the condition was related to a granulomatous response of histiocytes to undefined stimulus that leads to the increase of lipid uptake of macrophages.[5]

JXG arises asymptomatically either on the face and neck or scattered throughout the body. Lesions are well defined red-brown papules and nodules which rapidly turn yellowish. Ocular involvement is the most common extracutaneous manifestation presented with hyphema and glaucoma.[4,6] Other organ involvements such as lung, liver, nervous system, bone, kidneys, colon, and genitourinary system have also been reported.[4] The cases of adult-onset JXG with bone and lung involvement is referred to as Erdheim-Chester disease (ECD).[3,4] Systemic symptoms can be present depending on organ involvement such as dysphagia, and dyspnea. Moreover, diabetes insipidus due to xanthoma cells infiltration of pituitary glands (40-50%), osteolytic lesions, multiple myeloma, Waldenstrom macroglobulinemia and monoclonal gammopathy can be observed. Chronic bone pain is the hallmark of ECD.[4-6] Twenty percents of papular JXG occur together with café-au-lait macules and can be considered as a great indicator to make the diagnosis of neurofibromatosis type 1 (NF-1) during the first year of life even without other reliable diagnostic criteria.[4] Furthermore, JXG in children with NF-1 has been reported to be a marker for developing juvenile chronic myeloid leukemia (CML).[4] In contrast, adult-onset XG has a benign course with rare extracutaneous involvement. Most of the adult cases have persistent lesions without spontaneous resolution. There has been no report of abnormal laboratory tests associated with adult XG except for 6 cases of XG developing before, during and following the presentation of hematologic malignancy; acute lymphoblastic lymphoma, adult T-cell lymphoma/leukemia, B-cell acute lymphoblastic lymphoma, and chronic lymphocytic leukemia.[7]

The histopathology of JXG reveals monomorphous, small and oval appearance, sometimes spindled with lipidized (xanthomatous) histiocytes with foreign-body giant cells, and Touton giant cells. In adult variants of JXG, they usually consist of various cellular features of histiocytes, which have been categorized into five types: vacuolated, xanthomatized, scalloped, oncocytic, and spindle-shaped.[8] A mixed inflammatory cell of lymphocytes, neutrophils, and eosinophils has been observed in various numbers. There tends to be more chronic inflammatory cells as well as stromal fibrosis in a very aged lesions. Immunohistochemically, JXG lesions mostly stain CD68/Ki-M1P and factor XIIIa but negative for CD1a and S100 protein. Clusters of comma-shaped bodies can be observed on electron microscopy (EM). The cytoplasm of foam cells is completely filled with lipid vacuoles, cholesterol clefts, and myeloid bodies.[4,9] The spindle-cell component, as found in the lesion of our case, expressed CD68 which is marker for macrophages and revealed negative for S100 and CD1a. However, the diagnosis of spindle cell xanthogranuloma requires a major component of spindle cell histiocytes of more than 90% with storiform arrangement which was not a prominent feature in our case.[4,5] Therefore, the differential diagnosis of other fibrohistiocytic spindle cell tumor, such as dermatofibroma, should be considered. In our case, the clinical presentation of multiple yellowish papulonodular eruptions would be likely to exclude the diagnosis of dermatofibroma.

No treatment is required in JXG because of its asymptomatic and self-healing features.[4,7] JXG lesions usually resolve spontaneously within a few years, whereas no spontaneous resolution is found in AXG patients except for only few case reports.[1,10-11] Several treatments for ECD and other forms of NLCH have been tried without success. Palliative therapies such as cryotherapy, intralesional

corticosteroids injection and radiotherapy can be applied in individual disfiguring lesions with partial response.[6,10] There is a report of clinical improvement after oral isotretinoin treatment in one multiple AXG case.[2] Our patient received no treatment and still has persistence of cutaneous lesions after 1-year follow up period.

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