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CONCISE COMMUNICATION

Case series of volar juvenile xanthogranuloma: Clinical observation of a peripheral rim of hyperkeratosis

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ABSTRACT

Juvenile xanthogranuloma is a benign histiocytic tumor predominantly occurring in children as yellowish papules on the head and trunk. Presentations on the volar surfaces are rare and may cause diagnostic confusion with pyogenic granuloma, eccrine poroma and digital fibrokeratoma. We report two patients with unusual presentations of solitary juvenile xanthogranuloma on the palm or sole. Both had lesions lacking the classic yellowish color and demonstrating a well-defined, peripheral hyperkeratotic rim. Histopathological evaluation revealed prominent orthokeratosis corresponding to the rim. Additional histological features, including dermal histiocytes and Touton giant cells, were consistent with the diagnosis of juvenile xanthogranuloma. Given the unusual locations and colors of the lesions, we conclude that histopathological evaluation is central to diagnosing volar juvenile xanthogranuloma. We additionally suggest that juvenile xanthogranuloma should be included in the differential diagnoses of volar lesions displaying a peripheral hyperkeratotic rim.

Key words: **acral involvement, histiocytosis, hyperkeratosis, volar, xanthogranuloma.**

INTRODUCTION

Juvenile xanthogranuloma (JXG) is a benign, non-Langerhans cell histiocytic tumor. It primarily occurs in children as asymptomatic single or multiple cutaneous lesions that resolve spontaneously over several years. Infrequently, lesions involve extracutaneous locations, such as the eye or lungs.[1,2] JXG occurs 10-times more frequently in Caucasians than in African-Americans.[3]

On the skin, JXG typically presents as yellowish or tan, smooth, firm, dome-shaped papules or nodules on the head, neck and/or upper trunk. Lesions may initially appear pink to red with a yellow tinge.[2] Only 20% of cases involve the extremities,[4] and presentations of solitary JXG on the palm or sole are rare. Indeed, there have been only three cases of isolated JXG on the palm,[4–6] two in subungual locations[7,8] and three on the sole.[9–11]

Here, we describe two patients with unusual volar presentations of JXG. Interestingly, we noticed a well-defined hyperkeratotic rim at the periphery of each tumor. Hyperkeratotic rims have been observed in previous reports of volar JXG.[11] Therefore, we propose that JXG should be included in the differential diagnoses of volar lesions with hyperkeratotic rims.

CASE REPORTS

Case 1

A healthy 18-year-old Hispanic man developed a solitary, 5-mm lesion on the right palm. His primary care physician diagnosed the lesion as a wart. Despite cryotherapy, the lesion grew slowly over 2 months. He was, therefore, referred to our dermatology clinic.

The patient reported no bleeding or friability of the lesion. On examination, he had a 1-cm, dome-shaped, firm, mildly tender nodule in the center of the right palm. The nodule was dull red and had a well-circumscribed peripheral hyperkeratotic rim (Fig. 1a). On dermoscopy, a “setting sun” appearance was not noticed, and there was no identifiable pigment network. Our differential diagnoses included eccrine poroma, pyogenic granuloma and non-Langerhans cell histiocytosis, including solitary reticulohistiocytoma.

Following a shave biopsy, histopathological examination revealed a nodular tumor with irregular epidermal acanthosis and, at the edge of the lesion, prominent orthokeratosis corresponding to the hyperkeratotic rim (Fig. 1b). There was a dense superficial to deep dermal infiltrate consisting of xanthomatous histiocytes and Touton giant cells (Fig. 1c,d). These features were consistent with JXG.

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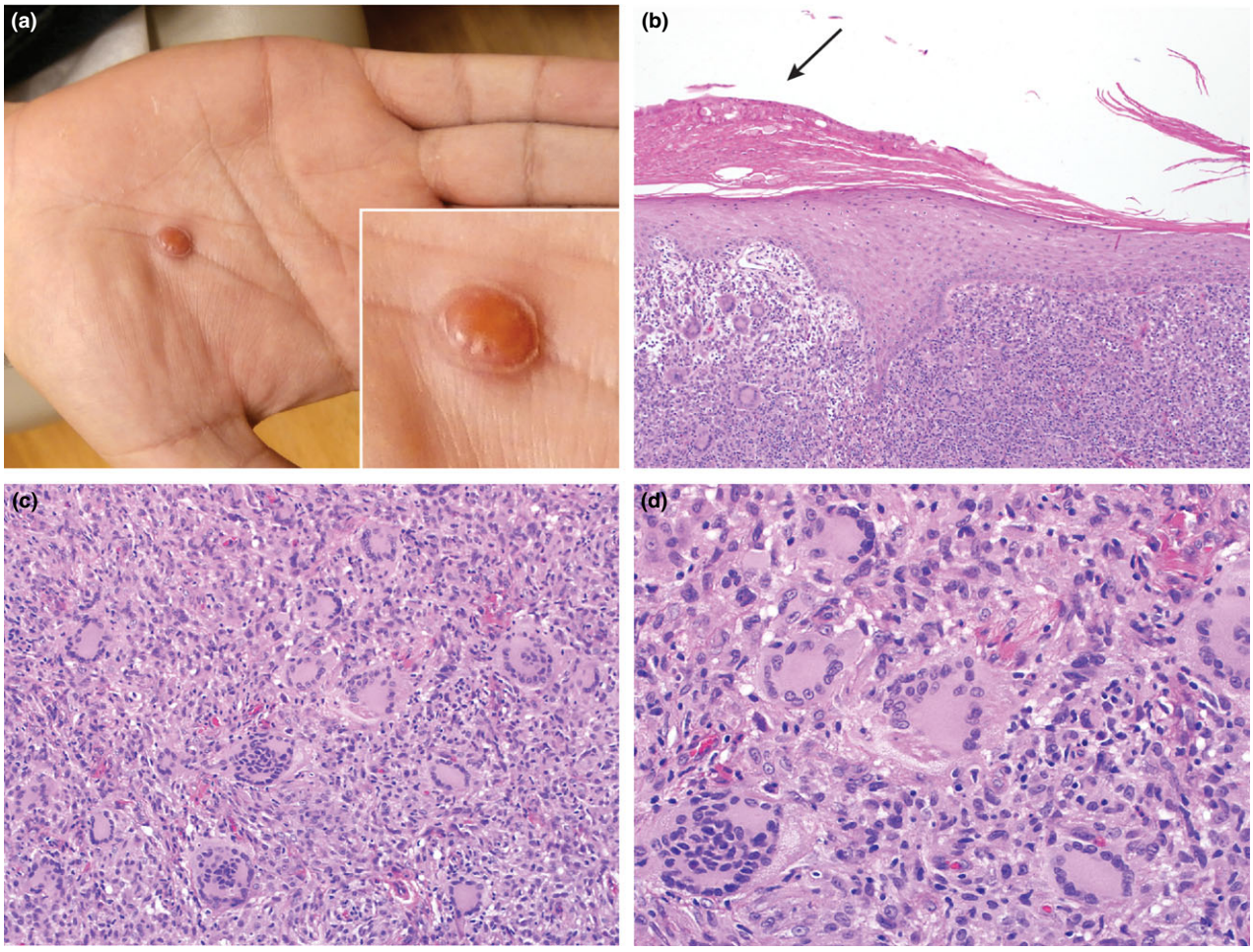

Figure 1. Rare volar presentation of juvenile xanthogranuloma with a hyperkeratotic rim (case 1). (a) Clinical appearance of the lesion as a well-circumscribed, rubbery, dull-red nodule on the central palm of an 18-year-old man. Inset highlights peripheral rim of scale. (b) Low-powered histological view of the edge of the lesion showing epidermal acanthosis and orthokeratosis corresponding to the hyperkeratotic rim (arrow) (hematoxylin-eosin [HE], ×100). (c) Also near the edge of the lesion, there is a dense superficial to deep dermal infiltrate (HE, ×200). (d) High-powered view of the previous image showing numerous xanthomatous histiocytes and Touton giant cells (HE, ×400).

Five months later, the patient returned with regrowth of the lesion. He reported pain and bleeding of the lesion with trauma. Examination revealed a 9-mm erythematous nodule on the right mid-palm. It was tender and again demonstrated a well-circumscribed peripheral hyperkeratotic rim. Similar lesions were not present elsewhere. The patient was referred to our hand surgery colleagues for excision.

Case 2

A healthy 11-month-old African-American girl was referred by her pediatrician to our clinic for a growth on the left sole between the first and second toes. The lesion had been present for 2 months and had bled intermittently.

Examination revealed an 8-mm, mildly hyperkeratotic, firm, non-tender, flesh-colored nodule with a prominent peripheral hyperkeratotic rim (Fig. 2a). On dermoscopy, no pigment network was apparent. Our differential diagnoses included traumatized nevus, foreign body reaction, infection, malignancy including amelanotic melanoma and infantile digital fibroma.

Following excision of the mass by our pediatric surgery colleagues, histopathological examination revealed prominent orthokeratosis at the periphery of the lesion, corresponding to the hyperkeratotic rim (Fig. 2b). Near the center of the lesion, there was hyperkeratosis and irregular epidermal acanthosis. In the dermis and subcutaneous tissue, there was a dense proliferation of histiocytic cells admixed with Touton giant cells (Fig. 2c,d). Based on immunohistochemical staining (data not shown), the histiocytic cells were CD68-positive, but negative for S100 and CD1a, consistent with a diagnosis of JXG. Our ophthalmology colleagues reported no evidence of ocular JXG. At 3 months post-excision, the lesion had not recurred.

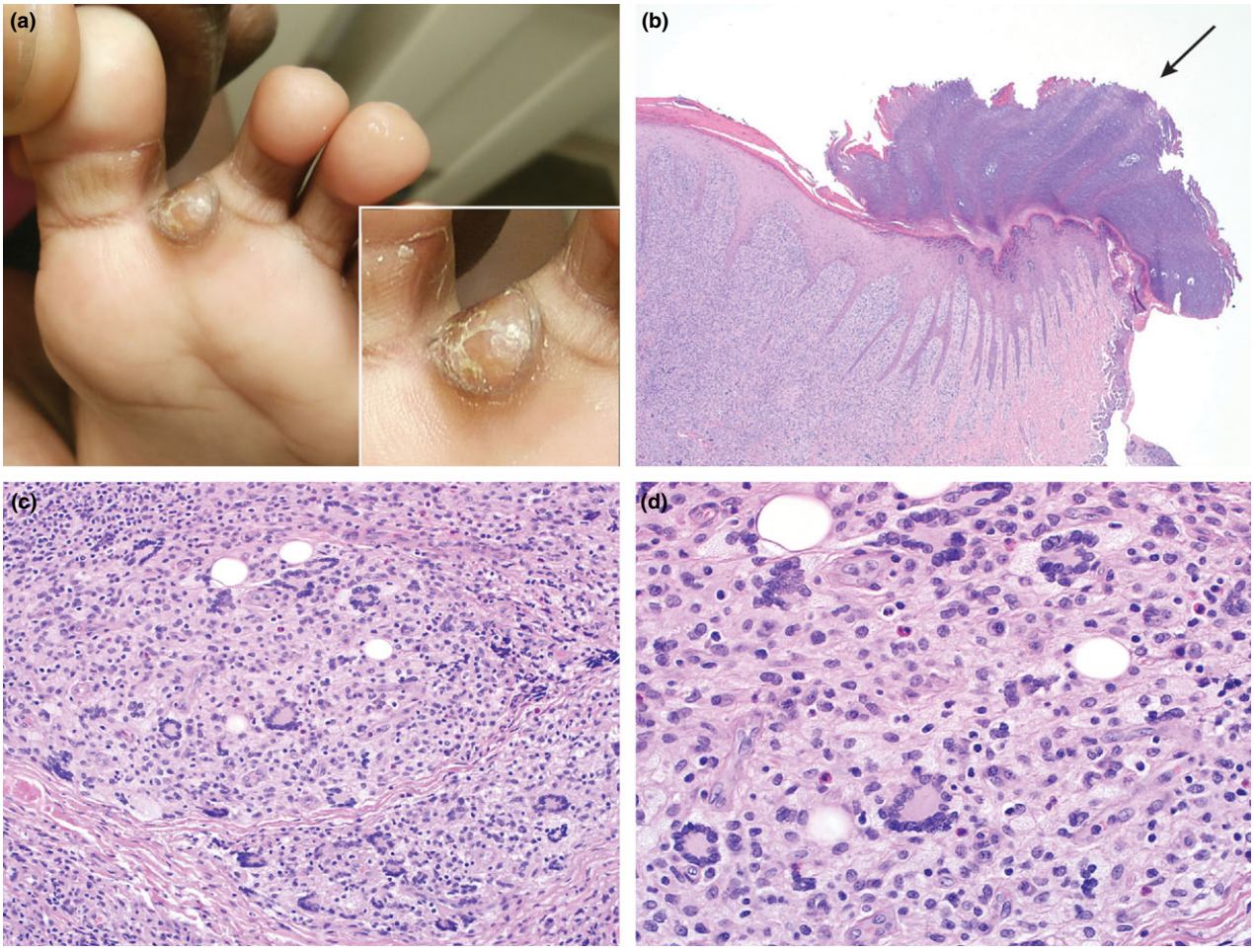

Figure 2. Another rare presentation of volar juvenile xanthogranuloma with a hyperkeratotic rim (case 2). (a) Clinical appearance of the lesion as a well-circumscribed, firm, flesh-colored nodule between the first and second toes of an 11-month-old girl. Inset highlights peripheral rim of scale. (b) Histological evaluation demonstrating prominent orthokeratosis at the periphery of the lesion corresponding to the hyperkeratotic rim (arrow) (hematoxylin–eosin [HE], original magnification ×40). (c) Low-powered histological view of the central portion of the nodule with a dense superficial to deep dermal infiltrate (HE, ×200). (d) High-powered histological view showing a proliferation of histiocytic cells admixed with Touton giant cells, lymphocytes and eosinophils (HE, ×400).

DISCUSSION

We present two patients who developed volar JXG, which is very rare.[5–11] Previous reports indicate that volar JXG may occur in a solitary fashion.[9–11] Consistent with these observations, our patients had solitary lesions without evidence of JXG at other cutaneous or extracutaneous sites, such as the eye. Furthermore, there is no evidence to suggest that volar JXG is associated with additional systemic findings, such as juvenile myelomonocytic leukemia, which may occur with increased frequency in patients with multiple JXG and neurofibromatosis type I.[2] Indeed, our patients were well developed and healthy.

Whereas JXG on the head, neck and trunk often appears yellowish, previous reports of volar JXG indicate that lesions can be erythematous, yellow-brown or dark brown.[6,9–11] Indeed, our patients presented with lesions that were dull red (case 1) or flesh-colored (case 2). Given the unusual colors and locations of the lesions, we did not initially consider JXG in the clinical differential diagnosis, which for volar neoplasms include eccrine poroma,[11] pyogenic granuloma,[9,10] digital fibrokeratoma,[12] dermatofibroma,[6] nevi, viral verruca, amelanotic melanoma[13] and solitary reticulohistiocytoma.[6]

Thus, histological evaluation is often necessary to diagnose volar JXG. Early lesions of JXG are composed of a dense dermal infiltrate of histiocytes lipidized to differing degrees and lacking Birbeck granules on ultrastructural examination, while mature lesions additionally contain Touton giant cells and other inflammatory cells, such as lymphocytes, eosinophils and neutrophils.[2] The histopathological differential diagnoses include Langerhans cell histiocytosis and dermatofibromas with numerous foamy histiocytes, including lipidized and histiocytic variants. To distinguish between these possibilities, immunohis-

tochemical staining is valuable. In contrast to Langerhans cell histiocytosis, the histiocytic infiltrate in JXG is negative for CD1a and S100.[2] Although both JXG and dermatofibroma stain with factor XIIIa, JXG is positive for CD68. Collagen trapping, seen in dermatofibroma, is not present in JXG. JXG also may show histological overlap with xanthomas and Rosai–Dorfman disease. However, most forms of xanthomas do not have intermixed inflammatory cells, and Rosai–Dorfman disease is distinguished by the presence S100-positive cells showing emperipolesis.

Additionally, as highlighted in Figures 1(b) and 2(b), the epidermis can display prominent orthokeratosis at the periphery of volar JXG. This feature corresponds to the well-circumscribed hyperkeratotic rim surrounding the lesions of our patients. While our study is limited by the small number of cases, we propose that volar JXG should be included in the differential diagnoses of acral lesions presenting with a peripheral hyperkeratotic rim. In a past report of volar JXG, a "well-circumscribed keratotic rim with a peripheral 'moat'" was also described.[11] Although it is unclear why such scaly rims may develop around volar JXG, one possibility is that this feature occurs as a function of growth on thick, volar skin.

Other types of volar lesions, such as pyogenic granuloma, eccrine poroma and acquired digital fibrokeratoma, can present with similar scaly rims.[10–12] As such, searching for additional clinical, dermoscopic and histological features will assist in making an accurate diagnosis. For instance, pyogenic granulomas are often more friable, moist and brightly erythematous than JXG, while eccrine poromas typically have a glossy red color. Digital fibrokeratomas are usually flesh-colored, and more hyperkeratotic and projectile in shape than JXG.

The use of dermoscopy can aid the accurate diagnosis of JXG. Dermoscopic findings of JXG include an orange-yellow "setting sun" appearance, yellow to white "cloud" deposits, whitish streaks and branched linear telangiectasias.[9,14] To our knowledge, rims of hyperkeratosis have not been reported in dermoscopic descriptions of JXG.

Non-volar JXG tends to resolve, especially in children,[6] but the natural history of volar lesions is unclear. Volar JXG may become traumatized or painful, thus interfering with physical activity.[9] Therefore, surgical excision is often recommended, which makes observing the natural course of lesions not always possible. Following removal, recurrence rates of volar JXG are unknown, given the rarity of lesions. As illustrated by case 1, lesions may recur after a superficial shave procedure, as opposed to complete excision. On the other hand, previous cases of volar JXG have not recurred at 3 months[6] and 1 year[11] following excision.

Finally, both of our cases involve non-Caucasian patients. This observation was unexpected, because JXG is reportedly more commonly in Caucasians.[3] It remains to be seen whether volar JXG occurs more frequently in non-Caucasian patients.

In conclusion, our cases demonstrate that JXG may not enter the differential diagnoses of volar growths, because JXG in this location is rare and potentially lacks the classic yellowish color. A high index of suspicion and, often, histopathological evaluation are required to make the diagnosis. Additionally, we propose that JXG should be included in the differential diagnoses of volar lesions displaying a peripheral hyperkeratotic rim.

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CONFLICT OF INTEREST: None.

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