

## Verruciform xanthoma of the thumb

Sir,

Verruciform xanthoma is a rare lesion with a predilection for oral mucosa. Recent reports revealed that it affected the skin and mucosa of parts other than the oral cavity, such as that of the penis and scrotum. We present a case of verruciform xanthoma involving the thumb.

An 80-year-old woman consulted our department for an asymptomatic lesion on her left thumb, which had gradually enlarged over the past 3 years. The patient had pared the lesion with a knife by herself several times; however, it recurred every time. The lesion was diagnosed as verruca vulgaris and frozen three times by liquid nitrogen, which was not effective. She had no known history of trauma or infection of the thumb. Physical examination revealed a single ill-demarcated yellow-tan papule 0.8 cm × 0.8 cm in diameter, on the skin of the left thumb [Figure 1]. The personal and familial medical histories of the patient were unremarkable, and no laboratory findings suggestive of hyperlipidemia were found.

The lesion was surgically removed and sent to pathology department for histopathological examination. Hematoxylin–eosin staining revealed a hard verrucous lesion, and the histopathology showed the epidermal hyperkeratosis and parakeratosis, and a papillomatous proliferation without atypia. The papillary dermis was filled with an infiltrate of lymphocytes and plasma cells; some foamy cells were observed in it [Figures 2 and 3]. But the foamy cells did not extend beyond the tips of the rete ridges. The immunohistochemical examination revealed positive staining of the foamy cells for CD68 [Figure 4], CD163, CD45, and CD3, and

negative staining for CD1a, CD117, EMA, CD20, and S100. Also, the lymphocytes in the dermis stained positively with CD45 and CD20, but were negative for CD3. The epidermis was extensively positive for cytokeratin (CK), but the positive pattern of the foamy cells to the same was punctiform. The foamy cells contained scanty periodic–acid Schiff (PAS)-positive diastase-resistant material and were negative for Giemsa (GMS) staining. The patient's histopathological diagnosis was established as verruciform xanthoma, and no recurrence had occurred at 8 months follow-up.

The histopathological pattern of our patient's lesion is identical to that of a typical verruciform xanthoma. It was generally accepted that this condition was first described by Shafer in 1971,<sup>1</sup> but Mario declared that the lesion of verruciform xanthoma had been reported by Otto in 1903.<sup>2</sup> It usually presents as a solitary, sessile, or pedunculated lesion with rough or pebbly surface,<sup>3</sup> and it may present as papules, nodules, or plaques. The lesion is generally asymptomatic, and it is about 2 mm to 2 cm in size with variable color, rarely bigger than 4 cm. Although verruciform xanthoma can occur at any age, it usually affects adults between 40 and 70 years with a slight male predilection. Oral verruciform xanthoma is common in males below the age of 50 years, and a reverse trend was noted in females.<sup>4</sup>

Verruciform xanthoma occurs as an isolated solitary lesion mostly. Multiple lesions were reported to be associated with other skin diseases or oral mucosal diseases, such as snuff dipper's keratosis, oral pemphigus vulgaris, carcinoma *in situ*, lichen sclerosus, solar keratoses, epithelial nevus, CHILD syndrome, etc.<sup>3</sup> Also, multiple

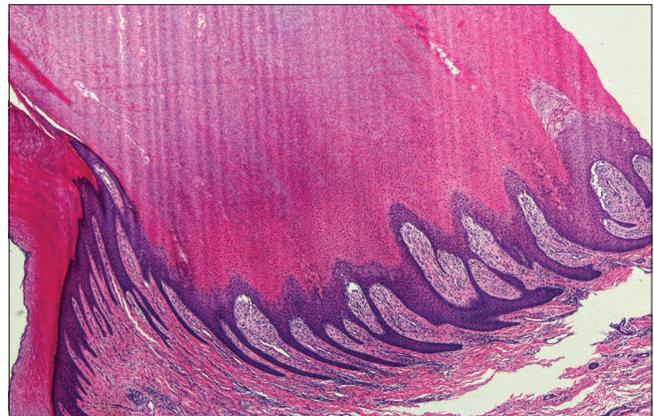
**Table 1: Some reports focusing on VX in the extraoral sites**

Location	Lesion	Publication date	Journal	First author
Scalp	Multiple verrucous plaques	1991	J Cutan Pathol	Meyers DC
Nose	Single verrucous papule	1986	Am J Dermatopathol	Duray PH
Lip	Single plaque	1993	Oral Surg Oral Med Oral Pathol	Allen CM
Ear	Multiple cyst	1991	J Am Acad Dermatol	Poblet E
Breast	Single cyst	2014	Am J Dermatopathol	Lomas-Garces-J
Right abdomen	Single verrucous plaque	2014	Am J Dermatopathol	Curto-Barredo L
Esophagus	Single granular mucosa	2012	Dig Endosc	Min KW
Vulva	Single polypoid lesion	2004	Int J Gynecol Pathol	Reich O
Penis	Single papule	2005	Arch Pathol Lab Med	Ersahin C
Scrotum	Multiple verrucous papules	2014	Dermatol Surg	Joo J
Glans	Singe plaque	2015	J Am Acad Dermatol	Arzberger E
Left forearm	Single papule	2013	J Cutan Pathol.	Blankenship DW
Left thigh	Single giant mass	2002	J Cutan Pathol	Agarwal-Antal N
Left inguinal	Single verrucous plaque	1980	J Cutan Pathol	Barr RJ
Left leg	Multiple plaques	2014	Cutis	Tang
Hand and foot	Multiple verrucous plaques	1989	J Am Acad Dermatol	Mountcastle
Right first toe	Single verrucous nodule	1987	J Am Acad Dermatol	Chyu

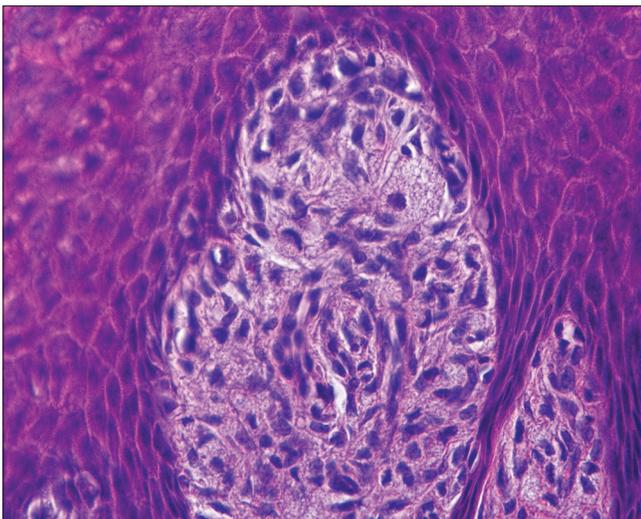
VX: Verruciform xanthoma.



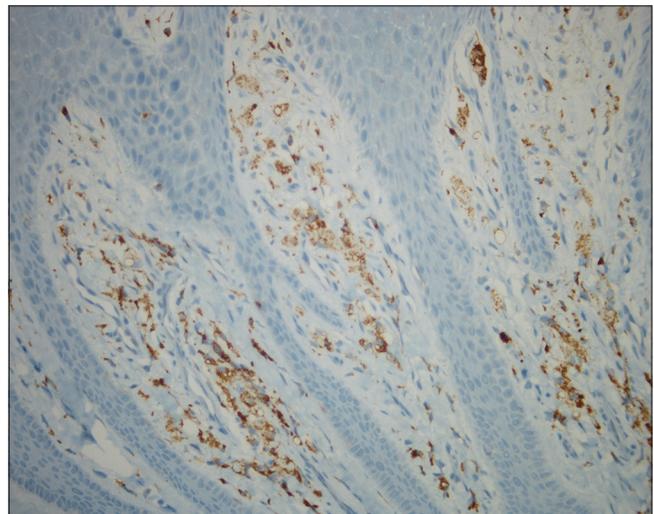
**Figure 1:** A verrucous papule on the left thumb



**Figure 2:** Hematoxylin–eosin (H and E) staining revealed a hard verrucous lesion, with the epidermal hyperkeratosis, parakeratosis, acanthosis, and a papillomatous proliferation. Atypia of epithelial cells was not present (H and E, ×40)



**Figure 3:** The papillary dermis between the acanthotic rete ridges was filled with an infiltrate of lymphocytes and plasma cells. And some foamy cells were observed in the papillary dermis (H and E, ×400)



**Figure 4:** The foamy cells are positive for CD68 ×200, a macrophage marker

lesions have been reported to occur in an immunocompromised patient and in hepatitis C virus carriers.<sup>5</sup> Verruciform xanthoma usually occurs intraorally, and cutaneous involvement is unusual. The extraoral occurrence has been reported mainly involving the anogenital skin and mucosa. There are various reports about verruciform xanthoma in other anatomic sites, for example, scalp, breast, thigh, etc. Some reports about verruciform xanthoma in extraoral sites are shown in Table 1. We had found several cases of verruciform xanthoma in the leg, finger, and toe.<sup>6-8</sup> One of the cases was reported by Mountcastle in 1989,<sup>8</sup> and the lesions were in the left third digit and right toes.

The diagnosis of verruciform xanthoma is based on the histopathological examination. It is characterized by papillomatous acanthosis, aggregations of xanthoma cells located within the papillary dermis, accompanied by infiltration of lymphocytes. The histopathological pattern of our patients was atypical to that, and the foamy cells were suggested to be monocyte-macrophage lineage by immunohistochemical staining. The negativity of foamy cells to S-100 ruled out the original possibility of them originating from dermal dendritic cells. The xanthoma cells are large cells with foamy cytoplasm. They stained positively with periodic acid Schiff and are diastase-resistant, implying that the material in the foamy cells is not glycogen.

The etiology of verruciform xanthoma is not fully characterized, and it did not seem to be related to any lipid metabolism abnormality.<sup>3</sup> It was suggested that verruciform xanthoma is a reaction pattern to an inciting event of epidermal keratinocyte damage. Keratinocyte damage has been attributed to a wide variety of instigators including recurrent cutaneous irritation or trauma, bacterial colonization, fungi, virus, and other inflammatory damage. The keratinocyte necrosis and degeneration may lead to the release of intracellular lipids, which are then engulfed by histiocytes in the dermis, giving rise to foamy cells. Moreover, inflammation was considered to be the primary trigger. In our patient, the positive pattern of cytokeratin staining for the foamy cells confirmed this opinion. Mehra *et al.* studied nine cases of verruciform xanthoma, and revealed that two of them showed a novel somatic missense mutation in exon6 of the 3-hydroxysteroid dehydrogenase (NSDHL) gene, and no mutation of exon4 was found in any case.<sup>9</sup> It is of interest that the lesion of our patient was on the thumb. Also she had neither evidence of any disease except verruciform xanthoma nor obvious history of any local infection or trauma in the thumb.

Therapeutic options for verruciform xanthoma included topical steroids, carbon dioxide laser, cryotherapy, wireloop electrosectioning, and radiation therapy. But none of these was completely effective and safe. Guo *et al.* had successfully treated multiple lesions on the vulva with imiquimod in a 2-year-old girl.<sup>10</sup> Anyways, the surgical excision is the most effective treatment for verruciform xanthoma to date. The lesions did not reappear after excision in our patient.

#### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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#### Conflicts of interest

There are no conflicts of interest.

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