Verruciform Xanthoma of the Earlobe in an Immunosuppressed Patient

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Practice Points

- Verruciform xanthoma clinically resembles verruca, condyloma acuminatum, verrucous carcinoma, or squamous cell carcinoma.
- Most lesions present on the oral mucosa or genitalia but rarely may present on other sites.
- The exact etiology of verruciform xanthoma remains unclear.
- Histologically, foamy histiocytes are present.

Verruciform xanthoma (VX) is an uncommon mucocutaneous lesion of uncertain etiology. Originally thought to be limited to the oral mucosa, its occurrence in other mucosal and nonmucosal sites also has been documented. Histologically, VX is characterized by subepithelial foamy histiocytes associated with papillomatosis, parakeratosis, and dyskeratosis. Subepithelial foamy cells are lipid-containing, non–Langerhans cell histiocytes. A variety of etiologies have been proposed without much consensus, including infectious (bacterial, viral, and fungal), degenerative, reactive/reparative, inflammatory, metabolic, reactive/multifactorial, and immunosuppressive factors. Verruciform xanthoma of the external ear is exceedingly rare. Herein, we report a rare case of VX occurring on the earlobe at a piercing site in an immunosuppressed patient and provide a discussion of the possible pathogenetic mechanism(s).

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Verruciform xanthoma (VX) is an uncommon, benign, mucocutaneous lesion of uncertain etiology. It was first described by Sachs[1] in 1903 and called a xanthoma-like nevus. In 1971, Shafer[2] referred to it as *verruciform xanthoma*, the name by which it currently is recognized. Verruciform xanthoma originally was thought to be limited to the oral mucosa; however, subsequent studies have shown its occurrence in other mucosal and nonmucosal sites. To date, several hundred cases have been reported in different anatomic locations including the oral cavity,[3-11] lip,[12-14] penis,[15-21] vulva,[22-24] anal region,[25] nose or nasal vestibule,[26,27] ear,[28,29] feet,[30] and scrotum,[31-33] as well as in other sites. Two cases of VX have been reported in internal organs, the upper aerodigestive tract, and the esophagus.[34,35]

Most patients with VXs are normolipemic and otherwise healthy. Clinically, lesions typically are asymptomatic, slow-growing, red to yellow, verrucous papules that vary in size. Lesions usually arise on normal mucocutaneous surfaces but have been reported to present in association with other lesions, such as warty dyskeratoma[36] (mucous membrane) and discoid lupus erythematosus[37] (skin). Histologically, VX shows accumulation of xanthoma cells (foamy histiocytes) in the submucosa or papillary dermis between the elongated rete ridges, which also is associated with papillomatosis, parakeratosis, dyskeratosis, variable numbers of intracorneal neutrophils, and a subepithelial lymphoplasmacytic infiltrate.[38]

Cutaneous VX occurring in areas other than the anogenital region is uncommon, and VX of the

external ear is extremely rare. Two cases involving the helix and the posterior pinna or postauricular area of the ear have been previously reported.[28,29] Herein, we report a rare case of VX occurring on the earlobe at a piercing site in an immunosuppressed patient.

Case Report

A 76-year-old woman presented with a skin growth over a piercing site on the right earlobe that had been present for several years. The patient's medical history was remarkable for discoid lupus erythematosus, rheumatoid arthritis, and renal transplant at 9 years of age with retransplant 5 years prior to presentation. She also had undergone bilateral knee replacement. Her blood lipid profile was within reference range. Two months prior to presentation, the lesion was injected with intralesional steroids at another clinic. Clinical examination showed a 4-mm, flesh-colored, verrucous, keratotic lesion with no evidence of ulceration or bleeding. A shave biopsy was performed and sent for pathologic examination with a clinical impression of verruca versus benign keratosis.

A shave specimen measuring 4×4 mm was received in a fixative. Microscopic examination revealed a lesion with typical verrucous architecture (Figure 1); however, on higher magnification, characteristic features of VX were readily identified, including papillomatosis associated with confluent parakeratosis and dyskeratosis involving the crevices between the verrucous digitations and extending into the stratum malpighii (Figure 2). Xanthoma cells (foamy histiocytes) were noted within expanded dermal papillae between elongated rete ridges (Figure 3). Additional supportive features included neutrophils at the junction of the stratum corneum and stratum malpighii with loss of the granular layer (Figure 4) and a mild perivascular lymphocytic infiltrate at the base of the lesion.

Immunoperoxidase studies revealed that xanthoma cells stained positive for CD68 (Figure 5) and negative for S-100 protein and CD1a. Interestingly, the CD1a stain showed absence of positively staining Langerhans cells in the lesional epidermis, while the adjacent uninvolved epidermis showed retention of the normal Langerhans cell population.

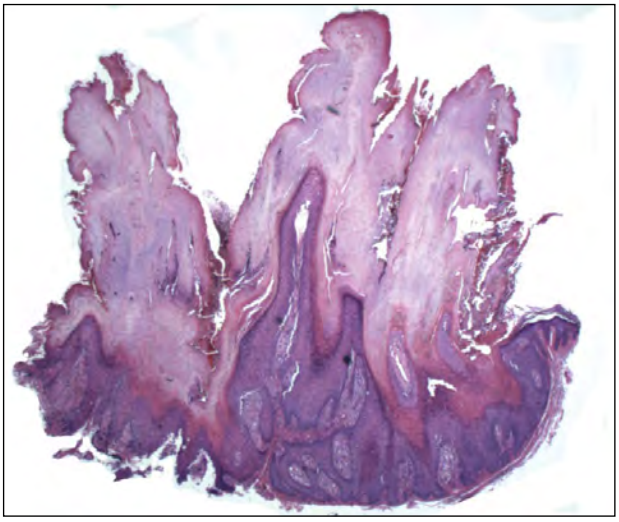

Figure 1. Scanning magnification showed a lesion with typical verrucous architecture resembling verruca vulgaris (H&E, original magnification ×20).

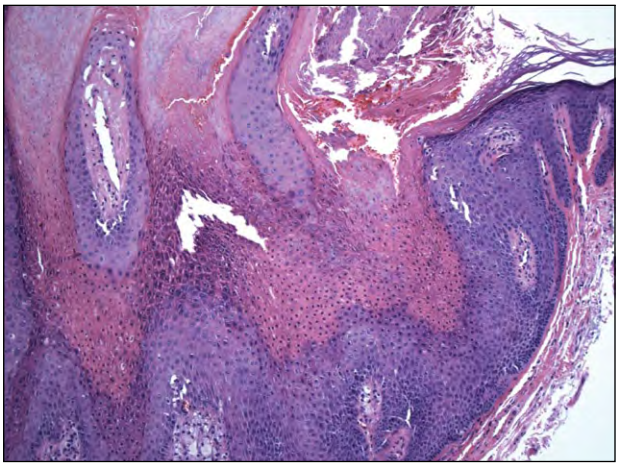

Figure 2. Higher magnification exhibited confluent parakeratosis and dyskeratosis involving the crevices extending deep into the stratum malpighii (H&E, original magnification ×40).

Comment

Verruciform xanthoma was first described in the right axillary region of an 8-year-old girl by Sachs[1] in 1903 in association with a set of abnormalities that would later be known as CHILD syndrome (congenital hemidysplasia with ichthyosiform nevus and limb defects), which is caused by a mutation in the NAD(P) dependent steroid dehydrogenase–like gene, *NSDHL*.[39-42] Many other lesions were subsequently reported in the oral cavity until occurrence in extraoral locations was documented. The majority of extraoral lesions were reported in the anogenital region, with a few cases described elsewhere on the skin. Cutaneous VX lesions may present in association with preexisting or concomitant conditions or may arise de novo in normal skin.[26,27,43] Clinically, cutaneous VX resembles verruca, squamous cell carcinoma, or verrucous carcinoma.[44]

The origin of the subepithelial foam cells has been established to be non–Langerhans cell histiocytes[5,8] with accumulated lipid[1]; however, the etiology and pathogenetic mechanism still are being debated. Over the years, a variety of etiologies have been proposed based on clinical, histologic,

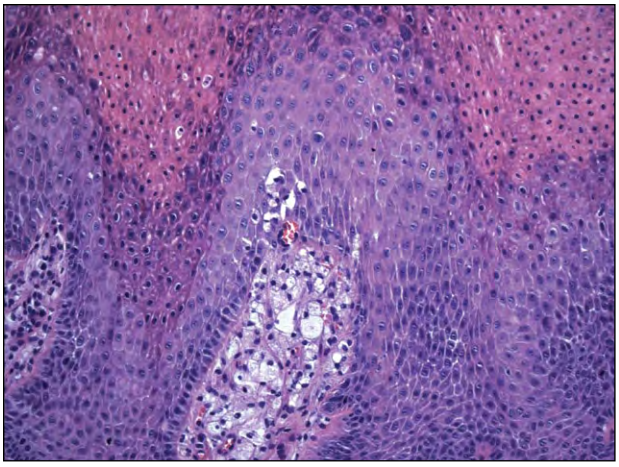

Figure 3. Xanthoma cells (foamy histiocytes) within dermal papillae between elongated rete ridges (H&E, original magnification ×100).

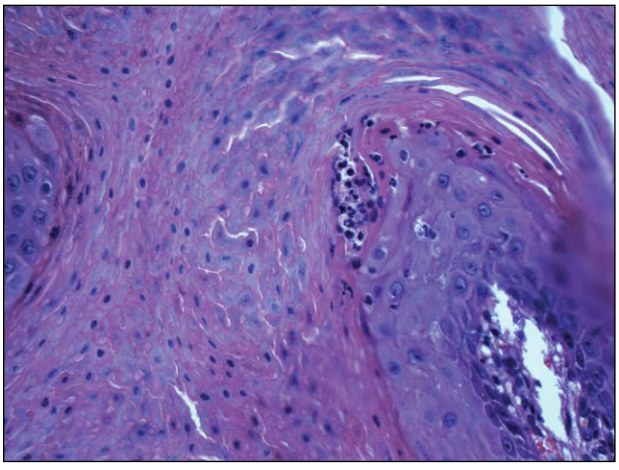

Figure 4. A collection of neutrophils at the junction of the stratum corneum and stratum malpighii with loss of the granular layer (H&E, original magnification ×400).

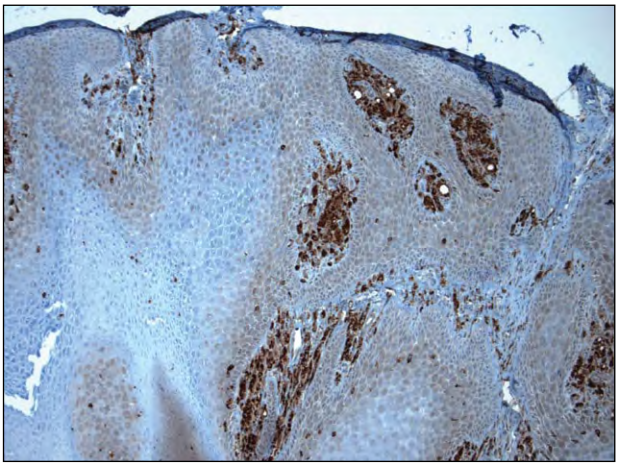

Figure 5. Immunohistochemical staining revealed xanthoma cells that stained positive for CD68 (original magnification ×40).

immunophenotypic, ultrastructural, and molecular findings including infectious (bacterial,[2,45,46] viral,[47,48] fungal[43,49,50]), degenerative,[45,51] reactive/reparative,[52] inflammatory,[53] metabolic processes,[34,38] reactive/multifactorial,[54] and immunosuppressive[55-57] factors, without much consensus.

Two cases of VX occurring in the external ear have been reported.[28,29] A 79-year-old man presented with VX on the helix of the left ear in association with actinic keratosis.[28] Regarding the causal relationship between the 2 conditions, the authors doubted the assumption made by Neville[49] that VX is a reactive lesion arising from degeneration of the overlying epidermis. The second case described a 22-year-old man with VX presenting on either the posterior pinna or the postauricular area of the ear (the authors did not specify). This lesion had the configuration of an epidermoid cyst with its lining showing the characteristic changes of VX; the authors called it cystic VX.[29] In contrast, our case involved an immunosuppressed 76-year-old woman with a lesion located over a piercing site on the right earlobe. The pathogenesis in our case may have included several contributory traumatic, infectious, and immunosuppressive factors, as well as a multifactorial etiology. According to Mohsin et al,[43] the lesion may have been caused by repeated microtrauma at the piercing site. Occurrence at this site and concomitant immunosuppression may have resulted in repeated clinical or subclinical infections. Furthermore, the role of immunosuppression in the development of VX through a decrease in Langerhans cells has been suggested. Verruciform xanthoma has been described in immunocompromised individuals, including bone marrow transplant recipients,[55] patients with chronic graft-versus-host disease,[56] renal transplant recipients,[57] and human immunodeficiency virus–positive patients.[58] It has been postulated that reduced epidermal Langerhans cell density and function as a consequence of immunosuppression results in increased products of keratinocyte damage, thus prompting dermal dendrocytes to phagocytose them and transform into foam cells.[57] Microscopic lichenoid destruction of the basal keratinocytes also may be implicated.[55] In human immunodeficiency virus–positive patients, increased levels of various cytokines (eg, tumor necrosis factor α, IL-1, and IL-6) are thought to play a role in epidermal proliferation and lipid metabolism, thus possibly predisposing the patient to the formation of VX.[58] In our case, a multifactorial etiology seems to be evident, combining the factors of epithelial damage due to repeated microtrauma, increased frequency of clinical/subclinical infection, and decreased ability to clear epithelial debris.

Conclusion

As in other instances of VX, our case demonstrates an architecture identical to commonly observed verruca on scanning magnification, emphasizing a need for examination with high-power magnification.

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