

## Dermatopathology quiz: Cerebriform papules of the scrotum

Cassandra Andreychik, Leonard J. Bernstein<sup>1</sup>, Dirk Elston<sup>2</sup>

The Commonwealth Medical College, Scranton, PA, <sup>1</sup>Laser and Skin Surgery Center, <sup>2</sup>Ackerman Academy, New York, USA

The 55-year-old male who presents with several scrotal cerebriform papules [Figure 1-3]. He is concerned that they may represent venereal warts.

The lesion most likely represents?

- A. Condyloma accuminatum
- B. Condyloma latum
- C. Porokeratosis ptychotropica
- D. Verruciform xanthoma
- E. Epidermolytic acanthoma

**Answer:** D. Verruciform xanthoma

Verruciform xanthoma is a papillary lesion observed primarily on the oral mucosa. They typically occur in adults between the ages of 40 and 70.<sup>[1]</sup> The pathogenesis is thought to involve an immune reaction to local trauma or inflammation.<sup>[1]</sup> Several agents have been implicated as possible etiologic factors for oral lesions of verruciform xanthoma, including tobacco, alcohol, drugs, sensitizing or allergic substances of foodstuffs and dental materials.<sup>[2]</sup> Due to the similar clinical appearance and distribution of verruciform xanthoma and condylomata, human papilloma virus (HPV) has been suggested as an etiologic factor, but *in situ* hybridization has generally failed to find evidence of a genuine association with HPV.<sup>[1,3]</sup>

Verruciform xanthomas most commonly involve the masticatory mucosa.<sup>[1]</sup> Other affected sites include the hard palate, tongue, buccal mucosa, soft palate, alveolar mucosa, floor of the mouth, and the junction between the hard and soft palate.<sup>[2]</sup> Extraoral cases commonly involve the vulva, anogenital skin and mucosa.<sup>[1,2]</sup> On examination, the lesions are typically solitary, sessile or pedunculated with a coarse surface. These growths are variable in color ranging from flesh-colored, pale, white, or red and approximately 2 mm-1.5 cm in size. They are slow-growing and asymptomatic.<sup>[1,2]</sup> While most cases occur as an isolated lesion, multiple lesions have been found



**Figure 1:** Cerebriform papules of the scrotum



**Figure 2:** At low power, orange-red V-shaped scale crusts are noted (H and E X 20)

to be associated with diseases such as psoriasis, snuff dipper's keratosis, epithelial nevus, discoid lupus erythematosus, solar keratosis, lichen sclerosus, oral pemphigus vulgaris, recessive dystrophic epidermolysis bullosa, CHILD syndrome, carcinoma *in situ*, and seborrheic keratosis. Verruciform xanthoma has also been reported in patients with hypercholesterolemia, hepatitis C carriers, immunocompromised patients and with other oral mucosal diseases such as lichen planus, leukoplakia, and amyloidosis. Verruciform xanthoma must be differentiated from verruca vulgaris, papilloma, verrucous carcinoma, and squamous cell carcinoma.<sup>[1]</sup>

Histopathological examination reveals foamy histiocytes present within elongated dermal

Access this article online

Website: [www.idoj.in](http://www.idoj.in)

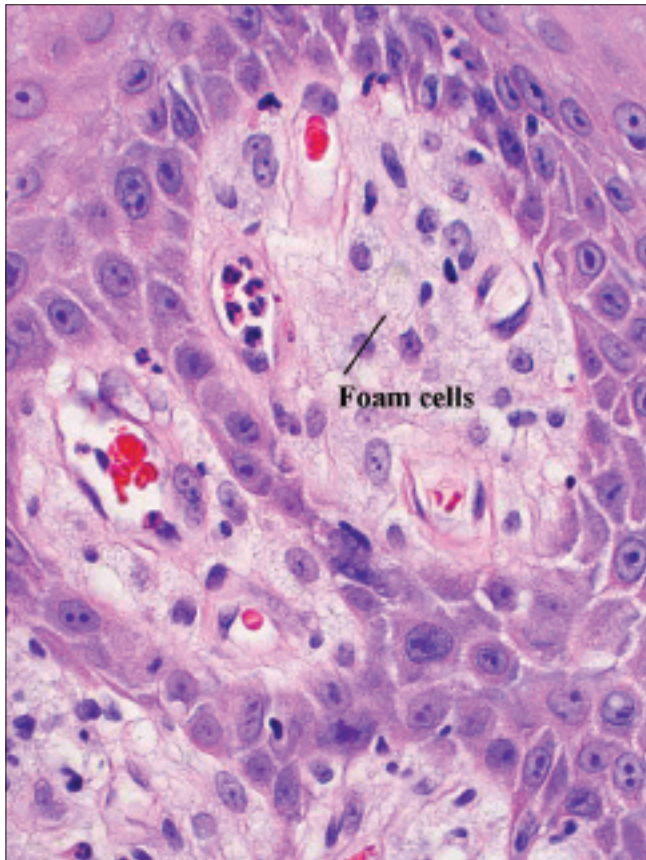
DOI: 10.4103/2229-5178.169719

Quick Response Code:



### Address for correspondence:

Dr. Dirk Elston,  
Department of Dermatology and Dermatologic Surgery  
Medical University of SC;  
MSC 578 135 Rutledge Avenue; 11th Floor,  
Charleston, SC  
29425-5780, USA.  
E-mail: [elstond@musc.edu](mailto:elstond@musc.edu)



**Figure 3:** Foam cells are present in the papillary dermis (H and E X 400)

papillae.<sup>[1]</sup> At scanning magnification, the appearance is characteristic, with an orange, red scale crust overlying an acanthoma with elongation of the rete ridges. Characteristic orange, red V-shaped areas of scale crust dip into the epithelium, resembling V-shaped arrows pointing to the xanthoma cells below.

It is postulated that verruciform xanthoma begins with the epithelial changes and progresses to the generation of foam cells.<sup>[4]</sup> T-cells are activated, and release cytokines are causing hyperplasia, which in turn expresses human leukocyte antigen-DR (HLA-DR) and interleukin 8 (IL-8) molecules. HLA molecules increase T-cell trafficking and IL-8 molecules cause neutrophil exocytosis into the parakeratin layer. An increase in epidermal lipids is seen in verruciform xanthoma. Another histological feature of this condition involves the flattening of keratinocytes caused by degeneration and squamatization of these cells, a sign of chronic epithelial damage.<sup>[1,5]</sup> The interactions of a potent monocyte/macrophage attractor, monocyte chemotactic protein-1, and chemokine ligand 2 (CCR2) cause upregulation of the macrophage and T-cell trafficking into the sub-basal papillae.<sup>[5]</sup> This is similar to mechanisms observed in gingivitis and periodontitis. The final step in the pathogenesis of verruciform xanthoma involves the transformation of

macrophages to foam cells. This occurs when activated T-cells recruit macrophages possessing CCR2 receptors causing macrophages to trap and internalize low-density lipoproteins (LDL) from epithelial cells and oxidize it. This results in the formation of foam cells.<sup>[1]</sup> Foam cells express macrophage scavenger receptor 1 (MSR-1) and oxidized LDL (Ox-LDL). MSR-1 allows verruciform lesions to sustain themselves and Ox-LDL serves as a chemoattractant for more T-cells and macrophages.<sup>[5]</sup>

Immunohistochemistry shows T-cells as the predominant cell type in the underlying inflammatory infiltrate, although neutrophils predominate in the crust. Foam cells are positive for CD68 antibody, a macrophage marker; therefore, they are considered to be of monocyte/macrophage lineage. Foam cells have also been shown to stain positively for cathepsin B, another macrophage marker, and negatively for S-100, weighing against the possibility of dermal dendritic cells as cells of origin.<sup>[1,5]</sup> Using immunohistochemical probes, Rawal *et al.* found that most foam cells found in verruciform xanthoma were of mature chronic inflammatory reparative phenotypes. This finding was consistent in the multiple clinically implicated sites such as gingiva, palate, and other mucosal sites.<sup>[1]</sup>

The clinical differential diagnosis primarily includes condyloma accuminatum, condyloma latum, porokeratosis ptychotropica, and the epidermolytic acanthoma. Condyloma accuminata is anogenital warts caused by the HPV, specifically subtypes 6 and 11. The pathogenesis of these lesions is related to sexual activity and is more common in immunosuppressed persons.<sup>[6]</sup> Lesions of condyloma lata are gray to white plaquelike lesions involving mucous membranes and may develop in patients with secondary syphilis.<sup>[7]</sup> Porokeratosis ptychotropica is a rare variant of porokeratosis characterized by a symmetrical pruritic eruption with erythematous papules and plaques classically involving the perinatal cleft and extending to the buttocks. These lesions have the classic histopathologic feature of multiple cornoid lamellae located at the periphery allowing a hyperkeratotic and verruciform appearance.<sup>[8]</sup> Epidermolytic acanthomas present as discrete keratotic papules typically located in the anogenital region with a histological analysis showing epidermolytic hyperkeratosis with vacuolar degeneration of keratinocytes within the granular and spinous epidermal layers and the presence of red and blue irregular keratohyaline granules. These lesions may also mimic condyloma accuminata clinically because of the extensive hyperkeratosis, papillomatosis, and acanthosis.<sup>[9]</sup>

The treatment of choice for verruciform xanthoma is excision, and no medical, chemical, or radiologic treatment is required after surgery.<sup>[2,4]</sup> No potential for malignant transformation has been observed till date.<sup>[10]</sup> Joo *et al.* recently showed successful treatment of lesions with shave debulking in combination

with fractionated CO<sub>2</sub> laser therapy with excellent cosmetic outcomes and decreased likelihood for recurrence.<sup>[11]</sup>

## REFERENCES

1. Hegde U, Doddawad VG, Sreeshyla H, Patil R. Verruciform xanthoma: A view on the concepts of its etiopathogenesis. *J Oral Maxillofac Pathol* 2013;17:392-6.
2. Dorankula SP, Ramani P, Premkumar P, Anuja, Sherlyn HJ. Verruciform xanthoma of the oral cavity-A case report. *J Clin Diagn Res* 2013;7:1799-801.
3. Joshi R, Ovhal A. Verruciform xanthoma: Report of five cases. *Indian J Dermatol* 2012;57:479-82.
4. Ryu da J, Lee SH, Yuk JI, Kim HJ, Huh JK, Park KH. Verruciform xanthoma of the palatal gingiva: A report of two cases. *J Korean Assoc Oral Maxillofac Surg* 2013;39:292-6.
5. Ide F, Obara K, Yamada H, Mishima K, Saito I, Kusama K. Cellular basis of verruciform xanthoma: Immunohistochemical and ultrastructural characterization. *Oral Dis* 2008;14:150-7.
6. de la Fuente SG, Ludwig KA, Mantyh CR. Preoperative immune status determines anal condyloma recurrence after surgical excision. *Dis Colon Rectum* 2003;46:367-73.
7. Begovac J, Lukas D. Images in clinical medicine. Condylomata lata of secondary syphilis. *N Engl J Med* 2005;352:708.
8. Yeo J, Winhoven S, Tallon B. Porokeratosis ptychotropica: A rare and evolving variant of porokeratosis. *J Cutan Pathol* 2013;40:1042-7.
9. Tan GF, Tan ES, Tey HL. Anogenital epidermolytic acanthomas: Effective treatment of pruritus with 0.1% tacrolimus ointment. *Dermatol Ther* 2014;27:113-6.
10. Bhalerao S, Bhat P, Chhabra R, Tamgadge A. Verruciform xanthoma of buccal mucosa: A case report with review of literature. *Contemp Clin Dent* 2012;3:S257-9.
11. Joo J, Fung MA, Jagdeo J. Successful treatment of scrotal verruciform xanthoma with shave debulking and fractionated carbon dioxide laser therapy. *Dermatol Surg* 2014;40:214-7.

**Cite this article as:** Andreychik C, Bernstein LJ, Elston D. Dermatopathology quiz: Cerebriform papules of the scrotum. *Indian Dermatol Online J* 2015;6:416-8.

**Source of Support:** Nil, **Conflict of Interest:** None declared.