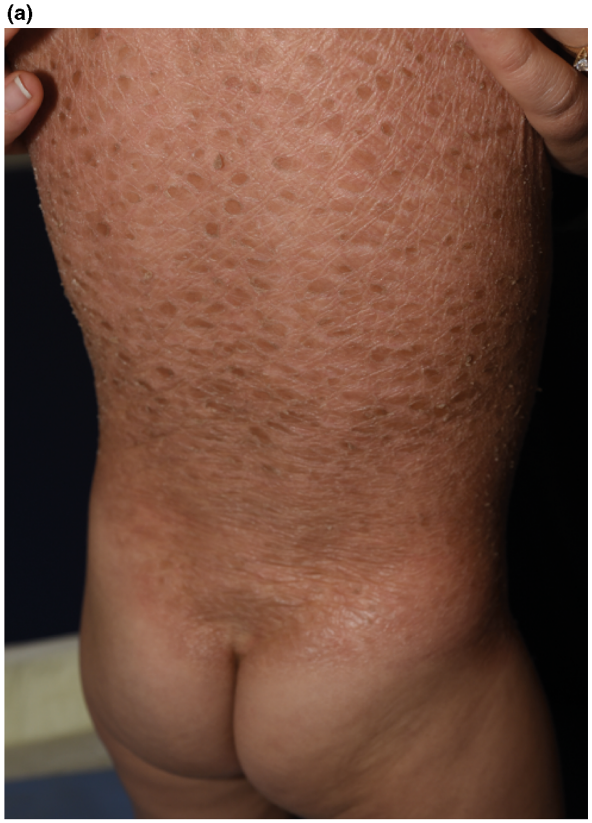
(a)



(b)

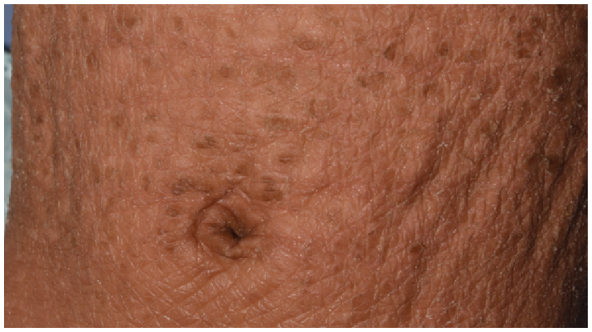


Figure 2 (a,b) Patient at the age of 1 year and 3 months showing lamellar scales located mostly on the trunk

Desquamation would appear on the warmer areas of the body, where the activity of mutant transglutaminase-1 (TGase-1) is significantly reduced as compared to the other body sites. On the other hand, there is a complete lack of the normal pericellular TGase-1 signal in affected skin, while there is a normal, less intense pattern in healthy skin.[2] Aufenvenne et al. showed that there is a reduction in the optimal temperature for the activity of the enzyme TGase-1 in patients with BSI. The optimum temperature for the normal enzyme is 37°C, while for the mutated one it is 31°C.[2] In this case, *TGM1* mutations are responsible for a temperature-sensitive phenotype. There is a resulting collapse of the stratum corneum lipid barrier, only reestablished at lower temperatures.[4] In BSI patients, hypohidrosis following extreme hyperkeratosis could lead to heat accumulation and hence summer exacerbation.[5]

The knowledge of the entity and its pathophysiology allows for better management and counseling for the families.

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***In lieu* of penectomy: complete resolution of penile melanoma *in situ* with topical imiquimod and tretinoin**

Dear Editor,

A 69-year-old Caucasian male with no personal or family history of skin cancer was referred to the dermatology clinic for a 15-month history of a pigmented lesion on the dorsal penile shaft with new-onset bleeding. Physical examination demonstrated a 2.5 × 2.3 cm, ulcerated, irregularly brown pigmented patch on the distal right shaft of the penis just proximal to the glans without palpable groin adenopathy (Fig. 1a). A diagnostic

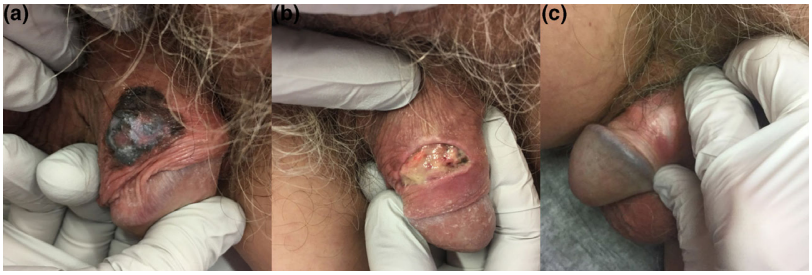

Figure 1 (a) Ulcerated melanoma on the distal penile shaft. (b) Wound on distal penile shaft after excision of melanoma. (c) Residual scarring and hypopigmentation at the excision site 1 month after completion of treatment with topical imiquimod

snip biopsy revealed an invasive melanoma to a depth of 0.79 mm with a positive margin. A 3.2 cm excision of the primary melanoma with narrow margins was performed (Fig. 1b). Histopathologic examination (Fig. 2a) demonstrated a proliferation of atypical melanocytes with ulceration and interspersed melanin. Breslow depth was 1.76 mm with 3-mitoses per square millimeter. Immunohistochemical staining was positive for Melan A and SOX-10, highlighting the melanocytic proliferation. Margins were histopathologically positive for melanoma *in situ* (MIS) (Fig. 2b). Wood's lamp examination of the wound edge demonstrated residual pigmentation. A subsequent staging bilateral superficial inguinal sentinel lymph node biopsy proved negative, consistent with T2b disease.

Various treatment options for the residual MIS were considered, including radiotherapy and intralesional chemotherapy. Consultations with urology and surgical oncology recommended definitive surgical removal via penectomy, which the patient declined because of quality of life concerns. *In lieu* of penectomy, a shared decision was made to start topical tretinoin 0.1% cream daily for 2 weeks followed by imiquimod 5% cream five times per week for 12 weeks. One month into treatment, the patient described mild erythema and pruritus at the treatment site and glans, the latter of which resolved with thorough application of a petroleum jelly barrier prior to treatment. At follow-up 1 month after completing the treatment course, the inflammation had resolved. At that time, there was mild scarring at the treatment site, no pigmentation with Wood's lamp examination, and no inguinal adenopathy (Fig. 1c). Confirmatory biopsy was planned at that time; however, the patient declined, opting for ongoing clinical monitoring every 6 months. No evidence of recurrence has been identified at 20 months follow-up.

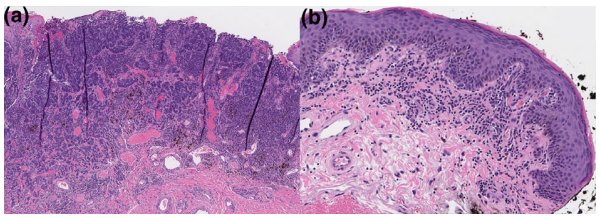

Figure 2 (a) Histopathology of ulcerated melanoma with Breslow depth of 1.76 mm and 3-mitoses per square millimeter (H&E, original magnification ×4). (b) The margins of the excised invasive melanoma were positive for melanoma *in situ* (H&E, original magnification ×14)

Primary penile melanoma is uncommon, with an incidence of approximately 1%, and has a higher mortality compared to cutaneous melanoma.[1] Over 80% of cases occur on the glans or prepuce, and less than 10% occur on the shaft.[2] Penile MIS is an even rarer entity.[3] Delay in diagnosis is common because of misdiagnosis, fear, or denial, with almost half of patients presenting with inguinal metastases.[1,4]

Surgical management remains the mainstay of both penile melanoma and MIS but may not be feasible because of functional or aesthetic complications, patient comorbidities, or patient preference. In this case, the presence of a significant *in situ* component was also considered the sufficient cause for disfiguring tissue removal/penectomy. The off-label use of topical 5% imiquimod has been reported for MIS, lentigo maligna, and cutaneous melanoma metastases with notable success in penile lesions.[3] This drug acts as an immune modulator by stimulating Toll-like receptors, and a robust immune response is responsible for the inflammatory side effects, including erythema and crusting. Imiquimod's penetration into the skin is often augmented by the addition of a topical retinoid, as in this case.[5]

When surgery may dramatically affect cosmesis or quality of life, such as in this case, off-label topical therapies like imiquimod can be an effective alternative. Further studies are needed in order to define the long-term prognosis and recurrence rate associated with the use of imiquimod for MIS.

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A healing case of orofacial granulomatosis with no medication

Dear Editor,

Orofacial granulomatosis (OFG) is an uncommon chronic inflammatory disorder which typically presents as recurring lip swelling, ulceration, and a cobblestone appearance of the buccal mucosa.[1,2] Histologically, the condition is marked by non-caseating granulomas.[1] The treatment of OFG is difficult, particularly in the absence of etiology.[3] Therefore, the aim of this study is to report a case of OFG which may be caused by tooth infection, and the healing of the condition was treated with no pharmaceutical application.

A 53-year-old woman presented to our Department of Oral Mucosal Disease in 2017 with a 2-year history of continuous right lower lip swelling and perioral skin fever. She had visited

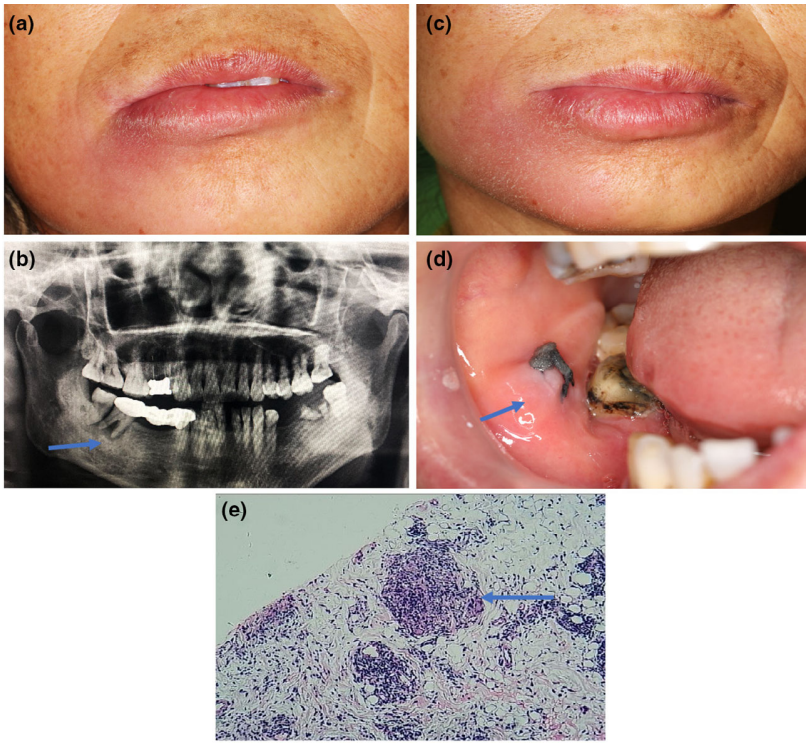

Figure 1 Symptoms of orofacial granulomatosis in a 53-year-old woman. (a) Pronounced right lower lip swelling, desquamation and perioral erythema. (b) Panoramic x-ray showed apparent periapical radiolucency of tooth #47 (arrow). (c) More apparent lip swelling and perioral erythema. (d) Biopsy on right buccal mucosa (arrow). (e) Histopathological examination revealed epithelial hyperplasia with submucosal inflammation infiltration that focally showed non-necrosis granulomatous features (arrow) (Hematoxylin and eosin, ×200)