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Genitogluteal porokeratosis in an HIV-positive man: a case report and review of the literature on genital porokeratosis

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Abstract

Genitogluteal porokeratosis is a disorder of keratinization that may present in men in their fourth decade of life. We describe a 52-year-old human immunodeficiency virus (HIV)-positive man with history of anal squamous cell carcinoma who developed verrucous lesions on the buttocks and genitals. The buttock lesions presented shortly after radiotherapy for anal carcinoma a decade prior, whereas the genital lesions presented three months prior in areas treated with injectable medication for erectile dysfunction. Skin biopsy revealed a cornoid lamella, leading to the diagnosis of genitogluteal porokeratosis. The buttock lesions were treated with shave excision and the genital lesions were treated with topical agents. Using the PubMed database, a literature search was performed with combinations of the following key words: acuminata, condyloma, cornoid lamella, genital, genitogluteal, HIV, penile, porokeratosis, verrucous, vulvar. The generated papers and their references were reviewed. To the best of our knowledge, we present the first reported case of genitogluteal porokeratosis in an HIV-positive man. Notably, these lesions developed in sites of prior radiation or injection. This condition should be included in the differential diagnosis of chronic lesions of the genitals and buttocks in patients with HIV and/or history of radiation treatment and/or trauma to the genitogluteal region.

Keywords: acuminata, condyloma, cornoid lamella, genital, genitogluteal, HIV, penile, porokeratosis, verrucous, vulvar

Introduction

Porokeratosis is a disorder of epidermal keratinization, which can be hereditary or acquired [1]. It is characterized histologically by the presence of cornoid lamellae within the outer layers of the epidermis. When present on the genitals, the condition can be easily misdiagnosed as condyloma [2]. We present a human immunodeficiency virus (HIV)-positive man, with a history of anal squamous cell carcinoma (SCC), who presented with verrucous lesions within the genitogluteal region; biopsy confirmed the diagnosis of porokeratosis. It is important to include genitogluteal porokeratosis in the differential diagnosis of genital hyperkeratotic skin lesions.

Case Synopsis

A 52-year-old HIV-positive man with history of anal SCC presented for evaluation of persistent, mildly pruritic, growths on the buttocks, penis, and scrotum. His social history included receptive intercourse with male partners. He had treated the buttock and genital lesions with topical tea tree oil with limited response.

The patient's anal carcinoma had been treated with surgical excision and chemoradiation a decade ago. Per self-report, the buttock growths began several weeks after completion of radiation treatment.

The patient also had a two-year history of erectile dysfunction, which he treated with an injectable

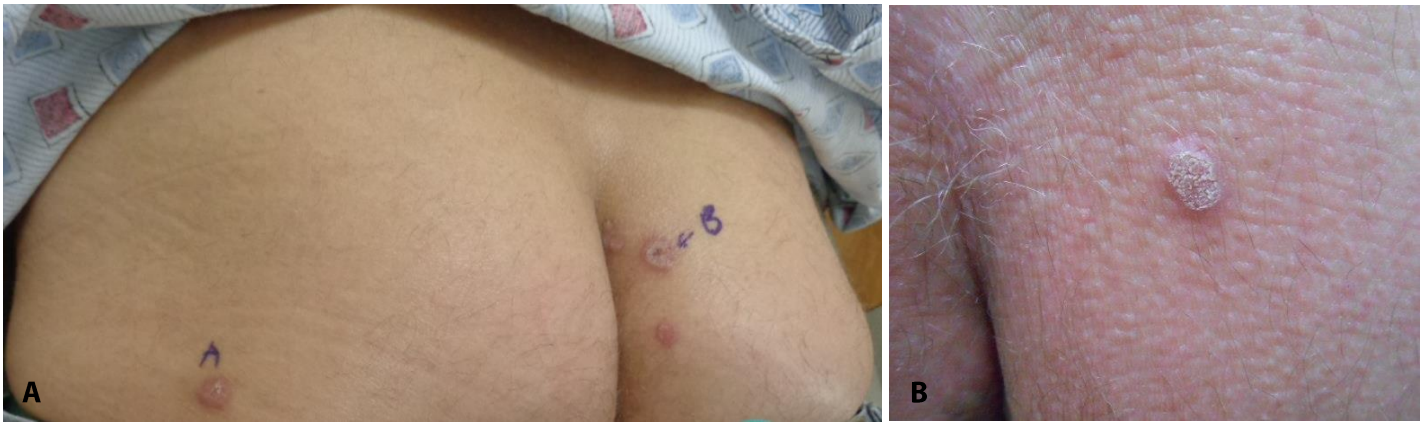

Figure 1. *Distant (A) and closer (B) views of the porokeratosis lesions on the buttocks. Closer view highlights the double-edged scale present at the periphery of a pink scaly papule. The left buttock shows a pink-to-red hyperkeratotic papule. Note that 'A' and 'B' denote biopsy sites.*

combination of alprostadil, papaverine, and phentolamine. The injections were delivered intracavernosally. The patient commented that his penile lesions were in areas he had previously injected. The penile and scrotal lesions began after two years of treatment; he stopped using the injectable medication with the onset of the lesions.

Cutaneous examination was remarkable for a pink hyperkeratotic papule on the left buttock, whereas the right medial buttock revealed multiple pink-to-red scaly verrucous papules (**Figure 1**). The right lateral penile shaft revealed several verrucous papules and plaques with white scale and raised borders; one hyperkeratotic papule was seen on the dorsal penile shaft (**Figure 2**). On the scrotum, a single skin-colored scaly papule with a raised, thread-like border was seen (**Figure 3**). Considering the patient's history, the clinical differential diagnosis of these lesions included primary SCC, condyloma acuminata, condyloma lata, cutaneous metastases, and genitogluteal porokeratosis.

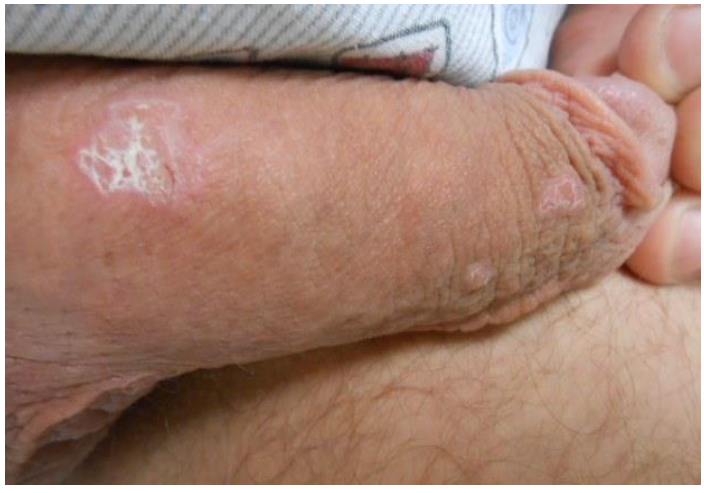

Figure 2. *Penile porokeratosis. The right lateral penile shaft has three hyperkeratotic papules and plaques.*

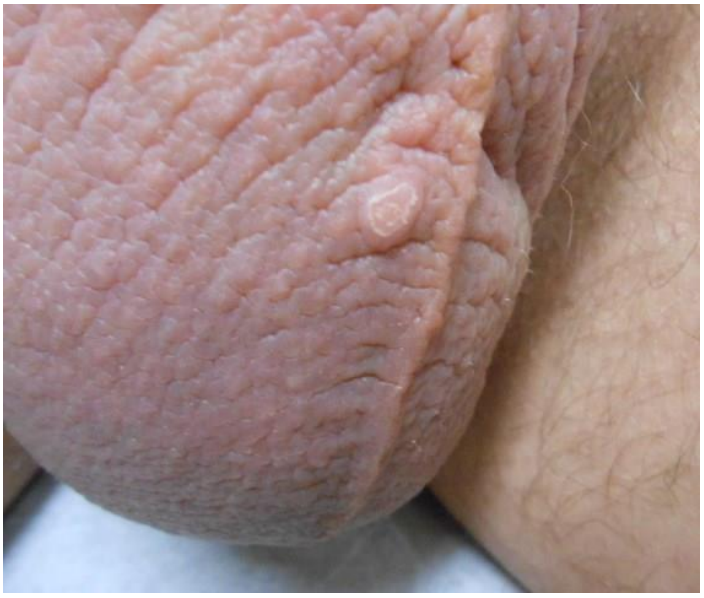

Figure 3. *Porokeratosis of the scrotum. One skin-colored scaly papule with a thread-like, double-edged border is seen..*

Biopsies were taken from the left and right medial buttocks; the patient deferred biopsy of penile and scrotal lesions. Histopathology revealed marked verrucous papillomatosis, psoriasiform epidermal hyperplasia, and cornoid lamella (**Figure 4**). The dermis showed a mild inflammatory cell infiltrate with telangiectatic vessels. No significant squamous dysplasia or evidence of malignancy was identified.

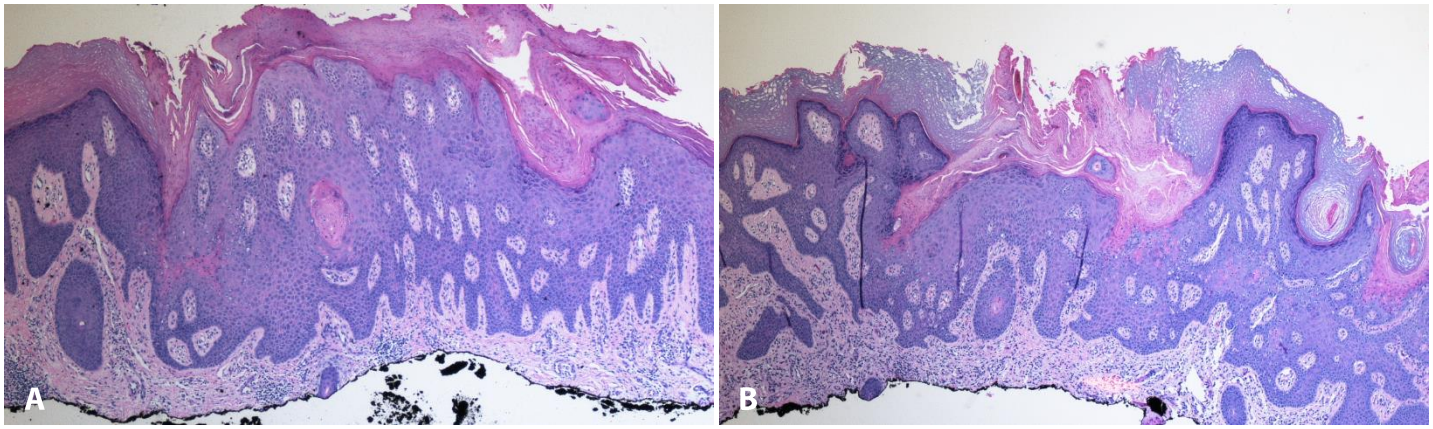

Figure 4. *Pathologic findings of genitogluteal porokeratosis. Microscopic examination of the right (A) and left (B) buttock lesions shows prominent verrucous hyperplasia and several epidermal invaginations with parakeratotic tiers (cornoid lamellae). There is underlying hypogranulosis and dyskeratosis. A mild inflammatory cell infiltrate is present in the dermis. H&E; A, B, 10×).*

Correlation of the patient's physical examination and histopathologic findings established the diagnosis of genitogluteal porokeratosis. At a follow-up visit two months later, well-healed biopsy site scars were seen. The remaining buttock lesions were removed with shave excisions (histopathology of which also showed porokeratosis) and he began daily application of topical 0.025% tretinoin cream and 5% imiquimod cream for the penile and scrotal lesions.

Case Discussion

Five variants of porokeratosis have been defined: classic porokeratosis of Mibelli, disseminated superficial actinic porokeratosis, linear porokeratosis, punctate porokeratosis, and porokeratosis palmaris et plantaris disseminata [3]. More recently, the terms verrucous porokeratosis and porokeratosis ptychotropica have been used to describe lesions involving the gluteal cleft [3, 4].

Porokeratosis involving the genitals is rare; it was first described in 1985 [5]. **Table 1** summarizes the characteristics of our patient and the 69 previously reported individuals [1-3, 5-33]. Median age at time of diagnosis is 39 years, with a range of eight to 75 years. Median duration of disease at time of diagnosis is three years, with a range of one month to 40 years.

Porokeratosis of Mibelli is autosomal dominant. However, porokeratosis involving the genitals appears to arise sporadically given lack of family history in these patients [6]. Genital involvement favors men; only 7% of the patients were women. Genital involvement appears to have a predilection for the Asian population; more than 80% of the patients for whom race information was provided were Chinese, Indian, Japanese, and Korean.

Porokeratosis involving the genitals has a polymorphic presentation (**Table 1**). Many patients presented with well-defined erythematous-to-brown annular papules and plaques with central atrophy and raised borders. Hyperkeratotic verrucous papules and plaques were also described, as in our patient. Pruritus was noted in about 75% of the patients if symptoms were discussed. Disease limited to the genitals was reported in approximately 65% of patients, with the remaining individuals displaying extension to the buttocks, perineum, or thighs. The clinical differential diagnosis includes Bowen disease, condyloma acuminata, condyloma lata, eczema, extramammary Paget disease, fungal infection, granuloma annulare, lichen planus, lichen sclerosus chronicus, lichen sclerosus et atrophica, and psoriasis [6-10].

Histologically, all variants of porokeratosis are characterized by the presence of the cornoid lamella [11]. This appears as parakeratosis overlying an epidermal invagination. The underlying epidermis demonstrates loss of the granular layer along with dyskeratotic keratinocytes.

The etiology of porokeratosis remains to be established. However, repeated trauma from friction or scratching has been considered to be a factor in

the pathogenesis [7, 12]. Our patient's lesions support a possible link to trauma; his buttock growths began soon after the completion of radiation treatments in the area 10 years prior, whereas his more recent penile lesions were in areas that had been repeatedly injected with the prostaglandin-based medication.

Porokeratosis may occur in the context of autoimmune disease, chronic liver disease, diabetes mellitus, HIV-associated acquired immunodeficiency syndrome (AIDS), and organ transplantation [36-42]. A compromised immune status is not common in patients with genitogluteal involvement, in contrast to porokeratosis involving the rest of the body that has been linked to immunosuppression [34, 35]. Our patient, to the best of our knowledge, is the first reported HIV-positive individual with genitogluteal porokeratosis. Two other patients were also found to have immune deficiencies; one patient had a reduced CD4-to-CD8 ratio without HIV infection, whereas the other patient had multiple myeloma [13, 14]. We hypothesize that local immune dysregulation secondary to prior radiotherapy, repeated trauma of injections, or HIV infection are possible mechanisms for disease pathogenesis in our patient.

Several therapeutic options for porokeratosis have been reported. Procedural methods of treatment include cryotherapy, laser ablation, and elliptical or shave excision [15]. Topical agents that have been applied include corticosteroids, diclofenac gel, 5-fluorouracil, imiquimod, salicylic acid, vitamin A derivatives, and vitamin D analogs [3, 9, 14, 15]. Oral acitretin has also been used [16, 17]. The topical agents may be successful in reducing the pruritus but often fail to clear the lesions. Excision has been successful in most patients [8, 12, 28].

Porokeratosis should be considered in the differential diagnosis of genital lesions. The condition may mimic ominous conditions such as primary SCC, particularly in our patient with a history of anal SCC. In addition, porokeratosis is considered to be premalignant since it is susceptible to malignant transformation. Overall, the risk of malignant transformation in porokeratosis ranges from 3.4% to 19% depending on the variant of porokeratosis present; the most common malignancies reported are basal cell carcinoma and SCC [43]. To date, the subsequent development of cancer has not been found in porokeratosis lesions involving the genitals. However, malignant transformation was observed in a woman with gluteal involvement; she developed invasive SCC on the buttock 18 years after her diagnosis of porokeratosis ptychotropica [44].

Conclusion

Porokeratosis involving the genitals is rare. The diagnosis should be considered in patients with chronic lesions in the genitogluteal region. Our patient, to the best of our knowledge, is the first HIV-positive individual reported with genitogluteal porokeratosis. The clinical morphology of his lesions mimicked condyloma and his history of anal SCC raised concern for recurrent or metastatic malignancy. Additionally, our patient is unique in that his lesions appeared in areas of prior trauma. Local immune dysregulation may have contributed to the development of genitogluteal porokeratosis in our patient. Patients with porokeratosis localized to the buttocks and genitals should be managed with careful monitoring since porokeratosis lesions may be associated with a risk of malignant transformation. Topical or procedural treatment can be considered.

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Table 1. *Summary of porokeratosis involving the genitals [1-3,5-33].*

Author, year	Cases	ARS	Location	Clinical manifestation	Dur (yr)	Num of lesions	Pruritic	IC	Mgmt	Response	Ref
Helfman, 1985	1	27 NR M	Penis, scrotum, thighs, inguinal folds	Salmon-colored plaques with elevated borders	5	Mult	NR	-	NR	NR	5
Levell, 1994	1	27 AA M	Penis, scrotum, gluteal cleft	Papules and plaques with hyperkeratotic borders	2	Mult	-	-	Topical agents[a], cryo	No response with topicals; no recurrence at 3 month FU with cryo	24
Neri, 1995	2	40,70 NR M	Penis	Annular plaque with raised hyperkeratotic borders and atrophic center	5	Sol	-	-	NR	NR	31
Tangoren, 1997	1	75 Ca M	Penis	Plaques with central atrophy and narrow hyperkeratotic borders	3	Mult	NR	-	Cryo	Resolved at FU	21
Trcka, 1998	1	70 NR M	Scrotum, Perianal area, thighs	Skin-colored papules and plaques with raised borders and atrophic centers	2	Mult	+	-	CO2 laser	Minimal scar at 6 month FU; 7 new lesions developed at 20 month FU	25
Robinson, 1999	1	39 NR W	Vulva	NA	30	Mult	+	-	Ultrasonic surgical aspiration	Resolved with procedure	20
Porter, 2001	1	56 NR M	Penis	Scaly annular plaque	2	Sol	-	-	Topical steroids, 5-FU	Resolved with 5-FU	19

Laino, 2004	1	36 AA M	Scrotum	NA	3	Mult	-	reduced CD4/CD8 ratio	NR	NR	13
Chen, 2006	10	36-59 NR M	Scrotum only (7), scrotum and buttocks (2), penis and thighs (1)	Erythematous to brown plaques with elevated borders	NR	NR	+ in 9 of 10	-	CO2 laser (4), topical agents (2), surgical excision (2)	At mean FU of 6 years, 4 of 8 had recurrence; excision patients lacked recurrence	12
Huang, 2006	6	29-66 NR 5M, 1 W	Scrotum, buttocks	Indurated keratotic plaques, white scaly plaques	1-9	Mult and sol	NR	-	Surgical excision and CO2 laser	No recurrence at 9 year FU	8
Kienast, 2006	1	15 NR M	Penis	Erythematous linear atrophic lesions	2	Mult	-	-	NR	NR	30
Perlis, 2006	1	64 K M	Penis	Erythematous lichenified plaques	Many	Sol	+	-	Topical steroid	Reduced pruritus	32
Kluger, 2007	1	68 NR M	Genitals in context of widespread body inv	Erythematous keratotic and erosive lesions	20	Mult	+	-	Topical agents[b], cryo, CO2 laser, surgical excision	Good response with cryo, laser, and excision; diclofenac and diflucortolone led to symptomatic relief only	28
Sengupta, 2008	3	34-36 I 2M, 1W	Vulva, scrotum, penis	Verrucous plaque on vulva; annular plaques with raised borders in the men	0.75 on vulva, 0.75 and 0.25 in the men	Mult and sol in men, sol in woman	+ on vulva, - in the men	-	Topical antifungal and steroids, surgical excision in woman, EDC in one man	Man with EDC had good response, NR in others	22

Valdivielso-Ramos, 2008	1	47 NA M	Scrotum	Plaque	NA	Sol	+	-	Surgical excision	NA	33
Benmously, 2009	1	50 NR F	Perineum	Annular plaques with keratotic borders and atrophic centers	1 month	Mult	-	MM	Topical tretinoin	No response at 3 month FU	14
Liang, 2009	1	22 NR M	Scrotum, penis, thighs	Annular plaques with thin, threadlike borders; inguinal fold with multiple verrucous papules and plaques	2	Mult	-	-	Podophyllin and cryo	NR	23
Schiffman, 2009	1	45 AA M	Scrotum, buttocks, groin	Patches and plaques with hyperkeratotic borders, some with atrophic centers	40	Mult	+	-	Topical steroids and retinoids, 5-FU	Some clearance and no recurrence	18
Garg, 2011	1	17 NR M	Genitals in context of widespread body inv	Linear annular scaly plaques	5	Mult	-	-	Oral acitretin, 5-FU	At 5 month FU all lesions flattened but did not clear fully	17
Gonçalves, 2012	1	39 Ca M	Penis	Linear areas with fine keratotic walls and atrophic, violaceous centers	15	Mult	-	-	Cryo	Improved at 2 year FU with no recurrence	27
Wanat, 2012	1	28 AA M	Scrotum	Thin red annular plaques with elevated borders	0.17	Mult	+ with burning	-	Cryo	Mildly improved then lost to FU	26

Dongre, 2013	1	34 I M	Scrotum and penis	Annular plaques with central atrophy	2	Mult	-	-	NR	NR	29
Ferreira, 2013	1	37 NR M	Scrotum, penis, gluteal cleft	Brown to red papules and plaques with raised borders	2	Mult	+	-	Topical steroids and antifungal	Limited response	6
Gu, 2014	11	8-61 Ch 10 M, 1 W	Labia majora, perianal area only (6), perianal with buttock (2), scrotum and penis (2), scrotum only (2)	Plaques with raised borders, verrucous papules	1-34	Mult and sol	+ in 9 of 11	-	Surgical excision (2); topical retinoic acid and topical steroid (9)	No recurrence at FU for excision patients; topical agents relieved itch only	11
Joshi, 2014	10	22-30 I M	Scrotum only (4), penis only (3), scrotum and penis (3)	Annular plaques with central atrophy and raised keratotic borders	Several months	Mult and sol	+	-	Topical steroids and antifungal, oral isotretinoin	Lesions flattened and itch subsided in 2 cases with isotretinoin	7
Ahmed, 2015	1	64 Ca M	Penis	Annular macule with collarette of scale and central atrophy	1	Sol	-	-	Shave removal	Remained clear at 6 month FU	9
Bhaskar, 2015	1	20 I M	Genitals in context of widespread body inv	Verrucous annular plaques with central atrophy	2	Mult	+	-	Oral acitretin, cryo	Lost to FU	16
Cabete, 2015	1	34 NR M	Scrotum	Annular plaque with raised hyperkeratotic borders	2	Sol	+	-	Topical steroids and antifungal, cryo, imiquimod,	No recurrence after excision	3

									surgical excision		
Guo, 2015	2	40,45 Ch NR, M	Scrotum	Annular hyperkeratotic plaque with raised borders	0.25, 0.5	Sol	+	-	Surgical excision	No recurrence at 1 year FU	1
Joshi, 2015	1	26 I M	Scrotum and penis	Erythematous atrophic plaques with raised keratotic borders	0.5	Mult	+ with burning	-	Topical steroids and antifungals, white paraffin	Pruritus subsided and lesions nearly cleared with paraffin	2
Khanna, 2015	1	22 I M	Scrotum and penis	Skin-colored scaly annular plaques with atrophic centers surrounded by hyperkeratotic borders	0.5-4[c]	Mult	+	-	Topical steroids and antifungals, oral isotretinoin with topical fluticasone propionate	Reduced itch and slight flattening of annular plaques with isotretinoin and steroid combination at 6 week FU	10
Mori, 2017	1	72 J M	Scrotum	Round flat brown plaque with raised borders	15	Sol	+	-	Cryo with topical maxacalcitol	Resolution within 3 months	5
Bari, 2017	1	52 Ca M	Penis, scrotum, buttocks	Hyperkeratotic verrucous papules and plaques with raised borders	Months to years[d]	Mult	+	HIV	Shave removal, topical tretinoin and imiquimod	No recurrence at 2 month FU from shave removal	CR

Abbreviations: +, positive; -, negative; 5-FU, 5-fluorouracil; A, age; AA, African American; Ca, Caucasian; Ch, Chinese; CR, current report; Cryo, cryotherapy; Dur, duration; EDC, electrodessication; FU, follow-up; HIV, human immunodeficiency virus; I, Indian; IC, immune compromised; Inv, involvement; J, Japanese; K, Korean; M, man; MM, multiple myeloma; Mgmt, management; Mult, multiple; NA, not available; Num, number; NR, not reported R, race; Ref, reference; S, sex; Sol, solitary; TBD, to be determined; Yr, years; W, woman

a: Topical agents included podophyllin, clotrimazole, clobetasol butyrate
b: Topical agents included betamethasone, vitamin D3, tazarotene, imiquimod, diflucortolone, and diclofenac gel
c: Lesions present for 4 years on the scrotum and 6 months on the penis
d: 9 years on the buttocks, several months on the penis and scrotum