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Vestibulovaginal Sclerosis in a Transgender Man on Testosterone

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Vestibulovaginal sclerosis (VVS) presents as a white plaque in the vestibule or vagina, previously reported only in perimenopausal and postmenopausal women[1–3] (see Table 1). This case expands the clinicopathologic definition of VVS: it may occur during reproductive age and the sclerosis may be focal. This case also highlights a knowledge gap regarding the impact of gender-affirming testosterone on vulvovaginal disease.

CASE REPORT

A 26-year-old transgender man presented with a painful white vulvar plaque present for 4 months. He denied injury, systemic illness, travel, change in medications, or traumatic sexual practices. Comorbidities included low back pain, pelvic pain with recent negative laparoscopy, restless leg syndrome, anxiety, bipolar disorder, and previous uncomplicated appendectomy. His medications were depot testosterone enanthate 125 mg every 10 days for 2 years, sodium valproate, escitalopram, and quetiapine. He was amenorrheic for 14 months, and cervical screening was normal and up-to-date. He received school-based quadrivalent human papillomavirus (HPV) vaccination. He smoked tobacco, used no other substances, and had a supportive relationship with a woman.

Vulvar examination demonstrated clitoromegaly and a white plaque over most of the hymenal ring that was tender to light palpation (see Figure 1). Cotton swab testing revealed scores of 7 to 9 over the abnormal skin, with a score at normal skin of 2. He consented to 4-mm punch biopsy of the hymen at 8 o'clock. Internal examination showed tight, tender levator ani muscles, and a mobile, anteverted, non-tender uterus.

The initial impression was chronic pelvic pain and vulvodynia with multiple associated factors. The etiology and clinical impact of the white plaque was unclear. The care plan included oral gabapentin, pelvic floor physiotherapy, and engagement with endocrinology, the pain team, and psychiatry.

Biopsy showed squamous epithelium with marked hyperkeratosis, hypergranulosis, irregular acanthosis, normal basal cell layer, absent lymphocytic infiltrate, and negative p16 immunostaining. The histopathologic diagnosis was benign hyperkeratosis and cannot exclude condyloma.

One month later, the lesion was unchanged. He had not accessed physiotherapy and took gabapentin 300 mg at night. He requested excision and was advised that this may not improve symptoms, but the larger specimen might provide a diagnosis. He underwent a posterior vestibulectomy with vaginal advancement, modified to remove the entire white plaque but leave normal skin in situ. For postoperative analgesia, a pudendal block with 0.25% bupivacaine was administered at the sacrospinous ligaments with 10 mL on each side.

The histopathology was consistent with vestibular sclerosis (see Figure 2). The hematoxylin and eosin stain demonstrated hyperkeratotic and acanthotic epithelium with a normal basal layer, sparse lymphocytic infiltrate, and focal sclerosis of the lamina propria. Periodic acid–Schiff (PAS) staining highlighted a thick basement membrane and focal subepithelial sclerosis. The specimen's negative HPV status was confirmed at a research laboratory with an L1 primer that detects any HPV type.

Three months after procedure, the surgical site was well healed with cotton swab scores of 0 to 2. Pudendal block provided 8 weeks of relief, followed by gradual return of myofascial pain. With time and multidisciplinary management, he reported intermittent pain-free periods. There was no VVS recurrence during 20 months of follow-up.

DISCUSSION

The incidence, etiology, and natural history of VVS are unknown.[1–3] Estrogen deficiency and trauma are proposed risk factors, but these are not universal across cases. The clinicopathologic features of VVS are (*a*) well-demarcated white plaque in the vestibule and/or vagina, sometimes incorporating a fissure, (*b*) subepithelial sclerosis, (*c*) absent or sparse lymphocytic infiltrate, and (*d*) normal or nonspecific epithelial appearance. Keratinization may occur but is not a diagnostic requirement.[2,3] This case is unusual for clinical and histopathologic reasons: VVS occurred in a young transman on gender-affirming testosterone, and the focal distribution of sclerosis meant that punch biopsy was nondiagnostic.

The differential diagnosis for a white vestibular plaque includes condyloma, high-grade squamous intraepithelial lesion, lichen sclerosus (LS), and epidermolytic hyperkeratosis.[2,4] The appearance was not typical for HPV-related disease, also excluded by negative p16 and HPV DNA. Mucosal LS is usually contiguous with vulvar disease; there was also no pruritus, no other dermatosis, and no lichenoid tissue reaction.[2] Epidermolytic hyperkeratosis is poorly understood, infrequently reported on the vulva, and has a benign clinical trajectory.

The role of VVS in his pain syndrome is unclear. The 2015 classification of vulvodynia emphasizes assessment for associated factors, to include hormonal status, musculoskeletal involvement, neurologic mechanisms, and psychosocial factors, each representing a potential treatment target.[5] Little is known about chronic pain in transmen. A study of transgender US Medicare beneficiaries found more claims for fibromyalgia and migraine compared with cisgender patients, with rates nearly doubled in those insured because of age rather than disability.[6] The impact of high-dose testosterone on vulvovaginal disease is unknown, but estrogen deficiency may alter local mucosal immune function and steroid receptor expression, potentially enhancing vestibular nociception.[7] Supporting the association between exogenous androgens and pain, a survey study of transmen identified that half reported pain with penetration while on testosterone, in contrast to rates of 20% before initiation of gender-affirming hormones.[8]

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The patient provided written consent for this case report and images.

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TABLE 1. Summary of Published Cases of VVS

	Age, y	Symptoms	Exogenous estrogen	Previous gynecologic procedures	Examination findings	Treatment	Outcome
Fadare[1]							
1	50	Dyspareunia	Nil	Nil	Multiple white plaques at distal vagina	Excision, topical estrogen	Not reported
2	52	Dyspareunia	Nil	Nil	White nodule at lateral vagina	Excision	Pain resolved, no recurrence
3	62	Dyspareunia	Topical estradiol	Hysterectomy and BSO	White nodule at distal posterior vagina	Excision	Not reported
Day et al[2]							
1	47	Dyspareunia	Topical estriol	Nil	Vestibular white plaque	Excision with flap repair	Pain resolved, no recurrence
2	56	Nil	Nil	Nil	Vestibular white plaque	Nil	NA
3	59	Dyspareunia	Nil	Nil	Pallor at posterior fourchette	Oral tricyclic antidepressant	Pain resolved
4	66	Nil	Nil	Nil	White plaque at distal vagina	Nil for white plaque	No change
5	69	Nil	Nil	Vaginal hysterectomy and prolapse repair	Nodular scar at posterior fourchette	Excision	No recurrence
6	70	Nil	Systemic estrogen and progesterone	Transobturator tape and pessary placement	Suburethral white plaque	Nil	NA
Croker et al[3]							
1	50	Nil	Nil	Not reported	Vestibular white plaque	Nil	NA
2	50	Dyspareunia	Topical estriol	Not reported	Subclitoral pallor	Topical potent corticosteroid and estriol	Minimal response
3	52	Dyspareunia	Nil	Not reported	Subclitoral white plaque	Nil	NA
4	54	Dyspareunia	Nil	Not reported	Subclitoral white plaque with fissure	Topical potent corticosteroid and estradiol	Minimal response
5	72	Dyspareunia	Nil	Not reported	Subclitoral white plaque	Topical potent corticosteroid and estradiol	Minimal response
6	83	Pain, itch	Oral estradiol	Not reported	White plaque at posterior fourchette	Topical mild corticosteroid	Minimal response

Abbreviations: BSO, bilateral salpingo-oophorectomy; NA, not applicable.

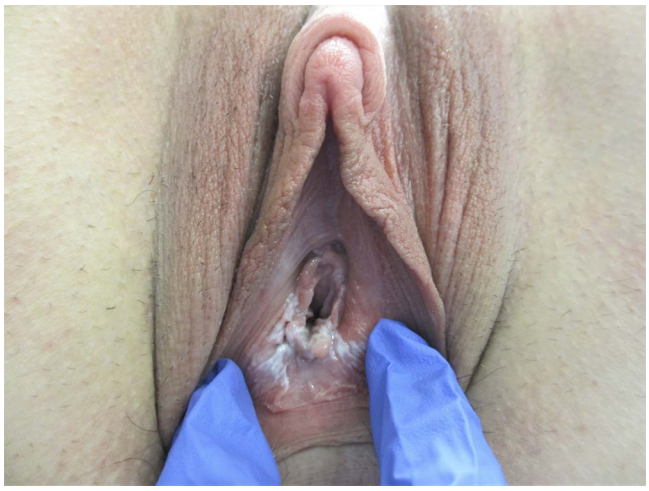

FIGURE 1. Clitoromegaly with otherwise normal vulvar architecture, and a white plaque extending over most of the hymenal ring.

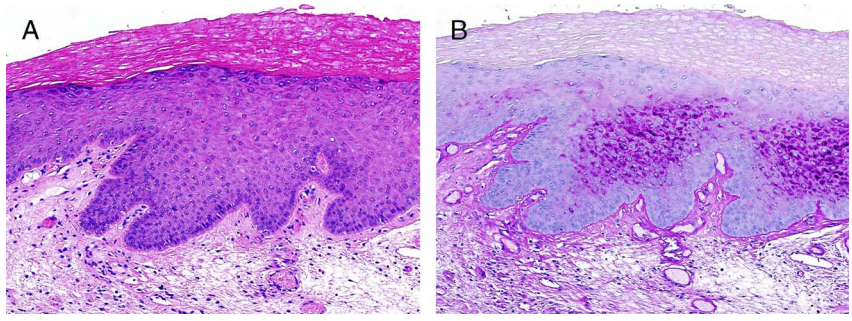

FIGURE 2. Vestibulectomy specimen showing (A) hyperkeratosis, irregular acanthosis, normal basal layer, thickened basement membrane, a focal thin band of sclerosis, and sparse lymphocytic infiltrate, hematoxylin and eosin, ×100, and (B) PAS stain highlighting the thick basement membrane and subepithelial sclerosis, ×100.

Excision is the only treatment reported as effective in series of VVS. In this case, diagnostic posterior vestibulectomy allowed for identification of focal sclerosis and comprehensive histopathologic assessment to exclude LS. It also yielded local symptom resolution, but pain at other sites only improved after persistent engagement with neuromodulators, physiotherapy, and psychological modalities.

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