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MEDICAL COMORBIDITIES (AT GOLDSTEIN, M MINER AND SJ PARISH, SECTION EDITORS)

Vulvar Dermatoses: Diagnosis, Management, and Impact on Sexual Function

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Abstract Physicians often feel challenged in the diagnosis and management of vulvar diseases and their effects on psychosexual health. Vulvar dermatoses must be considered in the differential diagnosis of women experiencing female sexual dysfunction or vulvovaginal pain. This review will focus on the diagnosis and treatment of common vulvar dermatoses, including vulvar contact dermatitis, lichen simplex chronicus, vulvar psoriasis, lichen sclerosus, lichen planus, and vulvar intraepithelial neoplasia. The impact of these disorders on sexual well-being will be emphasized. A detailed history and physical examination, backed by confident knowledge of vulvar dermatoses, will aid in diagnosis and management of these diseases. Current gold-standard treatments will be discussed as well as innovative therapeutic approaches currently being developed. With increased clinician awareness and further research, vulvar dermatoses and resulting sexual dysfunction can be appropriately managed.

Keywords Vulvar dermatoses · Sexual function · Lichen sclerosus · Lichen planus · Lichen simplex chronicus

Introduction

Urogenital complains are among the most common seen by a wide range of health care providers, including family practitioners, gynecologists, dermatologists, nurse practioners, physician assistants, and certified nurse midwives [1•]. Vulvar dermatoses can be difficult to diagnose as they present in a variety of ways. The differential diagnosis is broad and may include contact dermatitis, lichen simplex chronicus, lichen sclerosus, lichen planus, psoriasis, or potential malignancy [2]. To aid practitioners in diagnosis of vulvar dermatoses, the International Society for the Study of Vulvovaginal Disease (ISSVD) introduced a clinically orientated classification in 2011 [3].

Vulvar dermatoses may cause chronic pain, itching, and dyspareunia, all of which may negatively impact women's sexual function [4•]. As such, physicians and allied health care providers must be prepared to diagnose and treat vulvar dermatoses. This review will discuss the diagnosis and treatment of common vulvar dermatoses, with a focus on how these conditions affect sexual function and well-being in women.

An Approach to the Vulva

Most women do not realize that vulvovaginal symptoms are common and, in turn, may feel isolated due to their condition. Patients may become embarrassed discussing vulvar complaints, even with their physician. In this solitude, women might fear that their symptoms represent cancer or a sexually transmitted disease [5, 6]. Vulvovaginal disease can significantly affect sexual well-being, including sexual function and intimacy [4•, 7]. These conditions can present with dyspareunia, itching, fissuring, and post-coital bleeding [8]. Frustration and depression are common in most chronic pain conditions, and should be a consideration with chronic vulvar disease as well [9, 10]. Unfortunately, even with adequate medical management, sexual function may not return to normal [11].

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A comprehensive history and physical examination is essential in the management of vulvar conditions. Details of onset and duration of symptoms, aggravating and alleviating factors, and current sexual practices are necessary. A dermatologic history is extremely important, including a history of atopy, autoimmune disease, and dermatologic conditions including psoriasis and candidiasis, as well as any therapies and responses to treatment. A full sexual history, including sexually transmitted infections, should be obtained. It is important to review all medications, especially any topical or over-the-counter preparations. A history of genital surgery, including labiaplasty, should also be elicited. Lastly, exercise regimens and vulvovaginal care habits should be discussed.

A general physical examination, including the skin, eyes, thyroid, and mouth, should be performed, as some vulvar dermatoses are associated with autoimmune conditions and extra genital lesions. Examination of the vulva should be systematic and thorough. Proper lighting is essential, and vulvoscopy is recommended, as magnification may aid in diagnosis. Sometimes, a mirror may be helpful to allow the patient to communicate the location of concern. An optimal vulvar examination is performed with the patient in dorsal lithotomy position. Observation of the vulva includes identification of atrophy, erythema, induration, fissures, lichenification, ulceration, erosions, changes in pigmentation, and scarring, including phimosis of the clitoris and narrowing of the introitus. A cotton swab may be used for gentle palpation of the area to detect tenderness or decreased sensation. A speculum examination is necessary to detect vaginal findings, such as ulceration, synechiae, loss of rugae, pallor, and petechiae. Vaginal discharge should be obtained for cultures, wet mount, and pH assessment [8].

Indications for vulvar biopsy include lesions that exhibit lichenification, hypo or hyperpigmentation, induration, ulceration, abnormal vascular changes, or do not respond or worsen during treatment. Providers should have a low threshold for vulvar biopsy in the setting of an uncertain diagnosis, especially in the case of abnormal findings, suspicion of malignancy, or in patients with a known autoimmune disorder or immunocompromised status [6]. A consultation with an experienced dermatopathologist may aid in accuracy of biopsy results. Bowen et al. [12] found that 61 % of patients with refractory vulvodynia (i.e., vulvar pain) were found to have a clinically relevant dermatoses, including lichen sclerosus, allergic/irritant dermatitis, lichen planus, or other inflammatory or neoplastic dermatoses, upon analysis of vulvar biopsy [12].

Contact Dermatitis

Contact dermatitis is one of the most common and often avoidable problems seen in clinics that specialize in vulvar disorders (Boardman 2013). The reported incidence of vulvar contact dermatitis in these settings ranges from approximately 15–30 %; however, with increased use of vulvar hygiene products, the incidence is rising [13]. Contact dermatitis has been reported to occur in 20 to 60 % of patients with chronic vulvar symptoms [14•].

In this condition, exogenous agents such as irritants or allergens cause inflammation of the skin. Irritants are directly cytotoxic to keratinocytes without prior sensitization, while allergens stimulate a type IV delayed hypersensitivity reaction in sensitized individuals [15]. Vulvar skin is especially vulnerable to dermatitis due to intrinsic as well as environmental factors [10]. Common irritants include body fluids, feminine hygiene products (such as pad or panty-liners), lubricants, condoms, soaps, laundry detergents, and fabric softeners. The most sited allergens are anesthetics (particularly Benzocaine), antibiotics, antiseptics, douches, fragrances, nickel, rubber, and spermicides [16–18]. Women with a personal or family history of atopy or eczema tend to be more prone to contact dermatitis [19].

Clinical examination may reveal a range of findings from mild erythema and swelling to severe erythema, fissures, skin thickening, erosion, and ulceration. Acute lesions of contact dermatitis characteristically develop within minutes to hours after exposure, and are typically localized to the area of exposure [14•, 19]. A detailed history and physical examination are keys to diagnosis; however, physicians should have a low threshold for biopsy to rule out coexisting conditions. Histologically, lesions are characterized by intraepidermal edema or spongiosis, as well as a dermal infiltrate of lymphocytes and possibly eosinophils [1•].

With continued exposure or chronic scratching, lichen simplex chronicus may develop. In the setting of contact dermatitis that is long-standing or unresponsive to treatment, secondary or iatrogenic causes, such as Candida infection, should be considered [1•]. It is also important to rule out lichen sclerosus, lichen planus, candidiasis, psoriasis, sebhorriec dermatitis, and extra-mammary Paget's disease. Patch testing can be used to detect a specific allergen [2, 13].

Identification and removal of the causative agent is essential for successful treatment. It is important to counsel patients on allergen and irritant avoidance [2]. Inflammation may be alleviated with topical steroids, including triamcinolone 0.1 % ointment twice daily for moderate cases and clobetasol 0.05 % ointment once daily for severe cases. If relief is not achieved within 4 weeks of treatment, therapy with oral corticosteroids may be indicated [10].

Ice packs and antihistamines are helpful for vulvar pruritis. Scratching during sleep can be especially difficult to treat. An antihistamine with sedative properties, such as hydroxyzine, may relieve nighttime symptoms. In more severe cases, a low-dose tricyclic antidepressant, such as amitriptyline, may be given at bedtime for this purpose [10]. Patients should be examined between 2 to 4 weeks after initiating treatment, with steroids and anti-depressants tapered after the resolution of

symptoms. Superimposed fungal and bacterial infections are common and should be treated with fluconazole and oral antibiotics, as indicated [5]. Patients who do not respond to treatment will need re-evaluation and biopsy to exclude other conditions.

Lichen Simplex Chronicus

Lichen simplex chronicus (LSC) of the vulva is a chronic eczematous condition characterized by intense and unrelenting pruritis, leading to scratching and lichenification. The disorder, also known as neurodermititis, pruritus vulvae, squamous hyperplasia, and hyperplastic dystrophy, represents an end-stage response to a causative process [8, 19]. In vulvar specialty clinics, LSC is found in 10 to 35 % of patients, with 65–75 % of these patients reporting a history of atopy [19]. Irritants and infections may lead to chronic scratching, resulting in the skin developing a leathery and coarse texture with increased skin markings called lichenification. The vulvar skin can exhibit variable pigmentation, appear edematous, or become excoriated with fissures and broken or absent pubic hair (Fig. 1). Excoriation and fissures can become infected with yeast or bacteria [8, 19]. A biopsy may be necessary to exclude lichen sclerosus, lichen planus, or vulvar intraepithelial neoplasia (Burrows 2008). Histology from LSC reveals hyperkeratosis, hypergranulosis, and superficial dermal fibrosis [1•].

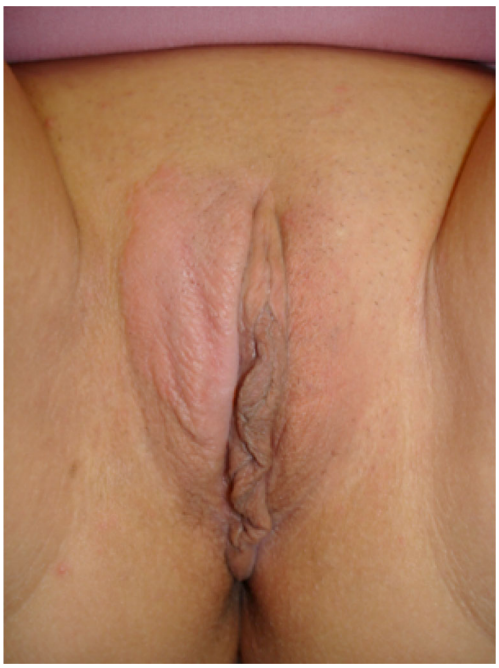

Fig. 1 Lichen simplex chronicus (LSC) occurs when an irritant leads to chronic scratching, resulting in a leathery and coarse texture of the vulvar skin. Lichenification may be more pronounced on one side. Source: Krapf, J.M., Goldstein, A.T. (2012) Vulvar dermatoses: part of the differential diagnosis for sexual dysfunction. The female patient, 37(4); 28–34

LSC affects quality of life, impacting both psychological and sexual well-being. Women with this condition report a constant "awareness" of their vulva, which may lead to self-consciousness in regard to sexual activity [8]. LSC has been associated with psychological problems, including demoralization, depression, anxiety, obsessive-compulsive disorder, and sleep disturbance [20]. In a study evaluating the effects of LSC on female sexual function, 43 women with LSC and 46 matched controls completed surveys evaluating quality of life and sexual function. Women with LSC scored significantly lower on the female sexual function index (FSFI) than healthy controls, especially in the domain scores of desire, arousal, lubrication, orgasm, and sexual satisfaction [21].

Identifying and eliminating all irritant and allergen exposure is the first step in treatment of LSC. It is also essential to break the itch-scratch-itch cycle, which can be difficult as women may scratch in their sleep. Nighttime pruritis may be alleviated with application of ice, antihistamines such as hydroxyzine, or oral amitriptyline for neuropathic-related itch [10]. Inflammation may be treated with topical application of high potency corticosteroids or topical calcineurin inhibitors. In a open-label study of 12 women aged 25 to 53 with biopsy-proven vulvar LSC, Pimecrolimus 1 % cream led to complete resolution of pruritis in seven participants, with improvement in erythema, excoriation, and lichenification for all the patients [22]. Decreases in pruritis were also found with Pimecrolimus treatment in a small series of postmenopausal diabetic women with LSC [23]. Correction of skin barrier function may be facilitated through use of Sitz baths, topical estrogen therapy in cases of vulvovaginal atrophy, and application of a thin layer of plain petrolatum jelly [19]. Concomitant infections should be treated accordingly.

Vulvar Psoriasis

Psoriasis is a chronic inflammatory proliferative skin disorder affecting up to 4 % of the population. Five percent of patients with persistent vulvar symptoms are found to have vulvar psoriasis [24]. Genital psoriasis typically involves the labia and perineum, with 65 % of patients presenting with vulva symptoms having psoriasis in other skin areas. Patients typically report pruritis, irritation, or pain, with almost 30 % of women experiencing dyspareunia [25]. Histologically, cutaneous lesions are characterized by parakeratosis containing neutrophils, epidermal psoriasiform hyperplasia with loss of the granular layer and spongiotic pustules of Kujol, and thinning of suprapapillary plates [1•]. However, in a large retrospective series of 194 cases, Kapila et al. [25] concluded that vulvar psoriasis is a clinical diagnosis, as biopsy is often not diagnostic [25].

Management focuses on symptom relief and avoidance of trauma to uninvolved skin. Up to one-third of patients may have a secondary infection with *Candida albicans* or

Staphylococcoccus aureus, which should be treated. Management options for vulvar psoriasis include application of mid-to-high potency topical corticosteroids, weak tar cream, topical retinoids, calcipotriol, and topical tacrolimus. Kapila et al. [25] recommends initial treatment with a potent topical corticosteroid such as betamethasone or clobetasol propionate 0.05 %, followed by maintenance therapy with a low-potency corticosteroid (methylprednisolone aceponate 0.1 % or hydrocortisone 1 %) combined with a low-potency tar preparation or calcipotriol, which were found to be well tolerated on the vulva. In cases of severe disease, systemic treatment with methotrexate may be indicated [25].

Lichen Sclerosus

Lichen sclerosus (LS) is a chronic inflammatory skin disorder that affects approximately one in seventy women [26]. The condition exhibits a bimodal onset with peak incidence in premenarchal girls and menopausal women. LS is generally accepted as an autoimmune condition; however, other potential causes have been explored including genetic predisposition, local immune response, estrogen deficiency, and specific infections [27, 28]. Vulvar itching, especially at night, is the most common presenting symptom, although LS may also be entirely asymptomatic and found incidentally on gynecologic examination. With disease progression, scratching and sclerotic changes lead to erosions and fissures; progressive scarring results in narrowing of the introitus [27, 28].

Seventy-nine percent of women with LS report chronic vulvar pain [29]. Lichen sclerosus can cause sexual dysfunction, with introital dyspareunia, decreased orgasm, and decreased coital frequency [11]. In a study of 45 women with LS, most common sexual issues included vulvar pain, introital dyspareunia, and reduced frequency of sexual intercourse [30]. Progressive scarring leads to narrowing and stenosis of the vulvar vestibule and vaginal introitus, resulting in loss of tissue elasticity and easy tearing at posterior fourchette during intercourse [27]. A questionnaire of 215 women with LS revealed that of all quality of life domains, sexual function was the most impacted. Compared to controls, LS patients scored significantly lower in sexual desire, arousal, lubrication, orgasm, satisfaction, and pain, causing significant sexual distress [31]. Even after adequate treatment confirmed by improvement in biopsy specimens, women with LS continue to have significant sexual dysfunction as assessed by the female sexual distress scale [11].

Physical examination reveals ivory white atrophic plaques with a "cigarette paper" appearance. Repeat scratching may lead to thickened skin with ecchymoses and hemorrhage. With disease progression, the labia minora may adhere to surrounding structures, and painful fissures can develop (Fig. 2). Inflammation and scarring lead to labial resorption, burying of the clitoris (phimosis), and narrowing of the introitus [27, 28].

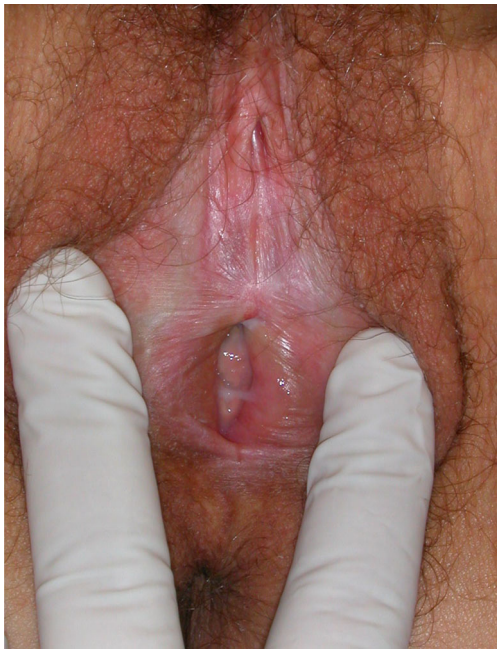

Fig. 2 Lichen sclerosus (LS) is characterized by ivory white atrophic plaques with a "cigarette paper" appearance, as well as resorption of the labia minora, fissures, and narrowing of the introitus. Source: Krapf JM, Goldstein AT. Lichen sclerosus. In The vulva: anatomy, physiology, and pathology, 2nd Ed. Farage and Maibach, editors. Springer Publishing; 2016

Skin changes may be difficult to distinguish from vulvar intraepithelial neoplasia (VIN). Vulvar LS is associated with the development of differentiated vulvar intraepithelial neoplasia (VIN) and squamous cell carcinoma (SCC), with risk of vulvar SCC estimated to be about 3–5 % [32–34].

Biopsy is preferred but may not be needed in typical presentations; however, with atypical features, diagnostic uncertainty, or failed response to treatment, histological examination is advisable [28, 35]. The classic histological features of uncomplicated LS include edematous superficial dermal area, or hylanized subepithalium with dilated vessels, loss of rete ridges, and red blood cell extravasation, as well as a lymphocytic infiltrate in the dermal layer. Often, histologic characteristics of superimposed lichen simplex chronicus, such as hyperkeratosis and epidermal hyperplasia, are also present [1•]. The pathology for LS is often difficult to interpret, especially after empiric steroid use [36].

Although there is no cure for LS, ultrapotent topical corticosteroids have shown the most promise in treating symptoms of vulvar LS [27]. A Cochrane review of seven randomized controlled trials with 249 participants evaluated five topical treatments, including clobetasol propionate 0.05 %, mometasone furoate 0.05 %, testosterone propionate 2 % cream, dihydrotestosterone 2 % cream, topical progesterone, and pimecrolimus [37••]. The recommended and first-line treatment of vulvar LS is the ultrapotent topical corticosteroid clobetasol propionate 0.05 % ointment [37••, 38•].

In a randomized control trial of 79 women with long-standing biopsy-proven vulvar LS, Bracco et al. [39] found that clobetasol proprionate 0.05 % applied twice daily for 1 month, then once daily for 2 months, was significantly better than placebo in improving symptoms, gross appearance, as well as histologic features [39]. Although there is no general consensus regarding optimal dosing regimen, most experts recommend application daily treatment for 2–4 weeks, followed by tapering over weeks to months [38•]. In a survey of 96 women with chronic vulvar LS treated with clobetasol, 69 % of patients achieved freedom from itching, with a global patient benefit index (PBI) of 3.06 and 93 % of patients reporting a PBI >1, indicating improvement in quality of life with treatment [40]. Formerly studied in penile LS, mometasone furoate 0.1 % has also recently been shown to be equally efficacious to clobetasol and well tolerated for the treatment of vulvar LS both with a tapering regimen and a continuous regimen for active disease, as well as maintenance therapy for up to 1 year [41–44]. Triamcinolone ointment, a medium-potency topical corticosteroid, has also shown to be effective in reducing patient symptom scores [45].

Topical calcineurin inhibitors, including tacrolimus and pimecrolimus, have also been studied in the treatment of LS. Goldstein et al. [46] conducted a double-blinded randomized trial of 38 women with biopsy-proven vulvar LS treated for 12 weeks with either clobetasol 0.05 % or pimecrolimus 1 % ointment. Outcome measures included inflammation on biopsy specimen and symptoms of pruritus, burning, and pain. Both clobetasol and pimecrolimus were found to be safe and efficacious in the treatment of vulvar LS, with clobetasol as the superior treatment in improving inflammation [46]. Funaro et al. [47] conducted a double-blind, randomized study of 55 women with vulvar LS, with 28 patients treated with tacrolimus and 27 patients with clobetasol. Both the groups showed a significant decrease in signs and symptoms of LS after a 3-month treatment period, but a significantly higher number of patients in the clobetasol group had complete resolution of signs and symptoms [47]. Given that the long-term safety profile is not yet established [48], topical calcineurin inhibitors are not to be used as first-line treatment.

There is no evidence in supporting efficacy of topical androgens or progesterone in treating vulvar LS [37••]. Cutaneous lysate, a topical compound composed of growth factors, anti-inflammatory interleukins, and interferons derived from cultured human fetal fibroblasts, has shown promise in improving symptoms of vestibulodynia, as well as lichen sclerosus [49, 50]. Additional studies of these newer treatment alternatives are needed.

Surgical treatment methods have also been reported. In a non-controlled study, Casabona et al. [51] reported improvement in itching and burning symptoms within 1 month after a surgical tissue regenerative technique involving injection of adipose-derived mesenchymal cells and platelet-rich plasma. All 15 patients with a histologic diagnosis of LS experienced total resolution of symptoms and restoration of sexual activity within 4 months after surgery [51]. High-intensity focused ultrasound (HIFU), which stimulates cell proliferation and revascularization, has also been investigated as a potential treatment for LS. In a review of 41 cases of lichen sclerosus, 38 cases of squamous cell hyperplasia, and 17 mixed cases treated with HIFU, 90 % of the patients showed symptom improvement or resolution 6 months after treatment, with decreased signs of inflammation on biopsy. However, almost 10 % of participants incurred skin burns with blistering [52]. In a clinical trial of 26 patients with vulvar LS randomized to treatment with UV-A1 phototherapy or application of clobetasol ointment, there was no significant difference between the treatment groups for clinical grading with both treatments reducing burning and pain. However, unlike the clobetasol group, the phototherapy group did not show a significant improvement in pruritis or quality of life [53]. Successful surgical treatment of both clitoral phimosis and vulvar scarring that inhibits comfortable coital function is relatively easy to perform provided post-operative treatment with corticosteroids, and vaginal dilators is used to prevent reactivation of active LS and recurrent adhesions [54]. Vulvectomy is not indicated in the management of uncomplicated LS and is reserved only for malignancy [27].

Patients should follow up 2 to 3 months after initiating treatment, followed by 6 months, and then annually if disease is well controlled. Poorly controlled women exhibiting ongoing hyperkeratosis or ulceration should undergo biopsy to evaluate for vulvar intraepithelial neoplasia and squamous cell carcinoma [35]. Although it was formerly unclear if medical treatments for LS prevented malignant transformation, a recent study showed that adequate treatment with corticosteroids significant lowers the risk of malignant transformation [55••]. Given these findings, asymptomatic patients exhibiting clinically active signs of disease require treatment, and treatment should likely be continued for a long-term course after resolution of active disease.

Lichen Planus

Lichen planus (LP) is an inflammatory mucocutaneous disorder that targets oral and vulvovaginal mucosa, in addition to the scalp, skin and nails. Estimates of prevalence for vulvovaginal LP are generally less than 1 %, with specialized vulvar clinics reporting prevalence up to 3.7 % based upon vulvar histology [28, 56]. Although the pathogenesis of LP is unknown, the condition is most likely a T cell-mediated autoimmune disease [57].

Patients with vulvovaginal LP may present with pruritis, burning, dyspareunia, post-coital bleeding, or purulent vaginal discharge [28]. Vaginal involvement is reported in up to 70 % of cases. Patients frequently report a copious yellow discharge,

which is comprised of leukocyte and parabasal cells (immature epithelial cells of the vagina). [28, 58]. The triad of erosive or desquamative vulvitis, vaginitis, and gingivitis comprises a unique syndrome called vulvovaginal-gingival syndrome [59]. This disease severely affects sexual interaction. In one published report from a referral practice, nearly 8 % of women examined for evaluation of vulvar pain were found to have LP [60]. Cooper et al. [61] found that 95 % of women reported sexual dysfunction, with dyspareunia in 60 % and apareunia in 35 % of women [61]. In a retrospective study of 95 patients with genital LP, over half reported dyspareunia as their primary complaint at the first visit, and 44 % of women had abstained from vaginal intercourse for at least a year [62].

There are three clinical types of vulvar LP: classic papulosquamous, hypertrophic, and erosive. Erosive LP (ELP), the most commonly recognized presentation of vulvovaginal LP, presents as glassy, brightly erythematous erosions accompanied by white striae (Wickham striae) (Fig. 3). The disease may markedly alter the vulvovaginal anatomy resulting in loss of the labia minora, narrowing of the introitus, phimosis of the clitoris, and narrowing or obliteration of the vaginal lumen [28, 58]. In a 2013 consensus paper, diagnosis of ELP can be made based upon at least three of the following clinical and histologic features: scarring, Wickham striae, mucosal involvement, vaginal erosions, pain and burning symptoms, vaginal inflammation, band-like infiltrate at the dermal-epidermal junction, lymphocyte predominance, and basal degeneration [1•, 63•]. Biopsy may be performed in the setting of unsure diagnosis or in the presence of hyperkeratotic lesions suspicious for malignancy, [2]. The histologic findings of ELP are often non specific, and only about

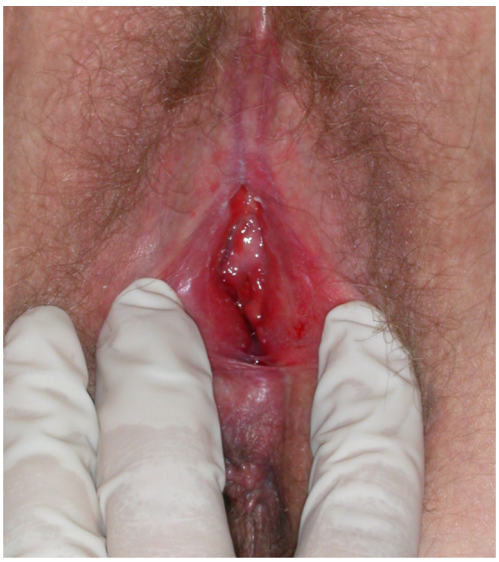

Fig. 3 Erosive lichen planus (ELP) presents as glassy, brightly erythematous. Erosions accompanied by Wickham striae. Source: Krapf, J.M., Goldstein, A.T. (2012) Vulvar dermatoses: part of the differential diagnosis for sexual dysfunction. The female patient, 37(4); 28–34

70 % of patients with clinical features of vulvar LP show histological evidence of disease [28, 64].

Vulvovaginal LP is difficult to treat; lesions are relatively resistant to available therapies. Based upon three large published studies, first-line treatment of vulvar LP is currently topical potent or ultrapotent corticosteroid ointments, although treatment failure rates have ranged from 25 to 70 % [59, 62, 65, 66]. Copper and Wojnarowska [65] found treatment with clobetasol 0.05 % ointment twice daily for 3 months led to symptomatic improvement in 94 % of women, with 71 % of the 114 patients achieving symptom resolution [65]. Kennedy and Galask [66] found treatment with topical steroids or calcineurin inhibitors led to resolution of symptoms in about one-third of the 113 patients [66]. In 85 patients treated with topical steroids, Santegoets et al. [62] found 70 % slight to moderate improvement [62]. Authors have reported improved disease control with individualized multimodal approaches of systemic (methotrexate or low-dose prednisolone) and topical (corticosteroid or tacrolimus ointment or vaginal pessary) therapies [67].

Flucocinonide 0.05 % or clobetasol propionate 0.05 % may be applied daily up to 3 months until lesions have resolved, then the topical can then be tapered slowly. Vaginal dilators can be used to apply the corticosteroids in the vaginal lumen to help prevent or disrupt synechiae. Soaking in warm water may aid in penetration of the topical through heavily keratinized lesions [58]. Vaginal LP may be treated with intravaginal hydrocortisone suppositories, which prevent obliteration of the vagina [2]. When topical medications fail, oral prednisolone 30–60 mg daily for 4 to 6 weeks is usually effective. [59].

Although not recommended for active LP, in cases of severe scarring of the vulva or vagina, surgery may be necessary to decrease urinary difficulties and restore a woman's sexual function [68, 69]. Suzuki et al. [69] found that surgery to release vulvovaginal adhesions allowed intercourse in 55 % of women, with 91 % of the patients reporting satisfaction. However, sexual difficulties may persist, as 50 % of the patients continued to fear pain with intercourse [69]. On follow-up visits, patients should be regularly assessed for signs of malignancy, with a low threshold to biopsy lesions refractory to treatment [2, 57].

Vulvar Intraepithelial Neoplasia

The classification of precursors for vulvar squamous cell carcinoma (SCC) has evolved over the past century. The most recent terminology, set forth by the International Society for the Study of Vulvovaginal Disease (ISSVD) in 2015, divides VIN into vulvar high-grade squamous intraepithelial lesion (HSIL) (formerly "usual" type VIN in the 2004 ISSVD terminology) and vulvar intraepithelial neoplasia, differentiated type [70, 71•]. This distinction reflects the different mechanisms of carcinogenesis. A human papillomavirus (HPV)-

related pathway leads to usual VIN, resulting in a warty or basaloid SCC. An LS-mediated pathway leads to differentiated VIN, resulting in keratizing SCC [71•, 72, 73•].

Differentiated VIN accounts for less than 5 % of VIN and often occurs in older women with LS or LP with a long-lasting history of pruritic symptoms. The risk of developing vulvar SCC in women with LS has been estimated to be 4.5 %, with an interval of about 10 years from diagnosis of LS to carcinoma. Studies indicate that p53 and PTEN mutations may play a role early in the pathway. A recent study showed that medical treatment of vulvar LS with topical corticosteroids may decrease risk of developing VIN and vulvar SCC [55••].

Differentiated VIN can be a diagnostic challenge. Lesions may appear gray or white with a rough and irregular surface. Any suspicious lesions that persist or are refractory to medical therapy warrant a biopsy [73]. Histology reveals prominent eosinophilic cells in the basal and parabasal areas with keratin formation within the rete ridges. Keratinocytes may display "pearl-like" changes and exhibit large vesicular nuclei. Differentiated VIN can be mistaken for benign lesions due to its high level of cellular differentiation [74].

Treatment options for VIN include surgical excision, laser ablation, and medical management. Vulvectomy is usually reserved for cases involving confluent, multifocal lesions or patients with persistent or recurrent disease. The aim of surgical therapy is to achieve free margins and preserve uninvolved structures in an effort to preserve normal anatomy [34]. In developing a therapeutic approach to VIN, many factors should be considered. Removal of areas at risk for malignant transformation may distort vulvar anatomy affecting sexual body image and result in dyspareunia. In addition, it not yet been fully proven that removal of VIN prevents invasive vulvar cancer in the future. In order to avoid vaginal stenosis and related dyspareunia, excision of vestibular sites should be reconstructed with advancement of the posterior epithelium [74]. CO_2 laser is a viable alternative to excisional therapy when cancer is not suspected, but requires increased depth of treatment and may result in increased scarring in hair-bearing areas [34].

Medical management is a treatment option that allows preservation of vulvar anatomy, but underlying cancer must be excluded. 5-fluorouracil has a response rate of up to 75 %, but is poorly tolerated and not used as a first-line medication.

Randomized controlled trials of the immune response modifier imiquimod show partial or complete response in treatment of VIN in over 80 % of patients, and is safe and effective for long-term treatment [75–77]. In a single case report, sinecatechins 15 % ointment, a botanical drug approved by the FDA for treatment of external anogenital condyloma, was used to successfully treat VIN in an immunocompromised patient who failed treatment with imiquimod. Prospective studies are needed to determine the role of this potential treatment option [78].

Conclusions

Vulvar pain and dyspareunia are common presenting complaints in the office setting. The effect of chronic vulvar conditions on psychosexual well-being is becoming increasingly recognized. Unfortunately, physicians often feel challenged in the diagnosis and management of vulvar disease and its effects on psychosexual health. Vulvar dermatoses must be considered as a part of the differential diagnosis for any women with sexual dysfunction or vulvovaginal pain. A detailed history and physical examination, backed by a confident knowledge of vulvar dermatoses will aid in diagnosis and treatment. The treatment of the vulvar dermatoses is still evolving, with innovative approaches currently being developed and examined in the literature. Novel treatments have targeted specific vulvar dermatoses.

Recent research has also focused on the sexual well-being component of vulvar dermatoses, but many questions remain unanswered. Sexuality is an important aspect in quality of life. Women with chronic vulvar conditions and their partners may be reluctant to broach sexual matters with their physician. This stresses the importance of the physician feeling comfortable identifying, counseling, and treating women with vulvar dermatoses. With increased clinician awareness and further research, chronic vulvar conditions and resulting sexual dysfunction can be appropriately managed.

Compliance with Ethical Standards

Conflict of Interest JMK declares that she has no conflicts of interest. ATG reports personal fees from Emotional Brain, research for Palatin, research for Bayer, and personal fees from SST, outside the submitted work.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- • Of importance
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