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Depigmentation's Disorders of the Vulva, Clinical Management

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Abstract

The cancer of the vulva is a rare disease with a positive association to poor developing countries. However, the incidence of vulvar cancer in situ nearly doubled in the last two decades and remained relatively stable. The main reason for this increased incidence of vulvar intraepithelial neoplasia (VIN) in women younger than 45 years is due to changes in sexual behavior, first intercourse at early age, multiple sexual partners, and sexually transmitted diseases that were increasing progressively. Furthermore, it is strongly associated with smoking and the increased incidence of HPV infection. The occurrence of early symptoms of VIN-like pruritus vulvae, pain, and lichen sclerosus led to early diagnosis to perform the adequate treatment. VIN tends to appear multifocal, while most invasive cancers are unilateral located and appeared with well-circumscribed lesions.

Keywords: lichen sclerosus vulvae, atrophic and hypertrophic disorders, vulvae, psoriasis

1. Introduction

1. The all vulva consisting of the mons pubis, the labia majora and minora, the clitoris, and the vulval vestibule, is covered by keratinized squamous epithelium as opposed to the vaginal mucosa covered by nonkeratinized epithelium of the same type. The labia majora carry hair and contain sebaceous and sweat glands. Embryologically, they correspond to the male scrotum. The lymph nodes of vulva drain to the external iliac lymph nodes via inguinal lymph nodes. The area is extremely vascular [1, 2].
2. After taking a detailed personal medical history regarding to hygiene techniques focusing on the use of antibiotic ointments, antiseptics, topical analgesics, lubricants should the gynecologist establish, whether the examining woman suffers from general skin conditions including dermatitis, psoriasis, lichen sclerosus, allergic contact dermatitis, or suspicious vulva disorders. It is commonly agreed that the rate of allergic dermatitis is high in combination to

vulvar symptoms [3]. During the examination, the clinician should carefully examine the vulva and pay attention to skin or mucosal color (erythema and intense red); texture can provide clues to correct diagnosis (e.g., slight hyperkeratosis and thickened skin) existence of any lesions, which seems unusual for such macules, papules, or ulcers [4, 5]. Ulcers of vulva are diagnostically challenging due to variation in clinical morphology [4, 5]. The primary morphology is clinically relevant for identifying because it can significantly narrow the differential diagnosis. Diagnosis of vulvar ulcers based solely on clinical findings is often inaccurate, in most cases depending on sexually transmitted infections, but the differential diagnosis can include also dermatoses, trauma, neoplasms, hormonal-induced ulcers, drug reactions, or ulcer of unknown etiology [6, 7].

Subsequent to the completion of detailed observation, the clinician can decide for the diagnosis, if additional tools are necessary like speculum examination, vulvoscopy, or dermoscopy. The benefit of vulvoscopy remains controversial [8]. The contribution of dermoscope is mainly for the evaluation of both pigmented and nonpigmented lesions, presence of scarring, and loss of architecture but required training to identified benign structures and suspicious, worrisome features. It is crucial to document the number, type, size, border characteristics, and depth of lesions, discharge if present, tenderness, and presence or absence of local lymphadenopathy, which could influence mode of treatment [9, 10]. Cultures should be taken if there is suspicion for an infection, and final genital biopsies were recommended without to be prerequisite for the completion of the definitive diagnosis. It is an all common finding for a clinician to be frustrated by pathology report because it is sometimes difficult for the gynecologist due to inherent challenges to approach the obtaining tissue from the genitalia.

In 1976, Freidich classified skin disorders of the vulva into three categories: (a) hyperplastic dystrophy, (b) lichen sclerosus, and (c) dystrophy with or without atypia. For example, the term of hyperplastic dystrophy was used to include completely different clinical features, such as psoriasis, chronic lichen planus, and Bowen's disease [11].

Due to diagnostic problems resulting from this classification, in 1989, the International Society for the Study of Vulvar Diseases established a new terminology, which has been maintained to date [12]. Nonneoplastic epithelial lesions were delineated as follows: (a) lichen sclerosus and atrophicus, (b) squamous cell hyperplasia (former hyperplastic dystrophy without atypia), and (c) other diseases of vulva, a category in which various injuries occur, such as psoriasis, lichen planus, fungal infections, and condyloma acuminata. Since cytological atypia is found in this category, the damage is "changing" category and now belongs to the VIN classification [12].

2. Disorders of the vulva

2.1 Dermatopathies

"Dystrophy" of the vulva is an abnormality of the vulva epithelium. Epithelial growth may be hypoplastic, hyperplastic, or abnormal in some other way [13, 14].

2.1.1 Atrophic and hypertrophic disorders

Atrophic and hypertrophic disorders of the vulva come under the general term of dystrophies (formerly characterized as "precancerous" conditions).

The skin, depending on the damage, may be appeared as white, dry, and thin or thickened, while hyperkeratosis and decreased vasculature are histologically present [15]. These alterations are mainly attributed to estrogen deficiency and, to this end, are often observed after menopause. The disorders may extend to the vaginal entrance, the perineum, etc. Usually there is intense pruritus, and the scratching it entails may result in an interception to the continuity of the skin. In addition to pruritus, there may be a burning sensation and dyspareunia, especially if the damage (usually atrophy) extends to the vaginal entrance [15]. For the treatment of pruritus, anti-inflammatory creams and topical corticosteroids are used (about two times a day). Antibiotic treatment is also administered in a transfection. In the absence of symptomatic treatment with conservative treatment and very intense annoyances of the patient, a simple vulvectomy can be chosen as “final” solution provided that the patient has been informed about the fact that in the half of the cases, the disease can relapse despite the surgical procedure [15].

Because of the fact that these disorders may coexist with malignancy, careful monitoring of the patient is required, and in doubt, multiple biopsies are required to exclude intraepithelial neoplasia (vulvar intraepithelial neoplasia/VIN) or cancer. Biopsies are often subjected to vulvovaginal screening after a 1–2% acetic acid solution is applied. However, the likelihood of developing invasive cancer in the soil of previous lesions is low. Given that these situations are well known, their descriptive “encyclopedic” terminology (in brackets, in italics) is not mentioned in the narrower “gynecological” or histological sense [16–21].

These alterations include:

- Lichen sclerosus
- Squamous cell hyperplasia
- Condyloma acuminata
- Psoriasis
- Lichen planus
- Mixed lichen sclerosus and atrophicus

The term dystrophic lesions of the vulva according to literature like writhing, leukoplakia, lichen sclerosus and atrophicus, it is preferable to not be used anymore [16, 20, 21].

2.1.1.1 Lichen sclerosus

“Lichen sclerosus” (LS) is a term used for a benign, chronic, progressive dermatological condition characterized by (intense) inflammation [22–25]. The epithelium is getting thinner, and some characteristic dermatological changes appeared accompanied by itching and pain.

In general, lichen sclerosus appears in the skin of the genitalia. It was first described by Hallopeau and Darier at the end of the nineteenth century as a variety of lichen planus, which is not acceptable today. The term lichen sclerosus (and/or atrophicus) should no longer be used, as forms of lichen sclerosus are not all atrophic. When there is coexistence of squamous cell hyperplasia, it is characterized as “mixed squamous cell hyperplasia and lichen sclerosus” [26–32].

Lichen sclerosis is considered as the most common chronic lesion in vulva, referred to a chronic atrophy that usually observed after menopause. Clinically, vulva is glossy and dry, with no folds. The lesions are often symmetrical. Although the condition is observed over a wide range of ages, it has an increased incidence in women aged 50–59 years. Postmenopausal women and young girls are usually afflicted before menstruation. There is no clear justification. There is sufficient evidence of involvement of autoimmune mechanisms in the pathogenesis of lichen sclerosis. It is known that 21% of patients with lichen sclerosis also suffer from autoimmune disease more often than with thyroid disease. It is reported that 22% of patients with lichen sclerosis have an inherited history, and that 44% have one or more autoantibodies. Also, there is a correlation with HLA II antigens. There are studies associating inflammatory factors, e.g., *Borrelia* infection, with the development of lichen sclerosis. It is also reported that there is overexpression of wild-type P53 protein in lichen sclerosis, which occupies areas adjacent to squamous cell carcinoma (SCC) in which HPV is not detected.

Typically, the rash of lichen sclerosis begins as white polygonal papules, which flock to plaques. Typically, candlesticks and/or clearly cracked plugs appear on the surface of the plate, and they are similar to attached nozzles. Over time, plugs and craters may disappear by dropping a smooth, often porcelain plaque, and they rarely show up. Thus, the skin appears white and thin, although it may be present in SCH [26–32]. Originally, lichen sclerosis may have a bubbling consistency and is characterized by edema of the prepuce clitoris and telangiectasia of labia and purpura. Stretch marks appear mainly in the middle perineal line. Bullous lichen sclerosis is often accompanied by bleeding within the lesion, and the fillet can disappear. Later, labia minora and structures around clitoris disappeared too. The epithelium of the vagina and the cervix is not affected. However, there may be lesions in the forehead of the skin, which will lead to its constriction. Perianal lesions are described in 30% of cases [26–32].

Lichen sclerosis is a benign vulva condition associated to chronic and often progressive character with dermatologic location. Among the clinical findings are included marked inflammation, epithelial thinning, distinct dermal alterations like pruritus, and pain by varying degrees. The described lesions appear most frequently in the labia minora, but the early disease course affects not the vulvar architecture. During the disease progresses, the following pathological signs may be possible to occur: sexual dysfunction, fissuring in perineal region and around the clitoris, distinction between labia majora and minora, edema from inflammation, purpural lesions, and excoriations ecchymoses given fragility of the affected skin region [5, 33]. The main symptom is pruritus. Pain occurs if there are corrosions and stretch marks. Itching is intense during the night and may be so intense that it stops sleeping. Discomfort occurs when there is erosion, stretch marks, or narrowing of vaginal orifice [26–32]. Some women are asymptomatic, and LS is a random finding. Most of them had active childhood disease, which resulted in skin atrophy without symptomatology. Occasionally, hyperkeratosis and ecchymosis occur, which should be treated [26–32]. In childhood, the lesions are similar to adult lesions. But the ecchymosis may protrude and can be so intense that it leads us wrongly to the suspicion of sexual abuse. The diagnosis in most patients is indicated by the clinical picture, but its confirmation by histopathological examination is considered necessary. LS should be differentiated from lichen planus, vaginal pemphigoid, psoriasis, VIN, and SCC, and this is done by biopsy under colposcopic control. Ulcers, nodules, and granulomas should be controlled to exclude malignancy. The formation of hyperkeratotic plaques and erosions, which do not exist despite the applied treatment, suspects malignant transformation [26–32, 34].

Histologically, there is a decrease in subcutaneous fat, atrophy of all skin layers, and destruction of elastic tissue. The dermis is of some degree vitreous degeneration and round cell collections [35–37]. Typical histological findings are also including a thinned epidermis with areas hyperkeratosis, acanthosis, a broad band of homogenized collagen under the dermo-epidermal ligament, and lymphocyte infiltration under the homogenate area [33, 38–39].

Few patients have thickening of the epidermis, and these are those who have not been responding to LS and who are at increased risk of developing SCC. Due to the frequent association of LS with autoimmune diseases, the appropriate control should be performed. In particular, the possibility of autoimmune thyroid disease should be investigated [26–32, 34].

Squamous cell carcinoma (SCC) in women with LS is a common malignancy described. There are also reports of basal cell carcinoma and melanoma. The risk of developing SCC is about 5%. However, histopathologic examination in woman with lichen sclerosus during follow-up revealed squamous cell carcinoma. The role of HPV as a causative agent in malignant transformation is not entirely clear. There are studies suggesting the existence of two types of SCC: one type occurs in older patients with chronic LS disease and the other type is in younger women without LS but with proven infection by oncogenic HPV types. Although there is no evidence of the role of HPV as a causative agent in the development of SCC on LS, there is the theoretical risk of developing SCC from the topical use of corticosteroids, which may promote the development of HPV oncogenic strains, since it was found that in 20% of cases LS, there may be HPV infection [40–43]. More recent reports support the strong relationship of vulvar invasive squamous cell carcinoma and LS, so that lichen sclerosus is considered as precancerous damage [33]. It is not uncommon for women with carcinoma of vulva from squamous cells to also have undiagnosed lichen sclerosis, which may also be asymptomatic [33, 38].

The role of midwives, especially those who have increased initiatives due to their position (e.g., the one who works in the Center of Health), is very important to properly direct these postmenopausal women. It is well known that empirical use of ointments in precancerous or cancerous lesions of the vulva delays proper treatment and requires a high degree of suspicion of the doctor and midwife for malignant malignancy [33, 38].

There is no universally accepted treatment for women with lichen sclerosus. The treatment includes education and support, change of behavior to ensure good pudding hygiene, medication, and, in a small proportion of cases, surgery or photochemotherapy. The medical treatment of the condition includes the topical use of corticosteroids, such as clobetasol [44–47]. The major importance of LS treatment is proved by the fact that about 80% of invasive squamous cell carcinoma (SCC) of the vulva in elderly patients was associated with untreated, long-term conditions of lichen sclerosus (the final stage of the vicious cycle of itching-scratching-itching). Generally, the management should perform in twofold.

The first step aims to resolve LS symptoms, vulvar, and vaginal pain.

The second step's goal is to reduce the disease signs like hyperkeratosis fissuring echymoses [44–47].

2.1.1.2 Squamous cell hyperplasia

The oldest term leukoplakia (“chronic inflammatory disease of the mucosa which results in keratinization of the epithelium and in the formation of white spots”) is still reported today. The disorder is characterized by white, tough, and overwhelmed, hyperkeratotic “plaques” of the vulvar epidermis, and a disorder of “hormonal homeostasis” in its etiology. Histologically, squamous cell hyperplasia is observed (**Figures 1 and 2**).

Figure 1.

VIN lesions are usually characterized by a change in color on the skin of the vulva. They are usually white and/or gray.

Figure 2.

VIN lesions: The rarities are lesions in red and brown. Their surface may be flat or abnormal.

This chronic and recurrent condition may occur at any age but is more common in older patients and usually manifests with pruritus. Less often, it occurs with dyspareunia or pain. It is an autoimmune condition and is associated with other autoimmune diseases such as malignant anemia, thyroid disease, diabetes mellitus, systemic lupus erythematosus, primary biliary cirrhosis, and bullous pemphigoid. Histologically, the skin appears thin with loss of the crevices found between the nipples. Surface skin is vitrified, and a set of chronic inflammatory cells is observed beneath it [48–53].

Clinically, the skin appears white, thin, and corrugated but may be overlapped and keratinized, if there is coexistence of squamous cell hyperplasia. There may also be symphysis of the clitoris or the vulva. The diagnosis is made by biopsy. Lichen sclerosus is a nonneoplastic condition but can coexist with vulvar intraepithelial neoplasia, while there is correlation with invasive squamous cell carcinoma of the vulva in 2–5% of cases. This is describing the reason why possible long-term monitoring is required every 6–12 months [26–32].

Treatment is required, especially if the condition is symptomatic, and a strong local topical steroid cream (e.g., Dermovate per 12-hour period) is usually used, which is gradually replaced by a milder formulation (e.g., hydrocortisone per hour, 24 h or less) as the symptoms require. Fluorinated corticosteroids or testosterone

ointment may also be helpful. Vulvectomy has no position in this case, as the recurrence rate after surgery is about 50% [26–32].

2.1.1.3 Psoriasis

Psoriasis is manifested as dry, red, and papular rash, which is usually clearly circumscribed and extends to the thighs. Diagnosis occurs easily when bleeding is observed during the removal of classic silver-like scars. It may be difficult to differentiate psoriasis from candida infection or dermatitis because the vulva is very often fluid. Candida infection should be ruled out. The lesions can be treated locally with coal tar preparations, ultraviolet maize, steroid creams, or other suitable drugs [54–56].

2.1.1.4 Lichen planus

It is a chronic papular rash with a bluish hue, which is located in the vulva and the bendable surfaces. It may be appeared in other areas like the mucous membrane of the oral cavity, and the diagnosis is enhanced by finding other lesions. Oral lesions precede genital lesions in one-third and simultaneously appear in half of women affected from the disease. After the vulva should be a vaginal examination, the walls of the vaginal may have following pathological abnormalities: erythema erosions and bleeding friable tissue. It is usually idiopathic but can also be related to medications. The treatment includes use of strong steroids locally or ultraviolet light, and the disease tends to subside within the next 2 years. Surgery removal should be avoided [57–62].

2.1.2 Others: vitiligo, intertrigo, aphthae

2.1.2.1 Vitiligo

The lesions of this disease can appear anywhere on the body with a predilection in the genital area. It can be confused with LS, associated to lack the classical signs of inflammation, possible coexistence with LS based on autoimmunogenity. In contrast to LS, which has predilection for hypooestrogenic states, vitiligo can be appeared at any age. No skin biopsies are necessary. Autoimmune thyroid disease is associated to vitiligo. Treatment includes administration of topical steroids and vitamins D, E, C, and B12. Surgery remains a viable option in unresponsive localized disease to conventional therapies [63–71].

2.1.2.2 Aphthae

They are vulva disorder associated to pain. Shallow ulcers most commonly occur on the oral mucosa and less commonly on the genital mucosa. The reasons are uncertain, and risk factors include stress, infections, hormonal factors, vitamin deficiency, and family history. The diagnosis result from exclusion of various genital ulcers causing in most cases in assumption of sexually transmitted infection. Aphthosis appears in simple and rare complex form, and the recurrence rate is about 20% of the general population. For the treatment, it is important to educate the patients to conform in skin and wound care and administration of topical corticosteroid propionate ointment in cases of complex aphthosis [63–71]. Aphthae should differentiate from Behcet syndrome, a disorder that causes inflammation of the blood vessels throughout the body, and could affect the vuvla causing open sores in the vulva. Furthermore, vulva aphthous ulcers could appear in patients with HIV infection, Chrohn disease, and ulcerative colitis.

2.1.2.3 Intertrigo combined with candida infection

Intertrigo is a wet inflammatory dermatitis, which can occur on any fold of the body because of the irritation of the exposed skin surfaces from friction between them. This is more likely to occur in women who are overweight but also in those who wear tight clothing.

The skin is painful, often red and flaky, showing wetness and stretch marks. Weight loss, local hygiene, and local exposure to air, such as the use of socks and cotton lingerie instead of synthetic underwear, should be envisioned. Powders (e.g., talc), astringents (e.g., zinc), or blocking agents in the area may also help.

Candida usually complicates intertrigo and should be treated as described according to clinical practice guidelines for the management of candidiasis [56, 57]. In order to relieve the inflammation, since there is no candida infection, steroid creams may be used.

2.1.3 Allergic/irritant dermatitis

The skin of the vulva, and especially the opening of vagina, is often affected by dermatitis. Dermatitis can be irritating (nonimmune) or actually allergic (immune-induced). Chemicals that cause skin hypersensitivity include, but are not limited to, cosmetics, perfumes, contraceptive lubricants, sprays, and vaginal washings. Detergents, dyes, softeners, bleaches, soaps, and bleach used to clean the underwear can also cause irritation. In severe cases, hypersensitivity may occur in topical application of anesthetic creams, as well as steroid preparations.

Women with contact dermatitis have an overgrowth inflamed vulva with eczema characters, and patch tests can reveal local irritants. Temporary relief can be achieved with lubricants of the vulva (e.g., Emulsiderm in a daily bath), softeners (e.g., local water creams), and topical corticosteroids (e.g., monthly treatment with Dermovate topical application). As before, nonresponsive lesions need biopsy to confirm the diagnosis [72–75].

2.2 Pruritus

The term pruritus describes an intense feeling of itching. It is more common in women over the age of 40 years, and symptoms are getting worse by stress or depression. There are many causes of itching.

Biopsy may be necessary for diagnosis, as well as patch tests may be also helpful. If no cause is found, it may be worth considering the possibility of previous sexual abuse or psychosocial problems.

It is important to stop the vicious cycle of irritation/itching cycle that is using strong local steroids for a short time in order to reduce the local inflammation induced by scratching. Applying strong steroid ointment daily for 3 weeks followed by 1% hydrocortisone cream once a day is useful, as well as soap substitutes (e.g., Oilatum).

Irritants, cosmetics added to bath, and synthetic pantyhose, as well as soap substitutes, should be avoided, and comfortable cotton underwear should be used. The area should be gently dry (e.g., with a hairdryer). Antihistamines can also help. If depression coexists, it may require treatment [76–84]. Reasons of vaginal pruritus

Infection (candida, luteum, filamentous worms)

Eczema

Dermatitis (patch tests)

Irritation due to vaginal excretion

Lichen sclerosus

Lichen planus

Vulvar intraepithelial neoplasia (VIN)
Vulvar cancer
Systematic diseases (diabetes mellitus, ureamia, or liver deficiency)
Psychogenic [82–84]

2.3 Vulvar intraepithelial neoplasia (VIN)

The term VIN was proposed to include dysplastic lesions and vulvar squamous in situ cancer and replace terms such as: (a) Bowen's disease; (b) Bowen's papilloma; and (c) dystrophy with atypia.

Depending on the degree of maturation of the neoplastic epithelium and the extent of atypia, three VIN classes, from I to III, are defined just like in CIN.

2.3.1 New terminology: previous terminology

VIN I: mild dysplasia
VIN II: moderate dysplasia
VIN III: Toy Bowen's disease, severe dysplasia
Squamous cell carcinoma in situ, erythroplasia of Queyrat

The lesion is characterized as VIN I when the cellular abnormalities, in comparison with absence of layout, are limited to the lower one-third of the vulvar squamous epithelium, VIN II when the abnormalities extend to the middle third of the epithelium, VIN III when they extend to the upper third of the epithelium, and CIS when lesions occupy all the epithelial layers. Approximately 40% of women present without accompanied symptoms and in the rest cases a background of inflammatory skin disease in the majority being lichen sclerosis exist.

The disease is not characterized as invasive carcinoma as long as the basal lamina remains intact [72–75].

2.3.2 Risk factors VIN

Common point: VIN is part of a total of epithelial changes in the woman's inferior genital system and may coexist (at least 15–20%). In particular, if there are acuminate warts in the vulva, the rate for CIN lesions is almost 50%.

2.3.3 Risk factors

1. Early onset of sexual activity
2. Switching (multiple) sexual partners
3. Immune system weakness
4. Cross-reaction or coexistence of high-risk HPV subtypes
5. Smoking, alcohol, and unbalanced diet
6. HPV infection
7. HSV-2 infection
8. Chronic irritation of the vulva
9. Warts

2.3.4 Biological behavior and prognosis VIN and CIN

In most VIN cases, instead of CIN, the damage is high risk. It is also uncommon to diagnose just VIN I lesion.

VIN:

- increased incidence in last two decades
- average age of development 30 years
- risk of progression to invasive cancer increased in women of the fifth decade (20%)
- the recession is twice as likely as invasion.

It is more common in women of 20–30 years, while VIN III in the fourth decade whereas invasive cancer mainly in the fifth decade [32, 34, 40].

2.3.5 Clinical finding and diagnose of VIN and CIN

VIN instead of CIN is not appeared during colposcopy with abnormal vasculature and mosaicism, but in the form of subtracted white or red plaques with clear borders.

Due to keratinization of the surface layer, in case of VIN, the cytological evaluation is more difficult.

VIN: itching, burning sensation, pain, single, or multifocal lesions (40%)

CIN: there are usually no symptoms or findings, single, or multifocal lesions

VIN: lesions often situated in the inner lips of vagina and the perineum

CIN: lesions frequently cited in the transformation zone

3 Basic principles in treatment of depigmentation disorders of the vulva

3.1 Clobetazone (Butavate*)

Treatment of choice is the topical administration of clobetazone, which blocks mitosis and induces synthesis of proteins reducing inflammatory response. It is also believed that it affects Ki67 as well as promotes p53 expression.

For those cases that diagnosed for the first time, it is recommended to apply once daily for 4 weeks, then every second day for 4 more weeks and during the third month of treatment, twice a week (once a day is based on pharmacokinetic studies). If symptoms reappear, the minimal clobetazone dose in which disease was controlled is administered.

A 30 g tube should be used for 12 weeks, and then, the original is reconsidered. If treatment is effective, hyperkeratosis, bruising, erosions, and stretch marks will disappear, but atrophy and color change still remain.

Clobetazone is continued as needed. Most patients usually need 30–60 g per year. If therapy is complete, no further treatment is needed, but other patients will have relapses and should continue to receive treatment [72–75].

An alternative option is triamcinolone ointments.

3.2 Testosterone and other hormones

Nowadays, estrogens or testosterone creams have no place in the LS treatment. Also recent studies have shown that testosterone is less effective than clobetazone

and has same effectiveness with petrolatum, the excipient used to make testosterone ointment.

3.3 Progesterone

It is referred to be extremely effective. It is prepared by mixing 400 mg progesterone oil with 4 oz Aqua-for. It is prescribed twice a day.

3.4 Retinoids

They are mainly used in the complicated LS on failure of corticoid treatment. It is considered that they reduce the degradation of the connective tissue.

3.4.1 Acitrecine (Nco-Tigason*)

Acitrecine (Nco-Tigason*) 25 or 50 mg/24 h per os in a single dose until symptom remission and continue 25–50 mg/24 hours go per os. The treatment stops when the lesions fall back.

3.4.2 Isotretinoin (Roaccutan*, Accurane*)

Isotretinoin (Roaccutan*, Accurane*) synthetic 13 is isomer of tretinoin. It reduces sebaceous gland size and sebum production and inhibits abnormal keratinization. The dose is 0.5–1 mg/kg/24 hours, and the duration of treatment is 4–6 months.

Topical administration of retinoids is not recommended due to the local irritation they cause.

Close attention should be paid to per os administration of retinoids to adolescents due to the teratogenicity they cause and is recommended avoidance of pregnancy for 2 months (isotretinoin) and 3 years (acitretin) at the end of the treatment [72–75].

3.5 Other medications

Positive results from the administration of potassium para-aminobenzoate, as well as psoralen with UVA therapy, stanozolol, antimalarials, antihistamines (e.g. oxatomide), and various antibiotics (possible cause or infection by *Borrelia*), were also observed.

3.6 Surgical treatment

In uncomplicated forms of LS, there is no evidence of removal of vulvar tissue. Surgical treatment should be applied exclusively in case of malignant transformation and recurrent forms.

When there is a narrowing of the opening of vagina, perineoplasty is performed, which improves dyspareunia in 90% of cases and improves the quality of sexual life in 86% of cases.

Simple vulvectomy should not be preferred because the symptoms do not always disappear, the signs reappear, and the likelihood of malignant transformation persists. Also, the operation creates many psychosocial problems.

3.7 Alternative treatment

Positive results are reported with LASER ablation treatment, which is applied with LASER CO, 1–2 mm deep with complete healing 6 weeks after surgery and low relapse rates. It is considered a method of nonresponse to other forms of treatment.

Photodynamic therapy (topical application of the 5-aminolevulinic acid photosensitizer and exposure to argon laser light for 1–2 alphas in 1–3 sessions) is also used with very good results.

3.8 General considerations for patients during treatment

Patients with LS have thin skin, which is not considered a “satisfactory” barrier to the loss of moisture, and it would be a failure not to mention some general measures.

1. Excessive drying after bathing should be avoided.
2. Gentle moisturizing products such as, e.g., Vaseline should be used to improve the moisture of the affected skin.
3. Good hygiene, avoidance of irritants and allergens, use of cotton lingerie, and avoidance of tight and hot clothes.

A lesion that resides in the vulva or in the vaginal opening and continues after the skin lesion is absent is secondary to a sensory disorder. This pain does not correspond to topical administration of corticosteroids. A 5% xylocaine ointment is therapeutically administered; on failure, administration of amitriptyline is recommended [72–75].

3.9 Failure of treatment

On unsuccessful treatment with corticosteroids, the following should be checked: patient compliance, misdiagnosis or coexistence of other disease entities, contact dermatitis, secondary candidiasis, VIN, SCC, psoriasis, or pemphigoid vulgaris.

If the symptoms persist after the medical repair of the damage, it is a secondary sensory disorder.

3.10 Follow-up

The risk of malignant transformation of LS is very small. Even if malignant transformation occurs, the progression of the disease is slow. However, patients should be screened at the end of the first trimester of treatment after 6 months and then yearly.

One-month follow-up requires patients with a poor response to corticosteroid therapy, and they are usually those in whom squamous cell hyperplasia coexists and are therefore susceptible to malignant transformation.

4. Conclusion

Vulva pathology is varied. Between all the described lesions, precancer conditions should be recognized early in order to stop the evolution. Strong dermocorticoids are the major local treatment on many vulvae chronic diseases. In specific conditions, local immune modulators or laser are necessary.

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