

Is there Any Reason of Irritating Vulvar Itching?

Magdalena Bizoń Szpernalowska* and Włodzimierz Sawicki

Chair and Department of Obstetrics, Medical University of Warsaw, Poland

*Corresponding author: Magdalena Bizoń Szpernalowska, Chair and Department of Obstetrics, Gynecology and Gynecological Oncology, ul. Kondratowicza 8, 03-242 Warsaw, Poland



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Abbreviations: LS: Lichen Sclerosus; PDT: Photodynamic Therapy; VIN: Vulvar Intraepithelial Neoplasia

ABSTRACT

Vulvar complains like itching, burning and pain are reported mainly by women in peri- and postmenopausal age. Severity of symptoms influence on well-being. The most frequent reason of vulvar symptoms is lichen sclerosus. Diagnose is given after vulvar biopsy, which is crucial in exact diagnosis. Sometimes histological result can also reveal hypertrophy of epithelium, acanthosis, lichen planus, vulvar intraepithelial neoplasia or even vulvar cancer. Lichen sclerosus cause leucoplacia, vulvar atrophy and narrowing of the vagina. Delay of diagnosis cause quicker progression of disease and intensification of vulvar symptoms. The first line of treatment is based on ointments according to glucocorticosteroids. If there is no response on this method, the alternative way is photodynamic therapy (PDT). The aim of the treatment is to protect against progression of lichen sclerosus and decrease vulvar symptoms.

Keywords: lichen sclerosus; itching; photodynamic therapy

Mini Review

Clinical vulvar symptoms like itching, burning and pain are irritable and annoying for women. Their severity and intensity induce scratching and in this way infection of the wound can appear. Epidemiological statistics show that every fifth woman complains of vulvar symptoms. It is estimated that 1,7% of all ambulatory visits in Outpatient Gynecologic Clinic concern on complains of vulvar symptoms [1]. The statistics show that women are more frequent diagnosed with lichen sclerosus than men in 6-10 times [2,3]. New changes of vulva sometimes causes patients problems and are a reason of visit to dermatologists, gynecologists, urologists, pediatrics, geriatricians and GPs. Methods of treatment are depended on specialists. Nevertheless, sometimes there is necessity of co-operation between specialists [4]. The purpose of this mini review was to expose these problems of vaginal lichen sclerosus.

Discussion

History of Lichen Sclerosus

Lichen sclerosus was described for the first time by Hallopeau in 1887. Changes in anogenital area were called atrophic form of lichen planus [4]. In 1892 Darrier publicated features of histological view. Another names of lichen sclerosus were kraurosis vulvae,

weissflecken dermatose and white spot disease [5]. Nomenclature include also term of lichen sclerosus and atrophicus [6]. In 1928 Stuhmer described similar disease in men with occupied urethra and glans penis, which was called balanitis xerotica. Nowadays it is male equivalent of lichen sclerosus [7]. Finally name of lichen sclerosus was accepted in 1976 by ISSVD (International Society for the Study of Vulvovaginal Disease) [4]. Despite many modifications in nomenclature of vulvar disease, the name of LS does not changed.

Epidemiology

Epidemiological research show lichen sclerosus as a risk factor of neoplastic disease. In primary lichen sclerosus risk of vulvar and vaginal cancer increases. Lower morbidity in cervical cancer can be correlated with lower risk of infection of HPV. Patients with advanced stage of lichen sclerosus intercourse less often or even not because of atrophy and narrowing of the vagina. In that way they avoid HPV infection, which is transmitted in transvaginal way. Higher risk of endometrial cancer and ovarian cancer was not reported [8]. The highest morbidity of neoplastic disease is breast cancer. Metastases of breast cancer in localization of vulva is rare and stands for 5-8% cases. Lobular cancer of the breast gives the most frequent metastases for vulva in 10-15% cases [9].

On the other hand, only 2 cases of metastases of vulvar cancer to breast were described. Definitely more often metastases in breast come from ovarian cancer, endometrial cancer, cervical cancer and choriocarcinoma. Every change on the anogenital area in patient with cancer in the past should be checked histologically [10]. However, lichen sclerosus was noticed also in postradiated skin after radiotherapy because of breast cancer. It was discussed a case study of patient with vaginal cancer with lichen sclerosus after brachytherapy [11]. Average time of ending of radiotherapy and first symptoms of lichen sclerosus was 2 to 12 years [12,13]. The main recommendation of all vulvar diseases is everyday care of vulvar skin and avoid irritating factors like artificial underwear, using of detergents and dyes. Good results are after emollients, soap substitute and soft, cotton underwear [14].

Risk Factors

One of the risk factors of lichen sclerosus is Human Papillomavirus Virus (HPV), like in cervical or vulvar cancer. There are registered more than 120 types of HPV virus [6]. Higher percentage of HPV infection in lichen sclerosus were recognized in male (29%) than female (8%) [15]. Human Papilloma Virus is a risk factor of cervical intraepithelial neoplasia and vulvar intraepithelial neoplasia. In metanalysis, correlation between infection of HPV and VIN was observed in 84% cases. Neoplastic transformation was claimed in 10% of patients [16]. What is a difference, higher expression of protein p16 was observed in vulvar HSIL and spinocellulare vulvar cancer dependend on HPV, which is the opposite to LS [17]. Undifferentiated VIN did not correlate with lichen sclerosus, but most frequent planoepitheliale vulvar cancer is observed [18]. In history, overexpression of p53 appears which can be a marker of vulvar cancer [19]. However, lichen sclerosus was recognized in area of differentiated VIN. Because of high risk of neoplastic transformation every new change should be biopied and histologically verify [20].

Morphology

The most often localization of lichen sclerosus, is anogenital area, which include labia majora, labia minora, area of clitoris and perianal area. Firstly, white plaques called leucoplacia appear, then they rupture. In that way cracks are presented, which cause scar and fibrosis till atrophy (Figure 1). Persistent symptoms induce reflexive scratching and can provide to subepithelial haemorrhages [21]. After years vulva becomes like elephant skin with progressing atrophy. Labia get shrunk, in clitoris area burning is presented (Figure 2). Fibrosis and degeneration cause narrowing of urethra and generate dysuria problems. Similar pathomechanism is correlated with narrowing of vagina and sexual disorders appear. Sometimes leukoplakia located in perianal area looks like „eight” [22]. There were also described cases of lichen sclerosus in anogenital area in monozygotic twins [23].

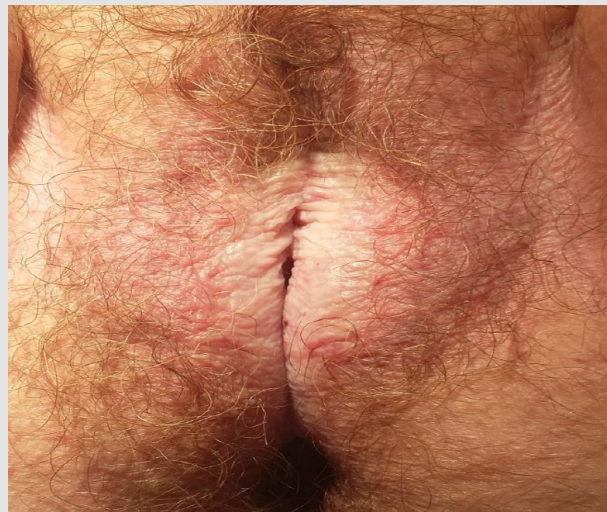


Figure 1: Lichen Sclerosus.

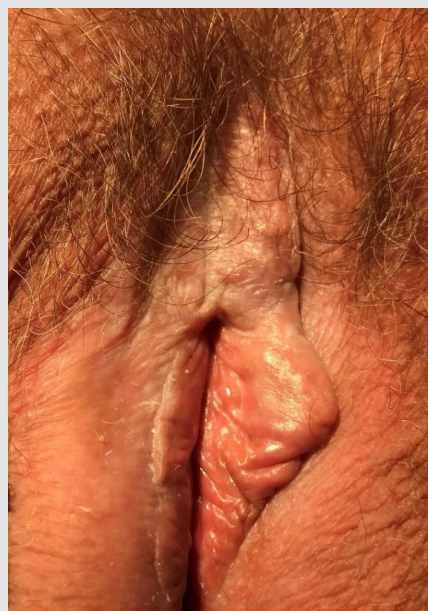


Figure 2: Lichen sclerosus.

It is also published co-existence of father and daughter [24]. On the other hand, family history of lichen sclerosus is a risk factor of vulvar cancer [25]. Children with lichen sclerosus had in 14% cases diagnose of autoimmune diseases, on the other hand autoimmune disorders were rejected in family history in 64% [26]. Higher correlation of autoimmune diseases and HLA antibodies were observed in women with LS than in men [27]. There are described many correlation with presence of LS. First of all, postmenopausal age with lower concentration of estrogens predispose for vaginal dryness and atrophy of vulva. Lichen sclerosus co-exists with autoimmune diseases. The most frequent are thyroid disease, malignant anemy, diabetes mellitus type 1, albinism and alopecia areata [14].

Treatment

The first line of treatment of lichen sclerosus was glucocorticosteroidotherapy, which was firstly used in 1991 year [28]. Propionate clobetasol has the most advantageous profits like reduction of symptoms and general improvement [14]. Unfortunately, this method should not be used permanently. After using specific algorithm remission of the disease should be seen. Index of recurrence of lichen sclerosus after locally steroids was 82% [29]. Clobetasol was so effective like mometasone and should be applied 8-12 weeks [30]. Totally remission of lichen sclerosus was after using propionian clobetasole [31]. There is a group of patients which stands 4-10% cases with no response on locally steroidotherapy in anogenital area. The second line of therapy stands for calcineurins inhibitors like tacrolimus and pimecrolimus [32]. But in comparison of clobetasol to pimecrolimus, the first one reduce inflammatory process and prevent neoplastic transformation of lichen sclerosus [33]. After therapy of pimecrolimus, higher concentration of antigen p53 in nucleus and keratinocytes is observed. Antigen p53 induces stress, anemy and inflammatory process. Spinocellulare vulvar cancer gives frequently neoplastic transformation than others [34].

Photodynamic Therapy



Figure 3: Lamp of photodynamic therapy.

The solar conception as a way of curing was known from ancient Egypt, India and Greece. In 1923 Alderson for the first time described phenomenon of heliotherapy in treatment of psoriasis [35]. Therefore alternative method of treatment of lichen sclerosus seems to be photodynamic therapy (PDT) (Figure 3). The first photosensitizer was hematoporphirin. In 80s of XX century δ -aminolevulinian acid was initiated as photosensitizer before PDT.

The first application in treatment of vulvar dermatose took place in 1993, when experimental research in vulvar intraepithelial neoplasia, cervical intraepithelial neoplasia and lichen sclerosus was conducted [36]. Positive effects of PDT was given also to extragenital localization [37].

Mechanism of PDT was based on oxidative proces after emission of light from photodynamic lamp towards vulvar skin with applicated prior 2 hours δ -aminolevulinian acid. Methylated form of photosensitizer infiltrate in the vulvar skin and is cumulated there [38].

Photosensitizer has to sensitize tissue to get better acces of electromagnetic wave. Fibrosis of tissues, reduction of intensity of skin are caused by keratinocytes, which under control of light from PDT produce higher concentration of IL-1, TNE, metalloproteinase-1 and metalloproteinase-3 [39]. Photodynamic Therapy is also used in indications like condylomata accuminata, acnes, psoriasis, Darrier disease, sarcoidosis and penile lichen planus. Thanks to profits on skin and value on flexibility PDT has application in rejuvenation of the skin [38]. Surgical treatment is not dedicated in LS. Postoperative adhesions and wound cause dysfunction in anogenital area connected with urinary problems and discomfort in sexual life. On the other hand, surgery is the first line of therapy as local incision in VIN. In this cases also reconstructive surgery can be considered to avoid decreasing of self esteem [14].

Conclusion

Lichen sclerosus is the most frequent vulvar disease. The knowledge of symptoms and clinical features allows to recognize disease and begin treatment. The most important clue for patients is to carefully adjust to hygienic rules of vulvar area. Everyday using of ointments protect against recurrence itching and burning. Earlier diagnosis and treatment, later atrophic complications appear. Neglected visit in gynecological outpatient clinic reduce quality of life. On the other hand, in some cases lichen sclerosus can transformed into VIN or vulvar cancer, where different methods of treatment are used.

Conflict of Interest

The authors have no conflicts of interest to declare.

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Magdalena Bizoń Szpernalowska. Biomed J Sci & Tech Res



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