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Pediatric vulvar lichen sclerosus: Does it resolve or does it persist after menarche?

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Abstract

Background and Objectives: Although data regarding the rates of remission and progression of the disease are still scarce, it is generally now acknowledged that pediatric vulvar lichen sclerosus (pVLS) can persist beyond puberty. Recent studies reveal that this condition may persist in as many as 75% of cases. The present study aims to answer the following query: how does pVLS evolve after menarche?

Methods: This observational retrospective study conducted on premenarchal girls diagnosed with pVLS in our institution between 1990 and 2011 describes 31 patients who returned for multidisciplinary clinical evaluation following menarche.

Results: The mean follow-up time was 14 years. At the post-menarche clinical examination, patients were classified as follows: 58% were still affected by VLS, 16% presented with a complete remission of disease, and 26% were completely asymptomatic although with persistent clinical signs of VLS.

Conclusions: In our series, pVLS persists following menarche in the majority of patients. These findings suggest the importance of a long-term follow-up even among patients who report resolution of symptoms following menarche.

KEYWORDS
adolescent, lichen sclerosus and atrophicus, pediatric, vulvar lichen sclerosus

1 | INTRODUCTION

Vulvar lichen sclerosus (VLS) is a chronic inflammatory disease that affects the anogenital region in both children and adults.[1–3] The disease follows a chronic, relapsing course and can evolve into vulvar squamous cell carcinoma (VSCC) in up to 21% of cases,[4] supporting the need for lifelong periodic follow-up. To date, the etiology of VLS is not fully known, although autoimmunity is thought to play an important role.[1,5–7]

Pediatric vulvar lichen sclerosus (pVLS) constitutes 10%–15% of VLS cases, with an estimated prevalence of 1:900 premenarchal girls.[2] However, this is probably an underestimate, as first signs and symptoms are usually nonspecific and the diagnosis may be missed.[1,8–12] Lagerstedt et al., claim that only 16% of patients with VLS are diagnosed at an early stage of the disease.[8] The mean age of pVLS onset is four to 6 years.[5,13]

pVLS presents with vulvar itching, soreness and burning of the vulvar and perineal region. In some cases, genital purpura due to

rubbing and mild trauma of the fragile and atrophic skin is also present. Dysuria may also occur, as well as constipation and painful defecation, which are reported in up to 67% of cases.[5,14–16] However, in 10% of patients the disease is reported to be asymptomatic.[5] Changes in vulvar architecture may also be present.[4,5]

Data regarding the natural course of pVLS are scarce and discordant due to the absence of long-term retrospective or prospective studies. In their recent review, Morrel et al. reported extremely divergent remission rates, varying between 11% and 70%.[17] Although clinicians do not agree on the rates of remission and progression of the disease, they now acknowledge that pVLS can persist beyond puberty.[17]

Early identification and treatment of VLS have a crucial role in disease remission and in avoiding long-term sequelae, which include persistence of symptoms, alteration of vulvar architecture, detrimental effects on sexuality, parturition, self-image, and development of VSCC.[7,8,18] The aim of the current study is to address the following query: how does pVLS evolve after menarche?

2 | MATERIALS AND METHODS

The current study was conducted at the Regional Referral Center for Diagnosis and Treatment of Vulvar Lichen Sclerosus and Prevention of Lower Genital Tract Diseases at the Department of Women's and Children's Health, Fondazione IRCCS Ca′ Granda Ospedale Maggiore Policlinico, Milan, Italy. Local Institutional Review Board (IRB) approval was obtained (#155875, 2022).

We analyzed clinical medical records of children and young girls referred to our prepubertal outpatient clinic with pVLS from1990 to 2011. Data retrieved were: age at time of VLS diagnosis, medical history, family history including familial VLS, symptoms and signs at time of diagnosis (i.e., genital itching, pain, burning sensation in the vulvar-perianal area, dysuria, bleeding due to skin fissures, hyperkeratosis, hypochromic areas with the classic "Figure of 8" or "hourglass" pattern involving the labia majora, labia minora, clitoral hood and the perianal region, white flat-topped papules), and pharmacological treatment for VLS at time of diagnosis.

Sixty-two post-pubertal patients were invited to our clinic for a re-evaluation, conducted by a multidisciplinary team composed of a gynecologist, a pediatric dermatologist with expertise in genital diseases, a pediatric gynecologist, and a pediatric urologist.

The primary aim of the post-pubertal clinical evaluation was to assess how pVLS evolves following menarche. The secondary aim of the study was to identify possible factors associated with the evolution of the disease. Data collected during the clinical re-evaluation included: age at menarche and coitarche, family history, medical history, obstetric history, presence of symptoms (i.e., itching, burning, dysuria, dyspareunia and vulvar discomfort), age at time of resolution of symptoms, if any. Moreover, we asked patients to confirm their age at the time of diagnosis and obtained information regarding type and length of treatment. All patients underwent clinical evaluation, consisting of a genital examination and vulvoscopy to allow a magnified vision of the genital area, and a dermatological evaluation of the extra-genital skin. When required, a vulvar biopsy was performed to establish clinical activity.

At the end of the clinical evaluation, the multidisciplinary team discussed clinical findings and evaluated if the patient should be considered: (1) still affected by VLS (defined as persistence of one or more post-pubertal symptoms or of one or more clinical signs of VLS); (2) completely recovered from VLS (defined as absence of both symptoms and clinical signs); or (3) classified in a third group characterized by the presence of one or more vulvar anatomical alterations occurring in VLS (i.e., resorption of the labia minora, adherence of opposing labia, burying of the clitoris and rarely, stenosis of the vaginal introitus), accompanied by a complete absence of clinical symptoms. Any disagreement among the four clinicians involved in the study was resolved by consensus.

We hypothesized that prescription of steroids at time of diagnosis, a positive medical history for other autoimmune diseases and familial LS could be factors associated with the presentation of pVLS following menarche. Therefore, we analyzed the association between the abovementioned items and categories 1 (still affected by VLS) and 2 (completely recovered from VLS).

Data was entered from medical records into Microsoft Excel (version 15.33; Microsoft, Redmond, WA). Descriptive statistics were achieved for demographic and medical data; continuous variables are presented as means with standard deviations (M ± SD), while categorical data is presented as percentages and frequencies.

3 | RESULTS

3.1 | Characteristics of patients with pVLS in childhood

During the period 1990–2011, 62 children were clinically diagnosed with pVLS. We were able to reach 31 patients, all of whom returned for re-evaluation (unfortunately we no longer had telephone contact information for the remaining 31 patients). Clinical characteristics at time of diagnosis were comparable between those who we were not able to contact and those who returned for re-evaluation. Mean age at time of diagnosis was 6.3 years (SD ± 2.58). A total of 22% had autoimmune comorbidities and 19.4% had genital or extragenital LS in their family history. The most prevalent symptoms (Table 1) at time of diagnosis were itching (77.4%) and burning (48.4%), while the main vulvoscopic findings were vulvar erythema (35.5%) and skin fissures (32.2%). More than half of patients (51.6%) had been prescribed ultra-potent topical steroids as first line treatment while less than half (45.3%) underwent maintenance treatment with vitamin E-based cream, which is used to improve skin hydration and elasticity, for an average period of 72 months (SD ± 34.2). Estrogen creams were also prescribed in cases in which moisturizers were not sufficient to improve skin hydration and elasticity. As many as 29% of patients admitted poor compliance to maintenance treatment.

3.2 | Post-pubertal re-evaluation of patients with pVLS

Patients were re-assessed in adulthood with a mean follow-up time of 14 year (SD ± 6.9). Mean age at time of re-evaluation was 20.3 years

TABLE 1 Symptoms and treatment type at the time of diagnosis in 31 patients affected by pVLS.

Symptoms at diagnosis[a]	
Itching	24 (77.4)
Burning	15 (48.4)
Dysuria	4 (13)
Signs at diagnosis[a]	
Erythema	11 (35.5)
Skin fissures	10 (32.2)
Hyperkeratosis	3 (9.7)
Hypopigmented areas in "Figure of 8" or "hourglass" pattern	3 (9.7)
Treatment at diagnosis[b]	
Vitamin E cream	25 (80.6)
Very high potency steroids	16 (51.6)
High/medium potency steroids	7 (22.5)
Lower/mild potency steroids	5 (16)
Calcineurin inhibitors	6 (19.4)
Local estrogen	9 (29)
No treatment	1 (3.2)
Maintenance treatment[c]	
Yes	14 (45.2)
No	17 (54.8)

[a]More than one item may be present for the same patient.
[b]Listed by potency according to the U.S. classification system.
[c]Maintenance treatment consisted in daily use of moisturizers. Topical steroids were administered for three consecutive days only when symptoms appeared.

(SD ± 6.68). Eight patients (25.8%) had meanwhile received a diagnosis of a second autoimmune disease (thyroid disease in seven cases, celiac disease in one). VLS was histologically confirmed at the time of re-examination in four patients (12.9%), while in the remaining 14 cases the diagnosis was rendered by clinical examination. A total of 19 patients (61.3%) reported no relevant symptoms at the time of re-evaluation. However, 4 (12.9%) reported itching, 4 (12.9%) burning, 4 (12.9%) vulvar discomfort, 2 (6.5%) dyspareunia and 3 (9.7%) vulvar dryness. Mean age at time of resolution of symptoms was 13 years (SD ± 2.9), while the mean age at time of menarche in these patients was 13.4 years (SD ± 0.8).

On the basis of clinical examination and vulvoscopic findings, the patients we were able to re-evaluate at time of follow-up were classified as follows: 18 (58.1%) were considered still affected by VLS, 5 (16.1%) presented with a complete remission of the disease, and 8 (25.8%) were completely asymptomatic although they presented with clinical signs of VLS.

When analyzing factors potentially associated with persistence of pVLS following menarche, we found a 0.8 RR (CI 0.6–1) for the prescription of steroids at time of diagnosis, a 1.4 RR (CI 1.0–1.8) for comorbid autoimmune diseases and a 1.4 RR (CI 1.0–1.8) for familial VLS. None of the associations resulted to be statistically significant.

4 | DISCUSSION

The current study evaluates children and young girls affected by pVLS to determine the persistence or resolution of pVLS after menarche. We found that in the post-pubertal period, 58% of patients diagnosed with pVLS were still affected by the disease (defined as persistence of symptoms or of clinical signs and symptoms of VLS). This study provides a relatively large cohort and long-term follow-up.

Most studies on pVLS are limited by cohort size and lack long-term follow-up, limiting our understanding of disease trajectory and long-term sequelae.[19–21] In their retrospective study, Kammire and colleagues observed a 60% remission rate among young girls with pVLS followed for a mean time of 39 months, although the follow-up duration ranged from 7 months to 6.8 years.[19] Moreover, clinical data were obtained by the means of a telephone interview, without clinical evaluation. In their study, remission was defined as complete absence of symptoms in patients who had previously received first-line treatment and were no longer receiving maintenance treatment.[20]

Similar results were obtained by Focseneanu et al., who described a 72% remission rate when retrospectively analyzing a population of 36 pre-menarchal girls with pVLS. Patients underwent a telephone interview to evaluate the presence of symptoms, which were used as an indicator of disease presence. The authors recognized this limitation as a weakness of their study and highlighted the importance of a clinical examination in the follow-up of patients with pVLS to document cases in which the disease persists despite the absence of symptoms.[21]

In contrast, in their review, Balakirski et al. reported a 31% remission rate in a population of 960 girls who were observed for a mean time of 16.3 months (range 1–168 months).[22]. A clear definition of the distinction between clinical remission and complete recovery of the disease is a fundamental issue which must be addressed in order to allow a comparison between different studies and to better understand the natural history of pVLS.

The most relevant result presented herein is that pVLS persists after menarche in 58% of cases. However, the majority of patients (61.3%) reported no active VLS symptoms at time of reevaluation.

Only 16% of patients were considered completely recovered following menarche. Interestingly, in our series, the dichotomous variable recovered/non-recovered was augmented by a third category of patients who presented with architectural changes, although were totally asymptomatic, raising the question whether these cases should be considered forms of pVLS that have completely recovered leaving permanent scarring or cases that are temporarily in a phase of disease quiescence. More information is needed to counsel this category of patients, as it is not yet clear what their prognosis is. Together with the patients whose disease persisted beyond puberty, this category of patients would likely also benefit from regular follow-up during adulthood. In our series, patients allocated in this category were invited to undergo annual follow-up.

We found no significant association between the prescription of steroids at time of diagnosis, a positive medical history for other autoimmune diseases, familial VLS and persistence of pVLS following menarche. However, studies on larger samples of patients may provide clarification whether such associations exist.

The main strengths of our study are the long follow-up with a mean time of 14 years and the in-person re-evaluation of patients

performed by a multidisciplinary team composed of clinicians of relevant specialities. Moreover, we clearly specified the difference between complete recovery, remission, and persistence of the disease.

The principal limitation of the current study includes its retrospective nature, which contributed to a 50% loss to post-pubertal re-evaluation, limiting sample size. Retrospective studies carry also the typical limitations of recorded patient information, including a high rate of unreported/missing data and possible bias/errors.

5 | CONCLUSION

These results suggest that pVLS persists following menarche in the majority of patients. Moreover, in approximately a quarter of patients, the clinical signs of the disease persist, although symptoms are no longer present. Although further studies on a greater number of patients are needed to confirm these results, we believe these findings are useful when counseling affected young girls and their parents on the trajectory of this disease and the need for future follow-up.

CONFLICT OF INTEREST STATEMENT

All authors declare that they have no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

PATIENT CONSENT STATEMENT

All patients gave their consent to the acquisition of images for research purposes.

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