Childhood vulvar lichen *sclerosus*: the consequences of diagnostic delay

Infância vulvar líquen *escleroso*: as consequências do atraso no diagnóstico

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ABSTRACT

Objectives: This series of 12 cases intends to raise awareness to Lichen *Sclerosus*, by illustrating its main clinical characteristics and complications, and by highlighting the importance of its early diagnosis. Methods: All of the patients discussed were attended at the Institute of Gynecology of the Federal University of Rio de Janeiro (UFRJ, Rio de Janeiro, Brazil), after being referred from primary care family medicine facilities. Results: We present 12 cases. The mean ages at the beginning of symptoms and clinical diagnosis were 6 and 9.25 years, respectively. The mean delay for diagnosis was 3.2 years. Vulvar pruritus and hypochromic macules were the most common initial symptoms. Complications included the fusion of the *labia minora* and clitoris entrapment. Cases with an earlier diagnosis had better

responses to treatment with ultra-potent corticosteroids such as Clobetasol propionate ointment 0.05%. Conclusion: Diagnostic delay of LS leads to its progression and long-term physical-psychological consequences. It must be remembered as a differential diagnosis of vulvar pruritus in childhood.

Keywords: lichen sclerosus et atrophicus, vulvar lichen sclerosus, pruritus vulvae, vulvar disease, pediatrics.

RESUMO
Objetivos: Esta série de 12 casos pretende sensibilizar o Lichen Sclerosus, ilustrando suas principais características clínicas e complicações, e destacando a importância de seu diagnóstico precoce. Métodos: Todos os pacientes discutidos foram atendidos no Instituto de Ginecologia da Universidade Federal do Rio de Janeiro (UFRJ, Rio de Janeiro, Brasil), após serem encaminhados de instalações de medicina familiar de atenção primária. Resultados: Apresentamos 12 casos. As idades médias no início dos sintomas e diagnóstico clínico foram de 6 e 9,25 anos, respectivamente. O atraso médio para o diagnóstico foi de 3,2 anos. Prurido vulvar e máculas hipocrômicas foram os sintomas iniciais mais comuns. As complicações incluíram a fusão dos lábios menores e o aprisionamento do clitóris. Os casos com um diagnóstico mais precoce tiveram melhores respostas ao tratamento com corticosteroides ultrapotentes, tais como pomada de propionato de Clobetasol 0,05%. Conclusão: O retardo diagnóstico de LS leva à sua progressão e consequências físico-psicológicas a longo prazo. Deve ser lembrado como um diagnóstico diferencial de prurido vulvar na infância.

Palavras-chave: lichen sclerosus et atrophicus, vulvar lichen sclerosus, pruritus vulvae, doença vulvar, pediatria.

1 INTRODUCTION

Lichen *Sclerosus* (LS) is a chronic dermatitis that can manifest in any area of the body, with a predilection for the anogenital region. LS most commonly occurs in postmenopausal, while also affecting pre-pubertal girls.[1]

The main risk factors for LS include a positive past family history and past medical history significant for autoimmune diseases, particularly Hashimoto Thyroiditis, Alopecia *Areata* and Vitiligo. Approximately 14% of the women and 3-5% of the girls diagnosed with LS have another concurrent autoimmune disorder.[2]

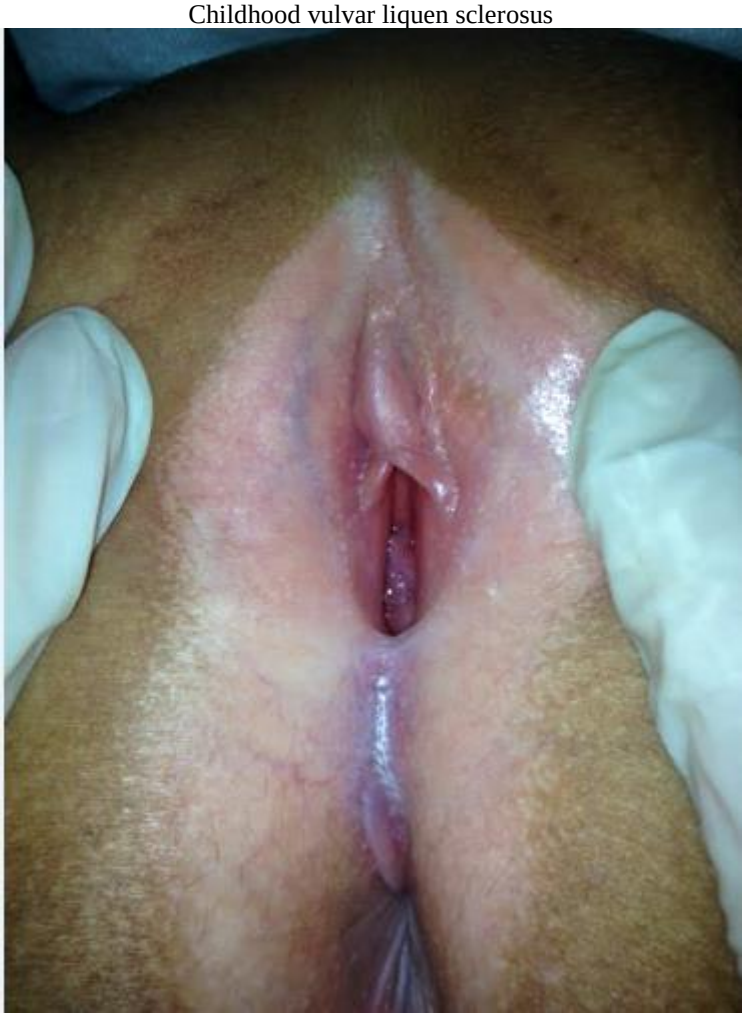
Among the main clinical features of childhood LS, vulvar pruritus is the most prevalent, affecting up to 90% of the patients. Other initial symptoms include vulvar pain, dysuria and gastrointestinal symptoms (such as constipation). Extra-genital manifestations at any age are less common, occurring in up to 10% of patients.[3]

The diagnosis of this disease is clinical, although atypical cases may require a biopsy (therapeutic failure or uncommon lesions). The characteristic vulvar lesions are atrophic white

macules, with papules coalescing into plaques that may form a classical "figure of eight" shape when the interlabial sulcus, perineum, and anus are involved. [3]

The treatment of LS aims to provide symptomatic relief, to prevent new or further anatomical disfiguration, and to, possibly, avoid malignant transformation to squamous cell carcinoma. Clobetasol propionate ointment 0.05% and other ultra-potent corticosteroids are the first-line in treatment.[3]

Figure 1. Photography of an infantile vulva with symmetrical hypochromic macules on the inner portion of the labia majora, extending from the anterior commissure to the perianal region ("figure of eight" shape). Notice the partial fusion of the labia minora and the formation of small synechiae at the posterior labial commissure. Childhood vulvar liquen sclerosus



Source: elaborated by the authors

Further development of sclerosis may cause fusion and retraction of the *labia minora*, as well as entrapment of the clitoris. This clitoris entrapment or burying, caused by advanced tissue sclerosis, leads to sensitivity deficits and possibly, sexual life impairments. Theoretically, in a minute part of the pediatric cases, the initial lesions may regress and even spontaneously disappear after puberty.

The clinical evolution of LS and all its complications may compromise their auto-esteem, self-body awareness, and prospective sexual lives. Early diagnosis and treatment is the only way to prevent such outcomes. However, current data demonstrate unacceptably high time delays between the appearance of symptoms and diagnosis, with averages of up to 10 years.[4]

This series of 12 cases intends to raise awareness to LS, by illustrating its main clinical characteristics and complications, and by highlighting the importance of its early diagnosis.

2 METHODS

Retrospective cross-sectional study in which archived medical records of care for children and teenagers diagnosed with vulvar lichen sclerosus at the Vulvar Pathology outpatient clinic at the Institute of Gynecology of UFRJ. These archived medical records were consulted to report as a series of cases this kind of disease.

The Research Ethics Committee of Federal University of Rio de Janeiro (UFRJ) of Maternity School approved under the number **CAAE** 92322217.7.0000.5275 on July 04, 2018.

3 CASES

All of the patients discussed were attended at the Institute of Gynecology of the Federal University of Rio de Janeiro (UFRJ, Rio de Janeiro, Brazil), after being referred from primary care family medicine facilities. Among the 677 patients diagnosed with LS between 2002 and 2017, only 2.5% (17/677) were pediatric patients; 29.5% (5/17) of them were excluded due to loss of follow-up. All of the utilized information was on their official medical records, and all the patients consented with their use for teaching and research purposes.

Highlighting the importance of the physical examination for the diagnosis of LS, only 16.6% (2/12) cases required a biopsy. One of them had atypical extra-genital hypochromic macules in the thorax and arms, and the other failed to respond to typical therapy.

Vulvar pruritus was by far the most common initial symptom, occurring in 91% (11/12) of our patients. It was the main factor that led families to look for health care assistance for their children. Hypochromic vulvar macules appeared solely or along with pruritus in three of the cases, but eventually, all of the patients developed this landmark LS characteristic. Vulvar pain was never the initial complaint, but ultimately occurred in ten cases. Interestingly, constipation was the first symptom for a 5-years-old girl. In all of the cases, symptoms started before menarche.

The location of the hypochromic macules differed in each case: vulva (four cases), vulva and perineum (four cases), and perianal “figure eight” pattern (four cases). Two patients had

vulvar lesions only in the *labia minora*, and two only in the *labia majora*. Unfortunately, 66.7% (8/12) of the girls already had some degree of architectural alteration accompanying hypochromia by the time they were finally referred and diagnosed, including total or partial fusion of the labia minora and clitoris entrapment.

After treatment with Clobetasol propionate ointment 0.05%, 58.3% (7/12) of the patients experienced complete relief of pruritus and vulvodynia, 33.3% (4/12) patients persisted with mild symptoms, and the remaining girl evolved with treatment-resistant intense pruritus. This patient's symptoms increased even though her hypochromic lesions partially regressed. Regarding architectural changes, complete clinical stabilization of compromised tissues occurred in 41.7% (5/12) of the cases and partial in 33.3% (4/12). The other 25% (3/12) of patients with irreversible anatomic changes had a 3 to 14 years delay to diagnosis. In this case, delay time resulted in *synechiae* formation, requiring reparative exeresis surgery.

Past medical histories were positive for genetic, autoimmune, and other multifactorial diseases: clitoris agenesis, vulvar vitiligo, Hashimoto thyroiditis and subclinical hypothyroidism, vaginal agenesis, and idiopathic precocious puberty.

The average time delay for diagnosis was of 3.25 years (ranging from 0.5 to 14). The mean age at the time the first symptoms and diagnosis were, respectively, 6 and 9.25 years. A summary of the 12 patient's clinical data is available in **Table 1**.

Table 1. Clinical evolution, ages, past medical histories, and outcomes of 12 pediatric patients diagnosed with Vulvar Lichen *Sclerosus et Atrophicus.*

Case	Age at 1st Symptoms / Age at Diagnosis	Initial Symptoms / PMH	Complications	Outcomes
1	11 / 12	Vulvar pruritus / Clitoris agenesis	Fusion of 2/3 of the *labia minora*	Asymptomatic; partial clinical stabilization
2	2 / 6	Vulvar hypochromic macules / Vulvar Vitiligo	Perianal hypopigmentation; total fusion of the *l*abia minora; clitoris entrapment	Partial symptomatic relief; partial clinical stabilization
3	5 / 8	Vulvar pruritus / Hashimoto Thyroiditis	Perianal hypopigmentation; partial fusion of the labia minora; clitoris entrapment	Partial symptomatic relief; no clinical stabilization
4	6.5 / 7	Vulvar pruritus; vulvar hypochromic macules / —	Bilateral *labia majora* fissures; partial fusion of the l*abiae minora*	Asymptomatic; total clinical stabilization
5	2 / 5	Vulvar Pruritus / —	Perianal hypopigmentation	Asymptomatic; total clinical stabilization

Case	Age at 1st Symptoms / Age at Diagnosis	Initial Symptoms / PMH	Complications	Outcomes
6	12	Vulvar pruritus	Vulvar hypopigmentation; total fusion of the *labia minora*; clitoris entrapment	Partial symptomatic relief; no clinical stabilization
	17	Vaginal agenesis; hematometrium		
7	4	Vulvar hypochromic macules; vulvar pruritus	Intense vulvar pruritus unresponsive to treatment; vulvar hypopigmentation	No improvement in vulvar pruritus; partial clinical stabilization
	7	Extra-genital LS; precocious puberty; subclinical hypothyroidism		
8	10	Vulvar pruritus	Clitoris hypopigmentation; partial fusion of the *labia minora*; partial clitoris entrapment	Asymptomatic; total clinical stabilization
	11	—		
9	5.5	Constipation; vulvar pruritus	Vulvar and perianal hypopigmentation	Asymptomatic; partial clinical stabilization
	6	—		
10	3	Vulvar pruritus	Total fusion of the *labia minora* with synechiae formation, requiring exeresis; total clitoris entrapment; extensive hypopigmentation	Partial symptomatic relief; no clinical stabilization
	17	—		
11	8	Vulvar pruritus	Perineal hypopigmentation; discreet fusion of the *labia minora;*	Asymptomatic; total clinical stabilization
	10	—		
12	4	Vulvar pruritus	Discreet vulvar hypopigmentation	Asymptomatic, total clinical stabilization
	5	—		

All the patients were treated with the potent corticosteroid Clobetasol propionate 0.5%; PMH: Past Medical History; LS: Lichen *sclerosus et atrophicus.* Childhood vulvar liquen sclerosus

Source: prepared by the authors

4 DISCUSSION

4.1 PRINCIPAL FINDINGS

LS is a diagnostic challenge in pediatric gynecology. Even though there are series of cases with larger samples in the literature, only the work of Cooper *et al. (2004)*[4] highlights the consequences of diagnostic delay, concluding that a possible regression of the LS vulvar lesions with Clobetasol propionate treatment directly depends on its early diagnosis. Cooper[4] demonstrated an average diagnostic delay of 2.8 years, with the worst outcomes occurring when that time was higher than three years. The study's mean onset and diagnosis ages, as well as the presenting symptoms, and complications were similar to what we observed in our series.

Squamous Cell Carcinoma occurs most frequently in older women, who experience much higher diagnostic delays, with reported averages around ten years.[5,6] Nevertheless, current American and British clinical recommendations indicate the necessity of long term follow-up of pediatric patients, with gynecological examinations every 6 to 12 months, to perceive disease relapses, complications, as well as new lesions suspicious for SCC.[3] Jensen and Bygum (2012)[6] report using the same strategy in Denmark, with positive results. The follow-up of our patients adheres to these recommendations.

4.2 CLINICAL IMPLICATIONS

Morrel *et al.* (2019)[7], in a systematic review, investigated the long-term consequences of LS in the youth. In their analysis of 37 studies, they concluded that its signs and symptoms persist after adolescence in the majority of cases and that permanent anatomical changes can occur. Nevertheless, they demonstrate that dermato-corticoids are highly effective in symptomatic control when the diagnostic delay is low. In our series, we observed that most of the symptoms improved with treatment, and vulvar clinical stabilization often occurred.

Schwegler et al. (2011)[8] indicate that patients are at higher risk for mental health disturbances and may experience regressions in quality of life. Most likely due to symptoms, stress, a decrease of social interactions, and impairments of sexual functioning. Accordingly, our experience shows that these patients frequently suffer with psychological and social disturbances, requiring interdisciplinary care along with the Consultation-Liaison Psychiatry Department.

In conclusion, the prevention of LS disfiguring and psychological complications relies on its early detection by primary care, and not by the vulvar pathology specialist who, unfortunately, first diagnoses already advanced disease.

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All the authors have met authorship criteria.

Yara Lúcia Furtado was one of the Professors mainly responsible for the care of the described patients. She gathered and interpreted data, drafted and revised the text, has approved its final version, and agrees to be accountable for all accuracy and integrity aspects of the work.

Caroline R. C. Gieler has reviewed the literature, organized and acquired data, drafted the text, approved its final version, and agrees to be accountable for all accuracy and integrity aspects of the work.

Filomena Aste Silveira was one of the Associate Professors mainly responsible for the care of the described patients. She gathered and interpreted data, drafted and revised the text, has approved its final version, and agrees to be accountable for all accuracy and integrity aspects of the work.

Gutemberg Almeida was one of the Professors mainly responsible for the care of the described patients. He gathered and interpreted data, drafted and revised the text, has approved its final version, and agrees to be accountable for all accuracy and integrity aspects of the work.

CONSENT

Written consent was obtained from all the patients included in this case series, including the one for which an image is submitted

ETHICS APPROVAL

The Research Ethics Committee of the Maternity School of the Federal University of Rio de Janeiro (UFRJ) was responsible for the approval of the research pre-project (Ethics Committee Regulation Number 2.753.641).

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APPENDICES

CHILDHOOD VULVAR LIQUEN SCLEROSUS

TWEETABLE STATEMENT: This article shows a series of 12 girls that have diagnosis of vulvar lichen sclerosus (children and teenagers) with a lot of clinical findings (itching is more frequent), time delays between the appearance of symptoms and the clinical diagnosis, complications, and response to treatment. They were referred from primary care to the Institute of Gynecology of the Federal University of Rio de Janeiro. Considering recent literature, this diagnostic delay is a very pressing issue in both developing and developed countries. Moreover, the physical and mental health consequences of the complications of Lichen *Sclerosus* are daunting

AJOG AT A GLANCE:

- Our study is important to draw attention to rare disease in children that compromises sexual performance in the future

- The lichen sclerosis is disease of probable autoimmune origin with two peaks of incidence – in childhood and in the sixth decade

QUESTIONS

A) Why was this study conducted?

This study was conduct because our desire to demonstrate the rare disease in children and teenager

B) What are the key findings?

The key findings are the characteristics and possibility of regression in childhood

C) What does this study add to what is already known?

This study adds the small frequency of regression in this group that is not consistent with most of the literature