

## CLINICAL CASE

## Vulvar ulcer in a 15-year-old girl: can we recognize adverse drug reactions?

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### ABSTRACT

**Background.** Pediatricians consider vulvar ulcer as an uncommon pathology. However, clinicians specialized in the care of young girls and teenagers with vulvar pathology actually consider vulvar ulcer not to be an infrequent primary complaint.

**Case report.** We report the case of a 15-year-old girl who presented fever and sore throat for which she was treated with trimethoprim-sulfamethoxazole. Two days after taking the drug she presented hyperpigmented patches with a bullous center that developed into a vulvar ulcer of ~4 cm in diameter. First considered infectious in origin, she received treatment with topical fluconazole and afterwards with amoxicillin clavulanate without any improvement. She was then assessed by a dermatologist, and the diagnosis of fixed drug eruption was established on the basis of the initial morphology of the lesion. She was treated with betamethasone and loratadine as well as topical 1% hydrocortisone. The lesions evolved to complete resolution.

**Conclusions.** In pediatric practice, it is important for the pediatrician to consider not only infectious and venereal causes in teenage girls with vulvar ulcer, but also allergic drug reactions.

**Key words:** vulvar ulcer, fixed drug eruption, adverse drug reaction.

### INTRODUCTION

The presence of a vulvar ulcer in adolescent patients is a diagnostic challenge for physicians and a cause of significant stress for parents and patients.<sup>1</sup> Vulvar ulcer is considered a rare condition. However, physicians who specialize in the care of adolescents and children with vulvar pathology consider vulvar ulcers to be a frequent complaint.<sup>2</sup> A structured approach facilitates the study of these cases and avoids unnecessary and costly diagnostic tests and cause anxiety for parents of patients with vulvar ulcers. Morphological findings are the most effective means for the determination of differential diagnoses rather than symptoms, which frequently are nonspecific.<sup>3</sup>

### CLINICAL CASE

We present the case of a previously healthy, 15-year-old female patient who denied the onset of sexual activity and chronic drug use. The patient arrived at the emergency department (ED) because for 3 days prior she had unquantified fever and sore throat. A diagnosis of bacterial pharyngitis was established. She was treated with trimethoprim-sulfamethoxazole, one tablet every 8 h for 2 days, (the contained dose per tablet was not specified). Two days later she presented with intermittent dysuria and a foreign body sensation in the vulvar area accompanied by itching. She was brought to the ED after detecting the presence of two vulvar lesions. On physical examination, vulvar lesions were observed. Lesions had an ovoid shape with purplish-erythematous plaques ~1.5 cm and 0.5 cm in diameter with central hyperpigmentation and a bullous appearance at the center. Lesions were located on the lower third of the lower lip on the right side and were unilateral and painful to manipulation (Figure 1A). When questioned, the patient reported moderate itching and dysuria. A diagnosis of candidiasis was established and the patient received nitrofurantoin and fluconazole as topical treatment.

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Two days later the patient returned to the ED. Upon inspection, lesions had an ulcerative coalescence with well-defined edges of ~4 cm in diameter. There was a halo of mild erythema and lesions were covered in a grayish-yellow exudate (Figure 1B). The patient reported continued and intense burning with urination, making urination difficult. She also presented with a temperature of 38°C. Bacterial superinfection was suspected and amoxicillin-clavulanate was prescribed as treatment. After 24 h she persisted with the lesions and severe dysuria that prevented urination. She returned to the ED where persistence of vulvar lesions and a distended bladder were detected. The patient was admitted to the hospital and a Foley catheter was inserted. Anesthesia was administered and a biopsy was taken (Figure 1C). During the patient's hospital stay, antibiotic treatment with amoxicillin-clavulanate was continued. An interconsultation with the Department of Dermatology was requested. Morphological diagnosis of fixed pigmented erythema was established. The patient was treated with loratadine/betamethasone (5 mg/0.25 mg) as well as 0.1% topical betamethasone. At 24 h she showed a decrease in lesion size and resumption of urination (Figure 2). Cultures were obtained from the secretion of the lesions and were

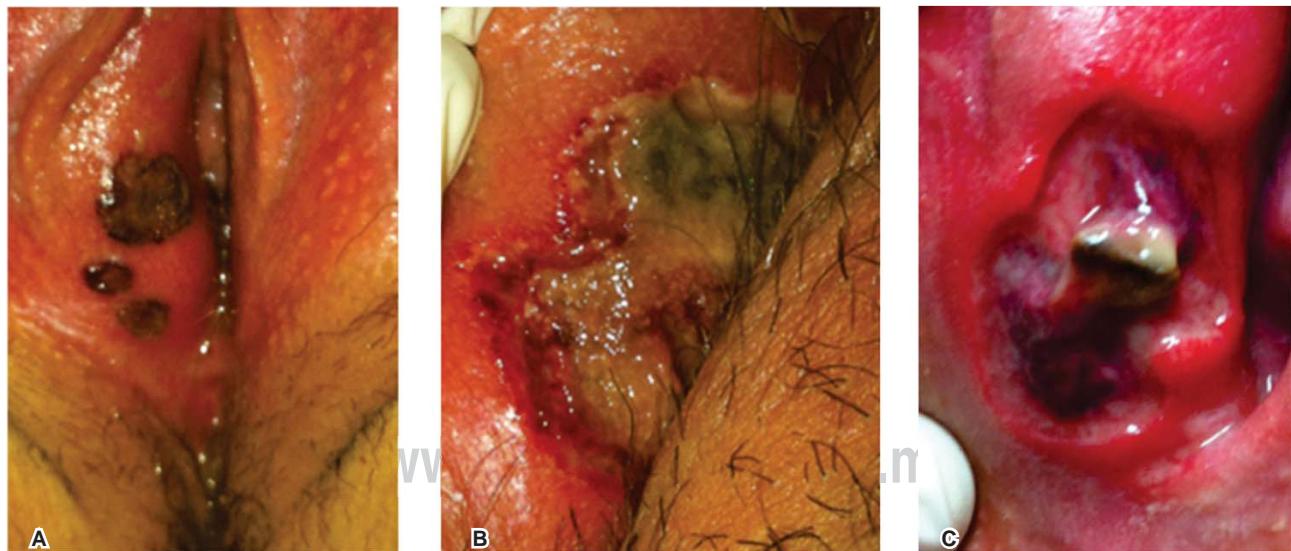
negative for aerobic and anaerobic bacteria. The patient was discharged after 96 h of hospitalization with instructions to continue with the topical treatment, using a less potent topical steroid (hydrocortisone 1%, for 3 days).

Biopsy reported necrotic tissue without evidence of neoplasm and with little reparative granuloma formation. The lesion resolved completely within 90 days of discharge.

## DISCUSSION

We report the case of a 15-year-old patient who experienced a delayed hypersensitivity reaction caused by a prescribed drug use. For the treatment of patients with vulvar ulcer, it is recommended that the pediatrician modify the diagnostic approach to which they are accustomed to.

In addressing an adolescent patient with vulvar ulcer, the first challenge of the pediatrician is to consider non-infectious causes of the lesion such as the case presented here. This case has significance because neither physicians nor patients recognize noninfectious causes of vulvar ulcers.<sup>2</sup> Adverse drug reactions are common problems that occur in up to 7% of the general population. There are more than 25 patterns of cutaneous manifestations that constitute an allergic response to the consumption of a drug.<sup>4</sup>



**Figure 1.** Description of the patient's clinical course. **(A)** Early stage with round, hyperpigmented, full-blown central lesions. **(B)** At the time of the hospital admission, the lesions have coalesced to form well-defined ulcer edges, covered by fibrinous exudate. **(C)** After the first course of treatment, the secretion was removed and they clearly observed the edges and bottom of the ulcer, well demarcated, with regular borders and the reaction of surrounding moderate erythema. (Photo courtesy of Dr. Alejandra Briones).



**Figure 2.** Appearance of the lesion after initial treatment with topical betamethasone loratadine.

Fixed pigmented erythema is a phenomenon in which exposure to a drug produces the appearance of a well-circumscribed, round or oval shaped erythematous single or multiple cutaneous lesion between 2 and 10 cm in diameter, which may appear anywhere on the mucocutaneous surface.<sup>5</sup> This is one of the most common forms of delayed hypersensitivity, only after exanthematic-type reactions.<sup>5</sup>

Ozkaya-Bayazit characterized the relationship between the drug and the location of the lesion. Trimethoprim-sulfamethoxazole was identified as the main causative agent of fixed pigmented erythema and genital mucosa was the most frequently affected site induced by this drug.<sup>6</sup>

Among the differential diagnosis of vulvar ulcer, the Lipschutz ulcer is found, a term that has been used to describe the ulceration of the vulva or lower vagina and whose appearance is not related to a history of sexual contact. A non-venereal vulvar ulcer has also been given the name of acute genital ulcers (AGU),<sup>1</sup> a term widely used in the literature. The differential diagnosis of AGU is extensive. The cause is identified after excluding systemic diseases. However, it is challenging to identify the existence of the etiologic agent of viral agents unrelated to sexually transmitted diseases, which have also been proposed as a cause of AGU in non-sexually active patients and in pediatric patients.

One of the most common viral agents reported in the literature is the Ebstein-Barr virus (EBV). However, few reports have described isolation of EBV directly from the ulcer, either by viral culture or by molecular techniques (polymerase chain reaction).<sup>2</sup>

In patients with a history of onset of sexual activity, we should consider, among the differential diagnoses, sexually transmitted diseases characterized by genital ulcers such as granuloma inguinale, lymphogranuloma venereum, syphilis, chancroid and herpes simplex virus. An individualized approach allows for guiding the practice of carrying out diagnostic tests for these diseases based on patient risk and sexual practices through diligent and thorough interrogation.<sup>1</sup> In this case, the patient's history facilitated her approach as a low-risk patient for sexually transmitted diseases. AGU is a diagnosis of exclusion, which is reached when specific systemic diseases and infections have been ruled out. The precise etiology of AGU is poorly understood and little studied, as occurs with oral ulcers. It is considered that these ulcers share a pathophysiological basis and clinical course.<sup>2</sup>

This patient's diagnosis was supported based on the morphologic appearance of the lesion as well as on the clinical behavior and treatment response. One of the diagnostic tests described for the confirmation of fixed pigmented erythema is the oral challenge test or challenge test, i.e., the patient's repeated exposure to the drug in smaller quantities pending presentation of the skin reaction. However, there is a contraindication with the practice of the oral challenge test because it increases the risk that, following exposure, the patient will experience a generalized reaction such as Lyell's syndrome and Stevens-Johnson syndrome.<sup>4</sup>

Vulvar pathology tends to be a field with little contact, both for gynecologists as well as for dermatologists. It is precisely the adolescent population that is most commonly affected by this type of skin lesion.<sup>2</sup> It is important for the pediatrician to keep in mind not only the infectious and venereal diseases in adolescent patients with vulvar ulcer. In this case report we highlight the importance of considering non-infectious causes of vulvar ulcers, among these is the possibility of adverse drug reactions.

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