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GENITAL ULCERS ASSOCIATED WITH SYSTEMIC LUPUS ERYTHEMATOSUS – WHAT ARE THE POSSIBLE CAUSES? A CASE REPORT

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ABSTRACT

Systemic lupus erythematosus (SLE) is a chronic systemic autoimmune disease that affects many organs. In this report, we discuss the case of a patient with SLE who presented to an out-hospital clinic, complaining of fever and pain with genital ulcers. Negative evaluations for other causes of genital ulcers, indicated these ulcers as related to SLE. This case highlights the importance of including SLE ulcers in the differential diagnosis of genital ulcers.

KEYWORDS

Systemic lupus erythematosus, genital ulcers, autoimmune diseases, systemic conditions

LEARNING POINTS

- Determining the cause of genital ulceration is a clinical challenge, especially in sexually active individuals.
- Genital ulcers associated with SLE are often underdiagnosed. Any patient with a history of SLE presenting with genital discomfort and/or pain must be evaluated for genital ulcers without delay.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a systemic autoimmune condition that targets healthy organs, with a higher incidence in females, especially of reproductive age[1]. Infection is a frequent trigger factor for SLE. Infection can also increase morbidity and mortality in SLE patients[2]. The differentiation of SLE flare and infection in a febrile patient is difficult, thus C-reactive protein, procalcitonin, and disease activity markers play a role[3]. Although only a few cases of SLE genital ulcers have been published, ruling out SLE in patients presenting with genital ulcers is important[4]. The precise etiology and pathogenesis of SLE remain unclear, however, it is described as an excessive immune response to infectious agents. Viruses, bacteria, parasites, and fungi are thought to trigger inflammation, autoantibody production and immune-mediated tissue injury[5]. Recently, molecular mimicry in genetically predisposed individuals has been hypothesized to exacerbate immune responses to self-antigens by immune mistake[6]. The first case of genital ulcer associated with SLE was reported by Fresko et al.[7]. We describe a case of a young female patient with SLE who presented with a history of painful genital ulcers.

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CASE PRESENTATION

A 28-year-old Syrian female presented to our out-hospital clinic in December 2021, complaining of fever and discomfort in the genital area for 10 days. She was diagnosed with SLE, according to the American College of Rheumatology/ European League Against Rheumatism 2019[8], as she had fever, fatigue, malar rash, oral aphthae, arthritis, pleuritis, and positive antinucleotides antibody (ANA). She had been treated with 200 mg/day hydroxychloroquine until admission. The remaining medical history was unremarkable. No family history of SLE was reported. On physical examination, multiple papular genital ulcers, sized 1-3 mm and well defined were found. Lymphadenopathy was present, but no vaginal discharge or ulcers were present. The remaining physical examination was unremarkable.

Hematologic and metabolic profiles were established, as well as a viral profile on blood and urine cultures. A vulvar biopsy and fungal swab test were ordered. CT of the pelvis and abdomen was ordered. The complete chemical and metabolic panels showed thrombocytopenia, with a platelet level of 93,000/µl (150,000-400,000/µl). Anti-double-stranded DNA (Anti dsDNA) antibody was 6UI/ml (normal). Urinalysis was notable for 1+ hematuria and 1+ proteinuria. Blood and urine cultures were negative for viruses. The COVID-19 test was negative. Serologies for herpes virus 1 and 2, Epstein-Barr virus, cytomegalovirus, *mycoplasma pneumonia*, parvovirus B19, toxoplasmosis, rubella, hepatitis, human immunodeficiency virus, and syphilis were negative. Bacterial vaginosis, gonorrhea, chlamydia, and trichomoniasis were ruled out. The fungal swab test was negative. Abdomen and pelvis CT were normal. A genital ulcer biopsy showed irregular acanthosis in the epidermis, ulceration, and lymphocyte infiltrations, with fibrinoid necrosis of the vessel wall, in the dermis. No granuloma was seen. We decided against immunofluorescence testing due to its high costs. Other causes of genital ulcers being ruled out, these ulcers were considered related to SLE, as one of its mucosal involvement. The patient was treated with 70 mg/day (1 mg/kg) prednisolone, continuing on 200 mg/day hydroxychloroquine. No antibiotic was prescribed. Improvement started after 2 days, and the ulcers were healed after 15 days. The prednisolone dose was eventually tapered to 5 mg/week. After 3 months, she was doing well, until the time of writing. Our case was submitted on the research registry database under UIN 8837.

DISCUSSION

SLE usually involves organs, including the skin[1]. Cutaneous manifestations are many and of wide spectrum[9]. In most cases, skin lesions in SLE occur in sun-exposed areas[10]. Mucosal involvement is frequently manifested in lupus as ulcers in the mouth, less frequently in the nose and throat and rarely in the genital area[11]. Behçet's disease presenting as genital ulcer was excluded in our patient as she had the diagnostic criteria of SLE[8].

SLE genital involvement presented as small–medium size, papular ulcers with well-demarcated borders. These lesions are seen in both discoid lupus and SLE[7,11,12].

The pathophysiology of ulceration in the setting of immune dysregulation remains largely unknown, although histologic examination has shown inflammatory infiltrate, likely involving activation of T cells, and release of tumor necrosis factor alpha[10,11].

In establishing a differential diagnosis of the genital ulcers, we considered sexually transmitted diseases, infections, dermatologic diseases-related, related systemic diseases such as Crohn's disease (CD), malignancies, traumatic ulcers, and idiopathic disease[12].The diagnosis of Behçet's disease can be confidently made if there are at least three reported episodes of mouth ulcers over the past 12 months and the presence of two of the following symptoms: genital ulcers, ocular manifestation, dermatologic manifestation and positive pathergy reaction[13]. The diagnosis is made when the patient meets the first critera: oral ulcer with 2 of the other 4 manifestations. Our patient did not fit the criteria of Behçet's disease, as she had only bipolar mouth ulcers.

Lipschütz ulcer is an infrequent, self-limited, nonsexually transmitted ulcer characterized by the rapid onset of vulvar edema along with painful necrotic ulcerations. It may be preceded by influenza-like or mononucleosis-like symptoms. In our case, we made a diagnosis of exclusion[14]. Our patient had fever, no edema in the genital ulcer, she had been diagnosed with SLE, and she did not report any prior symptom compatible with influenza or mononucleosis. The patient did not report any sexual relationship outside of marriage. She did not fit the diagnostic criteria for Crohn's disease[15].

Negative culture for microorganisms in genital ulcers can exclude infection[13], as in our case. In the 2019 ACR/EULAR criteria, ANA at a titer of ≥1:80 is a mandatory criterion. The more specific antibodies for SLE, anti-dsDNA and anti-Sm, are grouped in one domain and weighted equally by 6 points. Anti-dsDNA has been found to be positive in 70-90% of SLE patients[8,16].

Physical examination alone cannot distinguish genital ulcers associate with lupus from vulvar ulcers associated with CD. The only way to confirm and differentiate between genital CD and genital SLE is via biopsy[14], the procedure we followed.

The treatment includes non-steroidal anti-inflammatory drugs, antimalarial drugs like hydroxychloroquine, prednisolone, immunosuppressive drugs, and biologics, in addition to surgery in some cases[15]. Our patient had been treated with prednisolone and hydroxychloroquine, with a good response. An untreated ulcer could progress to squamous cell carcinoma[11].

Romiti and colleagues[16] prescribed prednisolone in two cases of discoid lupus erythematosus affecting the genital area, with widespread discoid lesions on the head. Paidi and colleagues[11] prescribed the same treatment to a young female patient with a history of CD, idiopathic thrombocytopenic purpura, SLE, and hypothyroidism,

presenting with recurrent chronic diarrhea, perianal ulcers, the passage of blood in stools, and anal pain.

The novelty of our case is that the genital ulcers were due to SLE, without a superimposed infection, or other diseases such as CD. The lesions responded well to Epstein-Barr and hydroxychloroquine, without using immunosuppressant drugs.

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