CASE REPORT

Lipschütz ulcer and group A streptococcal tonsillitis

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SUMMARY

Lipschütz ulcers (LU) are non-sexually related genital ulcers, rarely reported. We describe a healthy 11-year-old girl, who presented with fever and a painful vulvar ulcer associated with erythematous tonsillitis. Throat swab test for Group A Streptococcus (GAS) was positive. She was treated with amoxicillin. Further investigation was negative, including Herpes Simplex virus DNA from ulcer swab and serology for Epstein-Barr virus, cytomegalovirus and *Mycoplasma pneumoniae*. Antistreptolysin O titre was high. The ulcer healed in 2 weeks, with no recurrence in a 1 year follow-up period. The association of LU with GAS tonsillitis is very rare.

BACKGROUND

Lipschütz ulcers (LU), also known as reactive non-sexually related acute genital ulcers, are non-sexually transmitted genital ulcers characterised by an abrupt onset, intense local pain and dysuria. Their morphology is variable. 'Kissing ulcers' with a symmetric appearance on opposite sides of the vulva have been described. Labial oedema and painful inguinal lymphadenopathy may be associated. Prodromal mild mononucleosis-like or influenza-like symptoms are usually present.

LU used to be traditionally described in young virgin women. However, in the recent literature, they are more frequently reported in sexually active girls or women.[1]

Most cases of LU are idiopathic, but several non-sexually transmitted viral and bacterial infections have been reported.[1–14]

Etiopathogenesis of LU is poorly understood. Evidence suggests that local ulceration results from a systemic immunopathological response to an acute infection rather than a manifestation of an underlying chronic disease.[12 14]

LU are probably misdiagnosed by clinicians, who are unaware of their existence.[1 9 13]

CASE PRESENTATION

A healthy 11-year-old girl presented with an acute onset of intense vulvar pain and dysuria. Fever and odynophagia had begun 3 days before. A large and superficial ulcer of 2 cm in diameter, with a clean base and red border was identified on the inner surface of left labium minora, adjacent to the vestibule and part of the fossa navicularis (figure 1), along with mild labial oedema. No inguinal lymphadenopathy was found. The oropharynx showed swollen and erythematous tonsils, without oral ulceration. She denied menarche, active sex life or vulvar trauma. There was no history of oral aphthosis or genital ulceration.

INVESTIGATIONS

Complete blood count, serum urea, creatinine, chloride, sodium, potassium, transaminases, C-reactive protein and urinalysis showed normal values; throat swab test for Group A Streptococcus (GAS) was positive; antistreptolysin O (ASO) titre (8 weeks later) was 964.5 IU/mL (normal range <200 IU/mL).

Serology for Epstein-Barr virus (EBV), cytomegalovirus (CMV), *Mycoplasma pneumoniae* and Herpes simplex virus (HSV-1, HSV-2) was negative for acute infection; PCR for Herpes virus (HSV-1, HSV-2, EBV, CMV, varicella zoster virus and human HSV 6, 7 and 8) from ulcer swab was negative; genital ulcer swab cultures (bacterial and fungal) were also negative.

Human leucocyte antigen (HLA)-B51 allele was negative and the ophthalmic examination was normal.

DIFFERENTIAL DIAGNOSIS

The diagnosis of LU depends on the exclusion of other causes of genital ulceration. Laboratory tests may be helpful to exclude sexually transmitted infections and systemic autoimmune diseases.

Genital HSV is the most common cause of genital ulceration and may not be sexually acquired.[3 11] HSV PCR from ulcer swab was negative, making this an improbable diagnosis.[15] Genital ulcer swab cultures were also performed, without evidence of local pathogenic microorganisms. Our patient was sexually inactive and sexual abuse was not suspected, so we did not perform other tests related to a possible sexually transmitted disease.

LU are described along with evidence of several acute systemic infections, mainly EBV, followed by CMV and *M. pneumoniae*.[2] These were excluded by negative serological tests.

Febrile acute streptococcal tonsillitis was diagnosed, confirmed by a positive GAS throat swab test and an elevated ASO titre (8 weeks later). Although very rare, the association of LU with acute GAS tonsillitis has been reported.[14]

Behçet's disease seems to be more common in Portugal than in other countries.[1] At presentation, our patient did not fit the diagnostic criteria for Behçet's disease. However, HLA-B51 was studied to predict the risk for the development of this disease and was negative.[16] Other immune-mediated diseases, such as Crohn's disease or erythema multiforme were not considered based on the patient's history and clinical findings.

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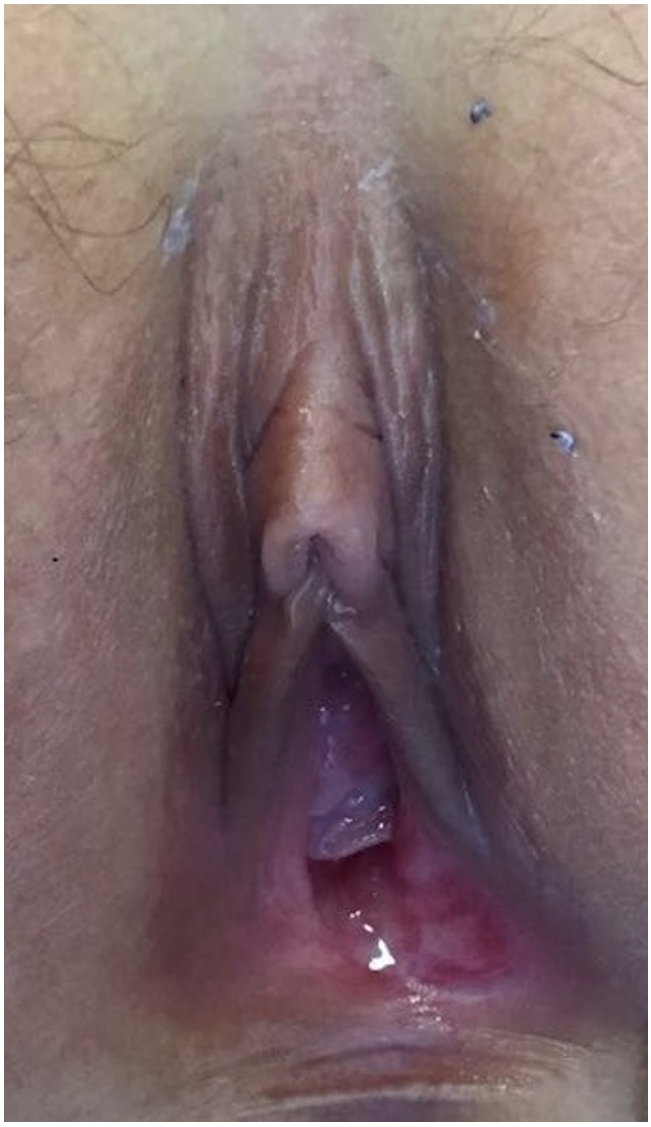

Figure 1 A large and superficial ulcer of 2 cm in diameter, with a clean base and red border on the inner surface of left labium minora, adjacent to the vestibule and part of the fossa navicularis.

TREATMENT

She was treated with a 10-day course of oral amoxicillin (500 mg twice a day). She also applied topical anaesthetic (lidocaine) and antiseptic healing ointment (dexpanthenol and chlorhexidine) until complete resolution.

OUTCOME AND FOLLOW-UP

The ulcer healed in about 2 weeks. Fever and odynophagia resolved in 2 days after initiating treatment with antibiotic. Regular follow-up appointments were scheduled by a paediatrician. There was no scarring or recurrence in the 1 year follow-up period. No oral ulcers were observed.

DISCUSSION

The diagnosis of LU is based on clinical findings and the exclusion of other causes of genital ulcers. Therefore, a complete clinical history and physical examination are essential.

There is no consensual laboratory protocol and the diagnostic management should be driven by clinical suspicion. Biopsy is usually unhelpful, as the histological findings associated with LU are normally non-specific.[1 2 7 10 13] Genital ulcer swab cultures should be restricted to cases that rise clinical suspicion of bacterial superinfection.[7]

LU have been associated with viral and bacterial acute systemic infections, mainly EBV infection, but also CMV, influenza virus, adenovirus, parvovirus B19, mumps, *M. pneumoniae* and *Mycoplasma fermentans*, *Salmonella paratyphi* and *S. typhi*, *Borrelia burgdorferi*, *Toxoplasma gondii*, ureaplasma and GAS. The exact pathogenesis of LU is uncertain and these associations have no proven linkage.[1–14]

LU are most of the times preceded by mild prodromal non-specific symptoms, which may be caused by an acute febrile illness, for example, an upper respiratory tract infection or a diarrhoeal illness.[7 14]

Acute streptococcal tonsillitis was diagnosed in our patient by a positive GAS throat swab test and an elevated ASO titre (8 weeks later). These findings, along with the clinical resolution following treatment with amoxicillin, are fairly consistent with an association between LU and an acute throat GAS infection.

Recent investigation suggests local ulceration to be the consequence of a type III hypersensitivity reaction to an acute viral or bacterial infection, resulting in a systemic host immunopathological response, rather than a local genital infection. Immune complex deposition in the dermal vessels and complement activation appear to play an important role in this process, leading to microthrombosis.[1 2 12] This explains why the microbiological tests from LU swabs are usually negative, as occurred in this case. In fact, few reports have described isolation of EBV directly from genital ulcers.[3 9 11]

The majority of the reported cases refer to previously healthy children, although most of the times an immunological study was not performed. LU have been described in two patients with immunoglobulin A deficiency. Interestingly, this immunoglobulin has an important role in mucosal immunity.[8]

LU are an acute self-limited ulcer and treatment is primary supportive, based on local hygiene, wound care and pain control.[2 3 5 10 13 14] Hospitalisation rate for pain control is not negligible.[14] Antibiotics are not indicated in otherwise healthy individuals, unless there is clinical suspicion of bacterial infection.[14]

Complete healing of LU varies from 2 to 6 weeks, generally with no scarring.[2 6 14] Recurrence has been reported in approximately one-third of the cases, although it is rarer in patients with acute genital ulceration associated with a viral infection or a systemic illness.[1 3 4 7] Lehman *et al* describe a recurrence rate of 60% and a history of oral aphthosis in 70% of the cases.[14] Neither occurred in our patient.

Learning points

- Lipschütz ulcers (LU) are non-sexually acute genital ulcerations that should be suspected in adolescent girls with vulvar pain and dysuria, along with influenza-like or mononucleosis-like symptoms.
- Laboratory investigation for genital ulcer should be based on clinical suspicion.
- LU are self-limited and appear to be a reactive response to an acute systemic illness.
- The association of LU with Group A Streptococcus acute tonsillitis is very rare.
- Treatment is supportive and prognosis is favourable, but follow-up is advised as the recurrence risk is not negligible.

Follow-up is advised to rule out an early stage of a systemic disease, mainly Behçet's disease.

Clinicians must keep in mind that genital ulceration may be very stressful to the patient and family. Thus, it should be reinforced that this is a non-sexually related condition and associated with good outcomes. Nevertheless, the possibility of sexual abuse should be kept in mind, specially in younger patients.

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