

Case  
report

# Genital ulcers associated with acute Epstein–Barr virus infection

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To date there have been only five reported cases of females with genital ulceration associated with primary Epstein–Barr virus infection. We describe two further patients and review the clinical features of all seven cases, noting the typical features, particularly purple ulcer margins and systemic symptoms, which should alert the physician to consider this diagnosis.

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## Introduction

Epstein–Barr virus (EBV) is a ubiquitous human herpesvirus. It is usually transmitted in saliva and primary infection is generally asymptomatic, although in a minority of those infected after infancy the immune response to primary EBV infection is manifest as infectious mononucleosis.<sup>1</sup> The virus replicates in the oropharynx and a latent infection is established in B lymphocytes enabling the virus to spread via the circulation. There is recurrent salivary excretion of virus, possibly resulting from continual reinfection from circulating B lymphocytes. Although EBV can also infect cervical epithelial cells *in vitro*, it has only rarely been described as a cause of genital ulceration.<sup>2–6</sup> We report two further cases that highlight features of the condition that may aid recognition and diagnosis. We believe the condition occurs more frequently than is currently recognised and is often wrongly attributed to herpes simplex virus (HSV) infection, with all the associated implications and concerns for the patient.

## Case reports

### CASE 1

A 14 year old girl presented with a 4 day history of painful vulval lesions, general malaise, and pyrexia. She had not yet reached the menarche and denied any sort of sexual genital contact. Her general practitioner had made a clinical diagnosis of genital herpes and prescribed aciclovir.

On examination, she had tender generalised lymphadenopathy, but no oropharyngeal lesions, rash, or hepatosplenomegaly. Genital examination revealed deep, 1 cm diameter, “kissing” ulcers on both labia majora. The ulcers had a central grey slough and vivid purple edges. Swabs (one taken before aciclovir therapy) were negative for virus culture, as were direct fluorescent antibody tests for HSV. Microscopy and culture of bacterial swabs revealed a mixed growth of organisms.

A full blood count showed a lymphocytosis with numerous atypical cells. The screen for heterophil antibodies was negative but viral serology revealed IgM antibodies to EBV capsid antigen (VCA) by immunofluorescence

(ATI Atlas) and an enzyme immunoassay (Biotest) for antibodies to nuclear antigen (EBNA) was negative, indicating a primary EBV infection. EBV DNA was detected in samples taken from the ulcer base by PCR DNA amplification using primers from within the BamH1 W repeat region of the EBV genome.

The patient’s systemic symptoms settled within a few days and the genital lesions within 2 weeks.

### CASE 2

A 14 year old girl presented with a 3 day history of acutely painful vulval sores associated with a generalised headache. She described an attack of oral herpes 7–10 days previously but had never suffered with genital lesions of any kind. The only sexual activity she claimed to have had was digital-genital contact 10 days previously.

On examination she had two ulcers with purple-red, ragged, edges and white centres. A diagnosis of probable HSV was made. She was prescribed aciclovir and analgesics. Three days later she returned having developed a temperature of 38°C and malaise. She had no symptoms or signs of pharyngotonsillitis, but she had bilateral, non-tender, cervical, and inguinal lymphadenopathy. The genital ulcers were resolving. The full blood count revealed a lymphocyte count of  $3.3 \times 10^9/l$  (a blood film was not performed), and a heterophil antibody test was negative. HSV culture and PCR were both negative at her initial visit. Serology showed the same pattern as in case 1. PCR for EBV DNA from the ulcers was negative.

Ten days after her initial presentation her ulcers had completely resolved and her systemic symptoms had cleared.

In a literature search via Medline we identified five other reported cases of female genital ulcers during primary EBV infection (table 1).

## Discussion

There are now several reports to show that, following acute infection, EBV shedding continues from both the oropharynx and the genital tract, suggesting that epithelial cells in both sites

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Table 1 Common features associated with genital ulcers caused by Epstein-Barr virus

Feature	Case 1 1997	Case 2 1997	Case 3 McKenna et al <sup>2</sup>	Case 4 Wilson <sup>4</sup>	Case 5 Portnoy et al <sup>6</sup>	Case 6 Brown and Stenchever <sup>3</sup>	Case 7 Navarro Llanos et al <sup>5</sup>
Sexual contact	none	digital-genital	none	none	oro-genital and genital-genital	oro-genital	none
Age	14	14	13	10	23	14	14
Description of ulcers	Two; painful; purple; rolled edges; deep; 1 cm diameter	Two; painful; irregular purple/red edge; deep, white base	Three; painful; vivid purple borders; deep; very large	Two; painful; 1.5 cm diameter	Three; painful; irregular purple/bluish-black margin	Multiple; painful; irregular erythematous margins; yellow/grey base	One; painful; erythematous edge; clean base; 2 cm diameter
Lymphadenopathy	generalised	generalised	generalised	cervical	inguinal	generalised	none
Fever and systemic symptoms	yes	yes	yes	yes	yes	yes, with rash	yes
Sore throat	no	no	yes with exudate	dry throat	no	yes, with ulceration	no
Atypical lymphocytes	yes	unknown	yes	unknown	yes	yes	no
HSV culture	-ve ×2	-ve	-ve	HSV ELISA -ve	-ve ×3	-ve	-ve
Heterophil antibody test	-ve	-ve	Monospot +ve	Monospot +ve	Monospot +ve	+ve 1:448	+ve
Serology	+ve IgM VCA, -ve EBNA 1 week after presentation	+ve IgM VCA, -ve EBNA 1 week after presentation	+ve IgM VCA 1 week after presentation	not obtained	+ve IgM VCA 2 weeks after presentation	+ve IFA 2 weeks after presentation	+ve IgM VCA 5 days after presentation
Culture/PCR for EBV	PCR +ve	PCR -ve	not done	not done	culture +ve	culture -ve	not done
Time until resolution of ulcers	2 weeks	10 days	not stated	1 week	5 weeks	2 weeks	3 weeks

may be continually reinfected by circulating B lymphocytes. It has been postulated that genital ulcers in infectious mononucleosis result from sexual transmission of the virus, either from genital-genital or oro-genital contact.<sup>3-6</sup> It is also important to note, however, that genital contact is not a prerequisite for the development of genital ulcers. In both of our cases and most of the others reported,<sup>2-4,5</sup> the ulcers occurred in young females before the onset of genital or oral sexual activity. Although autoinoculation cannot be ruled out, the ulcers are more likely to be a manifestation of lymphocyte migration to the genital tract.

It is noteworthy that in all the cases the acutely painful genital ulcers were by far the most important presenting symptom and were often present before the onset of any other features of infectious mononucleosis. Relying on the Monospot test or the presence of atypical lymphocytes in the peripheral blood film at the time of first presentation can be misleading, as in more than half the cases these were initially negative.

From the review of these two cases and the five others previously published, it is clear that the clinical appearance of the ulcers should suggest the diagnosis of EBV. The key features are the presence of acutely painful ulcers with a purple-red edge associated with systemic symptoms and lymphadenopathy distant from the site of ulceration. Confirmation of the diagnosis can be made by serology (the presence of IgM to EBV viral capsid antigen) or detection of EBV DNA by PCR examination of vulval swabs. Culture of EBV can take more than 4

weeks to become positive and this is not a test which is performed routinely. Patients who develop acute vulval ulcers due to EBV can be reassured that they will normally heal in about 2 weeks and there is no suggestion from the literature that they will recur.

We suspect that this clinical syndrome may be more common than has been previously recognised and is one that deserves wider recognition. It is important not to give patients an inaccurate diagnosis of genital herpes (with all its implications), especially in young women who may never have been sexually active. Genital ulcers in such cases will otherwise raise the question of sexual abuse and the recognition of EBV as a cause may thus avoid unnecessary distress.

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- Rickinson AB, Kieff E. Epstein-Barr virus. In: Fields BN, Knipe DM, Howley PM, et al, eds. *Fields virology*. Philadelphia: Lippincott-Raven, 1996:2397-445.
- McKenna G, Edwards S, Cleland H. Genital ulceration secondary to Epstein-Barr virus infection. *Gentourin Med* 1993;70:356-7.
- Brown ZA, Stenchever MA. Genital ulceration and infectious mononucleosis: report of a case. *Am J Obstet Gynec* 1977;127:673-4.
- Wilson RW. Genital ulcers and mononucleosis. *Pediatr Infect Dis J* 1993;12:418.
- Navarro Llanos A, Doménech Climent V, Elizalde Eguinoa J, et al. Primoinfección por el virus de Epstein-Barr: una causa poco conocida de úlcera genital aguda. Úlcera de Lipschütz? *Revista Clínica Española* 1996;196:570-1.
- Portnoy J, Ahronheim GA, Ghibu F, et al. Recovery of Epstein-Barr virus from genital ulcers. *N Engl J Med* 1984; 311:966-8.