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Ulcus vulvae acutum and SARS-Co V-2: an etiological role?

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A 10-year-old girl presented with a sudden onset of fever and vulvar pain. Genital examination revealed vulvar edema especially affecting the labia minora; on the inner face deeply penetrating ulcers were observed bilaterally, a larger one of about 3 cm in diameter on the left and two on the right of about 2 cm in diameter (kissing ulcers). They were well-circumscribed, centrally covered with a fibrinous membrane and with purple edges (Figure 1).

A clinical diagnosis of ulcus vulvae acutum was made.

The patient had never had sexual intercourse, was not affected by any disease and was not taking drugs.

Complete blood count was normal; laboratory findings showed elevated levels of serum C-reactive protein.

Serology was negative for a wide spectrum of infectious diseases, namely syphilis, HSV 1-2, parvovirus B19, adenovirus, and HIV; EBV and CMV serology was positive only for IgG.

Bacterial cultures were negative including Mycoplasma and Trichomonas Vaginalis.

SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) serology was requested; anti-SARS-CoV-2 IgM was positive with IgG antibodies negative. A molecular nasopharyngeal swab for the virus was performed with a negative result.

Due to the severity of the clinical picture and for preventing bacterial superinfection, the patient was treated with topical and systemic antibiotics before the laboratory results became available.

We empirically chose broad spectrum molecules, i.e. gentamicin cream and oral amoxicillin.

Because of the pain, she took ibuprofen for a total of 7 days.

Healing appeared within 2 weeks with scarring.

One month after healing, anti-SARS-CoV-2 IgG antibodies turned positive.

Ulcus vulvae acutum was first described by Lipschutz in 1913 and was therefore also called ulcus vulvae acutum Lipschutz (UVAL).

It is an uncommon clinical entity characterized by sudden painful vulvar ulcerations, of non-venereal origin, occurring mostly in young and virgin girls. Ulceration is often preceded by flu-like symptoms like fever, fatigue, malaise or chills.1

Guidelines for diagnosis and therapy are lacking.
A recently published systematic review of the literature, based on comparative and meta-analyses of the case reports described so far, proposes a diagnostic algorithm for a standardized diagnosis of UVAL (Table 1).

Our case fulfilled these diagnostic criteria.

The etiopathogenesis of UVAL is still unclear. Several infective agents have been associated with the disease in particular EBV, CMV, mycoplasma pneumoniae, flu virus, toxoplasmosis, mumps, salmonella, PVB19.

A hyperactivity of the immune system elicited by these infectious agents has been hypothesized as well as a type-III hypersensitivity reaction with vascular immune complex deposition, complement activation, micro-thrombosis and subsequent tissue necrosis.

In our patient, the initial flu-like symptoms and the current epidemiological situation made it mandatory to perform the serology for SARS-CoV-2.

During COVID-19 (Coronavirus Disease 2019) numerous and polymorphous skin and, to a lesser extent, mucosal manifestations have been described with different degrees of severity. Sometimes they can be observed in asymptomatic patients or in patients with very mild systemic symptoms of COVID-19 assuming therefore an important diagnostic value.

Some very severe cutaneous signs of COVID 19 are attributable to an immune disreactivity triggered by the virus with complement activation and possible interaction with coagulation pathways.

It is worthy of note that immune alteration and vascular damage are shared pathomechanisms for both UVAL and COVID-19 associated skin manifestations.

The necrosis and peripheral purpuric appearance of vulvar ulcers could also recall one of the typical skin patterns described during COVID-19.

The lack of definitive knowledge on the etiology of UVAL, as well as the limited use of histology in confirming the imputability of a specific infectious agent, does not allow us to affirm with certainty that SARS-CoV-2 is the cause of UVAL in our patient. However, the timing of onset and the unique positive serology for SARS-CoV-2 may suggest an etiologic role of this virus. During the COVID-19 pandemic it seems advisable to include SARS-CoV-2 as a possible cause of UVAL and to focus attention on the possible association with UVAL and its rare male counterpart, the juvenile gangrenous vasculitis of the scrotum.

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**Legend of Figure**

**Figure 1:** Clinical image of the vulva with the typical kissing ulcer
### Algorithm for diagnosis of UVAL

| Major criteria: |
|-----------------|
| - Acute onset of one or more painful ulcerous lesions in the vulvar region |
| - Exclusion of infectious and other non-infectious causes for the ulcer |

| Minor criteria: |
|-----------------|
| - Localization of ulcer at vestibule or labia minora |
| - No sexual intercourse ever (i.e. patient is a virgin) or within the last 3 months |
| - Flu-like symptoms |
| - Systemic infection within 2–4 weeks prior to onset of vulvar ulcer. |

Adapted from Sadoghi B. et al.²

### Legend of Table

**Table 1:** Diagnostic criteria of UVAL according to a recently published systematic review of the literature²
