





Acute Genital Ulcers in a Woman Secondary to COVID-19 Infection: A Case Report

Jia Zhang ^{1,*}, Danni Wang ^{1,*}, Mingjing Chen¹, Jiajun Li ², Wenxiang Huang ¹

¹Department of Geriatrics, the First Affiliated Hospital of Chongqing Medical University, Chongqing, People's Republic of China; ²Department of Infectious Diseases, the First Affiliated Hospital of Chongqing Medical University, Chongqing, People's Republic of China

*These authors contributed equally to this work

Correspondence: Wenxiang Huang, Department of Geriatrics, the First Affiliated Hospital of Chongqing Medical University, Chongqing, People's Republic of China, Tel +86 13883533808, Email wenxiang_huang@163.com

Abstract: Acute genital ulcers (AGU) have been associated with various pathogens, such as Epstein–Barr virus (EBV) and cytomegalovirus (CMV). However, cases of AGU associated with coronavirus disease 2019 (COVID-19) are rare, and this disease significantly impairs human quality of life. In this case, we report a 37-year-old woman who presented with a five-day history of a painful genital ulcer and fever. A month earlier, she had experienced a COVID-19 infection that resolved without medical therapy. Physical examination revealed that multiple asymmetric ulcers presented on labia minora covered with whitish exudates. The patient, without any high-risk sexual behavior, or a personal or family history of autoimmune disorders or inflammatory bowel disease, was diagnosed with COVID-19-related AGU after ruling out other infectious and immune diseases. Following a two-week treatment of oral prednisone, her vulvar edema, ulcers, and fever improved significantly. This case suggests that AGU may be triggered by a COVID-19 infection.

Keywords: COVID-19, SARS-CoV-2, acute genital ulcers, fever

Introduction

Acute genital ulcers (AGU), also known as Lipschütz ulcers, aphthous ulcers, or acquired genital ulceration, are characterized by acute, painful vulvar aphthous ulcers and typically occur in nonsexually active adolescent females.^{1,2} These ulcers, either singular or multiple, manifest as deep, sharply demarcated lesions with fibrinous coatings or greyish exudate.^{3,4} They frequently appear on the labia minora but also affect other regions, such as the labia majora and the perineal area.³ Affected patients often exhibit flu-like symptoms, including fever, fatigue, and lymphadenitis.⁴ The diagnosis of AGU is established by exclusion of other diseases.^{5–7} Although the etiology of AGU remains to be fully elucidated, it has been associated with various pathogens, including Epstein–Barr virus (EBV) and cytomegalovirus (CMV).⁴ In this paper, we report a rare case of a 37-year-old woman with exquisitely painful genital ulcers and persistent fever, which were attributed to COVID-19 infection after ruling out other common etiologies, thus highlighting the potential connection between AGU and COVID-19.

Case Presentation

A 37-year-old woman presented to our hospital with a 5-day history of exquisitely painful genital ulcers and persistent fever (38.5°C) on February 24, 2023. Over the previous month, she experienced a COVID-19 infection confirmed by a nasopharyngeal swab polymerase chain reaction. She referred to mild symptoms including fever, sore throat, and cough, which improved significantly within a week without medical intervention. She denied engaging in any recent high-risk sexual behavior. Additionally, she reported no history of autoimmune disorders or inflammatory bowel disease in herself or her family. Physical examination revealed multiple asymmetric ulcers with necrotic bases on the labia minora, which were covered in whitish exudates and exhibited well-demarcated borders (Figure 1A). No similar lesions

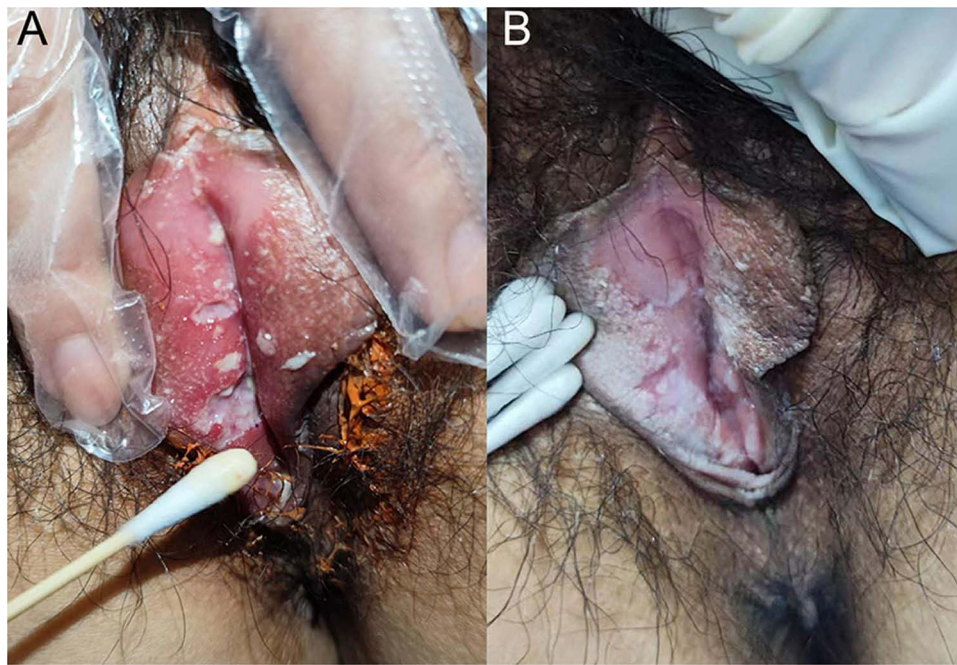


Figure 1 (A) Necrotic and fibrinous genital ulcers. (B) Follow-up image after 14 days of therapy demonstrating a resolving ulcerated lesion and vulvar edema.

existed elsewhere. Laboratory tests indicated a low lymphocyte count of $0.9 \times 10^9/L$ (normal range: 1.10–3.20) and a reduced percentage of lymphocytes at 10.5% (normal range: 20–50). The erythrocyte sedimentation rate was elevated at 84 mm/h (normal range: 2–26), and the C-reactive protein level was above normal at 13.9 mg/L (normal range: 0–8). After ruling out other common triggers such as herpes simplex virus, syphilis, EBV, human immunodeficiency virus, and CMV—all of which yielded negative serologic test outcomes—a diagnosis of AGU secondary to COVID-19 was established. Treatment with oral prednisone 20mg daily was initiated, the patient's fever subsided within 24 h, and vulvar edema and ulcers improved markedly (Figure 1B) after 14 days of therapy. At a 3-month follow-up, the patient remained asymptomatic.

Discussion

AGU, first identified by Lipschütz in 1913, mainly affects non-sexually active adolescent females and is characterized by the sudden onset of intense, painful, yet self-resolving vulvar aphthous ulcers.^{1,2,4,8} These ulcers often present with systemic infection symptoms and are associated with various pathogens, such as EBV, CMV, and influenza virus.⁴ The differential diagnoses for AGU encompass sexually transmitted infections, such as *Treponema pallidum*, herpes simplex virus, and Human Immunodeficiency Virus, as well as non-infectious conditions including Crohn's disease, Behçet's disease, erosive lichen planus, bullous disorders, localized trauma, and tumors.^{4,9} The characteristics of AGU and its differential diagnoses of Behçet's disease, Crohn's disease, and erosive lichen planus are shown in Table 1.

In this case, the patient exhibited sudden, painful ulcers on the labia minora, accompanied by fever. Laboratory tests targeting etiologies commonly associated with differential diagnoses of AGU yielded negative results. Considering the medical history, which indicated a COVID-19 infection 1 month earlier, the patient was diagnosed with AGU secondary to COVID-19 in accordance with the diagnostic criteria.⁴ Recently, five reported cases also highlighted the association between AGU and COVID-19.^{12–16} Of these, four were diagnosed with COVID-19 before the onset of genital ulcers, whereas one case was diagnosed 12 days after vulvar ulcers appeared. Notably, all cases presented flu-like symptoms alongside genital ulcers. Laboratory tests failed to reveal any positive findings for other potential causes of vaginal ulcers, leading to the final diagnosis of COVID-19-associated ulcers.^{12–16} The mechanism in these cases may be a dysregulation of the immune system accompanied by cytokine activation due to systemic illness. The fact that the SARS-CoV-2 virus

Table I Characteristics of Acute Genital Ulcers, Behcet's Disease, Crohn's Disease, and Erosive Lichen Planus

Disease	Aid to Differentiate
Acute genital ulcers ^{4,10}	<ul style="list-style-type: none"> • Commonly occurring in nonsexually active adolescent females • Typically deep with sharply demarcated borders • Frequently affects labia minora; may also appear on labia majora or perineal region • Accompanied by flu-like symptoms such as fever, fatigue, or lymphadenitis
Crohn's disease ^{4,10}	<ul style="list-style-type: none"> • Commonly occurring in premenopausal women • Recurrent ulcers and erosions primarily affect the anal or perineal region, with less frequency in the vulva and vagina. • Asymmetrical labial swelling (possibly affecting either labia minora or majora) • Predominantly fistulas • Accompanied by diarrhea or gastrointestinal problems.
Behcet's disease ⁴	<ul style="list-style-type: none"> • Primarily affects men aged between 20 and 40 years • History of recurrent oral aphthae and genital aphthae, as well as uveitis/retinal vasculitis • Bipolar aphthoid multiple ulcerations • May involve various other organs, including the skin, gastrointestinal tract, neurological system, vascular system, or joints.
Erosive lichen planus ¹¹	<ul style="list-style-type: none"> • The most frequent vulval signs are erosions, red and/or purple coloration, and scarring • Lesions have irregular shapes • The oral is often affected, other mucosal sites may also be affected • Do not resolve for at least several weeks

Abbreviations: AGU, acute genital ulcers; COVID-19, coronavirus disease 2019; EBV, Epstein-Barr virus; CMV, cytomegalovirus.

triggers a systemic autoimmune inflammatory response, impacting multiple organ systems, may explain the connection between the development of genital ulcers and COVID-19 infection.¹⁶

Treatment for AGU includes pain management, anti-inflammatory medication, and corticosteroid therapy.⁴ While corticosteroid therapy remains controversial, a systematic review suggests that systemic corticosteroids may prolong the disease's duration.⁵ However, a retrospective analysis of 26 patients with AGU indicates that corticosteroid therapy effectively resolves acute flare-ups and prevents AGU recurrences.¹⁷ Furthermore, given that four other reported cases of COVID-19-associated AGU have successfully utilized corticosteroid therapy with favorable outcomes,^{12,13,15,16} oral prednisone was administered to this patient, leading to the resolution of lesions within 2 weeks without any subsequent recurrences. Given the current context of the COVID-19 pandemic, we suggest clinicians adopt a low threshold for suspicion when evaluating AGU. Notably, for the rapid alleviation of symptoms related to COVID-19-associated AGU, oral steroid therapy continues to play a vital role in management.

Conclusion

In conclusion, we report a rare case to describe the potential relationship between the development of AGU and COVID-19 infection. Currently, the global COVID-19 pandemic remains far from over, clinicians should be alert to the presence of genital ulcers accompanied by flu-like symptoms in a clinical setting, and consider the possibility of COVID-19 infection as a potential trigger. Such recognition may prevent patients from delaying treatment, and timely and effective steroid therapy after diagnosis can avoid unnecessary interventions and alleviate patient distress.

Consent

Formal written consent for the publication of case details and associated images was obtained from the patient. Institutional approval was not required for publishing these case details.

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Disclosure

We declare that no authors of our work have conflicts of interest.

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