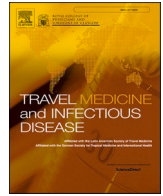




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Monkeypox proctitis treated with doxycycline in an HIV MSM returning to Italy from France

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ARTICLE INFO

Keywords:

Monkeypox virus

Proctitis

Anal pain

Doxycycline

Lymphogranuloma venereum

Dear Editor

Monkeypox (MPX) is caused by an orthopoxvirus and is typically a self-limiting disease with symptoms lasting between 2 and 4 weeks. WHO case definitions identify MPX as a rash illness; clinical suspicion requires the presence of symptoms and signs of a rash [1]. In addition, rectal pain is excluded from the list of significant symptoms. The earliest case descriptions of anal lesion and proctitis date back to June and July of 2022 respectively [2,3].

Here, we describe a case of monkeypox disease characterized by initial isolated anal lesion, inguinal lymphadenopathy, and rectal pain that occurred in August 2022 which was treated with doxycycline after being misdiagnosed by a specialist as lymphogranuloma venereum.

In August 2022, a 35-year-old HIV-positive MSM presented with a high fever, anorectal pain, and tenesmus to the Infectious Diseases department of University of Palermo-Italy.

He had previously engaged in unprotected anal receptive sexual activity in France and had not taken antiretroviral therapy (ARVT) for two months. His medical history included multiple episodes of syphilis, for which he was treated four times, as well as other sexual infections.

On examination, he had a left inguinal lymph node that was swollen, erythematous, and tender, as well as a left perianal papule. The blood tests revealed elevated levels of C-reactive protein (CRP). On the suspicion of gonococcal proctitis, testing for syphilis and HIV viral load was

performed, and single doses of ceftriaxone and azithromycin were administered as an empirical treatment. Syphilis serology was negative for active infection and HIV viral load was 9050 copies/ml. Also, CD4 cell count was performed, and the value was of 658 cells/mm³. ARVT was resumed.

Two days later, the patient returned to the department of Infectious Disease due to a worsening of the perianal lesion (Fig. 1A) and lymphadenopathy (Fig. 1B). His anorectal pain was moderately responsive to nonsteroidal anti-inflammatory drugs. As an evolution of the previous papule, he was found to have a perianal painful draining nodular lesion, a single pimple on the right buttock, and increased inguinal node inflammation. He refused hospitalization. *Chlamydia trachomatis* was investigated using polymerase chain reaction (PCR) on lesion swabs due to a suspicion of lymphogranuloma venereum (LGV), and treatment with doxycycline was initiated. PCR was negative for *Chlamydia* and other sexually transmitted diseases (gonorrhea, *Mycoplasma genitalium*, *Trichomonas vaginalis*). Due to the suggestive clinical picture of LGV and the risk of bacterial superinfection, doxycycline therapy was however continued for three weeks.

In the subsequent two days, there was an initial worsening with the spread of purplish erythema from the left inguinal region to the perianal region and the appearance of macular-vesicular lesions on the buttocks (Fig. 1C), followed by a rapid improvement of symptoms and disappearance of local inflammation (Fig. 1D and E). One-week follow-up

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<https://doi.org/10.1016/j.tmaid.2022.102469>

Received 17 September 2022; Received in revised form 20 September 2022; Accepted 21 September 2022

Available online 27 September 2022

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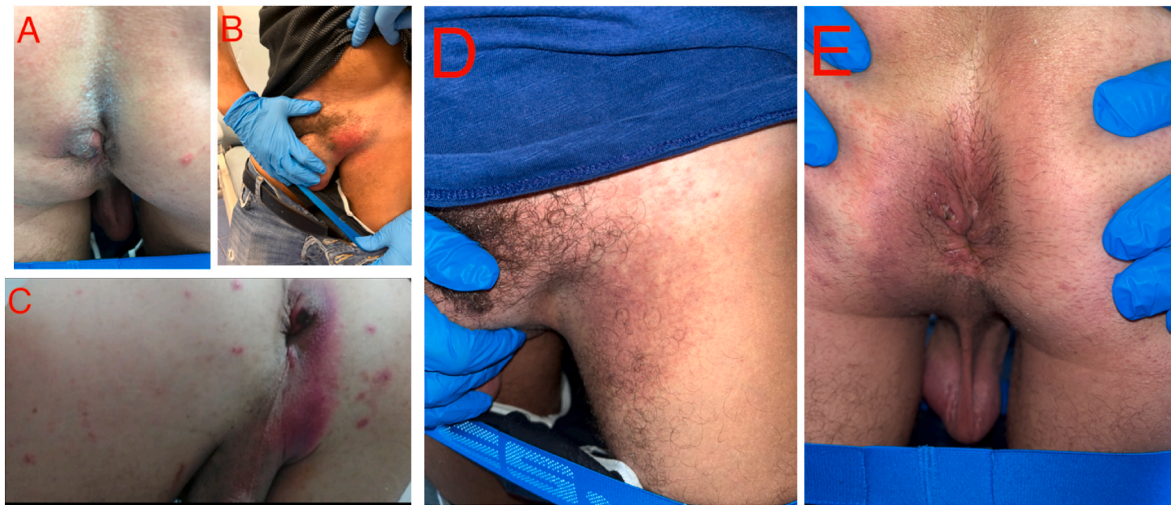


Fig. 1. Evolution of the anal lesion and inguinal lymphadenopathy: **A** nodular lesion at the second visit with single pimple; **B** lymphadenopathy and erythema at the second visit; **C** self-mirror collected image showing worsening of the anal lesion with purplish erythema and macular-vesicular lesion on the buttocks; **D** improvement of lymphadenopathy and erythema; **E** improvement of the anal lesion and erythema.

exams revealed a normal CRP value. Given growing evidence that monkeypox virus (MPXV) may be responsible for atypical cases of proctitis, PCR was performed one month after the first visit on the initially extracted DNA. The result of the test was positive.

The clinical manifestations of the 2022 outbreak of monkeypox may differ from those previously described, and there are an increasing number of reports of isolated perianal lesions and proctitis. A PubMed search combining the terms “monkeypox AND (proctitis OR anal)” yielded 14 papers describing single cases or case series with one single paper [3] published before August 2022.

Isolated anal lesion and proctitis, as in our case, make difficult diagnosis. In such circumstances the clinician first hypothesizes to classical diseases such as gonorrhoea, chlamydia, or syphilis. In our case, LGV was the most likely due to the lymphadenopathies and the anal lesion associated with proctitis. Bacterial superinfection can be a serious complication, and the initial site of the viral infection is likely to favor its development. Following doxycycline treatment, both the symptoms and the appearance of the lesion improved in our case. This was likely due to the resolution of a bacterial superinfection that had not been identified. However, tetracyclines and derivatives as doxycycline and minocycline has been studied in viral diseases with limited therapeutic options like dengue, sometimes with encouraging results. Doxycycline has anti-inflammatory and antioxidants effects by decreasing the expression of various pro-inflammatory cytokines (tumor necrosis factor and interleukin) and could prevent co-infections and superinfections due to broad-spectrum antimicrobial activity [4–7]. We cannot rule out the possibility that doxycycline may interfere with the pathogenesis of MPXV infection by promoting healing. Should further similar evidence emerge, a specific multi-center proof of concept study could be considered.

In conclusion, monkeypox is an emerging sexual transmission infection, and specific molecular biology should be performed in all patients with suspected sexual infection disease characterized by proctitis, anal pain and/or pustular rash.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of competing interest

Nothing to declare.

Funding for your research

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CRediT authorship contribution statement

Luca Pipitò: Investigation, Writing – original draft, All authors have read and agreed to the published version of the manuscript. **Marcello Trizzino:** Investigation, All authors have read and agreed to the published version of the manuscript. **Donatella Ferraro:** Investigation, All authors have read and agreed to the published version of the manuscript. **Antonio Cascio:** Conceptualization, Writing – original draft, All authors have read and agreed to the published version of the manuscript.

Declaration of competing interest

A conflicting interest exists when professional judgement concerning a primary interest (such as patient’s welfare or the validity of research) may be influenced by a secondary interest (such as financial gain or personal rivalry). It may arise for the authors when they have financial interest that may influence their interpretation of their results or those of others. Examples of potential conflicts of interest include employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/registrations, and grants or other funding.

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