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Hospitalisation for monkeypox in Milan, Italy

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A B S T R A C T

During the current multi-country outbreak of human monkeypox the hospitalisation rate observed in Milan, Italy was 8.8%. Bacterial superinfection and severe perianal pain were the main cause of hospitalisation requiring antibiotic treatment and analgesic therapy. One patient was treated with Cidofovir. All hospitalised patients were discharged and the outcome was favourable with full recovery.

The multi-country outbreak of human monkeypox (MPX), spreading all over the world since May 2022 with an epicentre in Europe and affecting mainly men who have sex with men (MSM), seems to be characterised by a milder course than in previously reported outbreaks in Africa [1–6]. For MPX infection observed in Africa it has been estimated an overall case fatality of 8.7% with difference between the involved MPX virus (MPXV) clade: 10.6% for Central African Clade (CAC) and 3.6% for West African Clade (WAC) [7]. In the 2003 outbreak of MPX in USA among 34 confirmed cases of MPXV infection caused by the WAC no fatalities were registered but 26% of patients required hospitalisation for >48 h [8]. Two young patients required hospitalisation in the intensive care unit for encephalitis and tracheal airway narrowing due to a retropharyngeal abscess. Among the adult population, a bacterial superinfection and a keratitis with corneal ulceration was reported [8].

Up to July 18, 2022, 34 confirmed cases of MPXV infection were diagnosed at the Department of Infectious Diseases of Luigi Sacco Hospital in Milan, Italy. Overall, 4 patients (11.7%) required hospitalisation (Table 1) but only in three cases (8.8%) it was directly due to clinical worsening of MPX infection and bacterial superinfections. Patient # 1 presented initially with several vesicular lesions localised on the nose followed by the onset of high fever and a possible bacterial superinfection. Despite antibacterial treatment the lesions coalesced with ulceration and development of a large eschar (Fig. 1). He was hospitalised and treated with cidofovir (twice administration) - because of tecovirimat unavailability - associated with antibiotics. He had an encouraging healing in of the lesions within 3 weeks and a complete recovery with scarring in about 6 weeks (Fig. 1). Patient # 2 required hospitalisation for severe anal pain and peripheral leucocytosis. He received only analgesic therapy with recovery in a few days. Patient # 4 following the diagnosis of MPX presented a cellulitis with ulceration and important edema localised to the shaft of the penis and scrotum (Fig. 2). Staphylococcus aureus and Streptococcus pyogenes were cultured from the ulcerated lesion requiring prolonged antibiotic therapy and hospitalisation. The duration of hospital stay ranged from 5 to 13 days. As far as alterations of laboratory exams, all four patients had a mild increase of C-reactive protein (median value 26.5 mg/dL), and one patient each showed leucocytosis, thrombocytopenia and increase of D-dimer. During the current MPX outbreak the rate of hospitalisation has been reported between 2 and 3.7% in two Spanish series [2,3], 8.3% in Germany [9], 9.2% in UK [1] and 11.1% in Portugal [10]. Our experience considering only patients with a clinical cause of hospitalisation (8.8%) is in agreement with previous studies.

Bacterial cellulitis localized to the penis as observed in one of our patients has been described initially by Hammerslag [11] and was reported in 11.1% of UK patients [1]. Proctitis and severe perianal pain directly caused by MPXV seems to be another frequent complication reported in up to 30% of subjects [12,13]. In conclusion, the proportion of hospitalised cases affected by human MPX during the current outbreak is about one out of ten with pain or bacterial superinfection.

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representing the main responsible clinical condition. Despite the small number of patients observed in our experience clinical outcomes were reassuring with complete recovery.

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**Institutional review board statement**

The study was conducted according to the guidelines of the Declaration of Helsinki. The study was approved by the Comitato Etico Interaziendale Area 1 (Protocol number 2022/ST/124).

**Ethics**

All patients provided written consent for the use of their case details and medical images in this publication.

**CRediT authorship contribution statement**

Davide Moschese: Conceptualization, Data curation, Formal analysis. Andrea Giacomelli: Conceptualization, Data curation, Formal analysis. Martina Beltrami: Data curation, Formal analysis. Giacomo Pozza: Conceptualization, Data curation. Davide Mileo: Validation, Formal analysis. Serena Reato: Data curation, Formal analysis. Martina Zacheo: Data curation, Formal analysis. Mario Corbellino: Data curation, Formal analysis. Giuliano Rizzardi: Conceptualization, Data curation, Formal analysis. Spinello Antinori: Conceptualization, Formal analysis, Writing – review & editing.

**Declaration of competing interest**

The authors declare no conflict of interest.

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### Table 1

Characteristics of hospitalised subjects with monkeypox.

| Gender/Age | M/26y | M/35y | M/34y | M/37y |
|-----------|-------|-------|-------|-------|
| HIV status | Negative | Negative | Positive | Positive |
| Clinical manifestations | Lesion on the nose followed by high fever (39.3 °C), chills, sweats, lymphadenopathy | Vesicular rash on mouth, head, limbs, trunk followed by fever (38 °C), lymphadenopathy | Perianal lesion followed by fever (38.3 °C), lymphadenopathy | Skin lesion of inguinal areas, shaft of penis, scrotum followed by fever (38 °C), headache, lymphadenopathy |
| Location of skin lesion | Nose, limb | Head, limbs, trunk | Perianal, foot, face, arm | Inguinal, penis, scrotum, face |
| Samples positive for MPXV PCR | Vesicule (skin, nose), anal swab, pharynx, seminal fluid | Vesicule, pharynx | Vesicule, pharynx, anal swab | Vesicule, pharynx, anal and uretral swab |
| Cause of hospitalisation | Worsening nasal lesion with suspected bacterial infection | Severe anal pain | Inability to self isolate | Bacterial infection (S. aureus, Streptococcus pyogenes) |
| Time of hospitalisation (days) | 8 | 5 | 8 | 13 |
| Abnormalities of laboratory findings | Increased C-reactive protein (45.1 mg/L) | Increased white blood cells (11,440/μL, N 40% L 50%), increased C-reactive protein (12 mg/L) | Mild thrombocytopenia (146,000/μL), increased C-reactive protein (30 mg/L) | Increased C-reactive protein (23.1 mg/L), increased D-dimer (1930 ng/mL) |
| Treatment | Amox/clav 3 g/d for 8 days; Cidofovir 5 mg/kg/day 1 and 7 | Analgesic therapy | None | Ceftriaxone 2 g/d for 7 days + daptomycin 500 mg/d for 5 days |
| Outcome | Recovery | Recovery | Recovery | Recovery |

N, neutrophils; L, lymphocytes; Amox/clav, amoxicillin/clavulanic acid; C-reactive protein normal value 10 mg/L.

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![Fig. 1. Evolution of nasal lesion of patient #1: A-I (in order): day 7, 9, 13, 19, 20, 22, 29, 33, 41. Cidofovir infusion at day 13 and 20.](image-url)
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