Travel Medicine and Infectious Disease

Hospitalisation for monkeypox in Milan, Italy

--Manuscript Draft--

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Abstract:	During the actual multi-country outbreak of human monkeypox the rate of hospitalisation 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.
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Declarations

Travel Medicine and Infectious Disease requires that all authors sign a declaration of conflicting interests. If you have nothing to declare in any of these categories then this should be stated.

Conflict of 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.

Please state any competing interests

None

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UNIVERSITA' DEGLI STUDI DI MILANO

DIPARTIMENTO DI SCIENZE BIOMEDICHE E CLINICHE

Milano, 24/07/2022

To The Editor-in-Chief

Travel Medicine and Infectious Diseases

Prof. Alfonso Rodriguez Morales

Dear Editor,

please find enclosed our manuscript entitled: "**Hospitalisation for monkeypox in Milan, Italy"** submitted for consideration in your Journal as Short communication .

We report the experience about hospitalization among subjects with monkeypox diagnosed at the Department of Infectious Diseases in Milano (Italy) from May to July 18, 2022. Our data are in agreement with previous published experience; however, we detail (a feature not reported in other papers) the cause of hospitalization and the follow-up of the patients.

The final version of the manuscript has been approved by all the authors. We declare that the manuscript has not been previously published and it is not submitted elsewhere

Yours sincerely

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Hospitalisation for monkeypox in Milan, Italy

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Abstract

During the actual multi-country outbreak of human monkeypox the rate of hospitalisation 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 (Figure 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 week (Figure 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 (Figure 2). *Staphylococcus aureus* and *Streptococcus pyogenes* were cultured from the ulcerated lesion requiring prolonged antibiotic therapy and hospitalization. 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 showed leucocytosis, thrombocytopenia and increase of D-dimer. During the actual MPX outbreak the rate of hospitalisation has been reported between 2-3.7% 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 Hammershlag [11] and was reported in 11.1% of UK patients [1]. Proctitis and severe perianal pain directly caused by MPXV is another frequent complication reported in up to 30% of subjects [12,13]. In conclusion, about one out of ten subjects affected by human MPX during the actual outbreak need to be hospitalised for pain or bacterial superinfection but the prognosis seems to be good with full recovery.

Figure legends

Figure 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.

Figure 2. Patient # 4: penile pustule in its stages of complication.

1A: day 1; 1B: day 3 ; 1C: day 5; 1D: day 11; 1E: day 22

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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).

Declaration of competing interest

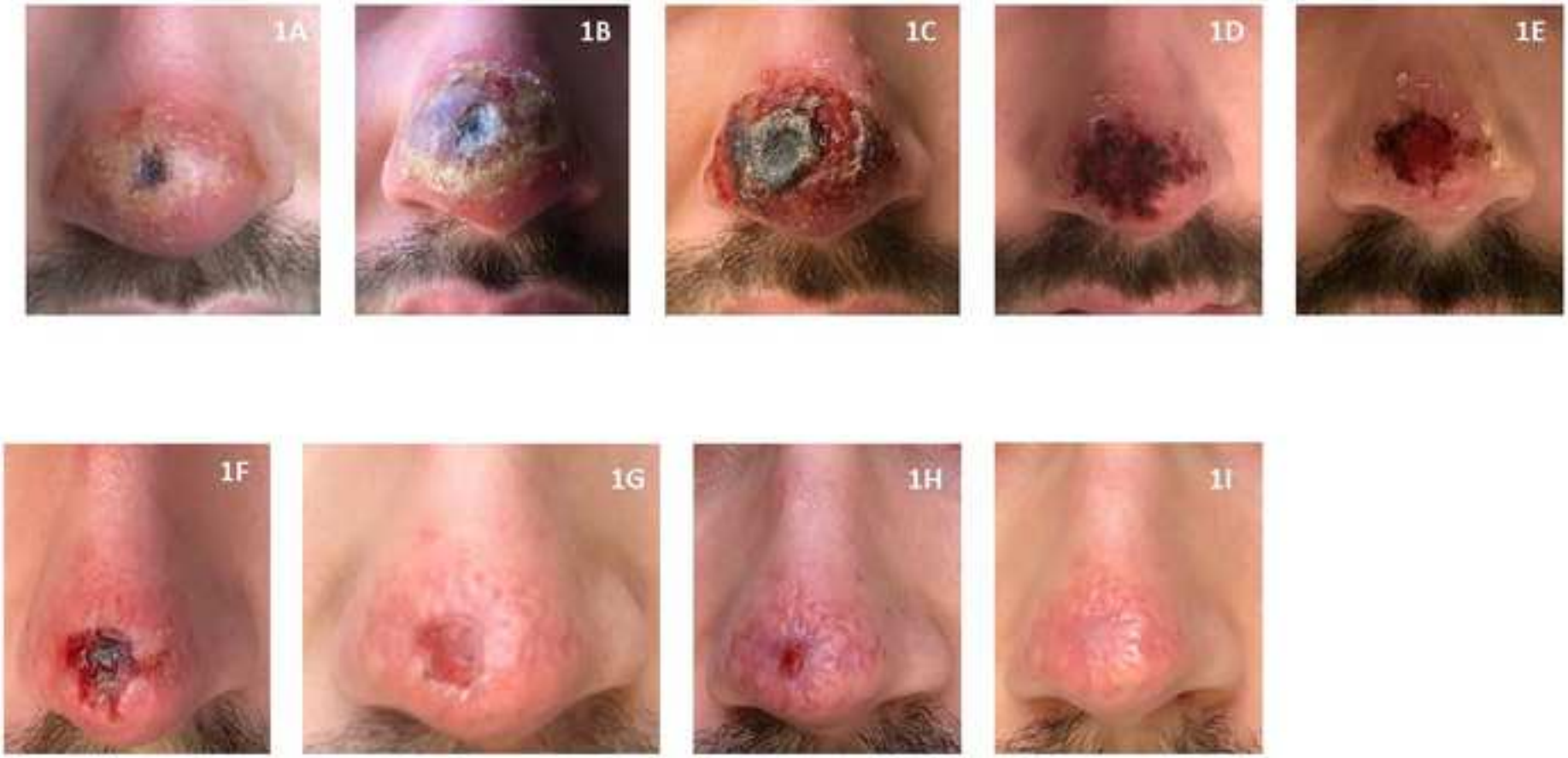
The authors declare no conflict of interest

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 lesions	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% L50%), increased C-ractive 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 2g/d for 7 days+daptomycin 500 mg/d for 5 days
Outcome	Recovery	Recovery	Recovery	Recovery

N, neutrophils; L, lymphocytes; C-reactive protein normal value 10 mg/L

Figure



Figure