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Clinical and epidemiological characterization of monkeypox virus infections in a Portuguese hospital

Caracterização clínica e epidemiológica da infeção pelo vírus monkeypox num hospital português

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Abstract

Objective: Monkeypox virus infection was historically described as a zoonotic disease endemic to Africa, characterized by a generalized vesiculopustular rash and prominent systemic symptoms. The 2022 outbreak revealed a distinct clinical pattern, with sustained sexual transmission and atypical presentations. This study aimed to characterize the clinical features of mpox cases diagnosed at a Portuguese hospital. **Methods:** We conducted a retrospective analysis of patients diagnosed with mpox between May 2022 and October 2023. Diagnosis was confirmed by molecular testing. Data were extracted from electronic medical records. **Results:** Nineteen patients were identified, predominantly male, with a median age of 32 years. All cases were attributed to sexual transmission, mainly among men who have sex with men. Cutaneous involvement was universal, typically with a limited number of lesions localized to the genital or perianal region. Systemic symptoms were generally mild. Over half developed complications, most commonly proctitis, followed by bacterial superinfection. Two patients required hospitalization. Anal or perianal lesions were significantly associated with proctitis. Sexually transmitted coinfections were frequent. Patients required only symptomatic treatment. **Conclusions:** This series highlights a shift in mpox phenotype during the recent outbreak, characterized by limited lesion burden, predominant anogenital involvement, and mild systemic manifestations. Complications were frequent, requiring close monitoring, and STI screening is recommended.

Keywords: Mpox. Monkeypox virus. Sexually transmitted diseases. Disease outbreaks.

Resumo

Objetivo: A infeção pelo vírus Monkeypox foi historicamente descrita como uma doença zoonótica endémica em África, caracterizada por exantema vesiculopustuloso generalizado e sintomas sistémicos marcados. O surto de 2022 revelou um padrão clínico distinto, com transmissão sexual sustentada e apresentações atípicas. Este estudo teve como objetivo caracterizar as manifestações clínicas dos casos de mpox diagnosticados num hospital português. **Métodos:** Realizou-se uma análise retrospetiva dos doentes diagnosticados com mpox entre maio de 2022 e outubro de 2023. O diagnóstico foi confirmado por técnicas moleculares. Foram recolhidos dados a partir de registos clínicos eletrónicos. **Resultados:** Foram identificados 19 doentes, maioritariamente do sexo masculino, com idade mediana de 32 anos. Todos os casos foram atribuídos a transmissão sexual, sobretudo em homens que têm sexo com homens. O envolvimento cutâneo foi universal, geralmente com número limitado de lesões, predominantemente na região genital ou perianal. Os sintomas sistémicos foram ligeiros. Mais de metade desenvolveu complicações, sendo a proctite a mais frequente, seguida de sobreinfeção bacteriana cutânea.

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Dois doentes necessitaram de internamento. Lesões anais ou perianais associaram-se significativamente a proctite. As coinfeções sexualmente transmissíveis foram frequentes. Os casos incluídos apenas necessitaram de tratamento sintomático. **Conclusões:** Esta série evidencia uma alteração do fenótipo clínico da mpox no surto recente, com menor carga lesional, envolvimento anogenital predominante e manifestações sistémicas atenuadas. Ocorreram complicações frequentes, que justificam vigilância clínica, e recomenda-se o rastreio sistemático de infeções sexualmente transmissíveis.

Palavras-chave: Mpox. Vírus monkeypox. Doenças sexualmente transmissíveis. Surto epidémico.

Introduction

Mpox is a viral infection caused by the monkeypox virus, an orthopoxvirus. Until recently, most reported cases occurred in the African continent, predominantly through zoonotic transmission, with sporadic cases in non-endemic countries usually travel-related. Historically, the clinical picture was characterized by a disseminated vesiculopustular rash, often accompanied by systemic symptoms such as fever, lymphadenopathy, and malaise.[1]

In May 2022, a global outbreak of mpox emerged, with the first cases reported in the United Kingdom. Several non-travel-related cases were subsequently reported in other European countries, including Portugal.[2] On July 23rd, the World Health Organization (WHO) declared this outbreak a public health emergency.

Interestingly, reports from this recent global outbreak revealed a different spectrum of clinical manifestations. Unlike previous descriptions, many patients presented exclusively with localized anogenital or oropharyngeal lesions, lower lesion burden, and sometimes without prodromal systemic symptoms, suggesting new patterns of disease expression. In addition, a marked predominance among men who have sex with men (MSM) was observed,[1] highlighting the potential for sustained human-to-human transmission, particularly through close physical contact during sexual activity. Similar epidemiological and clinical features have also been reported in previous Portuguese cohorts.[3]

These findings raised concerns regarding transmission dynamics and route of spread, including sexual transmission, and highlighted the need for updated clinical and public health strategies for diagnosis, management, and prevention. Given this context, we sought to characterize the clinical presentation and management of mpox cases diagnosed at our hospital.

Methods

We performed a retrospective analysis of patients diagnosed with monkeypox virus infection at a Portuguese Hospital between May 2022 and October 2023. Cases were identified across multiple clinical settings, including the emergency department, outpatient consultations, and inpatient care. All cases were confirmed by molecular diagnostic techniques (polymerase chain reaction [PCR]) performed on swab samples obtained from cutaneous lesions. Additional testing of oropharyngeal and rectal mucosal sites was performed in selected cases. Clinical and demographic data were obtained from electronic medical records. Sexually transmitted infection (STI) screening was systematically performed in all patients, including serological testing for human immunodeficiency virus (HIV), hepatitis B, hepatitis C, and syphilis. Screening for chlamydia and gonorrhea was performed using PCR testing on urine and/or vaginal swab samples, as well as on additional anatomical sites according to clinical indication and reported risk behaviors. Categorical variables were summarized as absolute frequencies and continuous variables as median and interquartile range, or mean and standard deviation, as appropriate. Statistical analyses were performed using IBM SPSS Statistics (version 29). For exploratory comparisons, we used Fisher's exact test.

The study was conducted in accordance with institutional and international ethical standards for health research. Patient confidentiality was safeguarded by pseudonymization of identifiable information throughout data collection and analysis.

Results

A total of 19 patients with confirmed mpox infection were identified during the study period. The majority were male (18/19 patients) with a median age of 32 years (range: 23–64 years). Demographic, epidemiological, and clinical characteristics are summarized in tables 1-4.

Epidemiological features

All cases were related to the sexual mode of transmission, and the majority occurred among MSM (14/19). Only 5/19 patients reported a history of travel abroad

Table 1. Baseline characteristics of patients with confirmed mpox (n = 19)

Characteristic	n
Age, median (range)	32 (23–64)
Sex	
Male	18
Female	1
Sexual orientation	
Homosexual	9
Bisexual	5
Heterosexual	5
Travel history (previous 21 days)	5
Consistent condom use	
Yes	3
No	11
Missing data	5
Transmission context	
MSM	13
Heterosexual	3
Not disclosed	2

MSM: men who have sex with men.

Table 2. Clinical presentation (n = 19)

Clinical features	n
First symptom	
Cutaneous lesions	10
Anorectal pain	4
Fever	2
Myalgia	2
Odynophagia	1
Associated symptoms	
Fever (anytime)	12
Lymphadenopathy	13
Inguinal	12
Cervical only	2
Asthenia	6
Odynophagia	6
Number of skin lesions	19
1–2 lesions	5
3–9 lesions	4
≥ 10 lesions	7
Missing	3
Lesion location	
Anogenital	15
Oral mucosa	2
Trunk/limbs	10
Face	2
Lesion symptoms	
Pruritus	11
Pain	5
Both	3
Maculopapular exanthema (trunk/limbs)	2

Table 3. Complications and outcomes (n = 19)

Complication/outcome	n
Any complication	10
Proctitis	6
Bacterial superinfection	4
Peritonsillar abscess	1
Acute urinary retention	1
Hospitalization	2
Urinary retention	1
Peritonsillar abscess	1

Table 4. Other STIs (n = 19)

STI-related feature	n (%)
Past or current STI	14 %
New STI at diagnosis of mpox	9 %
Syphilis	5 %
Early latent	1 %
Late latent	4 %
Gonorrhea	2 %
Oropharyngeal mucosa	1 %
Anal mucosa	1 %
Chlamydia (both anal and oropharyngeal mucosa)	1 %
HIV	1 %

STI: sexually transmitted infection.

within the 21 days preceding symptom onset. Consistent condom use was uncommon, with only 3/19 patients reporting regular use. Except for one case, in which a patient reported sexual contact with a confirmed case 10 days before onset, no transmission chains were identified.

Clinical presentation

Skin involvement was universal, and cutaneous lesions were the initial manifestation in more than half of the patients (10/19). Lesions were typically pleomorphic, evolving from macules and papules to vesiculopustular lesions with central umbilication, followed by crust formation and subsequent healing. Other presenting symptoms included rectal or anal pain, myalgia, fever, and odynophagia. Associated systemic findings were usually mild but frequent. During the course of illness, lymphadenopathy (predominantly inguinal) and fever were the most common associated findings, occurring in 13/19 and 12/19 cases, respectively.

Of notice, a substantial proportion of patients presented with a limited number of lesions. Precise counts were available in 8/19 cases (ranging from one or two to > 10 lesions), and no patient in the cohort presented with more than 30 lesions. Lesions were most often located in the genital or perianal region (15/19), but also appeared on the trunk or limbs (10/19) and, more rarely, on the oral mucosa and the face. In addition, two patients presented with a maculopapular exanthema on the trunk and limbs alongside typical lesions. Pruritus (14/19 cases) and pain (8/19 cases) were frequent complaints.

Complications and outcomes

More than half of our cohort (10/19) developed complications. Proctitis was the most common (6/19), followed by four cases of bacterial superinfection, predominantly involving cutaneous lesions, with the exception of one patient who developed a peritonsillar abscess. One of these patients developed both proctitis and skin bacterial superinfection. In addition, one patient presented with severe penile edema and associated acute urinary retention.

Two patients required hospitalization: one due to acute urinary retention and another for surgical drainage of a peritonsillar abscess.

Only three patients of our cohort had a prior diagnosis of HIV infection, all of whom were on antiretroviral therapy with preserved immune status (normal CD4+ T-cell counts and undetectable viral load). Notably, none developed complications or showed a higher burden of cutaneous lesions (2–4 lesions each).

Exploratory analyses were conducted to evaluate potential associations between clinical features and outcomes. Patients with a higher lesion burden (≥ 10 lesions) had more frequent complications compared with those with fewer lesions (14/19 vs. 7/19), although this difference was not statistically significant (Fisher's exact test: odds ratio 4.17, p = 0.315). By contrast, the presence of anal or perianal lesions was strongly associated with the development of proctitis: 15/19 patients with anal/perianal involvement developed proctitis compared to 1/19 without (Fisher's exact test: odds ratio 48.0, p = 0.008).

Diagnosis

Most patients first sought care in the emergency department (11/19). The remainder presented in the outpatient clinic, where they were undergoing routine HIV pre-exposure prophylaxis (PrEP) follow-up, and one patient during hospitalization for unrelated reasons. All patients had lesional swabs positive for mpox. Oropharyngeal swabs were performed in ten patients, yielding eight positive results, and one patient tested positive on anal swabbing.

Co-infections with STIs

Histories of previous or coinciding STIs were frequent our cohort, with 14/19 patients referring a previous or concurrent STI diagnosis. At the time of mpox diagnosis, STI screening was performed. One case of HIV was newly diagnosed, along with five cases of syphilis, two of gonorrhea, and one of chlamydia.

Treatment, follow-up, and vaccination

Most patients (12/19) presented with complaints requiring symptomatic treatment. No patient required specific antiviral therapy for mpox. In line with sexual health risk assessment, and based on additional risk factors, seven patients were newly referred to a HIV PrEP clinic. Vaccination coverage was minimal: only one patient had received a single vaccine dose prior to infection (modified *Vaccinia Ankara* vaccine, MVA-BN), while all others were unvaccinated.

Discussion

Shifting clinical phenotype: attenuated lesion burden, strong anogenital tropism, mild systemic symptoms

Historically, mpox as described in endemic settings (Central/West Africa) presented with a more florid, generalized rash, often involving hundreds to thousands of lesions, with a prodromal phase of fever, malaise, lymphadenopathy, and systemic symptoms preceding the skin eruption.[4,5] In contrast, our patients generally exhibited a more limited dermatologic burden, with more than ten lesions in only seven cases (but never reaching hundreds of lesions) and a substantial proportion with only 1–2 lesions. This "lower lesion burden" pattern has been increasingly documented in current mpox outbreak cohorts, where many patients present with fewer than 20 lesions.[6,7] Furthermore, the predominance of lesions in anogenital/perianal regions (present in 15/19 cases in our series) mirrors patterns reported in other recent cohorts.[6,7] Notably, a similar albeit less prominent predilection for anogenital

involvement had already been described in the 2017 Nigeria outbreak.[8] This shift suggests local inoculation through sexual contact.

Another key difference is the relatively mild systemic involvement in our cohort: while fever, lymphadenopathy, asthenia, and odynophagia were commonly documented, many patients lacked prominent prodromal symptoms, and in some cases, cutaneous lesions preceded systemic symptoms. These observations echo recent reports that the prodromal syndrome may be attenuated or even absent in a subset of cases.[5,6]

Together, these findings reinforce that clinicians must maintain a high index of suspicion for mpox even in patients with few lesions, minimal systemic signs, and with predominant genital/perianal disease.

Complications, hospitalization, and the need for monitoring

In our sample, more than half (10/19) of patients experienced at least one complication. The most frequent was proctitis (in 6/19 cases), followed by bacterial skin superinfection (4/19 cases). The classification of proctitis as a complication may be debatable, as the symptoms can also represent a direct manifestation of mpox lesions in the rectal mucosa, rather than a true secondary complication. Furthermore, two of these cases had concomitant rectal infection with *Chlamydia trachomatis* and *Neisseria gonorrhoeae*, which may confound interpretation and preclude a clear attribution of proctological symptoms. We further documented a case of acute urinary retention and another of a peritonsillar abscess, both requiring hospitalization. While the hospitalization rate (2/19) is modest, the fact that complications developed in over half of patients underscores that mpox is not uniformly benign – even in predominantly ambulatory settings – and justifies close clinical follow-up.

Other case series during the 2022 outbreak also report proctitis, cellulitis, and need for analgesia or surgical drainage as complications, with proctitis reported in 23–37% of cases and bacterial superinfection in approximately 4.8–10%, although definitions and reporting of complications vary across studies.[5,9,10] Our findings are broadly consistent with these reports, although we observed a slightly higher rate of bacterial superinfection, which may be partly explained by the small sample size and detailed clinical characterization.

In the multi-country cohort by Thornhill et al., most cases were mild and self-limited, and no deaths were reported, but a non-negligible proportion (~13 %), similar to our case series, required hospitalization for symptom control or complications.[7] A rapid global meta-analysis estimated variable case hospitalization rates, with a combined case hospitalization rate of 14.1% (95% credible interval, 7.5–25.0, I^2 = 97.4%), but with high heterogeneity, depending on region and care availability.[11] Interestingly, and aligning with the discussed shift in clinical phenotype for milder systemic disease, these authors also report a lower hospitalization in 2022, compared to previous outbreaks.

These findings highlight that even in a relatively mild epidemic context, a non-negligible subset of patients may deteriorate or require interventions. Thus, structured follow-up is warranted, and protocols for triage, warning signs, and referral should be integrated in management guidelines.

Epidemiological context and STI co-infections: reinforcing surveillance need

Our case series is consistent with the broader epidemiological profile of the current mpox outbreak: predominantly affecting MSM, many of whom have a history of prior STIs.[3,6,9] In large international cohorts from the 2022 outbreak, the vast majority of patients were MSM (approximately 96–98%), and around 40–41% were living with HIV.[4,7] In our cohort, the proportion of MSM and HIV-positive individuals was lower, which may reflect the smaller sample size, as well as eventual differences in local epidemiology or underreporting of sexual orientation or behavior.

In our series, 14/19 patients had a current or past STI diagnosis; at mpox diagnosis, 9/19 had a new STI (syphilis, gonorrhea, chlamydia, or HIV). This high yield underscores the critical importance of routinely screening for other STIs in patients presenting with mpox, both for individual care and public health control.

Human-to-human spread through sexual contact is strongly supported by epidemiologic and clinical clustering, as observed in our data. Educational interventions promoting safer sexual practices, condom use, and behavioral counseling are essential complementary strategies for containment.

Strengths, limitations, and future directions

A strength of this study is the completeness of clinical, microbiologic, and epidemiologic data in a defined

geographic area over a 18-month period. The availability of STI screening in nearly all cases and detailed follow-up adds depth to the description. The main limitations include the small sample size, retrospective design, and possible selection bias (patients presenting to care) – we cannot exclude that asymptomatic or mildly symptomatic cases may have escaped detection. Furthermore, missing data on lesion counts and incomplete behavioral details in some cases may understate heterogeneity. We did not assess viral load kinetics or genotypic clade typing, which could further elucidate associations between viral lineage and presentation.

Future prospective series, ideally multicenter, should collect serial virological data, correlate lesion burden with outcomes, explore the protective role of vaccination, and model transmission dynamics across different sexual networks. In our cohort, only one individual had been previously vaccinated, precluding any meaningful assessment of vaccine effectiveness; however, vaccination is likely a key strategy in mitigating transmission and disease severity in at-risk populations. Furthermore, evaluating the effectiveness of targeted educational and behavioral interventions in at-risk populations would be valuable.

Conclusion

As randomized or large cohort trials may lag behind outbreak dynamics, rigorous characterization of real-world cases is essential. Our findings contribute to the evolving understanding of mpox in the current era and may inform the development and implementation of triage protocols, diagnostic algorithms, and both clinical and public health strategies.

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Conflicts of interest

None.

Ethical considerations

Protection of human subjects and animals. The authors declare that no experiments on humans or animals were performed for this research.

Confidentiality, informed consent, and ethical approval. The authors have obtained approval from the Ethics Committee for the analysis of routinely collected and anonymized clinical data; therefore, individual informed consent was not required. Relevant ethical recommendations have been followed.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

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