



## **Erythematous maculopapular rash in monkeypox virus infection: A retrospective case series of 30 patients**

Chloé Bertin, Anne-lise Beaumont, Marie Merlant, Morgane Mailhe, Diane Le Pluart, Laurène Deconinck, Michael Thy, Marie Cortier, Mathilde Garé, Marion Dollat, et al.

### **► To cite this version:**

Chloé Bertin, Anne-lise Beaumont, Marie Merlant, Morgane Mailhe, Diane Le Pluart, et al.. Erythematous maculopapular rash in monkeypox virus infection: A retrospective case series of 30 patients. Journal of the European Academy of Dermatology and Venereology, 2023, 37 (5), 10.1111/jdv.18876 . hal-04407121

**HAL Id: hal-04407121**

**<https://hal.science/hal-04407121>**

Submitted on 20 Jan 2024

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

**Title:**

**Erythematous maculopapular rash in monkeypox virus infection: a retrospective case series of 30 patients**

**Article type:** Letter to the editor, number JEADV-2022-2551

**Authors :** Chloé Bertin<sup>1</sup>, Anne-Lise Beaumont<sup>1</sup>, Marie Merlant<sup>2</sup>, Morgane Mailhe<sup>1</sup>, Diane Le Pluart<sup>1</sup>, Laurène Deconinck<sup>1</sup>, Michael Thy<sup>1</sup>, Marie Cortier<sup>1</sup>, Mathilde Garé<sup>1</sup>, Marion Dollat<sup>1</sup>, Mayda Rahi<sup>1</sup>, Véronique Joly<sup>1</sup>, Sylvie Lariven<sup>1</sup>, Christophe Rioux<sup>1</sup>, Audrey Truong<sup>3</sup>, Lydia Deschamps<sup>3</sup>, Valentine Marie Ferré<sup>4</sup>, Charlotte Charpentier<sup>4</sup>, François-Xavier Lescure<sup>1</sup>, Fabrice Bouscarat<sup>2</sup>, Vincent Descamps<sup>2</sup>, Yazdan Yazdanpanah<sup>1</sup>, Nathan Peiffer-Smadja<sup>1</sup>

**Affiliation :**

1. Université Paris Cité, Bichat, Assistance Publique - Hôpitaux de Paris - Claude-Bernard University Hospital, Department of Infectious and Tropical Diseases, Paris, France
2. Service de dermatologie, AP-HP, Hôpital Bichat-Claude Bernard, F-75018 Paris, France ;
3. Service d'anatomopathologie, AP-HP, Hôpital Bichat-Claude Bernard, F-75018 Paris, France ;
4. Service de Virologie, Université Paris Cité, INSERM, IAME, UMR 1137, AP-HP, Hôpital Bichat-Claude Bernard, F-75018 Paris, France.

**Correspondence :** Dr Chloé Bertin, Université Paris Cité, Bichat, Assistance Publique - Hôpitaux de Paris - Claude-Bernard University Hospital, Department of Infectious and Tropical Diseases, Paris, France. Phone: +33140247803, mail: [chloe.bertin@aphp.fr](mailto:chloe.bertin@aphp.fr)

**Keywords:** Monkeypox, atypical dermatologic lesions, Exanthema, pharyngitis, maculopapular rash

Manuscript words: 599 words, 1 table and 1 figure.

**Conflict of interest:** there are no conflict of interest

Funding source: none

Data availability statement: the data that support the findings of this study are available on request from the corresponding author.

**Dear editor,**

Monkeypox (MPX) is a zoonotic disease caused by an *orthopoxvirus* usually causing self-limiting outbreaks in Africa. Since May 2022, an unprecedented outbreak has spread globally (1). The classical presentation of MPX disease associates fever, headache, myalgia, lymphadenopathy, sore throat and pleiomorphic skin lesions. Typical skin lesions are papules, vesicles and pustules that ulcerate, become umbilicated and then crops. However, the clinical presentation of MPX disease is sometimes aspecific and can mislead diagnosis (2,3). We conducted a single center retrospective study in Paris, France, to analyze MPX patients presenting with an erythematous maculopapular rash. All patients gave oral consent to participate and the study was approved by a Research Ethics Committee. Between May 21st and July 28th 2022, 439 patients had a PCR-confirmed MPX infection in this center. Thirty patients (30/439, 6.8%) presented an erythematous maculopapular rash (Table 1 and Fig. 1). Patients were all men except one male to female transgender and 93% had sex with men. Among the 30 patients, 25 (83%) presented concomitant typical MPX vesiculopustular skin lesions and 15 (50%) presented concomitant pharyngitis (Fig. 1). Of note, 5 patients (17%) had no typical MPX skin lesions and presented only with an erythematous maculopapular rash and a pharyngitis. Rashes appeared in a median of 3.5 days [IQR 2-6] after symptoms' onset. Dermatological examination revealed aspecific maculo-papular rashes, always affecting the trunk and sometimes extending to the limbs or face. Three patients were hospitalized: one for aphagious pharyngitis, one for blepharitis and one for phimosis with urinary retention. All rashes resolved in a few days without specific treatment. The prescription of an antibiotic therapy before the apparition of the rash was reported in 17 cases (59%), mostly amoxicillin (n=13) for suspected bacterial pharyngitis. In patients with antibiotics, the rash followed antibiotic use after a median of 1 day [IQR 1-2]. Among the 13 patients for whom EBV blood PCR was done, all had a replication. Of note, EBV blood PCR was performed in 7 patients of the center with MPX without a rash and found EBV replication in the 7 cases. Histopathologic findings were similar in the 6 patients who had a cutaneous biopsy to rule out a severe drug reaction. It consisted of a superficial lymphocytic infiltrate consistent with maculopapular exanthema of drug or viral origin. The immunohistochemical EBV marker (EBER) was always negative and there was no specific MPX histologic pattern to guide diagnosis. In this center, rashes frequency is estimated at 6.8% of MPX patients, which makes it less frequent than other recent reviews (8.0-13.7%) (3–5). Half the patients in this study had an association of rash and pharyngitis leading to antibiotics prescription to treat a suspected bacterial pharyngitis. MPX diagnosis may reduce the use of unnecessary antibiotic prescribing. MPX rashes could be related to different

physiopathological mechanisms including an aspecific MPX cutaneous tropism or concomitant viral EBV replication with cutaneous manifestation (6,7). Rashes onset in 59% of patients after antibiotic therapy might also suggest a drug reaction or an infectious mononucleosis-like antibiotic reaction (8). A primary EBV infection is much less probable even though clinical presentation can be misleading (9). An erythematous maculopapular rash was observed in 13 patients without prior antibiotic therapy making it a specific skin manifestation of MPX infection. Maculo-papular rashes are not uncommon in MPX. They are associated to pharyngitis in half of the cases and to typical skin lesions in 83% of the cases. In an epidemic context, MPX infection should thus be considered in patients with an erythematous maculopapular rash even without associated skin lesions.

**Acknowledgments:** The patients in this manuscript have given written informed consent to publication of their case details.

## References

1. Gessain A, Nakoune E, Yazdanpanah Y. Monkeypox. *N Engl J Med*. 26 oct 2022;0(0):null.
2. Tarín-Vicente EJ, Alemany A, Agud-Dios M, Ubals M, Suñer C, Antón A, et al. Clinical presentation and virological assessment of confirmed human monkeypox virus cases in Spain: a prospective observational cohort study. *The Lancet*. 27 août 2022;400(10353):661- 9.
3. Patel A, Bilinska J, Tam JCH, Fontoura DDS, Mason CY, Daunt A, et al. Clinical features and novel presentations of human monkeypox in a central London centre during the 2022 outbreak: descriptive case series. *BMJ*. 28 juill 2022;378:e072410.
4. Girometti N, Byrne R, Bracchi M, Heskin J, McOwan A, Tittle V, et al. Demographic and clinical characteristics of confirmed human monkeypox virus cases in individuals attending a sexual health centre in London, UK: an observational analysis. *Lancet Infect Dis* [Internet]. 1 juill 2022 [cité 26 juill 2022];0(0). Disponible sur: [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(22\)00411-X/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00411-X/fulltext)
5. Mailhe M, Beaumont AL, Thy M, Le Pluart D, Perrineau S, Houhou-Fidouh N, et al. Clinical characteristics of ambulatory and hospitalised patients with monkeypox virus infection: an observational cohort study. *Clin Microbiol Infect Off Publ Eur Soc Clin Microbiol Infect Dis*. 23 août 2022;S1198-743X(22)00428-1.
6. Shiohara T, Kano Y. A complex interaction between drug allergy and viral infection. *Clin Rev Allergy Immunol*. oct 2007;33(1- 2):124- 33.
7. Ónodi-Nagy K, Kinyó Á, Meszes A, Garaczi E, Kemény L, Bata-Csörgő Z. Amoxicillin rash in patients with infectious mononucleosis: evidence of true drug sensitization. *Allergy Asthma Clin Immunol Off J Can Soc Allergy Clin Immunol*. 2015;11(1):1.
8. Ishida T, Kano Y, Mizukawa Y, Shiohara T. The dynamics of herpesvirus reactivations during and after severe drug eruptions: their relation to the clinical phenotype and therapeutic outcome. *Allergy*. juin 2014;69(6):798- 805.
9. Ciccarese G, Trave I, Herzum A, Parodi A, Drago F. Dermatological manifestations of Epstein-Barr virus systemic infection: a case report and literature review. *Int J Dermatol*. oct 2020;59(10):1202- 9.