Two cases of Monkeypox virus infection without detectable cutaneous/mucosal lesions

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Dear Editor,

in our case series of 16 human Monkeypox virus (MPX) infected patients diagnosed from 1th July until 31thAugust 2022 in the Dermatology Unit and in the Infectious Disease Unit of the San Martino Hospital, Genoa, Italy[1], two patients had no detectable cutaneous/mucosal manifestations at the time of MPX diagnosis.

The first patient was a 37-year-old Italian homosexual man presenting to the Infectious Disease Unit for the pre-exposure prophylaxis (PrEP) against HIV follow-up appointment. He had been complaining of anal pain without anal bleeding or secretions for 5 days and admitted risky sexual behaviors (unprotected sex with casual partners) in the previous two weeks, when he had travelled to Indonesia and France. His stable partner, a 24-year-old Italian homosexual man, complained of sore throat and reported the same risky behaviors. He had not travelled abroad in the last month.

At physical examination, the patients had not visible cutaneous/mucosal lesions. They performed a complete sexually transmitted infections (STIs) screening including serology for *T.pallidum* infection, human immunodeficiency virus (HIV), hepatitis B and C viruses, anal, urethral and oropharyngeal swabs for the search of DNA of*Chlamydia Trachomatis* , *Neisseria gonorrhoeae, Mycoplasma hominis, Mycoplasma genitalium, Ureaplasma urealyticum, Ureaplasma parvum, Trichomonas vaginalis* by polymerase chain reaction (PCR) and, lastly, anal and oropharyngeal swabs for the search of MPX DNA by PCR, as previously described[2,3]. The laboratory investigations resulted all negative, except for the detection of MPX DNA at the oropharyngeal and anal swabs, that resulted positive in both sites and in both patients. The clinical presentation of these patients could be misdiagnosed with other STIs, especially with non-gonococcal proctitis and pharyngitis. Indeed, we suggest considering MPX infection in all at-risk patients presenting with traditional or atypical STIs signs/symptoms to avoid incorrect diagnosis.

Unlike the patient with MPX virus infection manifesting as single cutaneous lesion that we recently described[4], these two patients had not detectable cutaneous/mucosal lesions but only signs/symptoms of systemic involvement. Indeed, MPX virus traditionally causes a systemic infection: once acquired through close contact with skin/mucosal lesions, large respiratory droplets or fomites, the virus replicates at the inoculation site, then it spreads to the local lymph nodes and subsequently to the bloadstrem (initial viremia), causing the viral spread to other organs. These infection phases represent the viral incubation period, lasting 7-14 days. Signs/symptom onset correlates with a secondary MPX viremia corresponding to 1-2 days of prodromal signs/symptoms (mainly fever and lymphadenopathy) before appearance of skin/mucosal lesions[5]. Noteworthy, the MPX systemic spread during the acute infection represents a potential threat to the safety of blood transfusion and organ transplantation[6].

According to one of the largest case series describing MPX related signs and symptoms, presentation of MPX infection without skin/mucosal lesions accounts for about 5% of all cases[7]. We can speculate that in such cases, as in our patients and in those described by Quattri et al.[8], the cutaneous/mucosal MPX viral load was so low to cause only localized, single or even undetectable lesions. Unfortunately, we were not able to quantitatively assess the MPX viral load in the swabs that resulted positive nor in the patient's blood samples to confirm this hypothesis.

In conclusion, MPX infection can represent a diagnostic challenge, especially when it occurs as a single cutaneous lesion of the genito-anal site[4,8] or with acute anal or oropharyngeal pain in absence of associated cutaneous/mucosal lesions. Physicians should be aware of the possible atypical and scant manifestations of the disease and, in case of high clinical suspicion, should not exclude MPX infection even if cutaneous/mucosal lesions are undetectable.

Authors' contributions : Giulia Ciccarese, Giorgia Brucci: conceptualization, methodology, writing-original draft; Francesco Drago, Antonio Di Biagio: investigation, resources; Bruno Caccianotti, Sergio Lo Caputo, Teresa Santantonio, Gaetano Serviddio: writing review and editing, supervision.

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