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Human monkeypox coinfections; lessons from available cases – Correspondence

Dear Editor,

Monkeypox virus (MPXV) is a zoonotic member of *Orthopoxvirus*, family *Poxviridae,* which was announced as endemic in West and Central Africa following the smallpox eradication. The disease was initially identified in Denmark after two outbreaks of pustular illness in a macaque colony in 1958 [1]. In the 1970s, the first human case of monkeypox was reported in the Democratic Republic of Congo (DRC) [2], and numerous human monkeypox outbreaks were recognized in 1996–1997, as well as from 2001 to 2004 [3].

In 2005, the first sporadic MPXV case was identified in Southern Sudan. Similarly in 2018–2021 WHO (World Health Organization) announced the case in the USA, Singapore, United Kingdom, and Portugal that is associated with importation or travel to West African regions [4–6]. According to the literature review, the monkeypox virus is classified into two distinct branches including Congo Basin (mortality rate 10%) and West Africa (mortality rate less than 1%). All these sporadic MPXVs originated from the West African lineage [7]. Since September 2017, Nigeria has been experiencing the largest human monkeypox outbreak following climate changes with heavy rainfall and flooding. There are two primary hypotheses to elucidate this reemergence i.e. climate changes cause animal and human populations into proximity, and weaning herd immunity after smallpox cession in these conditions [8]. However, monkeypox is rapidly disseminated in the USA and Western Europe in a short time span. Despite the growing global health authorities' concern, our knowledge of the monkeypox host spectrum and sylvatic maintenance is limited.

As of writing of this study, several human monkeypox cases have been confirmed in non-African regions while co-infections of monkeypox still remain a puzzle. Bhunu et al., 2012 showed that residents in Central and West Africa hunt monkeys due to poverty. Thus, the number of human monkeypox increases when the number of MPXV infected-animal increases, particularly among HIV-infected individuals [9]. Correspondingly, the WHO warranted similarities in clinical presentation between human monkeypox and primary infection with varicella-zoster virus (VZV), especially in regions where both circulate [10]. Hoff et al., 2017 documented the co-occurrence of MPXV and VZV in a single host that causes missing MPXV in routine medical examinations worldwide [11]. Therefore, coinfections could lead to human monkeypox misidentification that is associated with lacking a meaningful gap in MPXV virus tracking. Hughes et al., 2021 recently published a case report regarding coinfections of monkeypox and varicella-zoster virus from the DRC [12]. Human monkeypox is commonly confused with another febrile rash illness particularly varicella-zoster virus infection in endemic regions. Nevertheless, monkeypox cases frequently experience a febrile prodromal with a high fever for 1–4 days before rash onset, whereas a low-grade fever at rash onset is more common for VZV. In addition, lymphadenopathy draining the palms of the hands and soles of the feet are more often noted in MPX than VZV [12]. It appears that the true prevalence of MPXV remains uncertain due to these misidentifications. The mechanism behind the co-occurrence of MPX and VZV remains unknown. Initial infection with either virus may cause weakness of the immune system to be susceptible to a secondary virus infection. The presence of cutaneous lesion may provide a suitable condition for the entrance of MPXV following contact with infected animals. It is also possible that MPXV infection directly activates VZV reactivation subsequent to herpes zoster (HZ) infection. Recent evidence showed that human monkeypox could easily be transmitted by an inter-human route through close contact with lesions, body fluids, respiratory droplets, and contaminated materials rather than travel to African countries. Based on CDC reports, the majority of human monkeypox is transmitted to men who have sex with men (MSM) (https://i-base.info/htb/42896). The first case of human monkeypox infection in the Czech Republic was also by a 34-years gay man with syphilis and HIV co-infection [13].

The recent European multicenter investigations announced that most MPXV cases were neither linked to travel nor had contact with symptomatic individuals or animals. Therefore, it may be the possible undetected spread of MXPV in Europe that represents MPXV has been circulating during a lack of surveillance systems, particularly during sexual encounters [14].

In summary, the potential role of HIV co-infection has been shown in prior studies. Concurrent manifestations of sexually transmitted infections would most likely be delayed or omitted chance of MPXV diagnosis. However, It is essential to consider the diagnosis of human monkeypox in all MSM cases with a typical rash. The true monkeypox burden was under-detected due to MPXV coinfections particularly with VZV infection, especially in an endemic area. The evaluation of current monkeypox coinfections highlights the significance of atypical clinical presentations of human MPX. Moreover, sexually transmitted infection (STI) clinics are the most common places to identify new monkeypox cases. Re-introduce smallpox vaccination to a population that lives with a high prevalence of HIV/AIDS in West and Central Africa could be a helpful strategy in rapid control of MPXV reemergence.

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