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Serum Mpox-specific IgG titers before and after breakthrough Mpox infection in an HIV-infected individual with viral suppression and prior 2-dose Mpox vaccination

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Dear Editor,

Vaccination program for Mpox with the modified vaccinia Ankara-Bavarian Nordic (MVA-BN) vaccine was implemented in Taiwan in March 2023.[1] Here, we present the clinical course of an individual with HIV who developed breakthrough Mpox after having undergone two doses of MVA-BN vaccination.

A 36-year-old man had been in his usual state of health until three weeks prior to this admission, when anal pain and bloody diarrhea developed. One week later, some vesicles were noted on the anal region and a few pustules on the right elbow. No fever, sore throat, or dysuria was reported. HIV infection had been diagnosed nine years earlier, for which he had been receiving stable antiretroviral therapy with the latest plasma HIV RNA <20 copies/ml and CD4 count 579 cells/mm^3 determined two months prior to this admission. He was occasionally engaged in group chemsex with men. He had received two doses of MVA-BN vaccine administered 11 and 16 months prior to this event, respectively (Figure).

Physical examination was remarkable for anal vesicles with central umbilication and digital-rectal exam revealed some blood clot. PCR assays of clinical specimens revealed multiple sexually transmitted infections (STIs): anal and throat swabs tested positive for Mpox virus, a rectal swab for human simplex virus and *Neisseria gonorrhoeae*, and a stool sample for *Entamoeba histolytica*.

His anal lesions worsened with severe pain and confluent vesicles were noted five days later. Treatment with tecovirimat (600 mg twice daily) was started on the second hospital day in addition to intravenous acyclovir and metronidazole and intramuscular administration of ceftriaxone of 500 mg, followed by a 7-day course of doxycycline. He was discharged with oral tecovirimat and paromomycin. All vesicles resolved two weeks after completing the 14-day course of tecovirimat.

We established an in-house enzyme-linked immunosorbent assay using convalescent serum from an Mpox patient as positive control to determine antibody response, including anti-A29 and anti-H3L IgG. H3L protein is expressed on the envelope of mature virion, which could be found in both Mpox and vaccinia virus, while A29 antigen, a homolog of vaccinia virus A27 protein, is considered to be more specific to Mpox virus and thus was applied for the design of Mpox-specific serological assays.[2,3] The titers of anti-A29 and anti-H3L IgG of the serum sample obtained on the day of admission were 1:200 and 1:400, respectively. Archived serum samples obtained one month after the first and second dose of MVA-BN vaccination were retrieved for determinations of anti-A29 and anti-H3L IgG titers, which all showed negative results (Figure). Antibody determination was performed after written informed consent was obtained.

While several studies had demonstrated promising effectiveness of MVA-BN vaccines against Mpox, cases of breakthrough infection still occurred.[4] Suboptimal antibody responses after vaccination among immunocompromised individuals were reported to be associated with breakthrough infection. Bottanelli firstly demonstrated a non-responder to MVA-BN vaccination had suboptimal antibody responses due to concurrent use of corticosteroids and IL-5 monoclonal therapy for asthma, who subsequently had breakthrough Mpox one year after the second dose of vaccination.[5] Weerasinghe also presented two immunocompetent, HIV-negative individuals who underwent MVA-BN vaccination and developed mild Mpox with negative IgG and IgM in the archived serum samples.[6] While milder symptoms were observed among most of the individuals with breakthrough Mpox, cases of breakthrough infection with severe symptoms that required antiviral therapy have been reported. However, the association with vaccination non-response and breakthrough infection warrants more investigations. Furthermore, frequent sexual exposure was also proposed to be associated with breakthrough Mpox infection.[4,7,8] Our case further showed that, despite good viral suppression and a high CD4 count with antiretroviral therapy, non-response to two-dose MVA vaccination and unprotected sex put this

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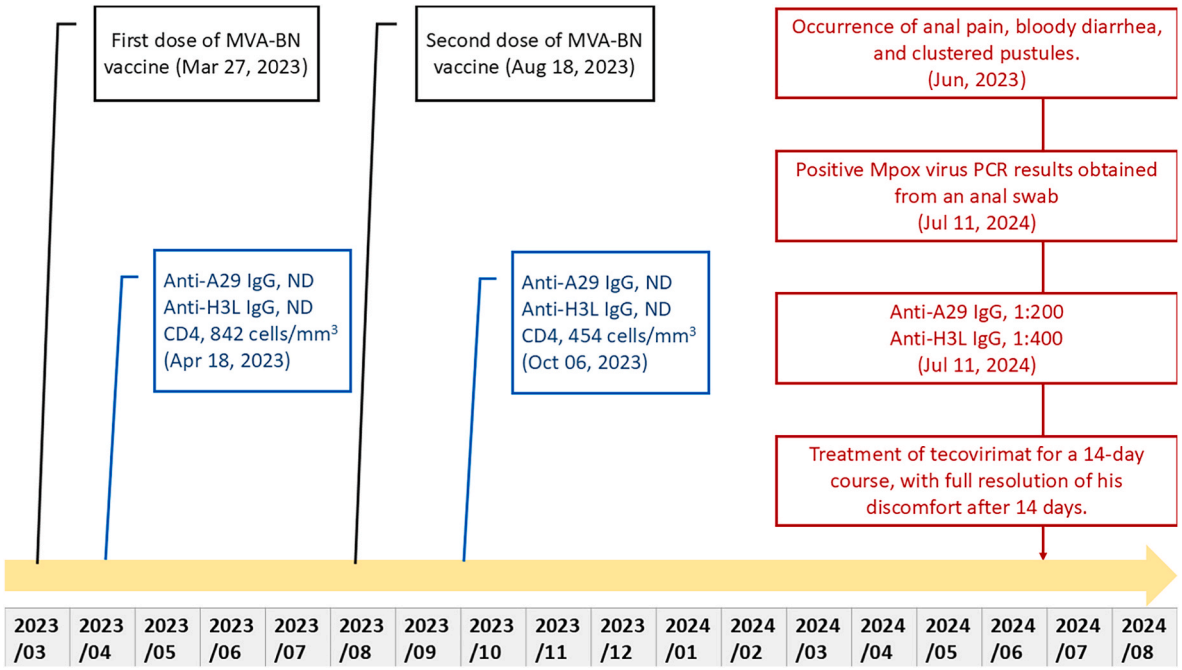

Fig. 1. Timeline of the patient's medical history. (ND, not detectable; PCR, polymerase chain reaction).

individual with HIV at high risk for breakthrough Mpox.

Nowadays, a more virulent cases of Mpox due to Mpox virus clade Ib is recently reported in Africa, Europe and some Asia countries, which could be likely to cause household transmission. Despite the lack of real-world study assessing the vaccine effectiveness against Mpox clade I, MVA-BN vaccine has been shown to confer protection from aerosol, intratracheal, or intravenous lethal challenge in animal models.[9] Therefore, in response to the reemergence of Mpox, Mpox vaccination should be promoted among the high-risk populations while more studies are warranted to assess the serologic responses to Mpox vaccination, vaccine effectiveness against Mpox clade Ib, and booster vaccination in vaccine non-responders.

CRediT authorship contribution statement

Wang-Da Liu: Writing – review & editing, Writing – original draft, Investigation, Conceptualization. **Tai-Ling Chao:** Methodology, Investigation, Data curation. **Sui-Yuan Chang:** Supervision, Conceptualization. **Chien-Ching Hung:** Writing – review & editing, Supervision, Conceptualization.

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