Biosafety and Health 6 (2024) 186–190

Contents lists available at ScienceDirect

Biosafety and Health

journal homepage: www.elsevier.com/locate/bsheal

Case Report

Human mpox co-infection with advanced HIV-1 and XDR-TB in a MSM patient previously vaccinated against smallpox: A case report

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ARTICLE INFO

Article history:
Received 24 January 2024
Revised 29 April 2024
Accepted 29 April 2024
Available online 01 May 2024

Keywords:
Mpox
Mpox virus (MPXV)
Human immunodeficiency virus type 1 (HIV-1)
Extensively drug-resistant tuberculosis (XDR-TB)

ABSTRACT

Mpox is a zoonotic infectious disease caused by the mpox virus (MPXV). Historically, the majority of mpox cases have been documented in Central Africa. However, since May 2022, there has been a notable rise in reported cases from regions beyond Africa. Currently, over 110 countries spanning Europe, North America, South America, Asia, and other territories have reported mpox infections. This report details a case involving a patient who identifies as a man who has sex with men (MSM) and is concurrently infected with MPXV, human immunodeficiency virus type 1 (HIV-1), *Pneumocystis jiroveci*, as well as extensively drug-resistant tuberculosis (XDR-TB). This patient had also received a vaccination for smallpox in the past. Additionally, we provide photographic documentation charting the progression of dermatological manifestations associated with mpox. This case highlights the significance of sexual intercourse as a crucial mode of transmission for mpox. The rapid and widespread dissemination of the MPXV across various regions, especially among MSM communities, underscores the importance of enhancing preventive education efforts targeted at high-risk populations.

1. Introduction

Mpox is a zoonotic disease caused by the mpox virus (MPXV), most cases have been reported in Central Africa. However, an increasing number of cases have been reported outside Africa since May 2022. More than 110 countries in Europe, North America, South America, Asia, and other regions have confirmed cases of mpox [1]. In China's mainland, there were 1,098 newly confirmed mpox infections between June 1 and August 31, 2023. All of these individuals were male, 96.3 % of whom were men who have sex with men (MSM). Some of these patients were diagnosed with acquired immune deficiency syndrome (AIDS), syphilis, condyloma acuminatum, and other infectious diseases. According to an international study that conducted a comprehensive systematic review and meta-analysis, three symptoms related to mucosal infection (skin rash, proctitis, and diarrhea) and a history of syphilis prevailed in patients with concomitant mpox and HIV. This study offers insights into the importance of clinical features of the primary invasion site of infection [2]. Here, we report the case of an MSM patient co-infected with MPXV, human immunodeficiency virus type-1 (HIV-1), *Pneumocystis jiroveci*, and extensively drug-resistant tuberculosis (XDR-TB) and was previously vaccinated against smallpox. In addition, we have added images of the natural evolution of dermatological lesions.

2. Case presentation

A 42-year-old man, a non-resident of Beijing City, was admitted to a local hospital with a history of recurrent fever since August 2022. He had a $CD4^+$ T-cell count of 35 cells/μL and an HIV-1 viral load of 90,000 copies/mL. Computed tomography (CT) of his chest revealed consolidation of the right lung field. Sputum smear was positive for acid-fast bacilli. Metagenomic sequencing of his peripheral blood indicated that the patient had been infected with *Pneumocystis yerinii*, *Mycobacterium tuberculosis* (MTB), and HIV-1. He was diagnosed with *Pneumocystis jiroveci* pneumonia (PJP), pulmonary tuberculosis, lymphatic tuberculosis, and AIDS/HIV. He was subsequently treated with sulfanilamide for PJP, prothioisonicamide, pyrazinamide, cycloserine, levofloxacin, and ethambutol for tuberculosis (TB), and bictegravir/emtricitabine/tenofovir alafenamide for HIV. During treatment, cycloserine and levofloxacin were discontinued owing to repeated manifestations of skin rash and allergy. Re-examination after three months of treatment in the local hospital revealed a $CD4^+$ T-cell count of 55 cells/μL and HIV-1 ribonucleic acid (RNA) load below the lower limit of detection. Chest CT revealed progressive consolidation in the

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https://doi.org/10.1016/j.bsheal.2024.04.005
2590-0536/

right lung field. Bronchoscopy was performed, and upon detection of drug-resistance genes in the alveolar lavage fluid, the mycobacterial infection was found to be resistant to isoniazid, rifampicin, ethambutol, fluoroquinolone, streptomycin, amikacin, kanamycin, and capreomycin.

On March 24, 2023, the patient visited Beijing Youan Hospital, affiliated with the Capital Medical University, for more intensive treatment. Laboratory results revealed a $CD4^+$ T-cell count of 74 cells/μL, CD4/CD8 ratio of 0.16, and HIV-1 RNA load below the lower limit of detection. The patient was diagnosed with drug exudation, XDR-TB (pulmonary and lymphatic tuberculosis), and AIDS. His anti-TB treatment was modified to linezolid (0.6 g, qd), clofazimine (200 mg, qd), and bedaquinoline (200 mg, 3 times/week: Monday, Wednesday and Friday); antiretroviral therapy (ART) protocol remained unchanged.

The patient visited Youan Hospital for a follow-up on July 19, 2023. He complained of genital herpes which manifested on July 7, and reported that on July 5 he had unprotected sexual contact (hugging, kissing, oral sex for more than 30 min, anal sex denied) with a man without knowledge of his health state. He presented with enlarged herpes with exudation in clusters that gradually spread to the face, scalp, nasal cavity, mouth, back, buttocks, and limbs. This was accompanied by swollen and painful inguinal lymph nodes without fever. No rashes were found in the meatus or perianal mucosa, and the patient reported no pain upon urination. On July 21, the Beijing Center for Disease Control and Prevention reported positive results for mpox using quantitative polymerase chain reaction (qPCR) on throat swabs, vesicle fluid, and anal swab samples. The cycle threshold (Ct) values were 21.74, 17.03, and 33.09, respectively. The diagnosis was confirmed as mpox and skin infection.

The patient was subsequently admitted to Youan Hospital and isolated in a single ward during treatment. Compound polymyxin B ointment was applied to the rash and covered with Kangfu Xin solution, and levofloxacin was added to prevent skin inflammation. Chest radiography showed that the tuberculosis lesion had significantly reduced compared to that 4 months previously (Fig. 1); therefore, conventional anti-TB treatment was continued. Laboratory test results showed a $CD4^+$ T-cell count of 101 cells/μL, CD4/CD8 ratio of 0.11, and undetectable HIV-1 RNA levels. The patient continued ART with bictegravir/emtricitabine/tenofovir alafenamide. During the course of treatment, a skin lesion biopsy was performed for pathological examination (Fig. 2). The skin biopsy findings under microscopic examination of the small skin tissue sample revealed partial necrosis of the entire epidermal layer locally, extending into the superficial dermis. There was residual mild hyperkeratosis and incomplete keratinization of the remaining epidermis. Focal epidermal cells exhibited swelling, and infiltration of neutrophils was observed. Mild epithelial hyperplasia was present, and the superficial dermis exhibited mixed inflammatory cell infiltration (including lymphocytes, neutrophils, and scattered eosinophils) along with areas of vascular hemorrhagic necrosis. Infiltration of mixed inflammatory cells was observed surrounding the small blood vessels within the dermal layer. In addition, gastrointestinal endoscopy did not reveal any involvement of the digestive tract mucosa. On July 21, 2023, the patient's whole-body rash began to crust, and on July 24 some crusts began to fall off (Fig. 3). By August 7 the patient's entire body had shed the rash (Fig. 4), and he was discharged from the hospital. Before discharge, the $CD4^+$ T-cell count was measured at 54 cells/μL and the CD4/CD8 ratio was 0.10.

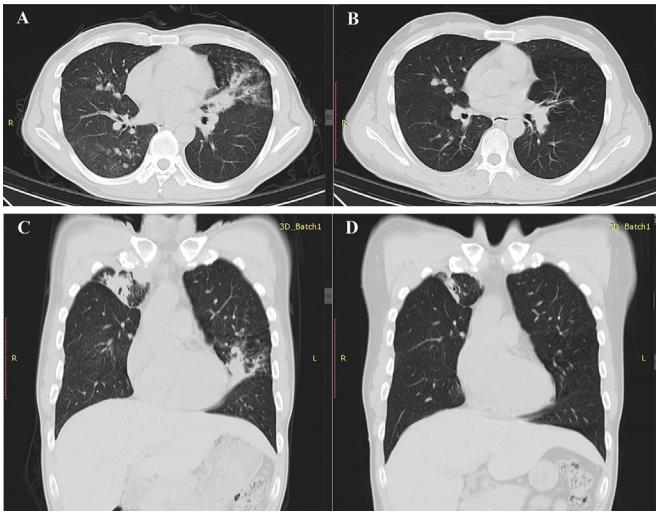

Fig. 1. Chest computed tomography (CT) images. A) and C) in March of 2023; B) and D) in July of 2023.

3. Discussion

Mpox is an emerging zoonotic disease that arises from an orthopoxvirus belonging to the Poxviridae family, which has complex double-stranded deoxyribonucleic acid (DNA). The virus was first isolated from a laboratory monkey in 1958, and the first human mpox case was reported in the Democratic Republic of Congo in 1970. Two clades of MPXV have been identified: the West African and Central African clades. The former has a case fatality rate of 3.6 %, with weak transmissibility and pathogenicity, whereas the latter has a case fatality rate

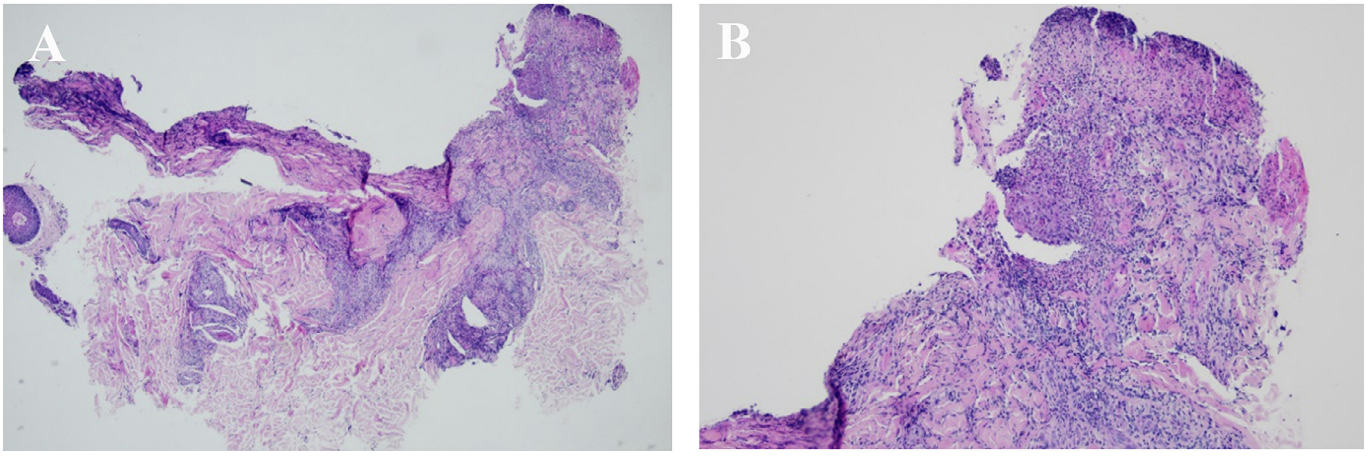

Fig. 2. Skin biopsy. A) Hematoxylin-eosin (HE) staining, 40 ×; B) HE staining, 100 ×.

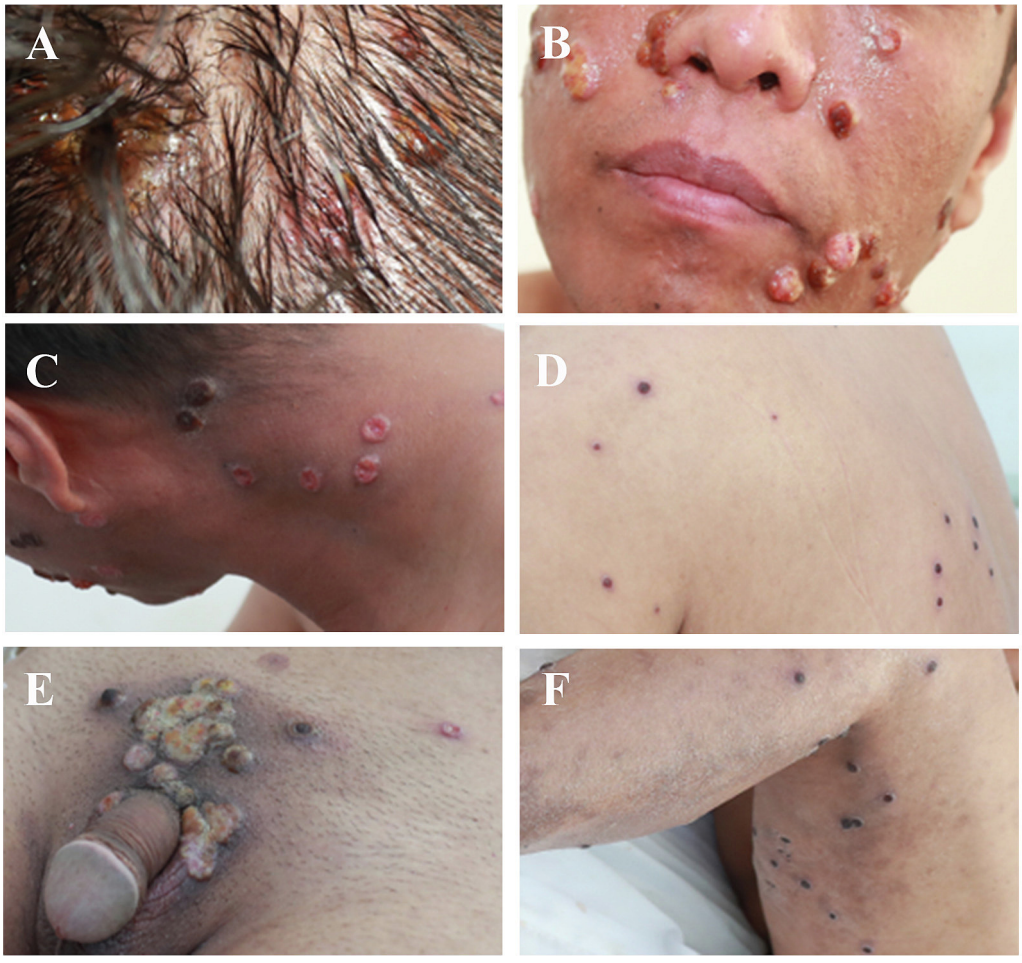

Fig. 3. Evolution of dermatological lesions on day 5 (A-F) after admission to hospital. A) Scalp; B) Face; C) Neck; D) Back; E) Genitals; F) Left lower limb.

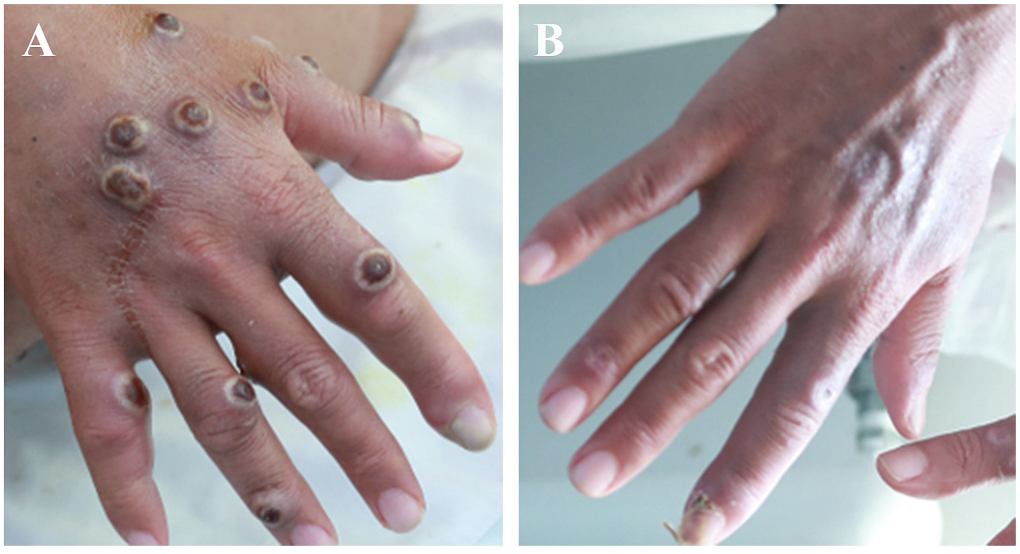

Fig. 4. Evolution of dermatological lesions on the left hand. A) On day 5 after admission; B) On day 18 after admission.

of 10.6 %, with relatively strong transmissibility and pathogenicity, and is primarily prevalent in Africa [3,4]. The virus involved in the current mpox outbreak is considered to be a mild West African variant as per the genetic sequencing results from cases reported outside Africa [5]. The symptoms in patients infected with this clade are milder, and the fatality rate is lower [6]. Researchers have investigated the global mpox prevalence and the differences in clinical manifestations and outcomes among patients with mpox between the pre-

outbreak (2003–2021) and the current mpox outbreak periods. MPXV clade IIb was found to exhibit higher infectivity, but it may cause mild symptoms, and its mortality rate is low [7]. The prognosis of patients co-infected with HIV and mpox exhibiting a $CD4^+$ T-cell count of < 350 cells/μL is unfavorable. O. Mitjà et al. [8] conducted a study that included 382 patients from 19 countries worldwide, all participants were co-infected with HIV and mpox, and had a $CD4^+$ T-cell count of < 350 cells/μL. Approximately 25 % (27/107) of the hospitalized patients died; notably, all deaths occurred in people with $CD4^+$ T-cell counts of less than 200 cells/μL.

The epidemiology of the current mpox outbreak varies significantly from that of the previous outbreaks, with most cases diagnosed in individuals who identify as MSM [9]. The majority of the cases are caused by unprotected anal sex, whereas a few involve unprotected oral sex or other forms of close sexual contact. MPXV DNA can now be detected in fluid from herpes sores on skin, throat swabs, venous blood, semen, and rectal specimens. Additionally, this indicates the possibility of MXPV transmission through direct contact with body fluids [10].

Mpox is a self-limiting disease with favourable outcomes. Severe cases are more commonly observed in individuals with a compromised immune system. A study involving over 1,900 patients with mpox found that more than 35 % of the patients were co-infected with HIV [11]. However, the possible role of HIV as an independent risk factor for MPXV infection remains to be elucidated. A mathematical model exploring the relationship between AIDS and mpox co-infection suggested that HIV may promote the spread of MPXV, and co-infection of mpox and HIV is associated with increased transmission rate of HIV [12]. O. Mitjà et al. [8,13] reported that 38 % – 50 % of patients with mpox over the past two years were co-infected with HIV. The clinical presentation appears to be more severe in patients with advanced HIV disease, characterised by diminished $CD4^+$ T-cell counts and higher HIV viral loads. These patients tended to manifest a greater number of skin lesions and experience a prolonged course of illness [14]. This may be related to the process of HIV replication interfering with immune responses against other pathogens.

Both mpox and smallpox are DNA viruses of the genus *Orthopoxvirus*, family of Poxviridae; therefore, the smallpox vaccine can confer partial cross-immunity against the MPXV. Typically, vaccination against smallpox provides some level of protection against mpox. As described in the present case, the patient was previously vaccinated against smallpox; however, the confluence of co-infection of HIV-1 and XDR-TB, $CD4^+$ T-cell counts of less than 200 cells/μL, and unprotected sexual contact, resulted in him acquiring the mpox infection and experiencing more severe clinical symptoms compared to patients infected with mpox only. The patient exhibited lesions of larger diameters, broader affected area, and involvement of deeper layers of skin. For example, skin lesions of patients with mpox infection demonstrates mixed inflammatory infiltration primarily at the dermal-epidermal junction with limited involvement of the dermis. In contrast the pathological examination of the skin lesion of the patient revealed local partial necrosis of the entire epidermal layer, extending into the superficial dermis. Additionally, infiltration of mixed inflammatory cells along with areas of vascular haemorrhagic necrosis was observed in the superficial region of the dermis, and infiltration of mixed inflammatory cells was observed surrounding the small blood vessels within the dermal layer (Fig. 2).

Notably the patient had a history of unprotected sexual contact (kissing, oral sex for more than 30 min, anal sex denied) with an MSM three weeks prior to the onset of symptoms. Gastrointestinal endoscopy performed during hospitalization did not reveal any mucosal damage or rashes. This indicates that the distribution of mpox lesions is associated with the mode of close contact and highlights the potentially increased risk of transmission during extended periods of intimate physical contact such as hugging and kissing for over 30 min. One study reported that unprotected sex was associated with an increased risk of mpox infection. A study conducted in Italy revealed that 67 % (43/64) of patients with mpox harboured MPXV DNA in their semen. Moreover, the viral DNA was cleared within six months with a median time of 10.5 days [15]. M. Du et al. [16] found that the prevalence of MPXV infection among MSM in China was nearly 1 %. In addition, the proportion (12.12 %, 8/66) of MSM who had a history of unprotected anal intercourse, commercial sex, and group sex in the past month and acquired mpox infection was much higher than that of other MSM.

Individuals with mpox should undergo regular screening for sexually transmitted infections such as HIV and other infectious diseases including TB, as mentioned in the present case. *The World Health Organization's Global Tuberculosis Report for 2021* estimated that approximately 9.9 million people globally were infected with tuberculosis in 2020, and 8.0 % of them were HIV-positive. Approximately 214,000 individuals with concomitant TB and HIV infection died in 2020. In individuals co-infected with HIV and MTB, both pathogens are involved in a complex interplay. These factors contribute to the progression of both diseases. Individuals co-infected with HIV and MTB often exhibit higher viral loads, larger viral reservoirs, more pronounced immune activation abnormalities, and an increased incidence of disseminated tuberculosis [17].

China accounts for approximately 72,000 patients with rifampicin-resistant tuberculosis (RR-TB) or multidrug-resistant tuberculosis (MDR-TB), which comprises 13 % of global cases [18]. The treatment of drug-resistant tuberculosis is extremely expensive. In recent years, some cases have demonstrated resistance to new drugs including bedaquiline and delamanid. There are also cases with no effective treatment options [19]. Currently, the success rate of XDR-TB treatment is 34 % [20]. High treatment costs, significant drug toxicities, lengthy treatment regimens, high mortality rates, and difficulty in adhering to the treatment protocol are the challenges faced by patients with drug-resistant tuberculosis. Close contact and airborne transmission of mpox among patients with positive sputum smears poses an additional threat to individuals with compromised immune systems, such as those with mpox or AIDS.

Our case emphasises that sexual intercourse is an important mode of transmission for mpox. The widespread transmission of MPXV over a short period across multiple regions, particularly among MSM populations, emphasises the need to strengthen preventive education for high-risk populations. A cross-sectional survey involving over 7,000 MSM in China found that those living with HIV demonstrated a greater willingness to accept mpox vaccination (4.11 % *vs.* 5.91 %, $P = 0.004$) and medical consultation (10.78 % *vs.* 16.22 %, $P < 0.001$) [21]. The preventive education program should cover topics such as proper condom use, pre- and post-exposure prophylaxis, initiation of antiretroviral therapy, voluntary HIV testing, vigilance against respiratory infections, and preventive measures against mpox. Given the limited medical treatment and prevention measures currently available, improving hand hygiene in the general population, limiting the import of African rodents and primates, prioritising the vaccination of people living with HIV, and reducing the risk of mpox infection are essential for preventing mpox among individuals at high risk for acquiring them.

Ethics statements

The Ethics Committee approved this study at Beijing Youan Hospital Capital Medical University (No. LL-2023-035-K). The participant provides signed written informed consent.

Acknowledgements

This work was supported by funds from the National Natural Science Foundation of China (Nos. 82241068 and 82241072).

Conflict of interest statement

The authors declare that there are no conflicts of interest.

Author contributions

Yuan Fang: Data curation, Investigation, Methodology, Validation, Visualisation, Writing - original draft. **Fuchun Wang:** Data curation, Investigation, Methodology, Validation, Writing - original draft. **Taiyi Jiang:** Data curation, Investigation. **Junyi Duan:** Data curation, Methodology. **Tao Huang:** Data curation, Visualisation. **Hao Liu:** Data curation. **Lin Jia:** Validation, Investigation. **Han Jia:** Data curation, Software. **Benyong Yan:** Data curation. **Mei Zhang:** Methodology. **Wen Wang:** Supervision, Visualisation. **Caiping Guo:** Conceptualisation, Supervision. **Lifeng Liu:** Data curation, Investigation. **Yuening Zhang:** Conceptualisation, Investigation, Methodology, Writing - review & editing. **Tong Zhang:** Validation, Visualisation, Conceptualisation, Supervision, Funding acquisition, Writing - review & editing.

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