CASE REPORT

How immunity shapes mpox severity: Insights from Sarawak Malaysia

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SUMMARY

Although uncommon in Malaysia, Mpox has emerged locally. Three cases of Mpox in Sarawak are presented, with the aim to describe clinical manifestations based on patients' immunity. All were MSM aged between 28 and 40 years of age. The first patient was HIV negative. He had 20 papules with central crusts on the penis and trunk. The disease duration in the first patient lasted approximately one month. The second patient was HIV-infected, and on HAART since 2022 with a CD4 of 208/μL. He had about 13 lesions over the hands, fingers, trunk, and perianal region. Recovery was achieved within two weeks, after which the patient was lost to follow-up. The third patient presented with a rapidly progressive eruption of multiple pustules over the genital area, face, scalp, trunk, and limbs two weeks before hospitalization. The lesions were most severe at the scrotum and perianal region with vesicles coalescing, resulting in necrosis with deep induration, and subsequent ulceration. His total lesion count was nearly 50. He tested positive for HIV, Hepatitis B, and RPR, with a CD4 of 15/μL. The ulcers were secondarily infected with *Acinetobacter baumannii*. He was hospitalised and isolated for a total of 75 days, receiving IV augmentin, tazocin, tecovirimat, IM benzathine penicillin, in addition to HAART consisting of dolutegravir, tenofovir, and emtricitabine. He improved very slowly. The clinical patterns of Mpox infection described in Sarawak reflect the typical presentation of Clade IIb MPXV. The disease was more severe and of longer duration in HIV-infected individuals with very low CD4 counts.

INTRODUCTION

Mpox (previously known as monkeypox) is caused by the Mpox virus (MPXV), a zoonotic orthopoxvirus that was first discovered in a colony of monkeys with pox infections in 1958.[1] There are two distinct clades of Mpox: Clade I (subclades Ia and Ib), which is associated with a threefold higher fatality rate than Clade II.[2] Clade II Mpox (subclades IIa and IIb), is associated with a self-limiting disease with a lower mortality rate.[2] Both clades, however, are disseminated in the same way. For decades, Mpox was endemic to West and Central African countries.[3] However, a major outbreak of Mpox clade IIb occurred in May 2022, leading to the declaration of Mpox as a Public Health Emergency of International Concern.[4] Since January 2024, more than 55,000 cases of clade I Mpox were reported globally. Since July 2023, Malaysia has reported a total 28 confirmed Mpox.[5]

Mpox typically presents with a febrile prodrome accompanied by generalised headache and fatigue.[6] Skin lesions initially appear as macules, progressing to papules, vesicles, and then umbilicated pustules with a prominent rim of erythema.[6] Ulcers will form subsequently with central scabs. Each morphology of the lesions appears at a single stage of development at a time; each lasts for one to two days. The number of lesions varied from a few to thousands.[7] Secondary bacterial infections may complicate the disease, resulting in abscess formation. In addition, lesions may coalesce to form large plaques and ulcers.[7-8]

Mpox in Malaysia reveals how heavily patient immunity shapes clinical presentations. Failure to recognise Mpox represents the greatest challenge in its management at the primary care level, leading to misdiagnosis and delays in contact tracing. Therefore, this case series aims to describe the clinical manifestations and disease progressions of Mpox in both immunocompetent and immunocompromised individuals.

CASE PRESENTATION

Mpox In Immunocompetent Individuals

The first case involved a 40-year-old gentleman with a history of latent syphilis, who had been treated and remained serofast since October 2015. He reported onset of painful vesicles at the genitalia four days after a casual sexual encounter at a sex party in Kuala Lumpur, involving three local and four foreign male partners. He developed high fever on Day 11 post-exposure, with scattered vesicles erupting over the trunk and limbs. Physical examination revealed multiple papules with central necrotic crusts over the penis and glans, associated with penile oedema (Figure 1A-1F). Similar discrete pustules with perilesional erythema were spotted over the trunk and limbs. The total lesion observed was 20. His inguinal lymph nodes were enlarged.

Penile lesion swab and scab tested positive for MPXV by PCR. Urethral swab culture grew *Staphylococcus aureus*. He was isolated in the ward for a week and treated with intravenous amoxicillin-clavulanate and analgesia. All lesions resolved without scarring one month later (Figure 1G-1H).

Mpox In Immunocompetent Individuals With HIV Coinfection

The second patient was a 28-year-old man who has sex with men (MSM) with positive retroviral infection. He had been

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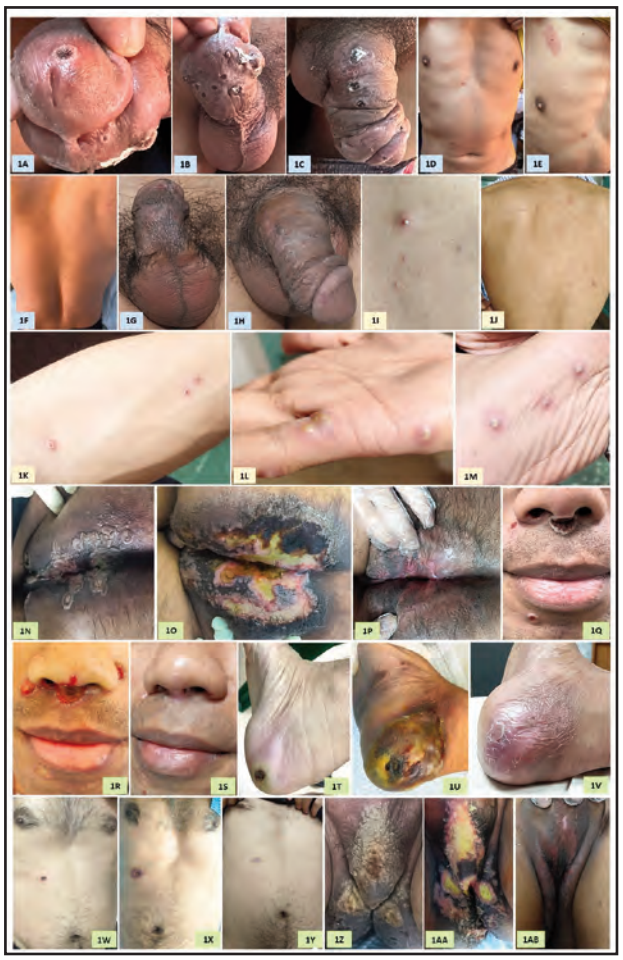

Fig. 1: 1A – 1F: Patient 1, Day 11 of illness at presentation, Figure 1G - 1H: Patient 1, penile lesion resolved without scarring 1 month following treatment, Figure 1I - 1M: Patient 2, Day 7 of illness at presentation, Figure 1N – 1P: Patient 3, Perianal lesion at Week 3(presentation), Week 7 (Day 11 Tecovirimat) and Week 19 of illness (day of discharge), Figure 1Q – 1S: Patient 3, Philtrum lesion at Week 3 (presentation), Week 7 (Day 11 Tecovirimat) and Week 19 of illness (day of discharge), Figure 1T – 1V: Patient 3, Right Heel ulcer at Week 3 (presentation) , Week 7 (Day 11 Tecovirimat) and Week 19 of illness (day of discharge), Figure 1W – 1Y: Patient 3, Trunk, Week 3 (presentation), Week 7 (Day 11 Tecovirimat), and Week 19 of illness (day of discharge), Figure 1Z – 1AB: Patient 3, Scrotal Base, Week 3 (presentation), Week 7 (Day 11 Tecovirimat) and Week 19 of illness (day of discharge)

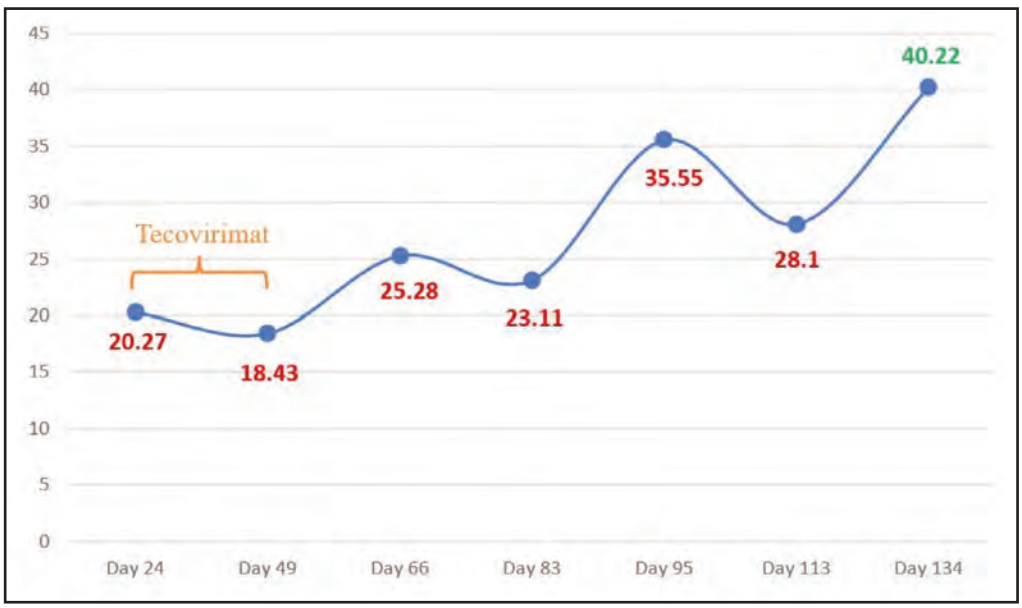

Fig. 2: Cycle of Threshold (Ct) of Mpox virus from perianal swab of Patient 30

commenced on antiretroviral therapy in 2022, but experienced treatment failure due to primary resistance, and was thus escalated to dolutegravir, lamivudine, and tenofovir since December 2024, with a CD4 count of 208 cells/µL. He presented with a one-week history of vesicles on the palms, soles, and arms, with fever for one day. His last reported sexual contact was two months prior, with a male partner from Penang. Clinically, scattered pustules were observed with erythematous rims over both palms, soles, and trunk (Figure 1J-1M). In total, 13 lesions were observed. Additionally, a single anal wart with multiple perianal erosions was noted.

Swabs and scabs over the lesion were positive for Orthopoxvirus DNA. Urethral swab was positive for *Ureaplasma urealyticum*. Screening for syphilis was reactive with a rapid plasma regain (RPR) titre of 1:1. Isolation in the ward was maintained for two weeks. Initially, oral acyclovir and doxycycline were prescribed for one week prior to Mpox confirmation. Three doses of intramuscular benzathine penicillin were administered at weekly intervals. The patient was instructed to perform potassium permanganate sitz baths. The patient was discharged in stable condition without complications. The patient was subsequently lost to follow-up.

Mpox In Immunocompromised Individuals With HIV Coinfection

The third patient was a 37-year-old MSM who first presented with multiple progressive, painful perianal ulcers for a week. No lesions were noted apart from the perianal ulcers. He was initially diagnosed with genital herpes and treated with a one-week course of oral acyclovir. Three weeks later, the lesions progressed, with an increasing number of crusted papules over the limbs, trunk, and face. Multiple scattered crusted ulcers with perilesional erythema over the scalp, hairline, face, neck, axilla, trunk, thighs, heels, and genitalia were observed. His perianal ulcers progressed into a large necrotic indurated plaque that extended from the perianal to the posterior scrotum and perineum region. (Figure 1N, 1Q, 1T, 1W, 1Z) The lesion count was almost 50.

His hepatitis B surface antigen, RPR (titre 1:8), and *Treponema pallidum* particle agglutination assay (TPPA) were positive. He was also diagnosed with retroviral disease with a CD4 count of 15 cells/µL. Polymerase chain reaction test from lesion scabs and swabs confirmed Mpox. A microbiological study of his genital ulcer grew Acinetobacter baumannii. He was hospitalised and isolated for a total of 14 weeks. During his isolation, he was initially treated with intravenous acyclovir for a 14-day course, which escalated to intravenous piperacillin/tazobactam without much improvement. He was then prescribed a 14-day course of oral tecovirimat 600mg bd in conjunction with anti-retroviral therapy consisting of dolutegravir, tenofovir, and emtricitabine. Clinical improvement was first observed at week 12 of the disease. All the crusts dropped off, leaving shallow ulcers except the ulcers at the perineum, which remained deep and undermining. Full recovery was achieved at week 16 of the disease. All ulcers healed with post-inflammatory dyspigmentation and atrophic scars, with scarring alopecia on his scalp. There were residual shallow ulcers at his perineum (Figure 1P, 1S, 1V, 1Y, 1AB). Repeated swabs of perineal ulcers at week 7, 9, 12, 14 of lesions showed persistent positive Mpox PCR. Figure 2 shows the trend of Cycle of threshold (Ct) value of the MPXV.

DISCUSSION

Unlike endemic regions where Mpox clade I is predominant, the Malaysia outbreak was associated with Mpox Clade IIb, affecting MSM primarily, and transmitted through sexual contact.[9] This case series illustrates the diverse clinical spectrum of Mpox, demonstrating that host immune status is pivotal in determining the disease presentation, severity, and duration. The contrasting clinical presentations of the second and third patients suggest that CD4 cell count is a key determinant of disease prognosis and duration. The second patient, with a CD4 count of 208 cells/µL, experienced a self-limiting course similar to that of the immunocompetent first patient. In contrast, the third patient, who had advanced immunosuppression with a CD4 count of 15 cells/µL, developed fulminant Mpox. These contrasting clinical presentations and disease courses emphasise the importance of host immune status in disease severity and recovery.

In a non-endemic country like Malaysia, the clinical presentation may be confused with human herpes virus infections. Specifically, the initial misdiagnosis of the third patient, who first presented with only perianal ulcers, may serve as a mimic of herpes simplex that may mask the diagnosis of Mpox. This serves as a reminder that healthcare professionals must maintain a high index of suspicion for Mpox infections, regardless of the patient's travel history. The discrepancies of the incubation period in second and third patients (ranging from weeks to months) deviate from the usual incubation period of 5 – 21 days. These discrepancies likely stem from underreporting or social desirability bias regarding sexual encounters. In Malaysia, the stigma surrounding HIV and homosexuality may result in intentional concealment of actual exposure timelines, posing a challenge for contact tracing and clinical diagnosis.

While Tecovirimat is the recommended agent for Mpox treatment,[10] Patient three clearly demonstrated that the standard 14-day course did not improve his condition as expected. A 14-day course of tecovirimat may be insufficient for individuals with profound immunosuppression. Persistently positive PCR results and low cycle threshold (Ct) values over 14 weeks suggest that, in the absence of functional immunity, viral clearance is markedly delayed. Extended duration of tecovirimat in combination with cidofovir has been described in severe Mpox infection in HIV infected patients in the United States.[10] Here in Malaysia, cidofovir and its prodrug brincidofovir are not available for the treatment of tecovirimat-refractory cases. The present experience suggests that whilst antivirals are important, recovery in advanced HIV cases remains achievable with gradual immune reconstitution provided by anti-retroviral therapy and high-quality supportive care. While the CDC recommends MVA-BN vaccination as post-exposure prophylaxis for individuals with known or presumed exposure to Mpox, currently, there are limited observational data on the effectiveness of post-exposure prophylaxis vaccination for Mpox.[1]

The clinical patterns of Mpox infection described here in Sarawak reflect the typical presentation of Clade IIb MPXV. The disease was more severe with longer disease in HIV-infected individuals with very low CD4 counts. All healthcare professionals should maintain a high index of suspicion, armed with vigilant screening and labouratory investigation, to diagnose the infection early. High-quality supportive care, together with immune reconstitution in advanced AIDS, is imperative for managing patients with fulminant Mpox.

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