# A Comprehensive Report on the First Mpox Case in the Philippines: From Clinical Presentation to Shotgun Metagenomic Sequencing Analysis

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**Case Report**

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# Abstract

*Background:* With the World Health Organization's declaration of the 2022 multi-country monkeypox outbreak as a Public Health Emergency of International Concern (PHEIC), we report the first confirmed case of monkeypox infection in a Filipino with clinical presentation different from the classic monkeypox cases previously reported in endemic countries of Central and West Africa before the 2022 outbreak. We describe monkeypox infection's gross and dermatopathological appearances on Southeast Asian brown skin. We also discuss the detailed process of monkeypox quantitative real-time polymerase chain reaction (qPCR) testing for diagnostic confirmation and the pioneering application of shotgun metagenomic sequencing to characterize the infecting virus.

*Case Presentation*: This was a case of a 31-year-old male Filipino with a travel history to several European countries. He developed five non-tender, well-defined, umbilicated pustules with erythematous borders on the upper lip, the left gluteal area, bilateral knees, and the left ankle. Skin punch biopsy findings were suggestive of a viral infection. Monkeypox infection from Clade II (previously known as the West African clade) was confirmed by detecting and amplifying the G2R_G, G2R_WA, and C3L gene targets using qPCR. Shotgun metagenomic sequencing subsequently identified a monkeypox genome sequence belonging to B.1.3 lineage of Clade IIb, associated with the current multi-country outbreak. The serologic varicella IgM test was positive but varicella PCR of the skin lesion and metagenomic sequencing did not indicate the presence of the varicella virus. The patient was discharged and continued isolation at home until all scabs had completely fallen off.

*Conclusions*: The presence of pustules among patients with risk factors such as possible close physical contact with infected individuals in areas with reported cases of monkeypox should raise suspicion for such an infection. Dermatopathological findings of the patient's skin lesions were consistent with a viral infection but were non-specific for monkeypox infection. The establishment and optimization of the qPCR protocol were necessary to confirm monkeypox infection from Clade II. Metagenomic sequencing successfully characterized the etiologic agent of the first laboratory-confirmed monkeypox case in the Philippines belonging to Clade IIb which is mainly responsible for the 2022 monkeypox global outbreak.


# Background

Monkeypox is a disease caused by the *Monkeypox virus* (MPXV), an orthopoxvirus first isolated from a group of infected monkeys in Denmark in 1959 (1). It was first identified in humans in 1970 and has become endemic in the Democratic Republic of Congo (2). The disease remained confined to African countries for several years, with two clades named after their areas of discovery: Central Africa and West Africa; however, cases were eventually detected in non-endemic countries such as the United Kingdom, United States, Israel, and Singapore at the beginning of the 21$^{st}$ century (3). A multi-country monkeypox

outbreak sprung in Europe in May 2022 and on July 23, 2022, the World Health Organization (WHO) declared monkeypox as a Public Health Emergency of International Concern (PHEIC) (3,4). Currently, there have been more than 50,000 reported cases and 18 deaths, from more than 100 countries, the majority of which came from the European region (5). The increasing number of monkeypox cases worldwide prompted a further investigation into the possible linkage of monkeypox viral evolution to the ongoing monkeypox outbreaks. Advanced scientific studies are currently utilizing metagenomic principles to identify genome sequences of the MPXV for phylogenetic characterization with the primary goal of determining a common origin for the recent outbreak and identifying the pattern of viral dissemination and evolution (6). Shotgun metagenomic sequencing is a method that broadly sequences all microbial genomes in a sample, with no specific pathogen target, and is hence hypothesis-free (6). This method has been widely used by responding sequencing laboratories worldwide, in the absence of targeted whole genome sequencing protocols of acceptable performance.

We then report the first ever confirmed monkeypox infection in a Filipino with a clinical presentation different from the classic monkeypox cases previously reported in endemic countries like Central and West Africa, before the 2022 outbreak. We demonstrate how monkeypox appears grossly on Southeast Asian brown skin, describe the dermatopathological findings of the umbilicated pustule, and extensively discuss the process of monkeypox quantitative real-time polymerase chain reaction (qPCR) testing for diagnostic confirmation and pioneering application of shotgun metagenomic sequencing to characterize the infecting virus. We also provide an explanation for the varicella serologic IgM test that was positive in this case.

# Case Presentation

*A. Clinical History*

This was a case of a 31-year-old Filipino, male, who consulted for pustules on the left ankle, the left gluteal area, the left upper lip, and one each on both knees. He had a history of recurrent folliculitis (one to two episodes per year). He had no known comorbidities, no known allergies to food or medications, and no previous Varicella or Measles infection. Vaccination against Varicella, Measles, and Smallpox was unrecalled. He was fully vaccinated against COVID-19 with two booster shots. He is a nonsmoker, an occasional alcoholic beverage drinker, and denied illicit drug use. He had a male sexual partner. He took a once-daily emtricitabine plus lamivudine combination tablet as human immunodeficiency virus pre-exposure prophylaxis (HIV PreP) for two months with the latest negative HIV test done just before PrEP initiation.

Four weeks before consultation, the patient began a 3-week-long leisure trip involving several European cities (**Figure 1**). He attended a concert and several social gatherings during his stay in Europe. He also

interacted with stray animals at parks. Thirteen days before consultation (16 days from arrival in Europe), he had one episode of undocumented fever with chills, which resolved after taking a combined anti-inflammatory tablet. He returned to the Philippines seven days before consultation (21 days from arrival in Europe) with no symptoms. Six days before consultation, pruritic vesicular rashes appeared on the left gluteal area, bilateral knees, and left anterior ankle. Five days before consultation, he had bloody stools prompting consultation at a private hospital, and was diagnosed with external hemorrhoids. He was sent home with prescribed diosmin + hesperidin tablets. Four days prior to consult, he developed an ulcer on the right upper lip and itchiness on the surface of his tongue. He also noted the increasing size of the lesions on his knees which urged him to consult.

On physical examination, the patient was seen awake, conscious, ambulatory, and with stable vital signs. A focused physical examination of the skin revealed five well-defined, non-tender pustules with umbilication and erythematous borders on the left gluteal, bilateral knees, left ankle, and right upper lip (**Figure 2**). No lymphadenopathies were noted. The patient was found to have satisfied the criteria for Monkeypox Suspect hence admitted to an isolation room for further evaluation. Initial laboratory tests showed a WBC count of 8.6 x $10^9$/L, neutrophils 53%, lymphocytes 35%, and the rest of the tests within normal limits including serum creatinine, SGPT, and SGOT. Several other possible causes of rash were ruled out: serologic measles Ag and Ab tests and herpes simplex virus (HSV-1 & 2) PCR of skin lesions were negative. Interestingly, Varicella IgM was positive but Varicella IgG and PCR of the skin lesions were negative for Varicella. The patient was also referred to the Dermatology service which performed skin punch biopsy, with results describing a viral infection. Specimens for monkeypox qPCR test and metagenomic sequencing were obtained and yielded positive results for monkeypox infection. The detailed qPCR and sequencing processes and results are described in the succeeding sections. The patient was discharged on the second hospital day. He was advised to keep the lesions clean and dry, using mild soap and moisturizing lotion daily as supportive management. Home isolation and daily monitoring of symptoms via online consultations were done until all crusts and scabs had completely disappeared. The patient's isolation period lasted for 23 days without any serious complications (**Figure 3**). No identified close contact became symptomatic nor developed any rash.

*B. Dermatopathologic Evaluation*

A skin punch biopsy of the umbilicated pustule on the left gluteal area was done by the Dermatology service. The epidermis revealed scale crusts and ulceration. Some of the keratinocytes in the epidermis and the upper dermis were large with convoluted steel-gray nuclei and the dermis revealed red blood cell extravasation and a moderately dense, perivascular, and interstitial inflammatory infiltrate of lymphocytes, histiocytes, and plasma cells (**Figure 4**). These findings supported a diagnosis of a viral infection.

*C. Specimen Collection and Processing*

A total of nine tissue/lesion specimens and nine swab specimens obtained from three sites (right and left knees, and left ankle area) were sent to the Special Pathogens Laboratory for confirmatory monkeypox real-time polymerase chain reaction (RT-PCR) test.

*C.1 Nucleic Acid Extraction from Dry Swab Sample*

At the laboratory, single dry swab of cotton was separated from the swab base and was added to the lysis buffer solution (400 µL phosphate-buffered saline (1x PBS), 20 µL proteinase K and 400 µL buffer AL). The solution was homogenized by vigorous vortex-mixing and incubated at 56°C for 10 minutes. Total viral DNA was extracted from the sample using the QiaAmp DNA Mini Kit (Qiagen, Hilden, Germany, Cat No: 51306) according to the manufacturer's instructions (7). The extracted DNA was eluted in 150 µL of nuclease-free water (NFW) and stored at -80°C until use.

*C.2 Nucleic Acid Extraction from Tissue Sample*

At the laboratory, 2.5mg (3mm in diameter) of the tissue sample was added to 80 µL phosphate-buffered saline (1x PBS) and was homogenized using a micropestle. The solution was briefly vortex-mixed after adding 100 µL buffer ATL and 20 µL proteinase K. Incubation at 56°C for 1 hour (vortex mixed every 20 minutes) and at 70°C for 10 minutes followed. Total viral DNA was extracted from the sample using the QiaAmp DNA Mini Kit (Qiagen, Hilden, Germany, Cat No: 51306) according to the manufacturer's instructions (7). The extracted DNA was eluted in 200 µL of nuclease-free water (NFW) and stored at -80°C until use.

*D. Real-Time Monkeypox PCR Testing and Results*

The PCR primers and probes were developed from the sequences described by Li, et al (8). Probe-based real-time PCR assay was performed using Applied Biosystem's AgPath-ID One Step PCR kit (4387424) (9) and Bio-Rad CFX96 Touch real-time PCR machine as PCR platform. RNase P was the assays' internal target control. A total of 23 µL of master mix (6.5 µL nuclease-free water, 12.5 µL 2x buffer, 1 µL 25 RT-PCR enzyme mix, 1 µL each of forward and reverse primers, 1 µL probe) and 2 µL of the extracted DNA

template was used. The following thermocycling protocols were programmed for monkeypox screening assay:  95 ºC for 10 minutes and 45 cycles of 95 ºC for 15 seconds, 60ºC for 20 seconds; for monkeypox differentiation assay: 95 ºC for 10 minutes and 45 cycles of 95 ºC for 15 seconds, 62ºC for 20 seconds. The optimized primer and probe concentrations were 10µM and 5µM, respectively for both screening and differentiation assays (**Table 1**).

**Table 1.** Primers and probes used in Monkeypox quantitative PCR test (8)

| Primer/ Probe Name | Sequence 5’ to 3’ | Assay Name |
|---|---|---|
| G2R_G Forward Primer | 5'- GGAAAATGTAAAGACAACGAATACAG-3' | G2R_G (Monkeypox Screening) |
| G2R_G Reverse Primer | 5'- GCTATCACATAATCTGGAAGCGTA-3' | |
| G2R_G Probe | 5' FAM-AAGCCGTAATCTATGTTGTCTATCGTGTCC-3' BHQ1 | |
| G2R_WA Forward Primer | 5'- CACACCGTCTCTTCCACAGA-3' | G2R_WA (Monkeypox Differentiation) |
| G2R_WA Reverse Primer | 5'- GATACAGGTTAATTTCCACATCG-3' | |
| G2R_WA Probe | FAM 5'-AACCCGTCGTAACCAGCAATACATTT-3' BHQ1 | |
| C3L Forward Primer | 5'- TGTCTACCTGGATACAGAAAGCAA-3' | C3L (Monkeypox Differentiation) |
| C3L Reverse Primer | 5'- GGCATCTCCGTTTAATACATTGAT-3' | |
| C3L Probe | 5' FAM-CCCATATATGCTAAATGTACCGGTACCGGA-3' BHQ1 | |

Two sets of the collected lesion dry swab and lesion crust were confirmed to be positive for monkeypox using real-time PCR screening assay with a mean cycle threshold (Ct) value of 19.54. The monkeypox real-time PCR differentiation assay revealed that the same samples were positive for the Western African clade (Clade II) only with a mean Ct value of 19.85 **(Table 2**).

**Table 2.** Monkeypox RT-PCR result with mean cycle threshold (Ct) values

| Target | Sample | CT Value | Mean CT Value | Result |
|---|---|---|---|---|
| G2R_G | Lesion Base Dry Swab Right Knee | 20.68 | 19.54 | Monkeypox Viral DNA Detected |
| | Lesion Base Dry Swab Left Knee | 19.09 | | |
| | Lesion Crust Right knee | 17.63 | | |
| | Lesion Crust Left Ankle | 20.76 | | |
| G2R_WA | Lesion Base Dry Swab Right Knee | 20.88 | 19.85 | Monkeypox Clade II** Viral DNA Detected |
| | Lesion Base Dry Swab Left Knee | 19.32 | | |
| | Lesion Crust Right knee | 18.18 | | |
| | Lesion Crust Left Ankle | 21.03 | | |
| C3L | Lesion Base Dry Swab Right Knee | - | - | Monkeypox Clade I* Viral DNA Not Detected |
| | Lesion Base Dry Swab Left Knee | - | | |
| | Lesion Crust Right knee | - | | |
| | Lesion Crust Left Ankle | - | | |

**formerly classified as Congo Basin clade*

***formerly classified as West African clade*

*E. Metagenomic Sequencing of Monkeypox Specimens*

To further characterize the etiologic agent of the first laboratory-confirmed Monkeypox case for the country, and properly classify its phylogenetic lineage, four specimens that tested positive for monkeypox RT-PCR were processed by the Molecular Biology Laboratory for metagenomic sequencing. Additionally, two confirmed target-negative samples were included in the sequencing run to be used as MPXV-negative specimen control. The standard Illumina DNA Prep protocol was followed (10). Fifty microliters (50 ul) of DNA extracts were purified using Agencourt AMPure XP (Beckman Coulter Genomics, IN, USA, Cat no. A63881), and quantified using Qubit HS dsDNA reagent kit (ThermoFisher Scientific, MA, USA Cat no. Q32854). The purified DNA extracts were normalized to 148 ng starting DNA input and were used for the

Illumina DNA prep kit (Illumina, Inc., CA, USA) library preparation. Constructed libraries were quantified using a Qubit HS dsDNA reagent kit and Agilent D1000 ScreenTape system (Waldbronn, Germany). The samples that passed the QC criteria were pooled and subjected to shotgun metagenomic sequencing using the Illumina Miseq sequencing instrument. Out of the four specimens that tested positive for monkeypox real-time PCR, only three samples qualified for shotgun metagenomic sequencing.

The publicly available ‘monkeypox-nf’ workflow developed by the Public Health Agency of Canada's National Microbiology Laboratory (11) was adapted for generating the MPXV consensus sequence. 10x and 5x depth thresholds and the MT903343.1 sequence from the B.1 hMPXV (human MPXV) lineage was used as the reference sequence for assembly. The script weeSAM was used to generate coverage depth plots (12). Nextclade was used for clade and lineage assignment, identification of single nucleotide variant (SNV) mutations, insertions, deletions, and for the phylogenetic placement of sequences on a reference tree. Tablet was used to inspect aligned reads supporting the identified SNV mutations.

**Table 3** and **Figure S1** of the supplementary file show the number of reads, sequencing depth, and genome coverage generated by the 3 MPXV positive samples. The total number of reads for each specimen ranges from 0.8M to ~1.2M reads wherein around 2.8k to 7.7k were mapped to the MPXV reference sequence (MT903343.1). Since all three samples were collected from the same patient, sequences generated by the three specimens were pooled to increase the number of reads and genome coverage. A total of ~5M reads with 14.5k reads mapped to the MPXV reference sequence and only 15% genome coverage using 10x default Illumina depth threshold. The genome coverage was increased to 80% when the depth threshold was lowered to 5x however this increases the likelihood of misclassifying mutations.

**Table 3.** Sequencing reads and MPXV genome coverage generated from the performed shotgun metagenomic sequencing

| Sample | No. of paired-end reads from sample | No. of reads mapped to MPXV reference | Mean sequencing depth | Depth threshold (default for illumina=10x) | # Ns in consensus | Coverage over MPXV genome (0.0-1.0) |
|---|---|---|---|---|---|---|
| MPOX22-0034CH | 1,210,779 | 3987 | 2.82958x | 10x | 197,134 | 0 |
| | | | | 5x | 189,399 | 0.0392373 |
| MPOX22-0034DSA | 829,239 | 2824 | 2.10975x | 10x | 197,134 | 0 |
| | | | | 5x | 189,831 | 0.037041 |
| MPOX22-0034DSE | 1,247,310 | 7721 | 5.1794x | 10x | 196,808 | 0.0016537 |
| | | | | 5x | 158,724 | 0.194801 |
| Pooled MPOX22-0034 | 5,402,912 | 14,532 | 10.1189x | 10x | 167,425 | 0.150705 |
| | | | | 5x | 38,363 | 0.805382 |

Assembly method: reference-based assembly with monkeypox-nf workflow (bwa, samtools, ivar)

The Nextclade analysis of consensus sequences generated from all three separate MPOX22-0034 samples, the pooled MPOX22-0034 sample, and using 10× and 5× depth thresholds with respect to a reference sequence from the hMPXV outbreak clade (i.e., MPXV_USA_2022_MA001 in NC_063383 coordinates or pseudo_ON563414) is shown in **Figure S2** of the supplementary file. Only up to three single-nucleotide variant (SNV) mutations were identified when comparing the consensus sequences to this reference sequence, which was from a sample collected in May 2022.

**Figure 5** shows the phylogenetic placement by Nextclade of the MPXV consensus sequences on a reference tree representing the different lineages under the hMPXV clade. The consensus sequences are placed in the B.1/B.1.3 lineage, showing that the first detected monkeypox case in the Philippines belongs to the B.1 or more specifically the B.1.3 lineage. Sequences with lower % coverage (MPOX22-0034DSA with 5× depth threshold and pooled_MPOX22 with 10× depth threshold) are placed at the base of the B.1.3 lineage while the sequence with the highest % coverage (pooled_MPOX22 with 5× depth threshold) is placed in a subtree within the B.1.3 lineage wherein the consensus sequence clusters with sequences from multiple European countries (including France, Germany, Finland, Switzerland, Spain, Belgium, and Slovenia) and the United States.

The three detected SNV mutations from the pooled_MPOX22-0034 consensus sequence are supported by 100% of reads covering their respective genome positions, which are the coordinates 55133, 64426, and 190660 in the pseudo_ON563414 reference sequence (for more details, see the supplementary

information, **Figure S3**). False positive mutations among these three SNVs are thus unlikely. Two of these mutations (G55133A/OPG074:R665C and C64426T/no amino acid change) are unique to B.1.3 (**Figure S3A and B**), supporting the validity of the lineage assignment of the consensus sequence. C64426T in particular is unique to the cluster of B.1.3 sequences originating from multiple European countries. One of the three mutations (G190660A/NBT03_gp174:R84K) appears in both B.1.3 and in B.1 sequences. Because of the positive varicella IgM result, metagenomic sequence data were reviewed to verify if there is a co-infection. No sequence data indicating varicella was present in the sample which supports the finding that there is no co-infection.

# Discussion

This report presented the first imported and travel-related case of monkeypox virus (MPXV) in the Philippines in a patient with a three-week travel history to several European countries and clinical symptoms of a few umbilicated pustules and a mild prodrome. The classic monkeypox infection reported from endemic areas had been known to have three stages: an incubation period of approximately 6-21 days; a prodromal phase characterized by the presence of fever, severe headache, lymphadenopathy, malaise, myalgia, and fatigue; and a rash period when the patient shows the typical rash progression: initially macular to papular/pustular lesions progressing to vesicular then umbilicated and later on becomes crusted), appearing more commonly on the face and limbs (13,14). The cases reported during the 2022 multi-country outbreak of monkeypox were presented differently (13). The symptoms described as “atypical” include fewer skin lesions (<10 lesions), mostly occurring at oral and anogenital areas, sparing the palms and soles, rectal pain and/or bleeding, and prodromal symptoms that occur after the rash or sometimes does not even occur at all (15–17). The solitary or few lesions occurring in the mucosal and anogenital areas as seen in our patient may have been acquired via direct skin-to-skin as in that involved during sexual intercourse (18). While hemorrhoids might be the cause of the patient’s rectal bleeding, it is possible that other less obvious mucosal lesions or monkeypox-associated proctitis might have contributed to the rectal pain and bleeding as is reported in other case series (14,16).

Fortunately, the monkeypox real-time quantitative PCR assay has been optimized and set up more than four weeks earlier than the patient’s consultation in our institute (19). This highlights the importance of increased disease information for early case detection, and timely establishment of national diagnostic capacity for confirmation of infection for emerging diseases as part of a comprehensive, multisectoral response plan. PCR remains to be the gold standard in diagnosing MPXV infections. The Ct values generated by the MPXV positive samples from the patient were low (Ct value range of 17 to 20) which denotes high viral load; however, nucleic acid extract concentrations were quite low (4-12 ng/ul) even after purification which may be the reason for the low genome coverage during metagenomic sequencing. The virus was identified to belong to hMPXV Clade II, formerly known as the West African Clade, and its sequence was placed in the B.1.3 lineage. Using Nextclade analysis (**Figure S2** of the supplementary file), three SNV mutations were detected from the pooled consensus sequence when compared with the reference sequence, two of which are unique to the B.1.3 lineage and the other one can be found in both B.1 and B.1.3 lineages (**Figure S3** of the supplementary file). Undetected mutations

remain a potential limitation but, if present, are not likely to change the assigned lineage given the presence of B.1.3 unique mutations. This limitation can be resolved by sequencing with higher coverage depth. The nomenclature we used for describing the phylogenetic lineage is already consistent with WHO's announcement last August 2022 referring to Clade I as the former Congo Basin clade and Clade II as the former West African clade. The primary basis for the new clade classification is the differences in the coding regions of each clade that relates to the immunomodulatory and host recognition antigenic determinants such as H3L and B12R (20). Clade II is now divided into two subclades Clade IIa and Clade IIb, the latter being the cause of the current multi-country MPXV outbreak and infecting our patient after traveling to Clade IIb-reporting countries in Europe (21).

The positive varicella IgM result, in this case, could indicate a monkeypox-varicella co-infection or a false positive varicella serology result. By history, the patient had no previous history of Varicella infection and none of his close contacts developed any recent vesicular lesions. MPXV and varicella co-infection among several cases in the Democratic Republic of Congo have been reported (22). This co-infection is possible because initial infection with either virus may have caused the immune system of the patient to have increased susceptibility to secondary infection (22). Varicella lesions may cause breaks on the skin surface which may serve as an ideal entry point for MPXV infection after high-risk exposure or contact with infected individuals and vice versa (22). However, confirmatory PCR testing of skin lesions for Varicella infection was negative and no reads were detected via metagenomic sequencing, ruling out a varicella co-infection. Previous studies have reported that IgM serologic testing is less sensitive and specific than the Varicella PCR test of the skin lesions (23). False positive results for serologic IgM tests have been previously reported even for measles and other infections. At least three reasons have been identified: the presence of cross-reacting antibodies, interference by other existing autoimmune conditions that produce broadly specific heterophile IgM antibodies, and the increased false positives when a test is conducted in a low disease prevalence setting, similar to monkeypox in the Philippines (24).

Currently, there are no available definite treatments for MPXV. There are also no drugs or vaccines against monkeypox approved by the Philippine Food and Drug Administration as of the writing of this manuscript (25). Management is supportive and focused on symptom management and prevention of superinfection (25). Current local guidelines advise strict isolation of MPXV-confirmed cases until all symptoms have resolved. The patient reported, in this case, was advised to undergo isolation until all the scabs were gone to avoid further transmission, which lasted for 23 days. No serious complications that required further hospitalization were reported by the patient during his home isolation. He did not receive any antibiotics or antivirals.

# Conclusion

Timely case detection and establishment of diagnostic capacity for testing and confirmation are important components of the country's response against monkeypox. With more confirmed monkeypox cases detected in non-endemic countries, the presence of pustules among patients with risk factors such

as possible close physical contact with infected individuals who travel to areas with active transmission should raise suspicion for monkeypox infection. Dermatopathological findings of the skin lesions in this confirmed case were consistent with a viral infection. The establishment and optimization of a qPCR protocol were necessary to confirm monkeypox infection from the West African clade in this case. This case report demonstrates the pioneering use of shotgun metagenomic sequencing in characterizing the etiologic agent. Based on the sequence analysis results, the first monkeypox case in the Philippines belongs to the hMPXV Clade IIb, a subclade of the former West African clade (now called Clade II), and more specifically, to the B.1.3 lineage associated with the ongoing monkeypox outbreak in different European countries. The negative varicella PCR of the skin lesions supported by the absence of varicella DNA on the sequencing makes the varicella serologic IgM results as more likely false positive.

# Declarations

### ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This case report was not part of a research study, hence, ethics approval was not sought. Written and signed consent was obtained from the patient.

### CONSENT FOR PUBLICATION

Written and signed consent for the preparation and publication of a case report was provided by the patient.

### AVAILABILITY OF DATA AND MATERIALS

Not applicable.

### COMPETING INTERESTS

All authors declare that they have no competing interests.

### FUNDING

Not applicable.

### AUTHORS' CONTRIBUTION

E.Y. and M.BS contributed to the study conceptualization, investigation, methodology, and visualization. P.G. contributed to study conceptualization, investigation, project administration, and visualization. A.R., A.G., G.A., and T.J.D. contributed to conceptualization, investigation, and supervision. L.D., A.N., F.P., R.P., C.C., E.M., S.O., J.M., M.C., and M.A. contributed to study data curation, formal analysis, investigation, methodology, resources, software programming, validation, and visualization. All authors contributed equally to the manuscript writing. All authors critically reviewed the manuscript for intellectual content, approved the final version of the manuscript for submission, and agreed to be accountable for all aspects of the work.

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## Abbreviations

MPXV: Monkeypox virus; hMPXV: human monkeypox virus; RT-PCR: Real-time Polymerase Chain Reaction; PBS: phosphate-buffered saline; NFW: nuclease-free water; CT value: cycle threshold value; HIV: human immunodeficiency virus; PrEP: Pre-exposure Prophylaxis; DNA: deoxyribonucleic acid; NFW: nuclease-free water; SNV: single nucleotide variant

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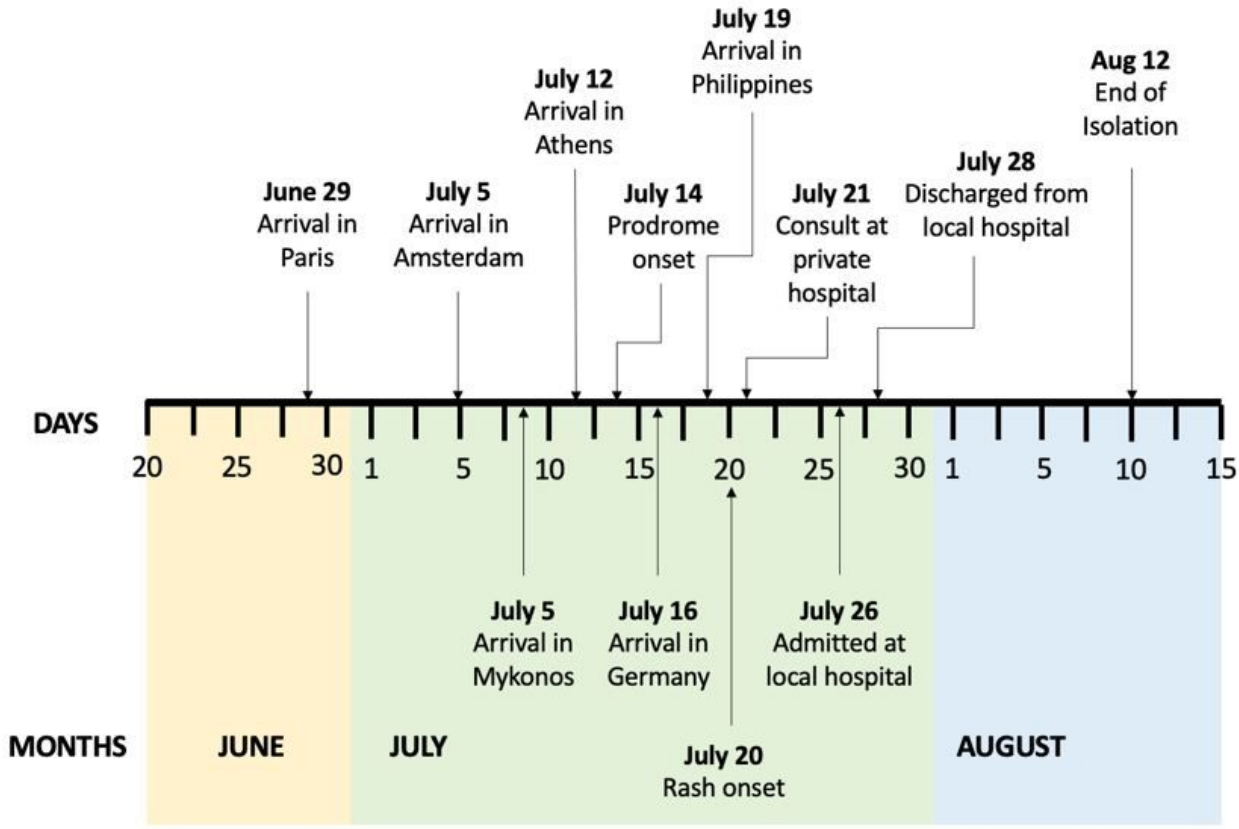
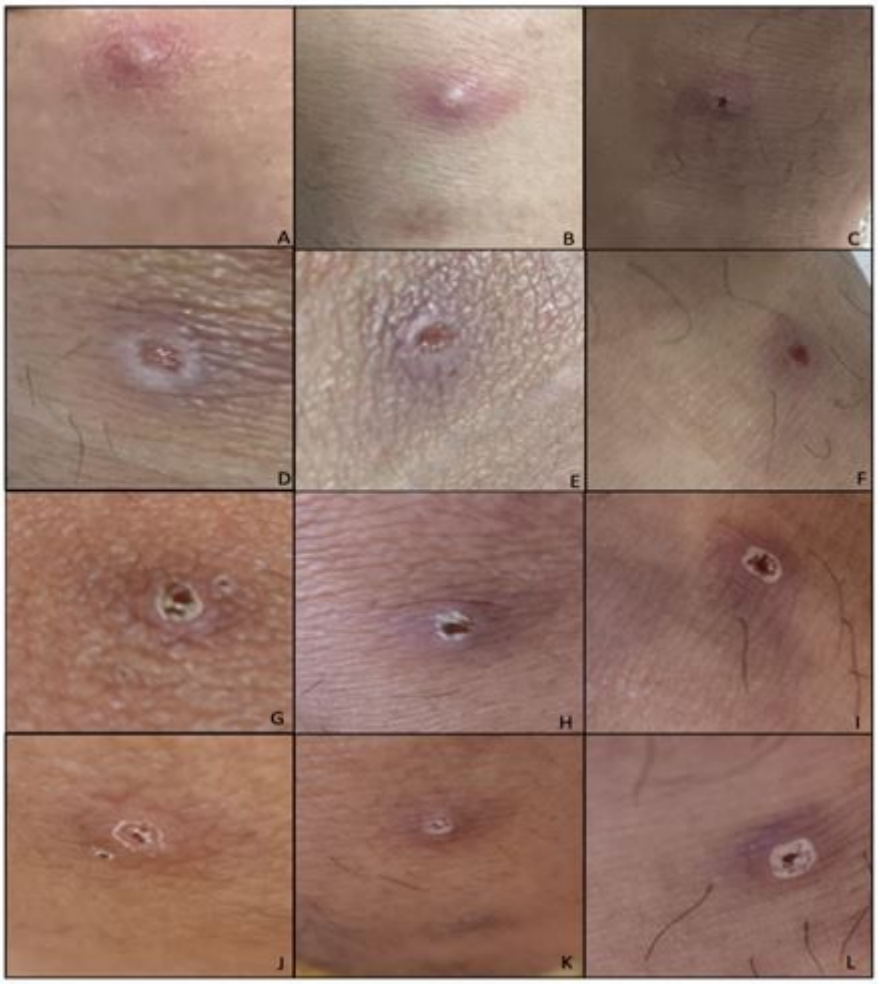
# Figures



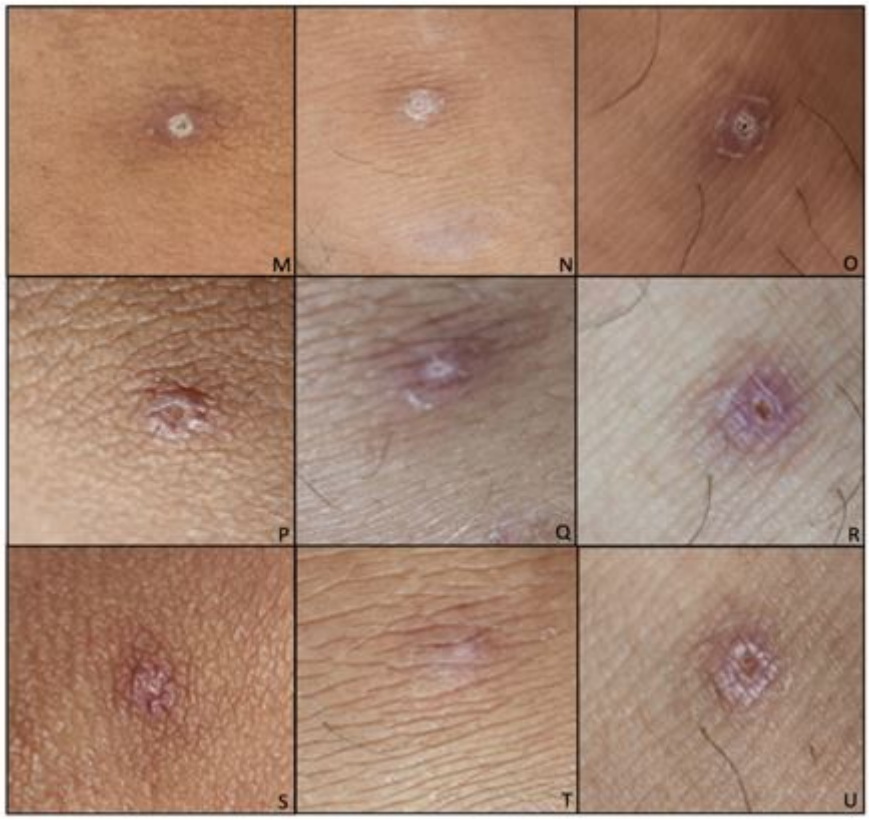

## Figure 1

Timeline of patient activities and potential exposures to Monkeypox virus, June-August 2022




## Figure 2

**Initial lesions of the patient during admission.** Lesions located at: (A) Left Knee (B) Right Knee (C) Left Ankle. Lesions after unroofing and swabbing on (D) Left Knee (E) Right Knee (F) Left Ankle. Lesions upon discharge from the hospital (G) Left Knee (H) Right Knee (I) Left Ankle.  Day 12 of Lesions on (J) Left Knee (K) Right Knee (L) Left Ankle.




## Figure 3

**Lesions during home isolation.** Day 17 of Lesions on (M) Left Knee (N) Right Knee (O) Left Ankle. Day 21 of lesions on (P) Left Knee (Q) Right Knee (R) Left Ankle. Lesions upon the end of isolation on Day 24 (S) Left Knee (T) Right Knee (U) Left Ankle.

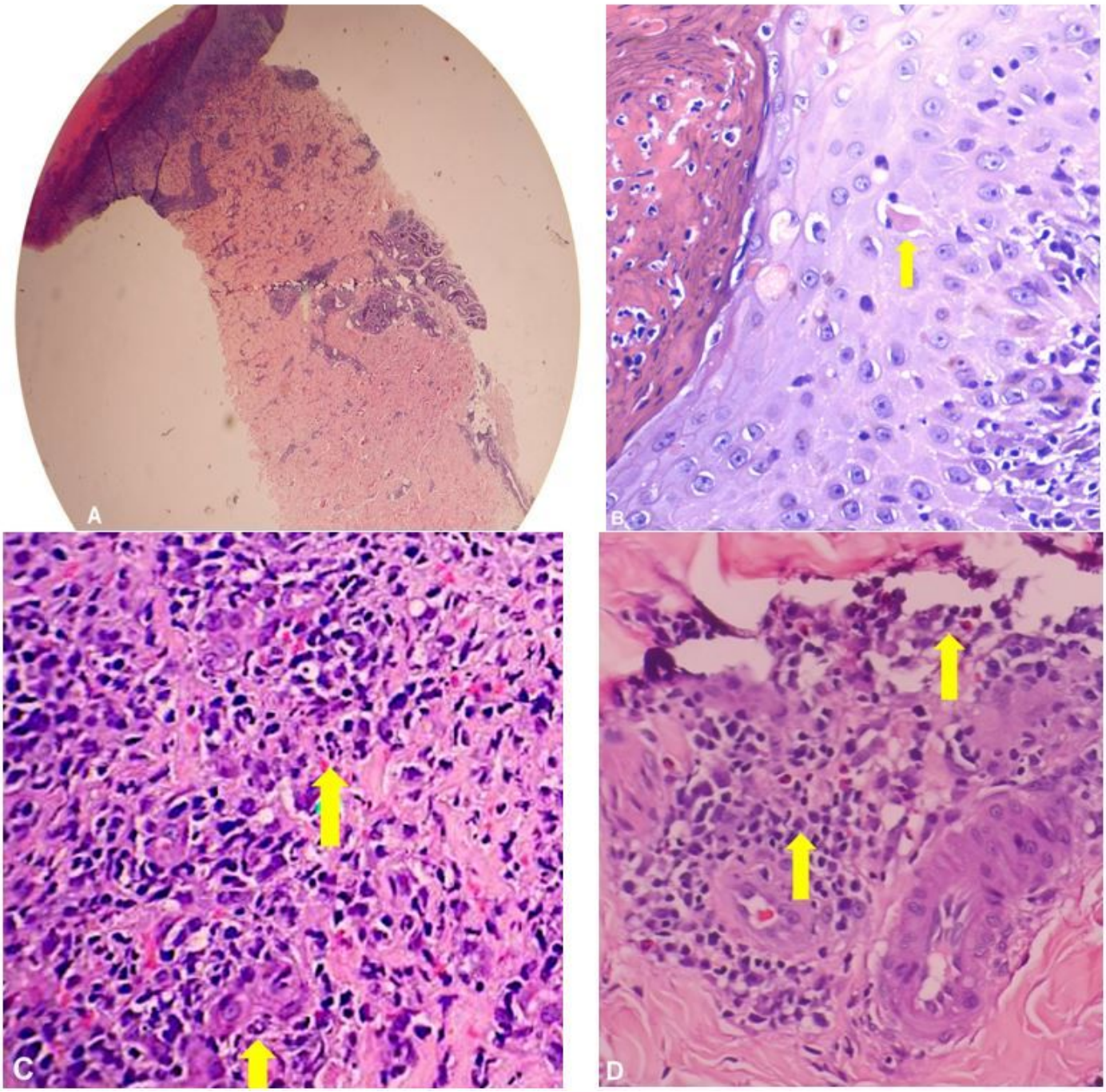
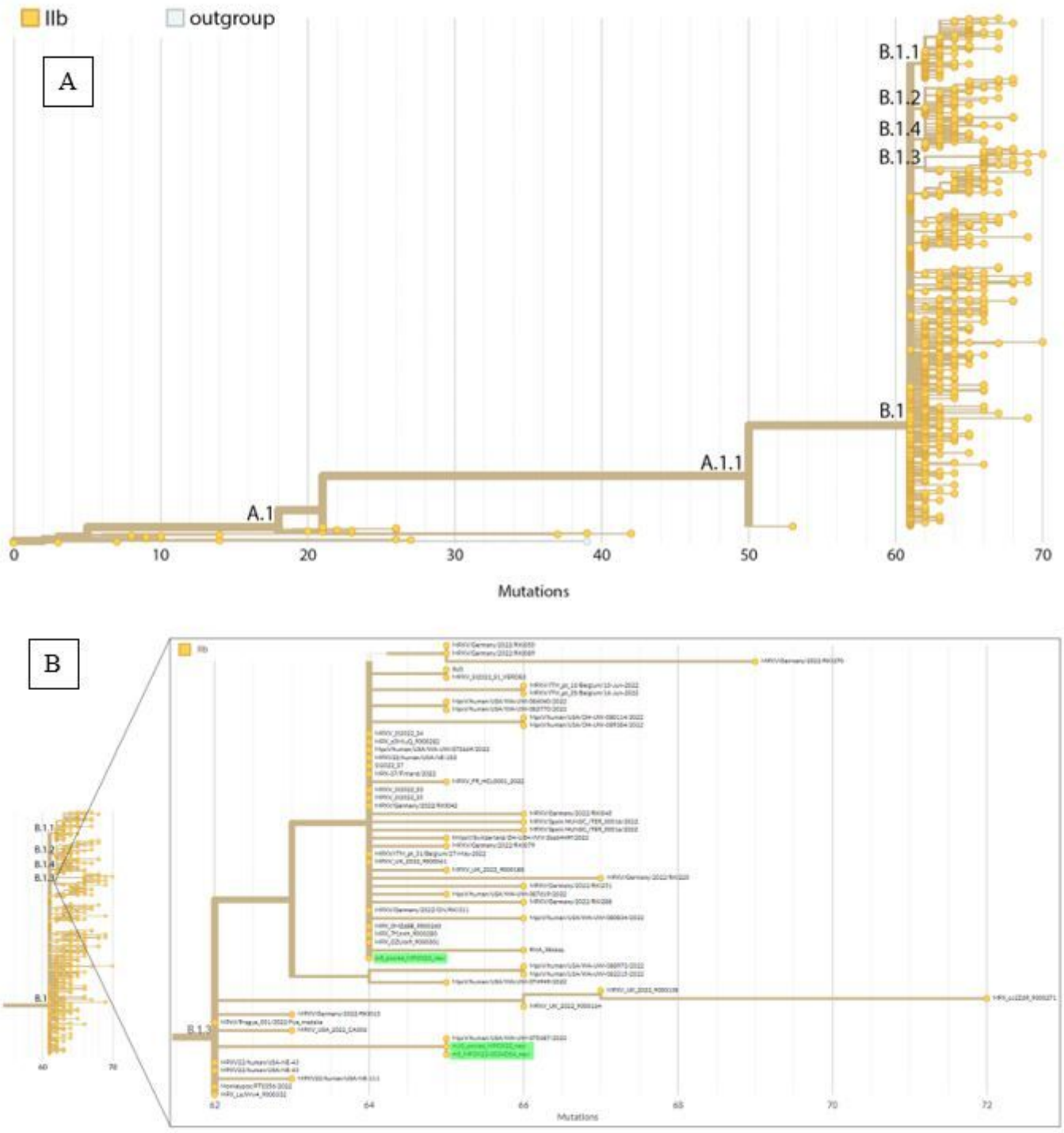



**Figure 4**

**Skin punch biopsy (H&E).** (A) On scanning view, the section shows full-thickness epidermal necrosis with (B) necrotic keratinocytes and a moderately dense, superficial, and deep perivascular infiltrate of (C) neutrophils, lymphocytes, and (D) plasma cells




## Figure 5

**Phylogenetic placement by Nextclade of the MPXV consensus sequences.** (A) Phylogeny represents the different hMPXV lineages including A, B, and their sublineages. (B) Zoomed-in view of the B.1.3 sublineage with consensus sequences from sample MPOX22-0034 (highlighted in green) placed within this sublineage.

# Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- MonkeypoxCaseReportPhilippinesSupplementaryFile.docx