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Not every skin rash in a returning adult male traveler is monkeypox

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\textbf{A B S T R A C T}

In May 2022, several European countries including Spain reported cluster of monkeypox cases with no apparent travel to endemic areas. We report a suspected case of monkeypox in Saudi Arabia in a healthy 30-year-old man who returned from Spain and the Netherlands with fever and rash for six days duration during the same time period of the outbreak, he was suspected to have monkeypox but was ultimately diagnosed with chickenpox.

\section{1. Introduction}

Monkeypox virus is an enveloped DNA virus belonging to the genus \textit{Orthopoxvirus} which includes the Smallpox virus which was officially eradicated in 1980. Monkeypox is a zoonotic disease, and since its identification in monkeys in captivity in the Netherlands in 1958, and in humans in Africa in 1970, the disease became endemic in Central and West Africa with sporadic travel related cases/clusters outside of Africa. Since the beginning of May 2022, a multi-county outbreak of Monkeypox cases were reported with the majority of cases having no links to travel from Africa with clustering among young men who identify as gay or men who have sex with men [\textsuperscript{1}]. From 1 January through August 7, 2022, 27814 laboratory confirmed cases of monkeypox and 11 deaths have been reported to WHO from 89 countries/territories/areas [\textsuperscript{2, 3}]. The largest number of cases/clusters were reported from the United Kingdom (UK), Portugal, Spain, other European countries, Australia, Canada, and the United States of America (USA). The exact source of this outbreak is not known to date. Here, we report a suspected case of monkeypox in Saudi Arabia in a traveler who returned in late May 2022 from Spain and the Netherlands during the same time period of the reported Monkeypox clusters, and after careful evaluation and laboratory investigation he was diagnosed with chickenpox.

\section{2. Case presentation}

A 30-year-old previously healthy male presented to King Saud University Medical City emergency department on May 25, 2022, complaining of generalized rash for six days duration. On May 3, 2022 he traveled from Riyadh to Dubai where he stayed overnight in transit, then traveled to Amsterdam where he spent 7 days attending a course. Later, he traveled to Barcelona, Spain, where he spent three nights, then he traveled to Ibiza where he spent three nights and attended a music concert with over 3000 attendees. On May 20, 2022, he started to feel feverish with malaise, next morning he developed an itchy skin rash that initially started on the scalp then by night it involved most of his face, the next day it went down to his chest, trunk, back, arms, legs, and soles but not his palms. Malaise continued with a mild headache and generalized body aches. He then traveled to Barcelona again where he spent two nights not leaving his hotel room due to malaise, then flew back to Riyadh via Dubai. Upon arrival to Riyadh, he immediately sought
medical attention. He denied any sexual activity during the entire trip, he did not visit any massage parlors or spas, and did not use any hot tubs. He had no animal contacts. During the five days prior to his presentation to the emergency room, few of the skin lesions drained yellowish discharge then dried. During the entire trip he only used a face mask to protect against coronavirus disease 2019 (COVID-19) while inside airport terminals, but did not wear it in the concert or any other social gathering. No history of any febrile illnesses in the past, no history of chickenpox, nor any contact with a known case of chickenpox, monkeypox or any persons with fever and rash. He was born in Riyadh, Saudi Arabia and is fully vaccinated with his routine vaccinations including varicella vaccine. He received three doses of COVID-19 vaccine, his last booster dose with BNT162b2 vaccine was in January 2022. He is single, lives in Riyadh with both parents and four siblings, none have had any similar symptoms. He traveled with a relative who did not develop any symptoms.

On physical exam he appeared generally well, his vital signs were normal with a temperature of 36.6°C. He had multiple maculopapular skin lesions involving the face, neck, chest, abdomen, back (Figure-1), upper thighs, legs, feet, and soles. Some lesions were crusted, some were maculopapular, and some were scabbed. No pustular lesions were seen. He had palpable bilateral deep cervical lymphadenopathy, mobile and non-tender, less than 1 cm in size. No axillary or inguinal lymph nodes. No genital lesions, perianal lesions, oral lesions, nor conjunctival lesions. Abdominal exam revealed a slightly enlarged liver with a span of 13 cm. Cardiovascular, chest, and neurological examinations were normal.

Laboratory investigations showed a normal complete blood count and differential, alanine transaminase was 69 U/L (Normal 6–42 U/L), total bilirubin was 27 µmol/L (Normal 1.71–20.5 µmol/L), nasopharyngeal swab for COVID-19 polymerase chain reaction (PCR) was negative. Three skin lesions were scrapped and sent to the central laboratory for monkeypox PCR using BGI Monkeypox Virus Nucleic Acid Detection Kit.

Upon presentation he was immediately placed in a single room in an airborne infection isolation room (AIIR) under both airborne and contact precautions, and no medications were prescribed. On day two of admission skin scrapings PCR returned to be negative for monkeypox but positive for varicella zoster virus (VZV). Serology for human immune deficiency virus (HIV-1) was negative, and HIV 1/2 PCR negative. However, VZV IgM was positive. The patient was diagnosed as a case of chickenpox and discharged the next day in good condition.

3. Discussion

Monkeypox was first discovered in 1958 and the first human infection was reported in 1970 [4]. It is endemic in West and Central Africa, with the largest outbreaks occurring in Nigeria [5]. The largest outbreak of cases outside of Africa was reported in 2003 in Wisconsin, USA, when the virus was imported from Ghana along with Gambian giant rats for an exotic pet market, the virus was transmitted to prairie dogs housed in the same pet shop as the rats and jumped from there to their owners, infecting 71 people in total with 19 hospitalizations [6]. Recently, it is interesting to note that there was transmission of Monkeypox virus from humans to a dog [7]. Between 13 and 25 May, 2022, during the time our case was traveling, the World Health Organization (WHO) reported a total of 226 laboratory-confirmed cases of Monkeypox, and many additional suspected cases in 21 non-endemic countries mostly in Spain [8]. However, the number of cases as of August 7th, 2022 had reached 27814 laboratory confirmed cases with 11 deaths [2,3]. The current patient visited two European countries during the time of the outbreak and presented with clinical features highly suspicious for monkeypox which include fever, followed by the generalized rash and his epidemiological link to an area with an ongoing monkeypox outbreak all made the clinical suspicion of monkeypox very high. However, the different ages of his skin lesions were atypical.

Human-to-human transmission of monkeypox has been well documented, one report from Sudan of 10 laboratory-confirmed cases and 9 suspected cases were identified with up to 5 generations of human-to-human transmission [9]. In 2021 an imported case of monkeypox from Nigeria to the United Kingdom (UK) caused a secondary transmission from the index case to another family member and a toddler [10]. Even though the disease is endemic in central and west Africa for many years, huge knowledge gaps exist in our knowledge about the disease, specifically, the disease reservoir, modes of disease acquisition, human-to-human transmission, best infection control measures and therapeutic and preventative measures. In our patient, the clinical suspicion was high, but with careful evaluation of the atypical rash, testing for other febrile illnesses causing generalized rash were warranted, and proved to be essential in his case. Co-infection with both monkeypox and VZV has been described in 134 cases in the Democratic Republic of Congo between 2009 and 2012 [11]. The current case had IgM and PCR confirmed VZV infection with a negative monkeypox PCR. Atypical features of VZV involving soles have been previously reported as suspected monkeypox [12]. Although both Monkeypox and Chickenpox diseases share many characteristics, there are certain accompanying symptoms that are more frequent in one or the other. A comparison of both diseases is shown in Table 1. In a study from Zaire, of 730 patients mission from the index case to another family member and a toddler [10]. Even though the disease is endemic in central and west Africa for many years, huge knowledge gaps exist in our knowledge about the disease, specifically, the disease reservoir, modes of disease acquisition, human-to-human transmission, best infection control measures and therapeutic and preventative measures. In our patient, the clinical suspicion was high, but with careful evaluation of the atypical rash, testing for other febrile illnesses causing generalized rash were warranted, and proved to be essential in his case. Co-infection with both monkeypox and VZV has been described in 134 cases in the Democratic Republic of Congo between 2009 and 2012 [11]. The current case had IgM and PCR confirmed VZV infection with a negative monkeypox PCR. Atypical features of VZV involving soles have been previously reported as suspected monkeypox [12]. Although both Monkeypox and Chickenpox diseases share many characteristics, there are certain accompanying symptoms that are more frequent in one or the other. A comparison of both diseases is shown in Table 1. In a study from Zaire, of 730 patients diagnosed clinically as chickenpox 3.3% were confirmed as monkeypox cases by laboratory [13]. Recent papers had also examined the features of Monkeypox and its resemblance to other diseases such as chickenpox and smallpox [14,15].

With the ongoing international outbreak of several clusters of cases of monkeypox in several non-endemic countries [16], and the re-opening of commercial flights internationally after relaxing COVID-19 mitigation measures, public health officials and clinicians should remain vigilant with a high index of suspicion for monkeypox and should continue careful evaluation and investigation for other febrile illnesses manifesting with rash like chickenpox.

Consent to participate

Patient consented to the publication of this report.

Fig. 1. Maculopapular rash on back with scabbed lesions near left shoulder.
A comparison between Monkeypox and Chickenpox Characteristics.

| Organism | Virus | Mode of transmission | Incubation period (days) | Rash on palms and soles | Rash features | Lymphadenopathy | Fatality | Diagnosis |
|----------|-------|----------------------|--------------------------|-------------------------|--------------|-----------------|----------|-----------|
| Monkeypox virus | Poxviridae family, Chordopoxvirinae, subfamily, and Orthopoxvirus genus | Close contact, respiratory droplets, contact with skin lesions, recently contaminated objects | Often 6–13 (range 5–21) | Yes | Deep-seated, firm/hard, well delineated, often in different stages | Present | 1–10% | Monkeypox PCR |
| Variella-Zoster Virus | Herpesviridae family, alphaherpesvirinae, subfamily, Varicellovirus genus | Close contact, respiratory droplets, contact with skin lesions, recently contaminated objects | 10–21 | No | Superficial vesicles “dewdrop on a rose petal” | Absent | Rare | VZV PCR or IgM |

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