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Case report | Prikaz bolesnika

The first case of imported mpox infection in Split, Croatia in July 2022

Prvi slučaj dokazane importirane mpox infekcije u Splitu u srpnju 2022. godine

Svjetlana Karabuva[1,2], Antea Troglić[1], Vanja Kaliterna[3,4], Diana Nonković[5,*]

[1] Infectious Diseases Department, University Hospital of Split, Split, Croatia
[2] University of Split, School of Medicine, Split, Croatia
[3] Clinical Microbiology Department, Teaching Institute for Public Health of Split and Dalmatia County, Split, Croatia
[4] University Department of Health Studies, Split, Croatia
[5] Epidemiology Department, Teaching Institute for Public Health of Split and Dalmatia County, Split, Croatia

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Summary

Monkeypox (mpox) infection is a zoonotic disease caused by an *Orthopoxvirus* – the mpox virus. A multi-country outbreak of mpox infection has been ongoing since May 2022. The number of cases reported globally peaked in August 2022, and has been steadily declining since. Most patients infected with the mpox virus during the current outbreak are men who have sex with men. The most common clinical symptoms include fever, followed by the development of papular, vesiculopustular and ulcerative lesions that progress to scabs on the body surface, chills and lymphadenopathy. Clinicians should report any suspected cases immediately to local and national public health authorities. Contacts of probable and confirmed cases should be monitored, or should self-monitor daily, for a period of 21 days following the last contact with a case or their contaminated materials during the infectious period.

During this outbreak, there were 31 reported cases of mpox infection in Croatia up to January 2023, with only one case registered in the Split-Dalmatia County. Here, we report the first case of proven imported mpox infection in Split, accompanied by photographs of skin lesions during the acute phase and recovery period.

Sažetak

Infekcija majmunskim boginjama (mpox) je zoonoza uzrokovana virusom majmunskih boginja iz roda *Orthopoxovirus*. U zemljama diljem svijeta epidemija ove bolesti traje od svibnja 2022. godine. Najveći broj prijavljenih slučajeva zabilježen je u kolovozu 2022. godine, te se od tada bilježi stabilan pad novooboljelih. Oboljele osobe uglavnom su muškarci koji imaju spolne odnose s muškarcima. Najčešći klinički simptomi su vrućica praćena razvojem papuloznih, vezikulopapuloznih, ulcerativnih lezija koje progrediraju do krusti na tjelesnim površinama, zimičavost i limfadenopatija. Kliničari bi nadležnim lokalnim i nacionalnim epidemiolozima odmah trebali prijaviti svaku sumnju na mpox infekciju. Kontakti vjerojatnih i potvrđenih slučajeva trebali bi biti svakodnevno nadzirani ili samonadzirani, tijekom 21 dana od posljednjeg kontakta s oboljelim osobama ili kontaminiranim materijalom.

U Hrvatskoj je do kraja prosinca 2022. godine službeno prijavljen 31 potvrđeni slučaj, od kojih je samo jedan zabilježen u Splitu u Splitsko-dalmatinskoj županiji. U ovom radu prikazujemo prvi dokazani, importirani slučaj infekcije majmunskim boginjama u Splitu, uz prateće fotografije kožnih lezija tijekom akutne faze bolesti i rekonvalescencije.

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✉ ***Corresponding author:**
Diana Nonković, MD., PhD., Epidemiology Specialist
Epidemiology Department, Teaching Institute for Public Health of Split-Dalmatia County,
Vukovarska 46, Split, Croatia;
E-mail: diana.nonkovic@nzjz-split.hr

Introduction

The mpox virus is a brick-shaped, moderately large (about 200-250 nm), and enclosed by a lipoprotein with a linear double-stranded DNA genome of approximately 190 kb[1]. It belongs to the *Orthopoxvirus* genus of the *Poxviridae* family, together with the Vaccinia virus, Cowpox virus, Variola virus and several other animal pathogen poxviruses. These viruses are known to have a long-lasting stability in the environment, and viable mpox virus can be detected on household surfaces for at least 15 days after contamination[2].

The mpox virus was first isolated in 1958 from pox lesions during an outbreak of vesicular disease among captive cynomolgus macaques imported from Singapore into Denmark for polio-vaccine-related re-

search[3]. In 1970, the first human isolate of the mpox virus was reported in a child in the equatorial region of the Democratic Republic of the Congo (DRC)[4]. Sporadic cases were reported from rainforest areas in Central and West Africa, and large outbreaks were identified, mainly in the DRC, where the disease is currently considered endemic[5]. Mpox virus was reported outside of Africa for the first time in 2003, when an outbreak occurred in the United States[6]. Since early May 2022, more than 60 000 cases of mpox virus have been reported in countries with no historically reported cases, particularly in Europe and the USA, among individuals who have not travelled to endemic areas[7]. Confirmation of one case of mpox virus, in a country, is considered an outbreak[2]. On 23 July 2022, the World Health Organization (WHO) declared that the multi-country outbreak of mpox virus is a public health emergency of international concern[2].

Mpox virus can be transmitted through direct or indirect contact with body fluids, cutaneous, mucosal lesions, or sores of infected individuals, or with materials that contain infected body fluids such as clothing or linens[1]. Most patients infected with mpox virus during the current outbreak are men who have sex with men[3].

The incubation period of mpox infection ranges from 5 to 21 days[2]. Typically, the prodromal phase of clinical illness lasts 1-5 days, during which time patients may experience fever, headache, back pain, muscle aches, and lymphadenopathy. The second phase occurs after the fever subsides, with the appearance of skin and/or mucosal rash, which might include a single or multiple lesions[2]. The lesions progress through macules, papules, vesicles, and pustules, before crusting over and desquamating over a period of 2 to 4 weeks. These mucosal lesions are often localized in the genital or perineal/perianal area as well as in the mouth and on the eyes[1,8]. Lesions might appear at different stages of progression and it has been observed that the rash can develop prior to typical prodromal or constitutional symptoms. Lymphadenopathy remains a common feature, usually appearing early in the course of illness[5,6]. The WHO recommends 21 days of self-monitoring from the date of last exposure to a case [2].

Mpox infection is generally a self-limited disease, with clade-dependent case fatality rates ranging from 1% to 10%[3]. Complications include pneumonitis, encephalitis, keratitis, and secondary bacterial infections [3,8]. Young children and immunocompromised persons, including individuals with HIV infection, are at higher risk for severe outcomes, however, effective antiretroviral therapy can reduce this risk[8]. Individuals with HIV infection with a low CD4 cell count (particularly < 100 cells per mm^3) are at increased risk of severe disease.

During 2022, there were 31 reported cases of mpox infection in Croatia. We report the first case of imported mpox infection in Split, Split-Dalmatia County, Croatia, accompanied by images of skin lesions.

Case report

On July 20, 2022, a 37-year-old previously healthy man presented to the Emergency Ward of the Infectious Diseases Department at the Split University Hospital, on the 9th day of the acute illness with catarrhal symptoms, fever up to 37.9°C, skin rash and inguinal lymphadenopathy. The patient, a Croatian citizen working in a hospital in Germany, had arrived in Croatia on July 11, 2022 to visit family. His mother also had catarrhal symptoms between July 12 and 17. A rapid COVID-19 self-test proved negative. Initial examination showed normal vital signs (RR 130/85 mmHg, 80 bpm, SpO2 96%, Temp 37°C). Physical examination revealed three round crusts with mild surrounding hyperaemia in the genital area (Figure 1a), three scabs on the chest wall (Figure 2a), one papule on the right hand (Figure 3a) and one indurated crust on his back. Bilateral inguinal conglomerate of enlarged and painful lymph nodes and slightly catarrhal pharynx were noted. Routine laboratory tests were normal, except for slightly decreased platelet count 121 x 10^9/L (reference: 158-424 x 10^9/L) and slightly elevated CRP (23.7 mg/L; reference: <5 mg/L). The patient reported unprotected sex with both men and women in the previous months. Serology for hepatitis B and C virus, HIV and syphilis was negative. Real-time PCR test for SARS-CoV-2 was also negative. Real-time PCR test was taken for mpox virus (nasopharyngeal swab, smear of genital changes and changes on the chest wall) – all samples were positive for mpox virus. After DNA extraction (GeneRotex, Tianlong, China), Monkeypox Virus Real Time PCR Kit was used for the detection of DNA from the mpox virus (bioPerfectus technologies, China). Afterwards, the patient was under the epidemiological supervision during the isolation period. His mother was tested for mpox virus and was negative.

On August 9, 2022, the patient came for a follow-up examination and all the skin changes were completely dry (Figure 1b, Figure 2b, Figure 3b) and the patient was feeling well. On the 22nd day from the onset of symptoms, the isolation measures ended. There was no other epidemiological data for further monitoring.

Figure 1a. Three round crusts with mild surrounding hyperaemia in the genital area (9th day of the illness).
Slika 1a. Tri okrugte kruste s blagom okolnom hiperemijom u području genitalija (9. dan bolesti)

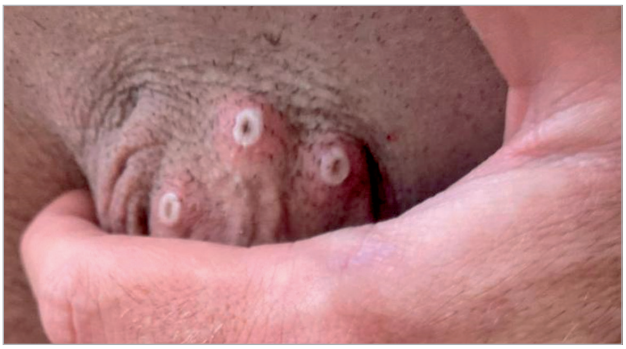


Figure 1b. Dry skin lesions in the genital area (22nd day of the illness).
Slika 1b. Suhe kožne lezije u području genitalija (22. dan bolesti)



Figure 2a. Three scabs on the chest wall (9th day of the illness).
Slika 2a. Tri kruste na prsnom košu (9. dan bolesti)



Figure 2b. Dry skin lesions on the chest (22nd day of the illness).
Slika 2b. Suhe kožne lezije na prsnom košu (22. dan bolesti)



Figure 3a. One papule on the right hand (9th day of the illness).
Slika 3a. Jedna papula na desnoj ruci (9. dan bolesti)



Figure 3b. Dry skin lesion on the right hand (22nd day of the illness).
Slika 3b. Suha kožna lezija na desnoj ruci (22. dan bolesti)



Discussion

From May 2022, the geographic pattern of mpox infection has changed from endemic to non-endemic regions. Recent outbreak in Europe included sexual transmission apart from other models of transmission. The cases were observed mainly in men who have sex with men because of the virus capacity to transmit through intimate close contact[1]. Our patient was also in the commonly affected group.

The clinical characteristics of mpox infection are mostly mild symptoms. The predominant clinical features are presence of rash located mostly in the anogenital and/or perineal area with inguinal lymphadenopathy, fever, asthenia and myalgia[2,7]. Photographs of skin lesions in our patient show the typical finding in the mpox infection. However, all patients with epidemiological data of unprotected sex must be tested for all routinely available sexually transmitted diseases. Possible causes of hospitalisation and death triggered by mpox infection include encephalitis and sepsis from skin and soft tissue infection. The difference in symptoms might be related to nutrition, immunosuppression, quality of the health care and viral evolution[8-10]. In our case, the disease was self-limited with no complications.

Most patients with mpox infection get better without medical treatment, as in our patient. If treatment is required, it is usually based on supportive and symptomatic therapy with focus on prevention and treatment of secondary bacterial infections.

Antiviral drug option for the treatment of mpox is tecovirimat. Brincidofovir and cidofovir is recommended for patients with severe disease[9].

The WHO has updated the interim guidance on vaccines and immunization for mpox virus. Updates include a clearer emphasis on the groups at risk of mpox infection for consideration for preventive vaccination, and updated terminology for pre- (PPV) and post-exposure (PEPV) vaccination[2]. PEPV is recommended for close contacts of cases, ideally within four days of first exposure (and up to 14 days in the absence of symptoms), to prevent onset or mitigate severity of the disease. PPV is recommended for individuals at high risk of exposure and for health workers at high risk of exposure, laboratory personnel working with *Orthopoxviruses*, clinical laboratory personnel performing diagnostic testing for mpox virus and outbreak response team members[2].

Conclusion

Mpox infection is caused by the *Orthopoxvirus* – mpox virus. A multi-country outbreak of mpox infection has been ongoing since May 2022, with 31 cases reported in Croatia by January 2023, including one confirmed case in Split, the only one documented in the Split-Dalmatia County, despite the tourist season. The mode of mpox virus transmission includes animal contact, direct/sexual contact, respiratory secretions or contact with active lesions. A detailed history, epidemiological data, and thorough clinical examination are essential for diagnosing all rash-accompanied diseases, especially in sexually transmitted and re-emerging diseases. Healthcare providers should be well-trained for early recognition of mpox cases, and facilitate easier access to health care.

Precautionary measures like hand hygiene and the use of mask are vital to prevent disease spread. Healthcare workers who have occupational exposure to patients with mpox virus or possibly contaminated materials should follow national infection control protocols. Tailored public health control measures are crucial, particularly for populations at increased risk of infection (men who have sex with men). Contact tracing during outbreak is essential for early detection and isolation of mpox cases. Implementing vaccination strategies—whether pre-exposure, post-exposure, or a combination thereof—for high-risk populations, alongside awareness-raising initiatives, is recommended as a targeted public health intervention to effectively reduce transmission.

Conflict of Interest

The authors have not declared any conflict of interest relevant to this work.

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