Chapter 2

Monkeypox Virus And The Anatomical Changes It Causes In Humans 👌

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Abstract

Monkeypox virus was first identified in Denmark in 1958. It was first seen in humans in 1970 in a 9-month-old male baby in the Democratic Republic of Congo. Monkeypox virus belongs to the orthopoxvirus genus within the pox virus family. This virus is detected locally and multiplies in the area where it is found, causing inflammation. It is carried to the lymph nodes, spleen, tonsils and bone marrow through the circulation in this region. The viruses that multiply here then reach target organs such as testicles and skin. The most common clinical symptoms of monkeypox virus disease are fever, fatigue, lymphadenopathy, and widespread rash all over the body. These rashes, which can be seen all over the body, including the mouth, genital area, palms and soles of the feet, start as macular and turn into papular, vesicular and pustular forms, respectively and these rashes end up crusting. This virus affects the skin, respiratory system, urogenital system, digestive system, nervous system and eyes in different ways and causes problems.

1. Introduction:

Monkeypox virus was first identified in 1958, after a study conducted on monkeys in Denmark, where symptoms similar to smallpox were observed (1). It is a zoonotic virus with enveloped double-stranded DNA and two different subspecies from the Orthopoxvirus genus, Poksviridae family, which has a lower spread rate and mortality rate than smallpox. It was first

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seen in humans in 1970 in a 9-month-old male baby in the Democratic Republic of CongoThe disease started to be seen outside Africa for the first time in 2003. It has been learned that all of these cases involved some form of interaction with imported animals (2). Later, the disease began to be seen in different countries at different times. Specifically, between 1970 and 1986, it was seen in 10 people in Sierra Leone, Nigeria, Liberia and Ivory Coast and in 394 people in Cameroon, Central African Republic and Democratic Republic of Congo. In the epidemic that occurred in Nigeria in 2017, 200 cases were detected and there were times when the epidemic rate reached a fatality rate of 3% (3). Data for June 2024 are shown in figure 1.

Number of confirmed mpox cases in 2024



Data as of June 30, 2024

Figure 1: World Health Organization (WHO) • Confirmed case means a laboratory-confirmed, clinically compatible case. No data is available for gray countries.

More than 14,000 cases of monkeypox have been recorded in the Democratic Republic of Congo since the beginning of 2024

Africa CDC announced that there were more than 14,500 monkeypox infections and more than 450 deaths from the beginning of 2024 to the end of July.

This disease is of serious importance for global public health because monkeypox is effective not only in African countries but also in other countries of the world.

2. Pathogenesis:

Monkeypox virus belongs to the orthopoxvirus genus within the pox virus family. The Poxvirus family is divided into 2 subfamilies: Poxvirus family chordopoxvirinae and entomopovirinae. Orthopoxvirus, which includes monkey virus, is among the subgenera that infect vertebrates.

Four subgroups have been identified in the Orthopoxvirus family that are pathogenic to humans. These are vario major virus, variola minor virus, cowpox virus and MPXV, which are the causative agents of smallpox, which were eradicated in the 1980s. Two genetic divisions of MPXV have been identified: West African and Central African (5).

This virus is detected locally and multiplies in the area where it is found, causing inflammation. It is carried to the lymph nodes, spleen, tonsils and bone marrow through the circulation in this region. The viruses that multiply here then reach target organs such as testicles and skin. This period covers approximately 15 days. As a result, the clinical features of the disease become clear and the diagnosis is made (6).

3. Diagnosis:

In epidemic and infectious diseases, it is very important to diagnose them in a short time to stop the epidemic and minimize the risk. This is possible thanks to laboratory tests. (7).

Confirmation of monkeypox infection is made by nucleic acid amplification testing using real-time or conventional polymerase chain reaction (PCR) to detect virus-specific DNA sequences. Samples are taken from skin lesions. Exudate swabs, lesion surfaces and crusts are suitable places for sampling.

Virus-specific Igm can be detected in serum taken on the 5th day of the disease, and IgG positivity can be detected in serum taken on the 8th day (7).

4. Clinical features and effects on human anatomy:

The most common clinical symptoms of monkeypox virus disease are fever, fatigue, lymphadenopathy, and widespread rash all over the body. The only clinical symptom that distinguishes monkeypox virus disease from smallpox and chickenpox, which have a similar clinical course, is lymphadenopathy. The initial phase lasts approximately 2-4 days. While fever, fatigue and lymphadenopathy are the most common symptoms in the initial phase, these symptoms may also be accompanied by headache and backache (6). Following the rise of fever, rash that begins on the face first and then occurs all over the body, resembling the rash of smallpox. Fever begins to subside 3 days after the rash appears. These rashes, which can be seen all over the body, including the mouth, genital area, palms and soles of the feet, start as macular, turn into papular, vesicular and pustular forms and end by crusting. This period in which rashes appear lasts approximately 2-4 weeks (7).

According to epidemiological studies in Africa, where it is endemic, most monkeypox infections have mild symptoms or are asymptomatic. The presence of fever, chills, weakness, muscle pain, lymphadenopathy and rash that develops especially on the face and extremities for 1-3 days in symptomatic individuals helps in the differential diagnosis of smallpox (8).

4.1. Changes in the skin:

Skin involvement in humans is the most prominent symptom of monkeypox virus disease. Classic skin rashes typically appear within 2 to 3 days after the onset of fever. Over the next 1-2 weeks, the lesions follow each other as macule, papule, vesicle and pustule. After remaining in the pustular phase for approximately 5-7 days, the lesions open, crusting and skin rashes begin. The patient usually recovers after 3-4 weeks from the first symptom, and the disease loses its infectious character, especially as the skin crusts spontaneously fall off. (9,10) (Figure 2).



monkeypox skin lesions

Figure 2: Monkeypox skin lesions

The rash tends to affect the extremities and face rather than the trunk. Facial involvement was observed in 95% of the cases, palms and soles were observed in 75%, oral mucosa involvement was observed in 70%, genital area involvement was observed in 30%, and conjunctiva and cornea involvement was observed in 20% (11).

In a study conducted by evaluating 54 cases diagnosed with monkeypox, skin lesions were found in all cases. When the anatomical locations of these lesions are evaluated, 33 (61%) in the genital area, 31 (57%) in the penis, 3 (6%) in the scrotum, 24 (44%) in the perineal region, 27 (50%) in the hip, 11 (20%) in the arms, and legs. 11 (20%), hands 11 (20%), face 11 (20%), oropharyngeal area 4 (7%), trunk 14 (26%), genital or perianal area 51 (94%), genital and perianal area It was observed that 6 (11%) (12). In another study conducted with 197 male cases, face 71 (36%), trunk 70 (35.5%), extremities 74 (37.6%), hands and feet 56 (28.4%), genital area 111 (56%). 4%), anus and perianal region in 82 (41.6%) cases, and oropharyngeal region in 27 (13.7%) cases (13). In a study conducted with 136 cases, 39 (30%) lesions were found in the facial region, 19 (15%) in the oral region, 60 (46%) in the trunk, 33 (29%) in the anorectal region, and 24 (19%) in the vaginal region (14).

4.2. Effects on the respiratory system:

Clinical findings such as pharyngitis, oral ulcers, and tonsillitis may be observed in monkeypox. In studies conducted, sore throat and pharyngitis were 16.8%; It has been seen at a rate of 20% (13,14). Lower respiratory tract involvement is less common. However, studies have shown that some monkeys exposed to the virus developed bronchopneumonia after a period of fatal necrotization (15). It is thought that the vaccine has an effect on these findings. In a 1987 case series of 282 patients with monkeypox in the Democratic Republic of the Congo, pneumonia and pulmonary distress occurred in 11.6% of unvaccinated individuals and 3.1% of vaccinated individuals (17).

4.3. Effects on the urogenital system:

The effects of monkeypox virus on the urogenital system are common enough to require medical care. Patients complain of intense skin lesions, especially in the genital area, penile edema and other sexually transmitted diseases. Testes, ovaries and uterus can be affected by monkeypox virus. Although the degree of this effect is not clearly revealed, the possibility of sexual transmission of this virus is high (18). In a study, sexual health screening was performed in 94% of the cases and urogenital system problems were found in all patients (12). In another study, 197 patients were evaluated and their urogenital system was evaluated. Of these, the rectum was infected in 25 (73.5%) and the urethra in 7 (20.6) cases, while Neisseria gonorrhoeae was seen in 34 (21.1%), Herpes simplex in 11 (7%) and Treponema pallidum in 6 (3.7%) cases. 56 (32.5%) of the cases had a sexually transmitted co-infection. Additionally, penile edema developed in 31 of the patients. Rectal pain or defecation pain was observed in 71 (36%) of the patients (13). Derin et al. In a case reported by , the patient was admitted to the hospital with a complaint of penile lesions and monkeypox virus was detected (19).

4.4. Effects on the digestive system:

Monkeypox virus affects the digestive system and organs and causes some clinical findings. Gastrointestinal system problems such as nausea, vomiting, diarrhea, dehydration and malnutrition are observed in patients. It has been reported that nausea and vomiting are more common, especially in pediatric patients, and less common in adults (20). Although involvement of the liver and other intra-abdominal organs is rare, its involvement can cause serious complications. Granulomatous changes and infections in the stomach, intestines and peritoneum have been observed in some studies. Some studies have shown that there may be effects on the liver and liver tissue (21).

4.5. Effects on the nervous system:

The most common neurological symptom encountered by patients with monkeypox is headache. A study showed that 24.9% of patients complained of headache (13). More serious neurological conditions may occur in the later stages of the disease. Encephalitis, meningoencephalitis and seizures are rare symptoms (22).

4.6. Eye effects:

Ocular findings in monkeypox include conjunctivitis, blepharitis, blepharoconjunctivitis, subconjunctival nodules, keratitis and corneal ulcers. Although eye pathologies are not very common, their presence is very important as it affects vision. In a study, it was determined that the rate of conjunctivitis was 20.3% and 16.4%, and keratitis and corneal ulcer were 4% (3).

5. Treatment, vaccination and prevention:

Supportive care, prevention of secondary infections and resolution of symptomatic problems are recommended in the treatment of the disease (23).

To prevent human-to-human transmission, surveillance and rapid diagnosis of new cases are critical. Close contact with infected people is the most important risk factor. Contact with skin debris and personal items of infected people should be avoided. Healthcare workers who live in the same house with the infected person and take samples from them and provide care are the group at the highest risk. Health workers, especially those taking samples, should be ensured to use personal protective equipment. It is known that the vaccine used against smallpox has 85% cross-protection. Therefore, it is recommended that healthcare workers be vaccinated against smallpox virus (24).

To prevent animal-to-human transmission, unprotected contact with wild animals, especially sick and dead animals, should be avoided. Animal meat and parts should be consumed well cooked. Contact with primates and rodents should be avoided, especially in endemic areas (25).

References

- TUNA Ayşegül MAYMUN ÇİÇEĞİ, GEÇMİŞTEN GÜNÜMÜZE Kırıkkale Üniversitesi Tıp Fakültesi Dergisi 2022;24(2):409-416
- Tepetaş M, Sungur S. Salgın Haberleri Maymun Çiçeği Virüsü Salgını. ESTÜ-DAM Halk Sağlığı Dergisi. 2022 Eki 31;7(3):550-56.
- Jezek Z, Gromyko AI, Szczeniowski M V. Human monkeypox. J Hyg Epidemiol Microbiol Immunol. 1983;27(1):13–28.
- https://www.bbc.com/turkce/articles/c4gep56x96go
- Sütlü S. Çatak B. Kılınç A.S. A New Epidemic Is At The Door: Monkeypox Virus. TJFMPC, 2023; 17 (2) :333-337
- Alshahrani NZ, Alzahrani F, Alarifi AM, Algethami MR, Alhumam MN, Ayied HAM, et al. Assessment of Knowledge of Monkeypox Viral Infection among the General Population in Saudi Arabia. Pathog Basel Switz. 2022;11(8):904. https://doi.org/10.3390/pathogens11080904.
- Gonzales-Zamora JA, Soriano-Moreno DR, Soriano-Moreno AN, Ponce-Rosas L, Sangster-Carrasco L, De-Los-Rios-Pinto A, et al. Level of knowledge regarding mpox among Peruvian Physicians during the 2022 outbreak: a cross-sectional study. Vaccines. 2023;11(1):167. https://doi. org/10.3390/ vaccines11010167.

- Centers for Disease Control and Prevention (CDC). Multistate outbreak of monkeypox--Illinois, Indiana, and Wisconsin, 2003. MMWR. 2003;52:537-40.
- Hobson G, Adamson J, Adler H, Firth R, Gould S, Houlihan C, Johnson C, Porter D, Rampling T, Ratcliffe L, Russell K, Shankar AG, Wingfield T. Family cluster of three cases of monkeypox imported from Nigeria to the United Kingdom, May 2021. Euro Surveill. 2021;26(32)
- http://www.veterinary.ankara.edu.tr/2022/07/05/ maymun-cicegi-monkeypox-hastaligi/
- Petersen, Eskild, et al. "Human monkeypox: epidemiologic and clinical characteristics, diagnosis, and prevention." Infectious Disease Clinics 2019: 33.4: 1027-1043.
- Girometti N, Byrne R, Bracchi M, Heskin J, McOwan A, Tittle V, Gedela K, Scott C, Patel S, Gohil J, Nugent D, Suchak T, Dickinson M, Feeney M, Mora-Peris B, Stegmann K, Plaha K, Davies G, Moore LSP, Mughal N, Asboe D, Boffito M, Jones R, Whitlock G. Demographic and clinical characteristics of confirmed human monkeypox virus cases in individuals attending a sexual health centre in London, UK: an observational analysis. Lancet Infect Dis. 2022 Sep;22(9):1321-1328. doi: 10.1016/ S1473-3099(22)00411-X. Epub 2022 Jul 1. PMID: 35785793; PM-CID: PMC9534773.
- Patel, A., Bilinska, J., Tam, J. C., Fontoura, D. D. S., Mason, C. Y., Daunt, A., ... & Nori, A. (2022). Clinical features and novel presentations of human monkeypox in a central London centre during the 2022 outbreak: descriptive case series. bmj, 378.
- Thornhill, J. P., Palich, R., Ghosn, J., Walmsley, S., Moschese, D., Cortes, C. P., ... & Orkin, C. M. (2022). Human monkeypox virus infection in women and non-binary individuals during the 2022 outbreaks: a global case series. The Lancet, 400(10367), 1953-1965.
- Goff AJ, Chapman J, Foster C, Wlazlowski C, Shamblin J, Lin K, Kreiselmeier N, Mucker E, Paragas J, Lawler J, Hensley L. 2011. A novel respiratory model of infection with monkeypox virus in cynomolgus macaques. J Virol 85:4898–4909. https://doi.org/10.1128/JVI.02525-10.
- Zaucha GM, Jahrling PB, Geisbert TW, Swearengen JR, Hensley L. 2001. The pathology of experimental aerosolized monkeypox virus infection in cynomolgus monkeys (Macaca fascicularis). Lab Invest 81:1581–1600. https://doi.org/10.1038/labinvest.3780373.
- Jezek Z, Szczeniowski M, Paluku KM, Mutombo M. 1987. Human monkeypox: Clinical features of 282 patients. J Infect Dis 156:293–298. https:// doi.org/10.1093/infdis/156.2.293.

- ELSAYED, Sameer; BONDY, Lise; HANAGE, William P. Monkeypox virus infections in humans. Clinical microbiology reviews, 2022, 35.4: e00092-22.
- Derin, O., Öztürk, E. N., Demirbaş, N. D., Sevgi, D. Y., & Dökmetaş, İ. (2023). Genital erüpsiyonla başvuran bir hasta: Türkiye'deki ikinci maymun çiçeği olgusu. Mikrobiyoloji Bülteni.
- Huhn GD, Bauer AM, Yorita K, Graham MB, Sejvar J, Likos A, Damon IK, Reynolds MG, Kuehnert MJ. 2005. Clinical characteristics of human monkeypox, and risk factors for severe disease. Clin Infect Dis 41:1742– 1751 https://doi.org/10.1086/498115.
- Weiner ZP, Salzer JS, LeMasters E, Ellison JA, Kondas AV, Morgan CN, Doty JB, Martin BE, Satheshkumar PS, Olson VA, Hutson CL. 2019. Characterization of Monkeypox virus dissemination in the black-tailed prairie dog (Cynomys ludovicianus) through in vivo bioluminescent imaging. PLoS One 14:e0222612. https://doi.org/10.1371/journal. pone.0222612.
- Huhn GD, Bauer AM, Yorita K, et al. Clinical characteristics of human monkeypox, and risk factors for severe disease. Clin Infect Dis, 2005; 41:1742–51.
- World Health Organization (WHO). Monkeypox Key facts. https://www.who. int/news-room/fact-sheets/detail/monkeypox. (accessed June 28, 2022)
- Fine PE, Jezek Z, Grab B, et al. The transmission potential of monkeypox virus in human populations. Int J Epidemiol 1988; 17:643–50.
- Center for Disease Control and Prevention. (CDC). Isolation and Prevention Practices for People with Monkeypox. https://www.cdc.gov/poxvirus/ monkeypox/prevention.html. (accessed June 30, 2022).