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Monkeypox virus; Epidemiology of the World and Turkey

Monkeypox virüsü; Dünya ve Türkiye Epidemiyolojisi

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Öz

Monkeypox virus has the potential to spread through zoonotic reservoirs. The virus reaches other geographical regions through displacements caused by war, migration, and other reasons. In previous years, human monkeypox was a rare zoonotic disease confined to West and Central Africa, however, this geographic range has expanded rapidly with the decline of smallpox vaccine-induced immunity in the world population. The multi-country monkeypox epidemic, which has been going on since the beginning of May 2022, was seen for the first time in many continents outside of Africa. Cases have been reported mostly from European countries and the Western Hemisphere of the World. Cases have been reported extensively from the European region and EU/EEA countries, most commonly Spain, Germany, France, and the UK. By 8 August 2022, over 28 000 confirmed cases and twelve deaths have been reported worldwide. Until 09 August 2022, 5 cases were reported from Turkey.

In this review, the epidemiology of Monkeypox and the general characteristics of the causative agent of Monkeypox is reviewed, with current information and data.

Anahtar Kelimeler Epidemiyology, Çiçek aşıları, Çiçek hastalığı, Maymun çiçek virüsü, Salgın.

Abstract

Maymun Çiçek Virüsü, zoonotik rezervuarlar yoluyla yayılma potansiyeline sahip bir virüstür. Virüs savaş, göç veya diğer nedenler kaynaklı yer değişiklikleri ile diğer coğrafik bölgelere ulaşmaktadır. Önceki yıllarda maymun çiçeği, Batı ve Orta Afrika ile sınırlı, nadir görülen bir zoonotik hastalık iken hastalığın bu coğrafik dağılımı, dünya nüfusunda çiçek aşısı kaynaklı bağışıklığın azalmasıyla birlikte hızla genişlemiştir. Mayıs 2022'nin başından beri devam eden ve birden çok ülkede izlenen maymun çiçeği salgını ilk defa Afrika dışında birçok kıtada görülmüştür. Bu vakaların çoğu Avrupa'dan ve Batı Yarımküreden bildirilmiştir. Vakalar, en sık İspanya, Almanya, Fransa ve İngiltere olmak üzere Avrupa Bölgesi ve EU/EEA ülkelerinden yoğun olarak bildirilmiştir. 8 Ağustos 2022'ye kadar dünya genelinde 28000'in üzerinde doğrulanmış vaka ve 12 ölüm bildirilmiştir. 09 Ağustos 2022 tarihine kadar Türkiye'den 5 vaka bildirilmiştir.

Bu derlemede, mevcut güncel bilgiler ve veriler ile maymun çiçeği hastalığının epidemiyolojisi ve maymun çiçek hastalığı etkeninin genel özellikleri gözden geçirilmiştir.

Keywords *Epidemiology, Monkeypox virus, Outbreak, Smallpox, Smallpox vaccines.*

INTRODUCTION

Monkeypox virus is a species of pox virus within the Orthopoxvirus genus of the Poxviridae family. This family of viruses can infect mammals, as well as reptiles, birds, and insects.[1] The Orthopox genus includes three other human pathogens, variola virus, cowpox virus, and vaccinia virus.[2] Numerous species of poxviruses are known to cause human infections, including Smallpox, Monkeypox, Cowpox, Vaccinia virus (VACV), and Molluscum contagiosum virus.[3] While the Monkeypox virus sporadically causes human disease, it also has a wide variety of potential host organisms to circulate for long periods in the wild.[3,4] Monkeypox virus was first isolated from monkeys. Also, squirrels, rats, and mice are natural hosts of the Monkeypox virus.[5]

Monkeypox can be transmitted through direct contact. Therefore, transmission is possible by direct contact with monkeypox rash, scabs, and bodily fluids of a person with monkeypox.[6] The virus can also be transmitted through contact with secretions such as saliva. Behaviors such as having sex with a person with monkeypox and using the same items can spread the virus.[6] Studies on the transmission route of the disease have shown that the monkeypox virus can be transmitted sexually. Epidemiological data up to June 2022 revealed that cases were particularly associated with men who had sex with men.[7,8]

In one study, various samples were taken from 12 patients and studied by PCR. Virus DNA was detected in all saliva samples of the patients and a high viral load was found in some of the saliva samples. In this study, rectal swab (11 of 12), nasopharyngeal swab (10 of 12), semen (7 of 9), urine (9 of 12), and stool (8 of 12) samples positivity were detected.[9]

In addition to the main modes of transmission of the infection, it is stated that the transmission via aerosol should not be ignored.[10] Respiratory transmission is possible by the release of large droplets by coughing or sneezing.[11] Although it is stated that it is possible to be transmitted through the placenta or by blood transfusion in addition to the mentioned modes of transmission, there is not enough data about this mode of transmission. In the current epidemic, the rashes on the genital areas of the patients support the transmission by sexual contact, but the transmission by sexual activity has not been clarified so far.[12]

Monkeypox virus has developed various mechanisms for entry into the host cell. In general, it is known that it enters the cell by micropinocytosis or fusion, releases its genome and proteins into the cytoplasm after entry into the host cell, and performs its replication here. As with other dsDNA viruses, it uses a DNA-dependent RNA polymerase enzyme to transcribe early viral mRNAs, followed by structural and non-structural viral proteins. After genome synthesis and protein synthesis, the virus is released from the cell after the assembly and envelope process and thus can pass to another cell.[13]

Transmission from animals to humans can occur through direct contact with one of the infected hosts (such as by eating the infected host's flesh) or their fluids.[1]

Studies have shown that the pathogen initially infects respiratory epithelial cells, spreads to lymph nodes, and then spreads systemically through monocytic cells.[14] The virus can infect most mammalian cells by attaching to structures abundant in cells such as chondroitin sulfate, heparin sulfate, and laminin.[15,16]

Epidemiology

Information on previous outbreaks and data on the latest outbreak

Monkeypox outbreak is an emerging infectious disease that is increasingly expanding geographically. The rapid spread of cases is a serious concern worldwide. Concern about the further spread of the outbreak is increasing as cases spread rapidly from Central Africa to other parts of the world.[17] This spread is thought to be due to the decline

in orthopox virus immunity worldwide following the cessation of the smallpox vaccine after smallpox was declared eradicated in 1980.[5,17]

Monkeypox was first isolated in 1958 in Denmark.[5] As with many other zoonoses, monkeypox is transmitted to humans by chance when they encounter infected animals. In 1970, the first human case was reported in Congo.[5] Before this new outbreak, human cases from outside Africa were rarely observed. In 2003, 71 cases of human monkeypox were reported in the USA. This outbreak started with the infection of prairie dogs housed in the same facility during the shipment of infected Gambia opossums, and human cases were seen after contact with these dogs.[18]

In sequencing studies with African and US isolates, two clades were determined by comparing the open reading frames of the genomes.[19] Monkeypox virus is currently classified into two clades (The West African clade and Kongo Basin clade), but a new classification has been proposed as clades 1, 2, and 3. Clade 3 is the cause of most human outbreaks in 2017, 2018, and 2022. It has been proposed that clade 3 can be divided into the lineages A, A.1, A.1.1, and B.1 (Figure 1).[19,20,21]

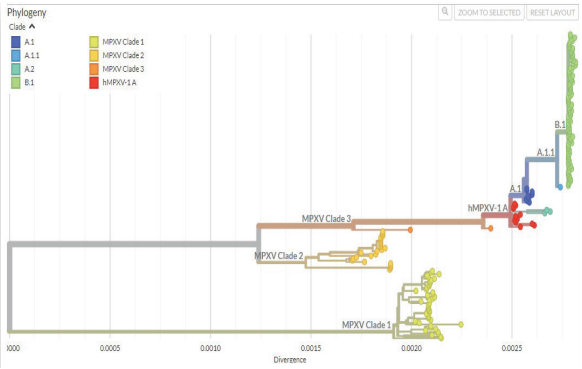

Figure 1. Genomic epidemiology of monkeypox virus.[21]

The West African clade is known to be detected from the western parts of Cameroon to Sierra Leone, whereas the Congo Basin clade (Central Africa) has been described from the central and southern regions of Cameroon to the Congo.[22]

Some differences in epidemiological and clinical features were identified between the two clades.[23] More significant morbidity, mortality, human-to-human transmission, and viremia have been detected in Congo Basin clade-related infections. Significant differences were also seen in morbidity factors such as disease severity and prominent rash. The West African clade is generally associated with milder symptoms than the Congo Basin clade.[1,23] Despite all these epidemiological and clinical differences, 0.55-0.56% nucleotide difference was found between the two strains.[23]

Case fatality rates of outbreaks in the Congo Basin have been reported as 1-10%. The clade circulating in this region appears to be associated with high virulence. The West African clade, responsible for outbreaks in Nigeria, is associated with a mortality rate of about 3%.[24]

Various ideas have been put forward as to the origin of the outbreak. Available data show that the sequences evaluated so far are nearly identical. Available data suggest that recent outbreaks outside of Africa may be associated with a single case. Studies have also shown that the sequences available in West Africa are similar to those from travel-related monkeypox cases that occurred outside of Africa in 2018 and 2019.[25]

Gene changes caused by mutations leading to loss of protein-coding genes or loss of regulatory regions detected in isolates from central Africa are thought to be associated with human-to-human transmission.[26]

The index case was confirmed in a person in the UK on 6 May 2022 and was associated with travel to Nigeria. Sequence analysis of the first isolate obtained in Portugal, collected on 4 May 2022, showed that these new isolates are genetically related to the Nigerian genome belonging to the West African clade.[27]

Other monkeypox genomes isolated in the USA and Belgium also show close genetic relatedness to West African

isolates.[28] Since the beginning of May 2022, thousands of cases have been detected, most of them without a history of travel to endemic countries. As of 28 July 2022, 21 067 cases have been confirmed worldwide, most of them in European countries and the USA (Figures 2 and 3).[29,30]

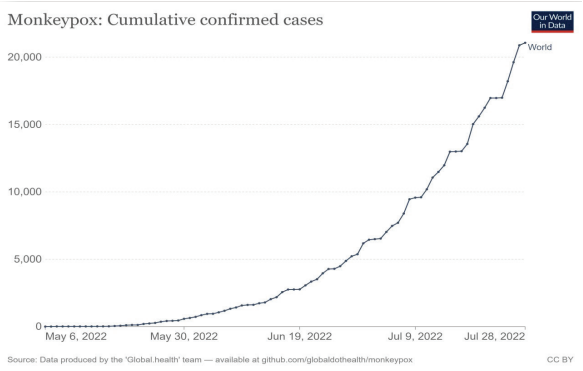

Figure 2. Confirmed cases.[29]

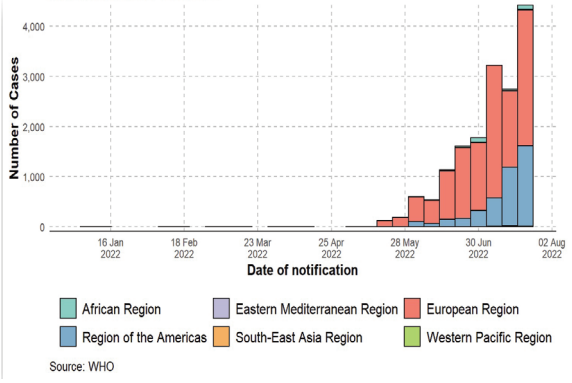

Figure 3. Cases reported up to 25 July 2022.[30]

As of 08 August 2022, 13 912 confirmed Monkeypox cases have been reported from 29 EU/EEA countries since the start of the outbreak with the leading cases from Spain (n=4 942 cases), Germany (n= 2 887) and France (n= 2 423 cases). Cases have been reported in almost all countries in this region. Until this date, five cases have been reported from Turkey.[31]

The first case in Turkey was detected at the end of June 2022. It has been reported that the patient is 37 years old and has an immune system deficiency.[32]

The geographical distribution of confirmed cases in the EU/EEA countries and Turkey until 2 August 2022 is shown in Figure 4.[33]

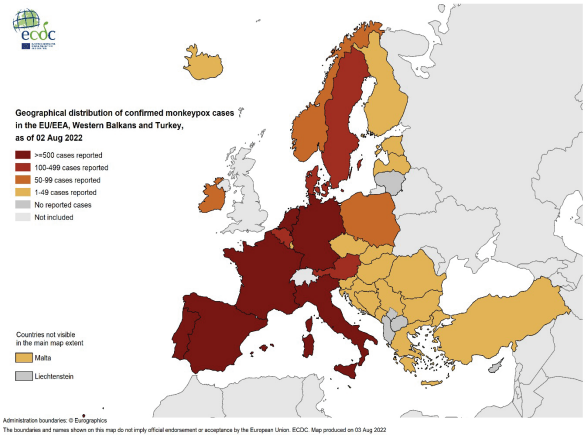

Figure 4. Geographical distribution of confirmed cases the in EU/EEA, Balkans, and Turkey.[33]

As of 06 August 2022, twelve deaths reported worldwide: Spain (n=2 deaths), İndia (n=1 death), Central African Republic (n=2 deaths), Nigeria (n=4 deaths), Ghana (n=1 death), Peru (n=1 death), and Brazil (n=1 death) (Figure 5).[34]

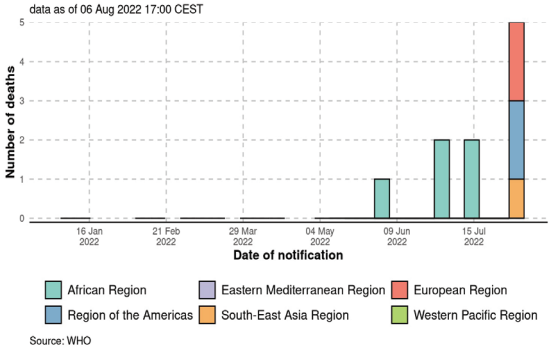

Figure 5. Reported deaths around the World.[34]

The outbreak was declared an International Public Health Emergency in late July 2022.[35]

Diagnosis, treatment options, and vaccines

Patients usually develop a rash on the genitals or anus or other contact areas such as hands, face, and mouth. The rash can be painful and sometimes manifested by itching. Although not all symptoms appear at the same time, other

symptoms are fever, headache, muscle pain, weakness, lymphadenopathy, and respiratory symptoms such as sore throat and cough.[36]

Although the disease is mostly self-limiting, the disease may be more severe in pregnant women, pediatric patients, and immunocompromised individuals.[37]

Swab samples taken from the lesion, mouth, and rectum or scab samples can often be used as examination specimens.[38]

Although other signs are useful in distinguishing vesiculopustular rashes of poxvirus infections from other infections, laboratory confirmation is required for definitive diagnosis. Various laboratory diagnostic tests such as virus isolation, electron microscopy, PCR, IgM and IgG ELISA, immunofluorescence tests, and histopathological examination can be used in the diagnosis of Monkeypox infections. Most of these methods cannot distinguish monkeypox infection from other poxvirus infections. Next-generation sequencing techniques continue to be used as the gold standard test for Monkeypox characterization.[1,39]

There are no licensed drugs for monkeypox so far. Brincidofovir and tecovirimat have been approved in the USA as treatment options for smallpox in case of a threat of bioterrorism.[40] Antivirals such as Tecovirimat have been recommended for those at risk of serious illness, such as those with compromised immunity.[41] Smallpox was reported to have been eradicated in 1977, due to the success of vaccination campaigns with the Vaccinia virus. As a result, it was recommended to stop the Vaccinia vaccine in 1980.[42] It is stated that the smallpox vaccine also has a protective effect against Monkeypox infections.[43] Vaccination is also thought to reduce the clinical manifestations of infection.[35] Currently, there are three smallpox vaccines available. Candidate vaccines are JYNNEOS and ACAM2000, licensed for smallpox, and Aventis Pasteur Smallpox Vaccine, an investigational vaccine for emergencies. JYNNEOS is indicated for adults at high risk.[43,44,45]

Vaccination is recommended for laboratory personnel working in the diagnosis of pox viruses and other healthcare workers at risk of exposure.[46] In case of exposure, it is recommended to start vaccination within 4 days after exposure. It is stated that vaccination 4-14 days after exposure can reduce symptoms but does not prevent the onset of the disease.[47]

Data show that the smallpox vaccine is at least 85% effective in preventing monkey disease. The risks from Monkeypox infections are greater than those from smallpox or monkeypox vaccines.[47]

Hyperimmune globulins are recommended for the treatment of serious complications of the vaccine (such as Eczema vaccinatum).[39] Immunoglobulins are also recommended in immunocompromised patients for whom the live vaccine is contraindicated.[39,48]

CONCLUSIONS

Monkeypox has been showing signs of becoming a global public health problem for many years, with minor outbreaks. The current epidemic is expected to spread gradually in the coming months. Therefore, it is necessary to work efficiently to control the epidemic. As we have learned from other outbreaks we have to share available resources early and efficiently.

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