

KLINIČKE KARAKTERISTIKE OBOLELIH OD MAJMUNSKIH BOGINJA PRILIKOM PRVE POSETE DERMATOLOGU – SERIJE SLUČAJEVA

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SAŽETAK

Uvod/Cilj: Majmunske boginje (engl. *Monkeypox* –MPX) predstavljaju oboljenje izazvano istoimenim *Monkeypox* virusom (MPXV) koje je endemsko u zemljama Centralne i Zapadne Afrike. Od maja 2022. godine beleži se epidemija majmunskih boginja u različitim regijama sveta, uključujući i Republiku Srbiju. Cilj ovog rada je bio da prikazemo kliničke karakteristike obolelih od majmunskih boginja prilikom njihovog prvog javljanja dermatologu.

Serijslučajeva: U rad je uključeno 7 pacijenata koji su tokom juna i jula 2022. godine došli na pregled kod dermatologa zbog promena u genitalnoj i analnoj regiji kod kojih je infekcija majmunskim boginjama potvrđena PCR (engl. *Polymerase chain reaction*) testom. Prosečan uzrast obolelih bio je 35,8 godina, svi su bili muškog pola i homoseksualne orijentacije, 3 osobe su bile HIV-pozitivne, a infekciju su dobili putem seksualnih odnosa. Tri osobe su se inficirale u inostranstvu, a četiri u Beogradu. Kod većine obolelih inkubacija je trajala kraće od nedelju dana i prodromalni znaci su bili odsutni. Kožne promene su se najčešće javljale na penisu u vidu beličastih umbilikovanih papula, pustula i krusta. Serološki testovi na sifilis su pokazali da nijedan oboleli nije imao recentnu infekciju.

Zaključak: Dermatolozi bi trebalo da budu senzibilisani na prisustvo ovog oboljenja u našoj sredini, da rano posumnjaju, upute pacijenta na laboratorijsku dijagnostiku i evaluaciju kod infektologa, kao i da pacijentu savetuju izolaciju i seksualnu apstinenciju jer se bolest može preneti i seksualnim putem.

Ključne reči: majmunske boginje, klinička prezentacija, epidemija, dermatolog

Uvod

Majmunske boginje (engl. *Monkeypox* – MPX) predstavljaju oboljenje izazvano istoimenim *Monkeypox* DNK virusom (MPXV) koji pripada familiji *Poxviridae* i rodu *Orthopoxvirus*. Virus je izolovan među laboratorijskim majmunima u Kopenhagenu 1958. godine (1), a oboljenje je prvi put opisano kod ljudi 1970. godine u Zairu i od tada se kao endemsko javlja u zemljama Centralne i Zapadne Afrike (2). Importovani slučajevi *monkeypox* infekcije opisani su kod osoba koje su putovale u endemske krajeve ili imale kontakt sa životinjama uvezenim iz Afrike (3,4). Početkom 2022. godine beleži se epidemija majmunskih boginja u različitim regijama sveta kod osoba koje nisu putovale u endemske krajeve. Od početka maja 2022. godine pa do 26. jula 2022. godine u zemljama Evropske regije registrovano je 13.043 slučaja osoba

obolelih od *monkeypox* infekcije, predominantno muškog pola, a od toga 10 registrovanih pacijenata bili su oboleli iz Republike Srbije (5).

Nakon inkubacije od jedne do dve nedelje, oboljenje najčešće počinje prodromalnom fazom u vidu povišene telesne temperature, glavobolje, bolova u mišićima i limfadenopatije, koju prati osip centrifugalnog rasporeda na licu i ekstremitetima uključujući dlanove i tabane, a kožne promene koje su kontagiozne i polimorfne (papule, vezikule, pustule i kruste) prolaze za nekoliko nedelja. Oboljenje se može preneti kapljičnim putem, bliskim fizičkim kontaktom, uključujući i seksualni odnos, kao i indirektno preko kontaminiranih predmeta (6,7).

Ono što karakteriše aktuelnu pandemiju su blagi prodromalni simptomi i pojava atipične kliničke prezentacije, sa primarnim lezijama u

CASE SERIES

CLINICAL CHARACTERISTICS OF PATIENTS WITH MONKEYPOX INFECTION AT THEIR FIRST VISIT TO DERMATOLOGIST – A CASE SERIESMilan Bjekic^{1*}¹City Institute for Skin and Venereal Diseases, Belgrade, Republic of Serbia

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SUMMARY

Introduction/Aim: Monkeypox disease (MPX) is caused by Monkeypox virus (MPXV) which is endemic in countries of Central and West Africa. Since May 2022 an outbreak of Monkeypox has been recorded in various regions of the world, including the Republic of Serbia. The aim of this study is to present the clinical characteristics of monkeypox cases during their first visit to a dermatologist.

Case series: The study includes seven patients who consulted a dermatologist during the months of June and July 2022 due to ano-genital rash and in whom Monkeypox infection was confirmed via PCR (Polymerase chain reaction) tests. The average age of patients was 35.8 years, all were men who have sex with men, three patients were HIV-positive and the infection was transmitted through sexual intercourse. Three patients were infected abroad and four in Belgrade. In most cases incubation lasted less than a week and prodromal signs were absent. Skin lesions most frequently appeared on the penis in the form of white umbilicated papules, pustules and crusts. Serological tests for syphilis showed that none of the patients had a recent infection.

Conclusion: Dermatologists should be sensitized to the presence of this disease in our country, they should suspect it early on, refer the patient to laboratory diagnostics and evaluation by an infectious disease specialist, and advise patients to isolate and abstain from sex because the disease can be transmitted during sexual intercourse.

Key words: Monkeypox disease, clinical presentation, outbreak, dermatologist

Introduction

Monkeypox disease (MPX) is caused by Monkeypox virus (MPXV) that belongs to the family Poxviridae and the Orthopoxvirus genus. The virus was isolated among laboratory monkeys in Copenhagen in 1958 (1), while the disease was for the first time described in people in Zaire in 1970, and since then it has been endemic in countries of Central and West Africa (2). The imported cases of monkeypox infection were described in persons who traveled to endemic regions or who had contact with animals imported from Africa (3,4). Since the beginning of 2022, an outbreak of monkeypox has been recorded in different regions of the world in persons who did not travel to endemic regions. From the beginning of May 2022 to July 26th, 2022, 13,043 cases of monkeypox infection were recorded in the countries belonging to the

European region, and they were predominantly males, while 10 registered patients were from the Republic of Serbia (5).

After the incubation period, the disease most frequently begins with the prodromal period in the form of fever, headache, muscle ache and lymphadenopathy, which is followed by rash on the face and extremities, including palms and soles with a central distribution, while skin lesions that are contagious and polymorphic (papules, vesicles, pustules and crusts) clear up in a few weeks. The disease may be transmitted by respiratory droplets, close physical contact, including the sexual intercourse, and through contaminated materials (6, 7).

Mild prodromal symptoms are characteristic of the current pandemic, as well as the appearance

anogenitalnoj regiji koje upućuju na bliski fizički kontakt tokom seksualnih aktivnosti, zabeleženi naročito u populaciji muškaraca koji imaju seksualne odnose sa muškarcima (5). Stoga, oboleli se neretko prvo javljaju u klinike za polne bolesti, dermatolozima koji nisu imali priliku da se susretnu sa *monkeypox* infekcijom u svojoj kliničkoj praksi. Cilj ovog rada je bio da prikazemo kliničke manifestacije *monkeypox* infekcije prisutne prilikom prvog javljanja obolelog dermatologu, kao i karakteristike inficiranih osoba.

Serijski slučajevi

U rad je uključeno 7 pacijenata koji su tokom juna i jula 2022. godine došli u ambulantu Službe za polno prenosive infekcije Gradskog zavoda za kožne i venerične bolesti u Beogradu sa simptomima koji su upućivali na *monkeypox* infekciju i koji su potom upućivani na Infektivnu kliniku Kliničkog centra Srbije gde je sa briseva kožnih promena i farinksa lančanom reakcijom polimerazom (engl. *Polymerase chain reaction* - PCR) dijagnostikovano *monkeypox* virus. Svi pacijenti su popunili anonimnu anketu vezanu za seksualno ponašanje u poslednjih mesec dana pre pojave simptoma (vrsta seksualnog odnosa, seksualna orijentacija, seksualni odnosi u inostranstvu), aktuelne simptome i HIV status. Svim pacijentima su urađeni serološki testovi na sifilis (VDRL – *Venereal Disease Research Laboratory*; laboratorijski test za istraživanje veneričnih bolesti; TPHA – *Treponema Pallidum Haemagglutination Assay*; *Treponema pallidum* hemaglutinacioni test). U ovom radu su prikazane samo inicijalne kožne manifestacije obolelih koji su nakon potvrđene dijagnoze lečeni prema preporukama infektologa i upućivani na kućnu/bolničku izolaciju.

Karakteristike obolelih i kliničke manifestacije *monkeypox* infekcije prikazane su u Tabeli 1. Prosečan uzrast obolelih bio je 35,8 godina (najmlađi pacijent imao je 26 a najstariji 44 godine) i svi su bili muškog pola i homoseksualne orijentacije, 3 osobe su bile HIV pozitivne, a infekciju su dobili putem oralnih i/ili analnih seksualnih odnosa. Tri osobe su se inficirale u inostranstvu (jedna u Nemačkoj, druga u Austriji, a treća u Grčkoj), a ostale u Beogradu. Kod većine obolelih inkubacija je trajala kraće od nedelju dana i prodromalni znaci su bili odsutni. Kod onih sa prisutnim prodromalnim znacima dominirala je povišena telesna

temperatura i blaga malaksalost. Kožne promene su se najčešće javljale na penisu u vidu beličastih umbilikovanih papula (slika 1), diseminovanih pustula (slika 2) i krustoznih lezija (slika 3). Promene u perigenitalnoj regiji su bile u vidu brojnih papulopustula okruženih eritematoznim haloom (slika 4) dok su kod pacijenta sa glutealnim lezijama dominirale pustule (slika 5). Kod dvojice pacijenata promene na koži su bile praćene osećajem bola i pečenja. Serološki testovi na sifilis su pokazali da nijedan oboleli nije imao recentnu infekciju, ali da je troje imalo pozitivan TPHA test usled ranije lečenog sifilisa.

Diskusija

Podaci iz Evrope o epidemiji majmunskih boginja ukazuju da je najveći broj registrovanih slučajeva u Španiji, Velikoj Britaniji, Nemačkoj i Francuskoj, da je većina obolelih muškog pola (99,4%),

Tabela 1. Izabrane karakteristike obolelih i kliničke manifestacije *monkeypox* infekcije

Karakteristike:	Broj (N)=7
Uzrast (prosečan):	35,8 godina
Seksualna orijentacija:	
Homoseksualna	7
Heteroseksualna	0
HIV status:	
Negativan	4
Pozitivan	3
Serološki test na sifilis:	
Negativan	4
Pozitivan*	3
Vrsta seksualnog odnosa:	
Oralni seks	2
Analni seks	3
Oralni i analni seks	2
Period inkubacije	
≤ 7 dana	4
8 - 14 dana	3
Prodromalni znaci:	
Prisutni	3
Odsutni	4
Lokalizacija lezija:	
Samo na penisu	5
Perigenitalna regija	1
Perianalna regija	1
Dominantna kožna lezija:	
Papula	3
Pustula	3
Krusta	1

* Pozitivan test usled ranije lečenog sifilisa.

of atypical clinical presentation, with primary lesions in ano-genital region which indicate a close physical contact during sexual practices, and which have been particularly recorded in the population of men who have sex with men (5). Therefore, patients often first visit clinics for venereal diseases, dermatologists who have not had the chance to see the monkeypox infection in their clinical practice. The aim of this study is to present the clinical manifestations of monkeypox infection during the first visit to a dermatologist, as well as the characteristics of infected persons.

Case series

The study includes seven patients with the symptoms of the monkeypox infection who came to the STD outpatient clinic of the City Institute for Skin and Venereal Diseases in Belgrade and who were referred to the Clinic for Infectious Diseases of the Clinical Center of Serbia, where the monkeypox virus was diagnosed by PCR (Polymerase chain reaction) tests on swabs taken from skin lesions and pharynx. All patients filled out the anonymous questionnaire relating to their sexual behavior during the last month before the symptoms appeared (type of sexual relation, sexual orientation, sexual relations abroad), current symptoms and HIV status. Serological tests for syphilis were done for all patients (VDRL – Venereal Disease Research Laboratory; TPHA – Treponema Pallidum Haemagglutination Assay). Only initial skin manifestations of patients, who were treated according to the recommendations of infectious disease specialist after the diagnosis was confirmed and who were referred to home/hospital isolation, were presented in this paper.

The characteristics of patients and clinical manifestations of monkeypox infection are presented in Table 1. The average age of patients was 35.8 years (the youngest patient was 26, while the oldest was 44) and they were all men who have sex with men, three patients were HIV positive and the infection was transmitted via oral and/or anal sexual intercourse. Three persons were infected abroad (one in Germany, second in Austria and third in Greece), while four were infected in Belgrade. In most cases incubation lasted less than a week, and prodromal signs were absent. Fever and mild weakness were dominant in patients with prodromal signs. Skin lesions most

frequently appeared on the penis in the form of white umbilicated papules (Figure 1), disseminated pustules (Figure 2) and crusted lesions (Figure 3). Lesions in the perigenital region were in the form of numerous papulopustular lesions surrounded by an erythematous halo (Figure 4), while pustules were dominant in patients with gluteal lesions (Figure 5). In two patients, skin lesions were accompanied by painful and itchy sensation. Serological tests for syphilis showed that none of the patients had a recent infection, but that three of them had a positive TPHA test due to the previously treated syphilis.

Discussion

Data from Europe on the outbreak of MPX show that the largest number of registered cases have been reported in Spain, Great Britain,

Table 1. Some selected characteristics of cases and clinical manifestations of monkeypox infection

Characteristics:	Number (N)=7
Age (average):	35.8 years
Sexual orientation:	
Homosexual	7
Heterosexual	0
HIV status:	
Negative	4
Positive	3
Serological test for syphilis:	
Negative	4
Positive*	3
Type of sexual practice	
Oral sex	2
Anal sex	3
Oral and anal sex	2
Incubation period:	
≤ 7 days	4
8 - 14 days	3
Prodromal signs:	
Present	3
Absent	4
Localization of lesions:	
Only on penis	5
Perigenital region	1
Perianal region	1
Dominant skin lesion:	
Papule	3
Pustule	3
Crust	1

* Positive test due to the previously treated syphilis



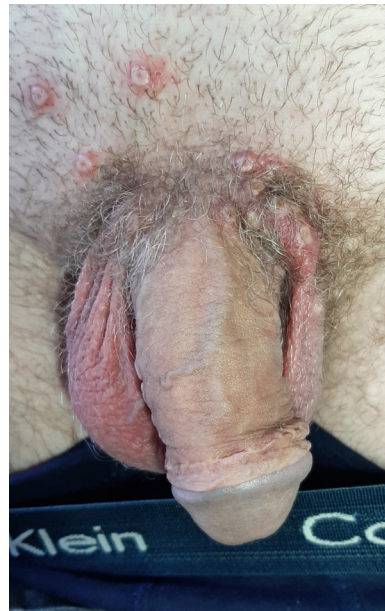
Slika 1. Beličaste papule sa centralnom umbilikacijom na glansu i telu penisa



Slika 3. Krustozne lezije na telu penisa



Slika 2. Brojne jasno ograničene pustulozne lezije na telu penisa



Slika 4. Brojne papulopustulozne lezije u perigenitalnoj regiji okružene eritematoznim haloom



Slika 5. Pustulozna ospa u predelu gluteusa



Figure 1. White papules with central umbilication on the glans and the shaft of the penis



Figure 3. Crusted lesions on the shaft of the penis



Figure 2. Multiple well circumscribed pustular rash on the shaft of the penis

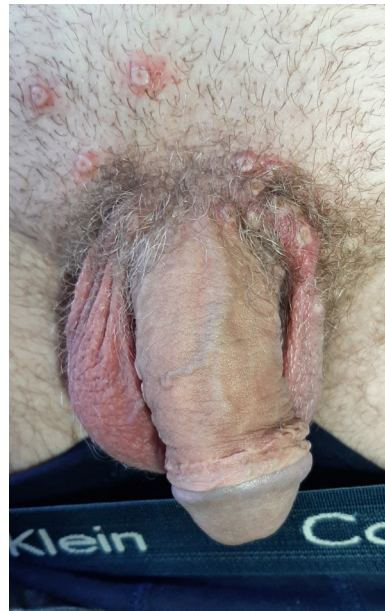


Figure 4. Multiple papulopustular lesions on the perigenital regions surrounded by an erythematous halo



Figure 5. Pustular rash on the gluteal region

uzrasta od 31 do 40 godina, da 37% obolelih ima HIV-koinfekciju, da je kod 94,7% obolelih prisutan osip na koži, a da su opšti simptomi poput povišene temperature, slabosti, bolova u mišićima ili glavobolje prisutni kod 67% slučajeva (5). I u našem radu svi oboleli su bili muškarci, prosečnog uzrasta 35,8 godina, a skoro polovina je imala HIV-koinfekciju. S obzirom na to da da opisujemo samo kliničku sliku prilikom prvog obraćanja obolelih zdravstvenoj službi (u ovom slučaju dermatologu), svi naši pacijenti su imali kožni osip.

Tipična slika majmunskih boginja je praćena pojavom febrilnog prodroma sa limfadenopatijom koji se javlja u proseku od 5 do 13 dana nakon infekcije, a njega prati kožni osip u vidu jasno ograničenih često umbilikovanih papula, vezikula, pustula i krusti sa centrifugalnom distribucijom, a nekad može biti diseminovan po čitavoj koži (8). Podaci iz Sjedinjenih Američkih Država tokom epidemije malignih boginja ukazuju na sve češću pojavu atipičnog osipa u ano-genitalnoj regiji, bez prethodnog prodromalnog stadijuma i opštih simptoma što može izazvati sumnju da se radi o *varicella-zoster* infekciji ili nekoj polno prenosivoj bolesti (9). U našoj studiji prodromalna faza je bila prisutna u manje od polovine obolelih, a sve inicijalne lezije su bile lokalizovane u genitalnoj ili perianalnoj regiji i bile su polimorfnog karaktera (umbilikovane papule, pustule ili kruste), ali kod svakog pacijenta su zabeležene promene u istoj evolutivnoj fazi (identične papularne ili pustulozne ili krustozne lezije) što je karakteristično za majmunske boginje (9). Lokacija ospe kod naših obolelih upućuje na direktan seksualni put prenošenja infekcije jer su kožne promene u svim fazama majmunskih boginja kontagiozne. Svi naši pacijenti su pripadali populaciji muškaraca koji imaju seksualne odnose sa muškarcima kod kojih su polne bolesti poput sifilisa i HIV infekcije u našoj zemlji češće (10), te ne čudi što je kod tri pacijenta bio pozitivan serološki test na sifilis koji ukazuje da su oni već bili lečeni od ove infekcije. Prva tri pacijenta su se inficirala tokom seksualnih odnosa u inostranstvu, a ostali u Beogradu što upućuje na to da je virus sve više prisutan i u našoj sredini, te dolazi do lokalne transmisije naročito u populaciji pod rizikom za polno prenosive infekcije. Iako je veći broj inficiranih u inicijalnoj fazi pandemije zabeležen među muškarcima koji imaju seksualne odnose sa muškarcima (5,9), ova infekcija nije ograničena ni na jednu populacionu grupu jer se

bolest prenosi bliskim fizičkim kontaktom sa inficiranim, te se svako može zaraziti.

U diferencijalnoj dijagnozi majmunskih boginja kod kojih su inicijalne promene u anogenitalnoj regiji u obzir dolaze polno prenosive infekcije poput ranog sifilisa (primarni i sekundarni stadijum), genitalnog herpesa, šankroida i *molluscum contagiosum* infekcije, ili, pak, infekcije izazvane *varicella-zoster* virusom (ovčije boginje i herpes zoster) stoga dermatolozi predstavljaju važnu kariku u ranoj dijagnostici ove bolesti.

Zaključak

Dermatolozi bi trebalo da budu posebno senzibilisani na prisustvo ovog oboljenja i u našoj sredini, da rano posumnjaju, upute pacijenta na laboratorijsku dijagnostiku i evaluaciju infektologu, a da pacijentu savetuju izolaciju zbog kontagioznosti oboljenja i seksualnu apstinenciju jer iako ne pripada u klasične polno prenosive infekcije, može se preneti i seksualnim putem.

Konflikt interesa

Autor je izjavio da nema konflikta interesa.

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Germany and France, and that the majority of them are males (99.4%), aged 31-40 years, while 37% of patients have HIV-coinfection, and that 94.7% of patients have skin rash, while general symptoms such as fever, feebleness, muscle ache or headache are present in 67% of cases (5). Also, in our study all patients were men, aged 35.8 years on average, and almost half of them had HIV-coinfection. Considering the fact that we have described only the clinical presentation during the first visit to the healthcare service (in this case a dermatologist), all our patients had skin rash.

A typical presentation of MPX is accompanied by febrile prodrome with lymphadenopathy, which appears on average 5 to 13 days after exposure, and it is followed by the skin rash in the form of clearly circumscribed papules that often umbilicate, vesicles, pustules and crusts with a centrifugal distribution, while sometimes it can be disseminated across the entire skin (8). Data from the United States of America during the outbreak of MPX have pointed to the atypical rash in the ano-genital region, without the previous prodromal period and general symptoms and therefore, *varicella zoster* infection or other sexually-transmitted diseases may be suspected (9). In our study, the prodromal period was present in less than half of patients, while initial lesions were localized in the genital or perianal region and they were polymorphic (umbilicated papules, pustules and crusts), but in each patient lesions were registered in the same evolution stage (identical papular or pustular or crusted lesions), which is characteristic of MPX (9). The location of rash in our patients indicates a direct sexual way of transmission because skin lesions are contagious in all stages of MPX. All our patients belong to the population of men who have sex with men, in whom venereal diseases such as syphilis and HIV are more frequent in our country (10), and therefore, it is not surprising that in three patients, serological test for syphilis was positive which indicates that they were previously treated due to this infection. Three patients were infected abroad during sexual intercourse, whereas other patients were infected in Belgrade, which points to the fact that the virus is increasingly present in our country, so there comes to the local transmission, especially in the population at risk of sexually-transmitted infections. Although a large number of cases in the initial phase of the pandemic was

reported among men who have sex with men (5, 9), this infection has not been limited to particular population groups because it is transmitted by close physical contact with the infected person, so everybody can get exposed.

In a differential diagnosis of MPX when the initial changes are in the ano-genital region, sexually-transmitted diseases may be taken into consideration, such as early syphilis (primary and secondary stage), genital herpes, chancroid and *molluscum contagiosum* infections, or infections caused by the *varicella zoster* virus (varicella and herpes zoster). Therefore, dermatologists are an important link in the chain of early diagnostics of this disease.

Conclusion

Dermatologists should be particularly sensitized to the presence of this disease in our country, they should suspect it early on, refer the patient to laboratory diagnostics and evaluation by an infectious disease specialist, and advise patients to isolate due to the contagiousness of this disease and abstain from sex because this disease can be transmitted during sexual intercourse although it does not belong to sexually-transmitted diseases in the classic sense.

Competing interests

The author declares no competing interests.

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