



A nephrology viewpoint on human monkeypox; a mini-review to current knowledge and new concepts

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Abstract

Monkeypox is a common disease between humans and animals. The cause of this disease is a member of the Poxviridae family. The transmission of this disease is mostly through aerosol, direct contact and insect bites. Monkeypox has different symptoms; its skin lesions are papules then; they progress toward vesicles and finally create classic pock lesions. The duration of lesions are 4 to 14 days and they are usually seen on hands, feet and face. This disease can cause fever, lymphadenopathy, encephalitis and keratitis. Thus, monkeypox in the course of its development involves several organs. Due to the limited number of studies conducted on this virus, we designed this study to investigate signs, symptoms and effect of monkeypox virus on kidneys and compare with other similar viruses such as other genera of *Orthopoxvirus* and varicella-zoster.

Keywords: Acute tubular necrosis, Monkeypox

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Introduction

Monkeypox is a viral disease common among humans and animals (1). Several people around the world have contracted the disease. The virus appears to be transmitted through aerosols, although direct contact and insect bites are more common and more likely to spread. Monkeypox virus is a member of Poxviridae family, *Chordopoxvirinae* subfamily, and is a genus of *Orthopoxvirus*. This genus includes variola (smallpox virus), vaccinia, and cowpox virus (2).

The first monkeypox outbreak was confirmed in 1959 Copenhagen of Denmark as a pox-like disease in monkeys (3). On 1 September 1970, the first human involvement of monkeypox observed in Congo. Between October 1970 and May 1971, six other cases of monkey pox were reported. Several thousands of monkeypox involvement have been reported in 15 countries until now (4).

Method of search

A search query was conducted through available international databases, including PubMed and Google Scholar. We searched the following keywords: acute tubular necrosis, monkeypox.

Clinical manifestation

The incubation period of monkeypox virus is computed

within 4 to 21 days. In this period, prodromal signs including fever, myalgia, malaise, pharyngitis, lymphadenopathy and back pain appear. After prodromal phase, exanthema phase appears with vesiculopustular lesions within 1 to 10 days. Lesions are pea-sized, monomorphic and similar with smallpox (5). Skin lesions are papules containing proliferative acanthocytes, which progress towards vesicles and then undergo umbilication, which finally creates classic pock lesions. The duration of skin lesions is usually within 4 to 14 days, and they are usually seen on the hands, feet, and face. Lung lesions are similar to skin lesions, but they also have hemorrhagic necrosis (2).

Bronchopneumonia, respiratory distress, encephalitis, keratitis, corneal infection with vision lost, secondary bacterial infection and gastrointestinal involvement have been reported in monkey pox (6).

Therefore, it can involve several organs in its progression. Due to the limited researches on this virus, we conducted this study to investigate other similar viruses such as other genera of *Orthopoxvirus* and varicella-zoster and infer issues with the monkey poxvirus especially on kidneys.

Kidney involvement following monkeypox

In a study which designed by Thornhill and colleagues from April to June 2022 across 16 countries on 528 cases,

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■ Implication for health policy/practice/research/medical education

Current case reports and the studies on the viruses similar to monkeypox show kidney involvement in this disease, is mostly acute tubular necrosis; however, this hypothesis requires more extensive studies.

there are two cases of hospitalization due to acute kidney injury and also no death reported from kidneys injury (7). In another study on varicella-zoster, the investigated case was a 34-year-old man with no history of specific diseases, suffering from varicella-zoster infection, who presented with fatigue and mild fever and symptoms of upper respiratory infection and had a skin rash four days before the admission. It was in the form of maculopapules and vesicles with an erythematous background, which first appeared on the head and ears, and then extended throughout the body and organs. The patient had severe cough and shortness of breath, serum creatinine on arrival was 0.8 mg/dL, blood urea nitrogen (BUN) was 8 mg/dL. In urine analysis, RBC was 10^{-8} and the quantity of proteinuria was within normal range. During hospitalization, serum creatinine increased up to 4.4 mg/dL then returned to the normal state after 12 days (8).

Acute renal failure in severe varicella-zoster in adults has already been detected. The connection between nephritis and varicella-zoster dates back to the year 1884, when Henocho examined four cases of nephritis in children with chickenpox, which had proteinuria, they had hematuria and edema three to eleven days following the skin rash (8).

In another study in 1921, 52 cases of acute nephritis related to chickenpox were investigated.

Likewise, in another study, one-tenth percent of 2534 patients with varicella-zoster had kidney problems (8), while the kidney disturbance appears after skin manifestations in patients (8).

Renal pathology following monkeypox

There is no extensive study on histopathological kidney samples of monkeypox patients. Due to its very similar appearance to chickenpox and the fact that both are viral infections that can affect different organs, we explain histopathological results of several cases from kidney biopsies and autopsies. We also reviewed a study that investigated monkeypox infection in rope squirrels.

A previous study reported a 16-year-old boy from India who referred to a medical center due to pre-orbital edema, edema of both legs, and oliguria, with a history of chickenpox 15 days prior to the visit. Upon admission, the patient's creatinine was 1.4 mg/dL and the patient's urea was 151 mg/dL. In the urine test, the patient had proteinuria +4 and a large number of red blood cells, also C-reactive protein (CRP) increased and serum C3 level decreased, but C4 was normal.

Abdominal ultrasound showed attenuated corticomedullary differentiation in both kidneys, in the

histopathological examination of the kidney biopsy, it was diffuse thickening and mesangial hypercellularity, splitting of the basement membrane with endocapillary and mild neutrophilic infiltration, which finally revealed a membranoproliferative glomerulonephritis suggested for this patient (9).

Additionally, a previous study, addressed a 59-year-old man diagnosed with varicella-zoster who was admitted to the hospital. During the first two days, the patient's urinary output decreased from 1500 mL/d to 500 mL/d. In the ultrasound examination, the size of the kidneys was normal and there was no evidence of obstruction. The patient was diagnosed with acute kidney failure. In the examination of the kidney biopsy, 10 glomeruli were examined, which did not have significant glomerular changes. He also had acute tubular necrosis in the examination of the electron microscopy. During the next 18 days, kidney function slowly returned to normal (10).

Here we also present another case report concerning, a 68-year-old woman with systemic blisters. This patient was diagnosed with nephrotic syndrome and cryoglobulinemic vasculitis three years prior to this admission. The patient was administered daily prednisolone and the proteinuria was controlled. Tzanck test was positive, and the patient was diagnosed with varicella-zoster. In the urine test, the patient had recent hematuria and proteinuria. The patient died after 24 days of hospitalization. In the autopsy of the kidneys, acute tubular necrosis was observed along with destructive glomerular lesions. Finally, in the autopsy of this patient, microabscess and necrosis due to varicella-zoster infection were shown in all organs, including the kidneys (11).

Falendysz et al investigated monkeypox infection on African rope squirrels. They found, in addition to epidermal and pulmonary lesions, which are typical, kidney lesions were also common in this disease and several cases in histopathological investigations showed renal tubular degeneration and multiple foci of perivascular lymphoid and plasmacytic inflammation in the region of the kidney pelvis and cortex (12).

Conclusion

This mini-review showed cases of renal involvement following monkeypox virus are very limited and our information in this field is incomplete. However, the study on African rope squirrels showed that renal lesions were also common. According to the study by Thornhill et al, two patients out of 528 hospitalized for acute kidney injury. Due to the studies conducted on the viruses similar to monkeypox and their effect on the kidney, as well as limited studies regarding the involvement of the kidney organ in the monkeypox virus, there is a possibility of kidney involvement in this disease, mostly acute tubular necrosis; however, this hypothesis requires more extensive studies.

Authors' contribution

Conceptualization, methodology, research, writing—original draft preparation, project management: SY and PS.

Resources: SY.

Data curation, visualization, supervision: EM.

Writing—reviewing and editing: EM and HRJ.

Conflicts of interest

SY, PS and EM was the researchers at Nickan Research Institute, however the process of peer-review was conducted like others.

Ethical issues

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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