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A Case of Hantavirus Renal Syndrome Detected in the COVID-19 Pandemic

COVID-19 Pandemisinde Saptanan Hantavirüs Renal Sendrom Olgusu

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ABSTRACT

Hantaviruses are enveloped RNA viruses in the Bunyaviridae family that cause rodent-borne zoonotic infections. They cause two separate diseases, hemorrhagic fever with renal syndrome (HFRS) and hantavirus cardiopulmonary syndrome (HCPS), as a result of transmission to humans through contact with rodent excrements and inhalation. The form seen more common in Türkiye is HFRS, which progresses with acute kidney injury and thrombocytopenia. Coronavirus disease 2019 (COVID-19) is an infectious disease that ranges from asymptomatic infection to pneumonia, respiratory failure, and death. Because of symptoms such as fever, weakness, and flu-like clinical findings in the early days, it can be confused with many infectious diseases. In this case report, a case of hantavirus renal syndrome admitted with fever, weakness, and flu-like symptoms during the COVID-19 pandemic was presented.
Keywords: COVID-19; hantavirus; thrombocytopenia.

ÖZ

Hantavirüsler Bunyaviridae ailesi içinde yer alan, kemirgen kaynaklı zoonotik enfeksiyonlara yol açan zarflı RNA virüsleridir. Kemirgen dışkıları ile temas ve solunum yoluyla insanlara bulaş sonucu renal sendrom ile seyreden kanamalı ateş (RSKA) ve hantavirüs kardiyopulmoner sendrom (HKPS) olmak üzere iki ayrı hastalığa yol açmaktadırlar. Türkiye'de daha çok görülen formu akut böbrek yetmezliği ve trombositopeni ile seyreden RSKA tablosudur. Koronavirüs hastalığı 2019 (coronavirus disease 2019, COVID-19) ise asemptomatik enfeksiyondan pnömoniye, solunum yetmezliğine ve ölüme kadar değişen klinik tablolara yol açan bir enfeksiyon hastalığıdır. Hastalık özellikle erken dönemde neden olduğu ateş, halsizlik, gribe benzer klinik bulgular gibi belirtiler nedeniyle birçok bulaşıcı hastalık ile karıştırılabilmektedir. Bu olgu sunumunda, COVID-19 pandemisi sırasında ateş, halsizlik ve grip benzeri klinik bulgular ile hastaneye başvuran bir hantavirüs renal sendrom olgusu sunulmuştur.
Anahtar kelimeler: COVID-19; hantavirüs; trombositopeni.

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INTRODUCTION

Viral hemorrhagic fevers are zoonotic infections that progress with fever and bleeding and are transmitted to humans mostly by ticks, mosquitoes, and rodents (1). Hantaviruses are enveloped RNA viruses that belong to the Bunyaviridae family and cause viral hemorrhagic fever. It is transmitted to humans mainly by contact with

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body exudates and secretions of infected rodents, and by inhalation (2). In addition, more rarely, it can be transmitted as a result of a rodent bite. Except for hantavirus pulmonary syndrome (HPS), which is caused by the Andes subtype, it is not transmitted from person to person by contact (3). While hantaviruses cause asymptomatic chronic infection in rodents, they occur in humans with two clinical manifestations characterized by fever with renal hemorrhage and pulmonary syndrome (4). However, nonspecific symptoms such as fever, and malaise in the prodrome stage of the disease before the present picture develops create a clinical similarity with the early stages of many diseases. In this report, a case that was initially followed up as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and then diagnosed with hemorrhagic fever with renal syndrome (HFRS) during the coronavirus disease 2019 (COVID-19) pandemic was presented.

CASE REPORT

A 57-year-old male patient with no known disease was admitted to an external clinical center with fever and flu symptoms five days ago. A COVID-19 polymerase chain reaction (PCR) sample was taken and symptomatic treatment was prescribed. He was admitted to the emergency room of our hospital with complaints of fever, fatigue, and abdominal pain. At the time of admission, body temperature was 38.5 ºC, heart rate was 118/min, arterial blood pressure was 120/75 mmHg, respiratory rate was 18/min, and other system examinations were normal. In laboratory tests, white blood cell (WBC) 11500/uL, neutrophil 7500/uL, platelet (PLT) 53000/uL, C-reactive protein (CRP) 11 mg/dL (0-0.5), urea 112 mg/dL, creatine 3.5 mg/dL, aminotransferase (ALT) 11 IU/L, aspartate aminotransferase (AST) 21 IU/L. The patient resides in the Yigilca district of Düzce, where there was a previous hantavirus epidemic, a history of going to the forest and drinking water in the forest 15 days ago. He was hospitalized with the preliminary diagnoses of hantavirus and leptospirosis. Hantavirus IgM, IgG, and leptospira PCR tests were requested. Methylprednisolone 80 mg 1x1 was started with the recommendation of internal medicine in the patient with urea 162 mg/dL, creatinine 9.1 mg/dL, and no urine output in the follow-ups, and the patient was taken to hemodialysis. Urea and creatinine values decreased after dialysis. After the results of leptospira PCR negative, hantavirus IgM (IFA) intermediate value and IgG (IFA) negative, the control hantavirus IgM and IgG antibodies studied one week later were both positive and hantavirus renal syndrome was diagnosed. During the follow-ups, the patient did not need dialysis, the patient in the polyuric phase was followed up with hydration and supportive treatment, the methylprednisolone dose was tapered off, and the patient was discharged on the 12th day of his hospitalization, whose symptoms and laboratory findings improved, and urea and creatinine values returned to normal.

DISCUSSION

The annual incidence of HFRS in the world is between 60 and 150 thousand and 90% of them are reported from China, Korea, and Russia. Almost 90% of the cases in Europe are reported from Scandinavian countries (Finland, Sweden, Norway). The presence of hantaviruses in wildlife rodents in Türkiye was first reported in a field study published in 2004. In a study conducted in Bartın, hantavirus seroprevalence was found to be 5.2%, and in a study conducted in Giresun, it was 3.2% (5).

While hantaviruses cause chronic asymptomatic infection in rodents, they cause two types of disease in humans. The incubation period of the HFRS form is 1-3 weeks, and there are five periods in the course of the disease: the febrile period, the hypotensive period, the oliguric period, the polyuric period, and the convalescent period. Fever, fatigue, and abdominal pain are the initial clinical findings. Although not all patients need dialysis, renal failure does not become chronic in patients who recover (6). Urea and creatinine elevation, thrombocytopenia, proteinuria, and hematuria are frequently detected in laboratory findings. In addition, high CRP values and leukocytosis, which are seen in many infectious diseases, can also accompany the disease (7). In our case, the disease started with prodromal complaints such as fever and malaise, followed by the need for hemodialysis as a result of increased urea and creatinine, followed by a polyuric period and recovery.

The incubation period in HCPS is between 2-3 weeks and there are four phases of the disease: the febrile/prodromal phase, the cardiopulmonary phase, the oliguric and diuretic phase, and the convalescent phase. The febrile period is characterized by fever, chills, and muscle pain. Increased pulmonary capillary permeability in the cardiopulmonary period leads to a decrease in cardiac output, acute respiratory distress syndrome (ARDS), and shock. This phase is also manifested by pulmonary edema, arrhythmias, and coagulopathy.

As with many viral infections, the diagnosis of hantavirus infection is made by serological tests and molecular tests. Demonstration of IgM-type antibodies in the serum in the acute phase of the disease or detection of at least a 4-fold increase in IgG titer in two separate serum samples taken during the acute and convalescence period is sufficient for the diagnosis of hantavirus infection. Another method is the detection of hantavirus RNA in serum and urine by reverse transcription-PCR (RT-PCR). The diagnosis of the presented case was made with positive results for hantavirus IgG and IgM (IFA) antibodies in the serum during the oliguric period.

The first human hantavirus epidemic confirmed clinically and serologically in Türkiye was detected in February 2009 in the Zonguldak-Bartin. 25 suspected cases were seen, 12 of them serologically detected Puumala virus (PUUV) subtype (7). Subsequently, two cases residing in Giresun, one of which was mortal, were reported, and the Dobrova virus (DOBV) subtype was found serologically in them (8). Finally, a hantavirus epidemic was observed in Düzce in April 2017, and the diagnosis of hantavirus was confirmed serologically in 20 of 50 suspected patients. While the PUUV subtype was detected in 18 of the patients, the subtype could not be determined in 2 patients. Of the 20 patients who were followed up with hantavirus positivity, 17 were living in the Yigilca district, which is defined as the hantavirus region, and the other three were living in neighboring districts. Except for one patient who died as a result of ARDS and cardiac arrest without renal involvement, the other patients were followed up with the diagnosis of HFRS and five patients (25%) received hemodialysis (9).

The present case is from the Yigilca district in April 2021 during the COVID-19 pandemic. The Yigilca is a region suitable for hantavirus infections due to its proximity to forests and habitats and the widespread spring water use. There are forest workers, farmers, and beekeepers in the risk groups for this disease. The presented case stated that he lived in a detached house in the countryside in the shade of the forest and drank the spring water from the forest.

Currently, there is no effective antiviral treatment for the hantavirus. However, in various studies, ribavirin treatment has been shown to reduce mortality (3). In hantavirus infections, treatment is limited to supportive treatment, and dialysis and platelet transfusion are applied when necessary. In this case, no antiviral treatment was applied for the hantavirus. Hydration and methylprednisolone therapy were used as supportive treatments. Hemodialysis was applied as a result of the patient's lack of urine output and increased creatinine. The patient, who entered the polyuric phase, did not need dialysis after the urea and creatinine values returned to normal.

Three hantavirus infections diagnosed in the COVID-19 pandemic have been reported in the literature (10-12). All cases are cardiopulmonary syndrome. All reported cases had a fever, thrombocytopenia, and bilateral pulmonary infiltration. And the history of hospitalization due to respiratory deterioration. While two cases were extruded after intubation and discharged, one case was fatal. The case reported from Argentina initially presented with headache and myalgia, and the SARS-CoV-2 PCR test was positive. In all of the cases, hantavirus tests were requested as a result of living in the endemic region, traveling to the endemic region, and learning about mouse contact in the detailed histories of the patients. While the diagnosis was made by serological methods in two cases, the diagnosis was confirmed by PCR in the mortal case. The present case was admitted with nonspecific symptoms such as fever, headache, and myalgia and was initially diagnosed with COVID-19. The patient had a negative SARS-CoV-2 PCR result and was tested for hantavirus at the first visit because he had thrombocytopenia and high creatinine and lived in the region where hantavirus is endemic. The patient with a positive hantavirus IgM, IgG test was diagnosed with hantavirus renal syndrome.

The present case is important in that it was first diagnosed as COVID-19 infection due to the pandemic period, and then diagnosed with a detailed history and clinical experience. Hantavirus infections should be kept in mind in the differential diagnosis of patients who live in or have a history of travel to the endemic region and present with fever, acute renal failure, and thrombocytopenia.

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