

CASE REPORT

Two cases of Hantavirus infection in Crimean-Congo Haemorrhagic Fever endemic region

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ABSTRACT

Crimean-Congo Hemorrhagic Fever (CCHF) and Leptospirosis are endemic in our region. Hantavirus infections may be confused with similar clinical picture zoonotic infections. Two patients with fever, malaise, cough, phlegm, nausea, vomiting, thrombocytopenia, renal failure, elevated transaminases, and a history of mouse contact were hospitalized in our clinic with a presumptive diagnosis of leptospirosis, pneumonia, CCHF and Hantavirus infections. Empirical antibiotic treatment was initiated and CCHF and leptospirosis was ruled out with laboratory tests. Hantavirus immunoglobulin (Ig)-G and Ig-M antibodies were detected positive by immunofluorescent antibody (IFA) method in both cases but, Dobrova virus was detected in only one patient with immunoblotting methods. Both patients were discharged after treatment. Hantavirus infections may be misdiagnosed as zoonotic infections since they have similar clinical picture. It should be considered in the differential diagnosis of patients with a history of contact with mouse. *J Microbiol Infect Dis* 2012; 2(3): 117-120

Key words: Hantavirus, hemorrhagic fever, renal syndrome, pulmonary syndrome

Kırım-Kongo Kanamalı ateşinin endemik olduğu bölgede iki Hantavirus enfeksiyonu olgusu

ÖZET

Kırım-Kongo Kanamalı Ateş (KKKA) ve leptospirosis bizim bölgemizde endemiktir. Hantavirus enfeksiyonlarını özellikle endemik bölgelerde bu hastalıklardan ayırt etmek kolay değildir. Çünkü semptomlar çok benzerdir. Ateş, halsizlik, öksürük, balgam çıkarma, bulantı, kusma, böbrek yetmezliği, transaminaz yüksekliği ve fare temas öyküsü olan iki hasta leptospiroz, pnömoni, KKKA ve Hantavirus enfeksiyonu ön tanılarıyla kliniğimizde hospitalize edildi. Ampirik antibiyotik tedavisi başlandı. KKKA ve leptospirosis laboratuvar testleri ile dışlandı. Hastalardan her ikisinde immünofluoresans antikor (IFA) ile immünglobulin (Ig)G ve IgM pozitifliği tespit edildi ancak sadece bir hastada immunoblotting metodu ile Dobrova virus saptandı.

Hantavirus enfeksiyonları benzer klinik tabloya sahip zoonotik enfeksiyonlarla karışabilir. Fare ile temas öyküsü olan hastalarda ayırıcı tanıda düşünülmalıdır.

Anahtar kelimeler: Hantavirus, viral kanamalı ateş, Hantavirus renal sendrom, Hantavirus pulmoner sendrom

INTRODUCTION

Hantaviruses cause two clinical pictures in humans: Hemorrhagic fever with renal syndrome (HFRS) and Hantavirus pulmonary syndrome (HPS).¹ Hantaviruses belong to the Bunyaviridae family of viruses (genus Hantavirus). The first Hantavirus was isolated in 1976.² Worldwide, approximately 150-200,000 patients/year

were hospitalized due to HFRS.¹ Crimean-Congo Hemorrhagic Fever (CCHF) and Leptospirosis are endemic in the Central Black Sea Region.³ A recent (January-May 2009) HFRS epidemic was reported from Zonguldak province⁴ and nearby towns and two HFRS cases were reported from Giresun.⁵ Two hemorrhagic fever cases with renal and pulmonary syndrome from the Ordu province are presented here.

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Case 1

A 57-year-old male farmer who lives in a garden house in a village that belongs to Ordu province was admitted to the Emergency Clinic of our hospital with the complaints of fever, malaise, chills, cold, cough, phlegm, nausea, and vomiting for five days. He has been working in a hazelnut garden 18 days before the symptoms onset and he noted that mice were living around his house. Physical examination: fever: 38.1°C; pulse: 98/minute; rate of respiration: 22/minute; arterial tension: 110/60 mmHg; oropharynx was hyperemic; one lymphadenopathy (1x1 cm diameter) was present at the right cervical region; and rales at the right basal of the lungs were found during auscultation. A P/A chest X-ray showed right paracardiac infiltration. Laboratory analysis showed: thrombocytopenia, elevated transaminases, proteinuria, and signs of acute renal failure (Table 1). The patient was hospitalized with a presumptive diagnosis of leptospirosis, pneumonia, and HFRS. Empirical therapy using ceftriaxone 2000 mg per day intravenously in two doses and clarithromycin 500 mg per day iv in two doses was initiated. At Refik Saydam Hygiene Center Presidency, Epidemic Diseases, Virology Reference and Research Laboratory, the following findings were identified by IFA test technique: IgM (+++) positive in the first serum sample, IgG (middle zone), IgM (+) and IgG (+++) positive in the control serum sample, which was obtained 10 days after the onset of the symptoms. Dobrova virus was positive with the immunoblotting method. At the sixth day of the treatment, thrombocytopenia and elevated aspartat aminotransferase (AST) were improved, and at the 10th day of the treatment, hypoalbuminemia was improved. The patient had acute renal failure; however, the serum creatinine levels were elevated to 4.4 mg/dL at the third day of the hospitalization, but it improved by hydration at the 10th day without hemodialysis. His body temperature fell to normal levels on the fourth admission day. Any platelet suspensions and albumin replacements are needed. Ceftriaxone and clarithromycin therapy which were given for pneumonia were completed at the 10th day and the patient was discharged without any complications at the 12th day of the hospitalization.

Case 2

A 70-year-old female farmer and breeder who lives in a village that belongs to Ünye, district,

Ordu, had complaints of fever, chills, cold, abdominal pain, diarrhea, nausea, and vomiting, which began one week before she admitted to our hospital. She was referred to our hospital with the complaints of dyspnea, epistaxis, and chest discomfort developed in the last two days. It is reported that the she has had contact with a mouse 10 days before her complaints, and a tick had been removed from her body during the same period. Physical examination: fever: 37.7°C; pulse: 98/minute; rate of respiration: 26/minute; Arterial tension: 80/40 mmHg; hemorrhagic foci on tongue; bilateral rales at the lower zones of the lungs were found during auscultation. Diffuse alveolar hemorrhage and pulmonary edema were found in the (P/A) chest radiography during admission. The patient had tachycardia and tachypnea, abdominal distention and sensitivity during palpation. The petechial rashes were found in her lower extremities. The acute coronary syndrome and acute abdomen were not considered for the patient. Laboratory parameters: the signs of acute renal failure as well as severe thrombocytopenia, elevated transaminases, and elevated cardiac enzymes were remarkable (Table1). The patient was hospitalized due to presumptive diagnosis of CCHF, Hantavirus infection, leptospirosis, and pneumonia. Empirical therapy using levofloxacin 750 mg per day intravenous was initiated. Nasal intermittent oxygen treatment (4 L/minute) was administrated for dyspnoea. The serum sample was evaluated by IFA technique for Hantavirus infection at Reference Laboratory, and Ig-M and Ig-G antibodies against hantavirus were found to be positive. During the follow-up period, thrombocytopenia and high AST and alanine aminotransferase (ALT), levels were decreased to normal levels at the 4th of day. Elevated creatinine levels were improved by hydration at the second day without hemodialysis. Creatine phosphokinase (CPK) was normal at the third day of the hospitalization. Hyperbilirubinemia was normal at the fifth day. She was afebrile, and tachypnea and tachycardia disappeared at the sixth day. Twelve units of random platelet and 4 units of apheresis platelet suspension were given to the patient during hospitalization. Diffuse alveolar hemorrhage and pulmonary edema improved at the 10th day of the follow-up period. Levofloxacin treatment was completed at the 10th day. The patient was discharged without complications at the 10th day of the treatment.

Table 1. Laboratory parameters of the patients on admission

Parameters (normal limits)	Case 1	Case 2
Leucocytes cells/mm ³ (4,100-11,200)	10,100	10,400
Neutrophils cells/mm ³ (1,800-6,400)	7,600	8,100
Hb concentration g/dl (11.7-15.5)	16.3	10.9
Thrombocytes cells/mm ³ (159,000-388,000)	44,000	6,000
ASTU/L (8-46)	52	531
ALT U/L (7-46)	36	86
Albumin g/dl (3.5-5)	2.59	3.26
LDH U/L (240-480)	946	1937
CK U/L (35-195)	275	2430
CK-MB ng/ml (5-25)	20	>300
C Troponin I ng/mL (0-1)	0	> 50
Creatinine mg/dL (0.4-1.4)	3.54	2
BUN mg/dL (5-24)	52	105
Amylase U/L (28-100)	30	133
Lipase U/L (13-60)	15	112
CRP mg/L (<3.36)	93	109
Proteinuria	Positive	Positive

Hb: Hemoglobin, BUN: Blood urea nitrogen, AST: Aspartat aminotransferase, ALT: Alanine aminotransferase, CK: Creatine phosphokinase, CK-MB: Creatine kinase-myocardial band, LDH: Lactate dehydrogenase, CRP: C-reactive protein.

DISCUSSION

Rodents are the main vectors of Hantaviruses. The transmission route is the bites of the infected animals or skin contact or mucosal contact with the excretions (urine or saliva) of the infected animals, or the inhalation of the contaminated aerosols.⁶ Puumala virus antibody was isolated in four of 65 *Microtus voles* types of rodents living in Black Sea and Aegean regions, three of which were seen in the Black Sea region.⁷

In our region, CCHF and leptospirosis are endemic.^{3,5,7,8} CCHF, Leptospirosis, and Hantavirus infections are difficult to differentiate in the endemic regions. Both of the cases are associated with mouse contact, which indicates Hantavirus infections. The symptoms of such diseases are similar. These similar symptoms are fever, thrombocytopenia, renal failure, and lung symptoms. There is alveolar hemorrhage in CCHF,

and pulmonary edema in Hantavirus infections. However, radiological differentiation of the clinical pictures is difficult. In the first case, the absence of history of tick bite, tends the possibility of CCHF is low.

Our two cases had similar complaints during admission. However, the second case had remarkable tachycardia, tachypnea, hypotension, dyspnea, chest pain, and elevated cardiac enzymes. CCHF was considered as a presumptive because of the existence of alveolar hemorrhage in chest radiography, diffuse petechial lesions secondary to serious thrombocytopenia, and hematuria. Since the CCHF PCR-RNA, and ELISA IgM and IgG were negative in serum samples, the disease was ruled out. The clinical course and laboratory parameters were improved rapidly, unlike with CCHF patients with fever, thrombocytopenia, increased AST, ALT, and CPK, and history of acarid contact. Therefore, Hantavirus infections that cause hemorrhagic fever were supposed. This diagnosis was supported with the rapid improvement of the transaminases and cardiac enzymes when the 12 units of random platelet and 4 units of apheresis platelet suspensions were given, even though the second case had serious thrombocytopenia and alveolar hemorrhage.

Leptospirosis was also considered as a presumptive because of fever, thrombocytopenia, increased creatinine, and the presence of history of mouse contact. *Leptospira*, microscopic agglutination tests and ELISA tests were negative in both cases. In the differential diagnosis, brucellosis and viral hepatitis, which may cause the same signs and laboratory results, were ruled out with several tests.

Thrombocytopenia, leukocytosis, and increased transaminases and creatinine were found in both of the cases. Platelet replacement is required in the serious CCHF cases; however, the need of replacement is less in the Hantavirus infections. Ribavirin was not given to any of the cases. Ribavirin is effective on CCHF virus in vitro, but its use as a treatment is controversial. The randomized-controlled studies are needed to determine its efficacy on the patients. Ribavirin is not recommended for Hantavirus pulmonary syndrome.^{3,8,9}

In conclusion Hantavirus infection can mimic other diseases and it should be considered in the

differential diagnosis of patients with a history of contact with a mouse. Early clinical diagnosis is important for the symptomatic supportive care in Hantavirus infections. The supportive treatment should be initiated before the results of the specific and serologic tests of Hantavirus are taken.

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