



A Rare Cause of Acute Renal Failure and Thrombocytopenia in Child: A Case Due to Hantavirus Infection

Çocuklarda Nadir Akut Böbrek Yetmezliği ve Trombositopeni Nedeni: Hantavirüs Enfeksiyonu Olgusu

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Abstract

17 years old male patient had applied to the primary care center for his complaints; fever, malaise and headache, and was he was investigated for causes thrombocytopenia of after thrombocytopenia had been detected in the workup. He had hyperaemia in oropharynx, 39°C fever, noticeable malaise, thrombocytopenia and renal failure at admittance to our clinic. No atypic cell was seen in peripheral blood smear of the patient. Laboratory tests for parvovirus, cytomegalovirus (CMV), Epstein-Barr virus (EBV), brucella agglutination and gruber widal test and markers for hepatitis were examined and the results were negative. A detailed patient history showed that we had informed that the patient had burned dead mice bodies. Serological investigation showed that IgG and IgM antibodies were positive in both Biot Analysis and indirect immunofluorescence assay (IFA). We observed a hantavirus infection causing haemorrhagic fever with renal syndrome (HFRS) and correspondingly applied symptomatic treatment.

Keywords: Thrombocytopenia, acute renal failure, hantavirus

Öz

On yedi yaşında erkek hasta 3 gündür devam eden ateş, halsizlik ve baş ağrısı şikayeti ile aile hekimliğine başvurmuş ve yapılan tetkiklerinde trombositopeni tespit edilmesi üzerine tarafımıza yönlendirilmiş. Hastanemize başvurduğunda orofarinkste hiperemi, 39°C ateş, belirgin halsizlik, trombositopeni ve böbrek yetmezliği olduğu görüldü. Hastanın periferik kan yaymasında atipik hücre görülmedi. Hastadan parvovirüs, sitomegalovirüs (CMV), Epstein-Barr virüs (EBV), hepatit belirteçleri, brucella aglütinasyon ve Gruber Widal testleri istenildi ve sonuçlar negatif saptandı. Hastadan alınan ayrıntılı anamnezde ölmüş fareleri yaktığı öğrenildi. Hantavirüsün serolojik tetkikinde hem indirekt immünfloresan assay (IFA) hem de Biot Analysis'de IgG ve IgM antikorları pozitif saptandı. Hastada kanamalı ateş ile seyreden akut renal sendroma yol açan hantavirus enfeksiyonu düşünüldü ve sadece semptomatik tedavi uygulandı.

Anahtar Terimler: Trombositopeni, akut böbrek yetmezliği, hantavirüs

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Introduction

Hantavirus is one of the RNA viruses which belongs to the family *Bunyaviridae*, just like Crimean-Congo haemorrhagic fever virus. Although transmission to human is transmitted by arthropods in the other viruses of the family *Bunyaviridae*, hantavirus is differently transmitted to human by rodents (1). In this case; we reported hantavirus infection after getting a detailed patient history and the child had both thrombocytopenia and renal failure at hospital admittance. We want to emphasize hantavirus infection, because we think there might be some overlooked cases who might cause acute renal failure in our region.

Case Report

17 years old male patient, who lived in Yigilca county of Duzce and did gardening in his spare times after school. The patient had applied to the primary care center for his complaints; fever, malaise and headache, and he was investigated for the causes of thrombocytopenia after thrombocytopenia had been detected in the workup (Table 1).

He had hyperaemia in oropharynx, 39°C fever and noticeable malaise was detected at his first physical examination. Other physical examinations were normal. The patient had thrombocytopenia and renal failure at admittance to our clinic (Table 1). The patient was hospitalized for treatment and clinical observation. The patient was followed up with IV hydration therapy. No atypic cell was seen in peripheral blood smear of the patient. Laboratory tests for parvovirus, cytomegalovirus (CMV), Epstein-Barr virus (EBV), brucella agglutination and gruber widal test and markers for hepatitis were examined and the results were negative.

Since fever and renal failure occurred in this case, leptospirosis was considered as a differential diagnosis. But bilirubin levels were not as high as expected in leptospirosis and serological tests were negative, so leptospirosis was excluded.

Thrombocytopenia persisted and progressive increases of serum urea, blood urea nitrogen and creatinine levels were detected on the fifth day of hospitalization (Table 1). The patient was not given a platelet suspension and was not dialyzed. We applied captopril treatment when hypertension was detected in clinical.

Table 1. Laboratory tests of the patient

| Haemogram | 1 st day | 5 th day | At discharge | Reference |
|---|---------------------|---------------------|--------------|-----------|
| Haemoglobin (g/dL) | 12.9 | 12.7 | 12.5 | 8-17 |
| Haematocrit (%) | 38.4 | 36.3 | 36.1 | 26-50 |
| Leucocyte (10 ³ /mm ³) | 2.1 | 5.7 | 5.2 | 3-15 |
| Neutrophil (10 ³ /mm ³) | 1.52 | 3.29 | 2.6 | 1.5-7 |
| Thrombocyte (10 ³ /mm ³) | 54 | 69 | 236 | 150-400 |
| Biochemistry | | | | |
| Ürea (mg/dL) | 23.9 | 82.1 | 34.6 | 13-43 |
| BUN (mg/dL) | 11.38 | 39.1 | 16.48 | 6-20 |
| Creatinine (mg/dL) | 0.88 | 4.5 | 0.99 | 0.7-1.2 |
| Üric Acid (mg/dL) | 4.6 | 8.6 | 7.6 | 3.4-7 |
| ALT (U/L) | 33.3 | 27.2 | 43.6 | 0-41 |
| AST (U/L) | 69.8 | 28.7 | 37.2 | 0-40 |
| CRP (mg/dL) | 2 | 1.11 | 0.19 | 0-0.5 |
| Urinalysis | | | | |
| pH | 6.5 | 6 | 6.5 | |
| Protein | Negative | +++ | Negative | |
| Erythrocyte | +++ | Trace | Negative | |
| Leucocyte | + | Negative | Negative | |
| Spot urine | | | | |
| Creatinine (mg/dL) | | 58.4 | | 39-259 |
| Protein (mg/dL) | | 126.3 | | 0-15 |

BUN: Blood urea nitrogen, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, CRP: C-reactive protein.

A detailed patient history showed that we had informed that the patient was living in a house with a garden, in which mice were living in the garden and the patient had burned dead mice bodies. We found a hantavirus infection causing haemorrhagic fever with renal syndrome (HFRS) because of his physical findings and there were some hantavirus findings detected in the neighbors in the village in which he lived. And we sent blood samples to the Public Health Institution Microbiology Reference Laboratory, National Arbovirus and Viral Zoonotic Diseases unit to investigate hantavirus antibodies. Blood samples were examined by two different procedures; indirect immunofluorescence assay (IFA) and Biot Analysis. IgG and IgM were positive in both procedures. We continued to apply symptomatic treatment to the patient. General condition of the patient was good and serum biochemical analyses were in the normal reference ranges on the 11th day of hospitalization. So then the patient got discharged with full recovery.

Discussion

A disease with 7% mortality rate, which was characterized by acute renal deficiency and shock, was seen in soldiers of United States of America and United Nations in the Korean War between 1951-1953. This situation was thought to be caused by a microorganism that transmitted to the soldiers who were settled in riverside of Hantaan river. The microorganism called Hantaan virus was described by Lee et al. in 1978. Every year 150,000-200,000 patients get hospitalized and diagnosed HFRS all over the World. Hantavirus infection has become a global health issue (1). In our country, the hantavirus infection was firstly detected in Zonguldak-Bartın region in February 2009 (2). Since rodents cause transmission of hantavirus, farmers, villagers, military personnel, campers and people who work in unaided circumstances are the high-risk groups (3).

Consumption of the food contaminated with infected excreta or saliva of rodents, contacting infected water or inhaling the particles of infected excreta or saliva lead to hantavirus infection. Aerosols are the most common reason of transmission from rodent to rodent or from rodent to human (4,5). Hantavirus causes two different diseases in human; more malignant form is hantavirus cardiopulmonary syndrome (HCPS) and the second one is HFRS. HCPS is characterized by acute respiratory failure and high mortality rate (1,2). On the other hand, HFRS may not be but should be taken into consideration if a patient has fever, thrombocytopenia, petechia and acute renal failure (6).

In hantavirus infections, immune system activation causes an increase in vascular permeability which leads to clinical symptoms. Clinical symptoms such as respiratory failure caused by pulmonary edema, oliguric renal failure, hyperten-

sion, hypotension and cardiogenic shock can lead to death (7). Incubation period of HFRS vary between 7-36 days. HFRS has 5 stages, but these stages are not always separable; fever (3-7 days), hypotension (few hours-2 days), oliguria (3-7 days), diuresis (1-2 weeks), convalescence (3-6 weeks) (1,2,6). HFRS disease causes deaths in oliguric stage with a rate of 50% and convalescence stage of this disease can last from days to weeks (6). Fever lasted 3 days before the patient admitted to our clinic, possibly indicated the prodromal stage. Increase in creatinine levels and decrease in amount of urination on 5th day of the hospitalization indicated oliguric stage. The patient improved on the 11th day of hospitalization.

Renal failure is commonly seen in HFRS. Oliguria is detected in 70% of the cases (8). 40% of the patients are being haemodialysed because of acute renal failure (2). Appropriate hydration can prevent patients from haemodialysis (7). Our patient also got well with hydration, without need of haemodialysis.

Laboratory tests may confirm to diagnose HFRS. The increase in serum urea and creatinine levels (starts increasing on 5-6th day, peaks on 9-12th day), leucocytosis, proteinuria, thrombocytopenia and haematuria are common signs of disease (3,9). Firstly, thrombocytopenia occurred in our patient, and creatinine peaked in oliguric stage, then returned to the normal reference range (Figure 1,2). CRP levels may also increase. Most common used tests to diagnose hantavirus infection are serologic tests. IgM and IgG antibodies can be detected in blood samples when symptoms show up. Enzyme linked immunosorbent assays (ELISA), western blot, IFA and strip immunoblot tests (SIA) can be used to detect these antibodies (3,10).

Serum urea-creatinine levels may also increase in leptospirosis, so leptospirosis should be considered as a differential diagnosis in HFRS. Contacting infected excreta or saliva of mice is the most important transmission way for both hantavirus and leptospira infections. Differentiation of epidemiologically and clinically similar two diagnoses is very important. Serological processes are easy and cheap, and commonly used to differentiate these two diseases (10). Since fever and renal failure occurred in this case, leptospirosis was considered as a differential diagnosis. But bilirubin levels were not as high as expected in leptospirosis and serological tests were negative, so leptospirosis was excluded.

Hantavirus infections do not have a specific treatment at the present time. Symptomatic treatments are being applied. The appropriate fluid-electrolyte treatment should be applied for proper tissue and organ perfusion. Renal functions, amount of urination and hydration level of patient should be observed closely. Haemodialysis may be needed in cases

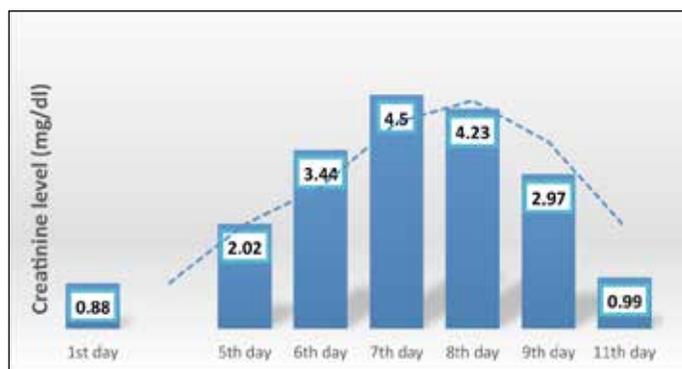


Figure 1. Creatinine change chart for eleven days.

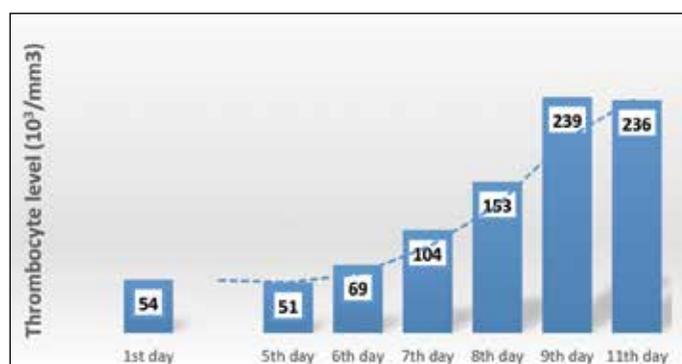


Figure 2. Thrombocyte change chart for eleven days.

of renal failure. Oxygen supply or even mechanical ventilation may be needed in cases of respiratory failure. Thrombocyte transfusion may be administered in case of decreasing of thrombocytopenia (3,7). There is no approved vaccine by world health organization against the infection (3). Interferon alpha treatment and ribavirin were used in China, but there was no specific treatment used in Europe (11). Our patient did not take any antiviral treatment and got well with symptomatic treatment and hydration, without need of haemodialysis.

Hantavirus infections may be mortal and there is no specific antiviral treatment against the infection, so protecting people from this infection is very important. Education of high-risk groups and keeping away from contact with contaminated rodents are fundamentals of avoiding infection (12,13). Considering there are unreported cases in the region in which our patient lived, water resources should be checked and people should be educated about protecting the habitat in endemic regions.

Conclusion

When fever, thrombocytopenia and renal failure occurred together in a patient, hantavirus infection should be considered and the patient should be questioned about professions, travelling to an endemic region, contacting rodents or their

excreta. In case of hantavirus infection is proven in a patient, other people who had similar complaints should be examined. Since there is no specific treatment for the disease, prevention measures should be done. Health workers should be educated about the disease and awareness stages should be updated regularly.

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