Kidney Res Clin Pract 31 (2012) 118–120

Kidney Research and Clinical Practice

journal homepage: http://www.krcp-ksn.com
Contents lists available at ScienceDirect

Case Report

Hemorrhagic fever with renal syndrome and coexisting hantavirus pulmonary syndrome

Young Min Hong, Jin Chang Moon, Hee Chan Yang, Kyung Pyo Kang, Won Kim, Sung Kwang Park, Sik Lee*

Division of Nephrology, Department of Internal Medicine, Research Institute of Clinical Medicine, Chonbuk National University Medical School, Jeonju, Korea

Article history:
Received 15 November 2011
Received in revised form
28 December 2011
Accepted 3 January 2012
Available online 24 April 2012

Keywords:
Hantavirus
Hantavirus pulmonary syndrome
Hemorrhagic fever with renal syndrome
Pulmonary hemorrhage

ABSTRACT

Hemorrhagic fever with renal syndrome (HFRS) is an acute viral disease with fever, hemorrhage and renal failure caused by hantavirus infection. Hantavirus induces HFRS or hantavirus pulmonary syndrome (HPS). HPS progression to a life-threatening pulmonary disease is found primarily in the USA and very rarely in South Korea. Here, we report a case of HFRS and coexisting HPS.

© 2012. The Korean Society of Nephrology. Published by Elsevier. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Introduction

Hantavirus comprises a genus of envelope viruses within the family Bunyaviridae. Infection with hantavirus may induce hemorrhagic fever with renal syndrome (HFRS) or hantavirus pulmonary syndrome (HPS). HFRS is not an uncommon disease in Korea and has several prominent features including fever, hemorrhage, hypotension and renal failure. Hantaan virus, which is usually associated with HFRS in Korea, may lead to more severe HFRS than any other strain [1]. Patients with severe HFRS typically progress sequentially from fever to abrupt hypotension and clinical shock, and then to oliguria. As thrombocytopenia and DIC develop, findings of diffuse hemorrhage may appear. Patients subsequently enter a diuretic phase and then a convalescent phase that often lasts for many weeks. Pulmonary manifestations are prominent finding in HPS and in epidemics in the USA. The mortality rate for patients with severe HFRS has decreased to $<5\%$ with advanced supportive care. However, HPS can progress to a severe degree more frequently than HFRS. To the best of our knowledge, there has only been one published case of HFRS with coexisting HPS in Korea [2]. We report on a 51-year-old man with HFRS and coexisting HPS who completely recovered without complications.

Case report

A 51-year-old man was admitted complaining of fever and petechiae over his entire body. He had visited family graves 10 day before presenting at our clinic. Three days prior to admission, fever, myalgia, chills, and petechiae developed and progressively worsened. He had a history of previous pulmonary tuberculosis, but no history of diabetes mellitus, hypertension, or hepatitis. A physical examination revealed a patient who appeared to be acutely ill, with a flushed face and petechiae over his entire body. He had mild dyspnea and tachypnea. The vital signs on admission were as follows: blood pressure, 100/60 mmHg; body temperature, 37.1 °C; pulse, 85 beats/minute; and respiratory rate, 24/minute. The laboratory findings on admission were as follows: hemoglobin, 10.0 g/dL; white blood cell count, 15.1×10^9/L; platelet count, 12×10^9/L; blood urea nitrogen, 51 mg/dL; creatinine, 4.5 mg/dL; aspartate

* Corresponding author. Department of Internal Medicine, Chonbuk National University Medical School, 634-18, Keum-Am dong, Jeonju, 561-712, Korea.
E-mail address: kidney@jbnu.ac.kr (S Lee).

2211-9132/$ - see front matter © 2012. The Korean Society of Nephrology. Published by Elsevier. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
http://dx.doi.org/10.1016/j.krcp.2012.04.318

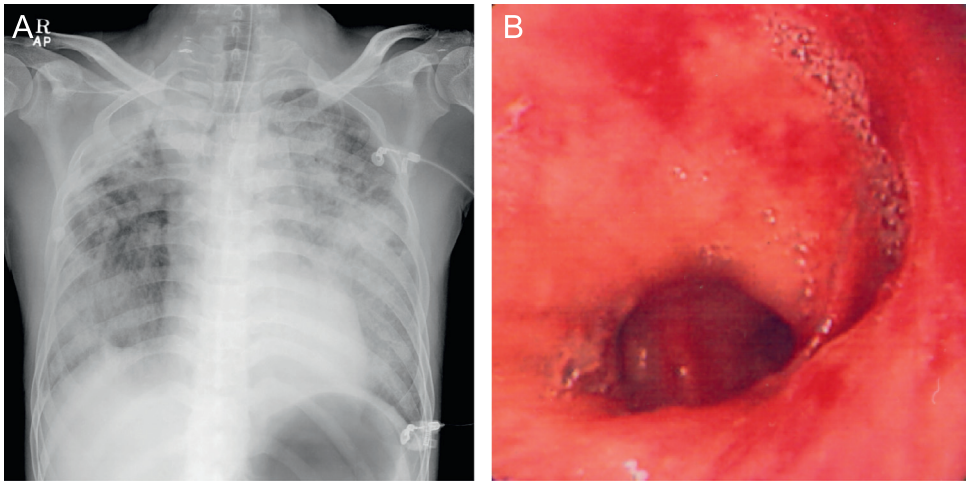

Figure 1. (A) On admission, a chest X-ray revealed pulmonary edema and hemorrhage. (B) Bronchoscopy showed a pulmonary hemorrhage and mucosal swelling in both lungs.

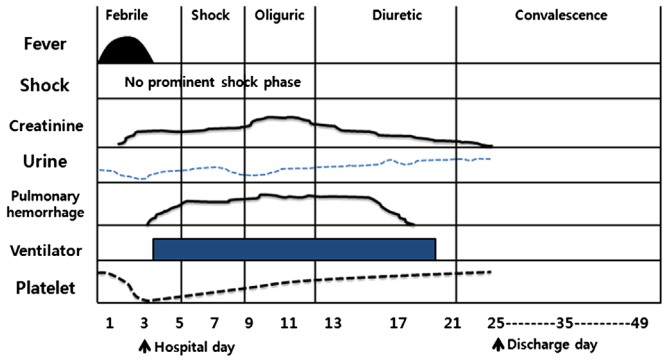

Figure 2. The patient's disease course. Unlike typical HFRS, there was no prominent shock phase and the patient continued to receive ventilatory care, antibiotics, platelet transfusions, and support for disseminated intravascular coagulation as indicated.

transaminase, 952 IU/L; alanine transaminase, 513 IU/L; amylase, 117 IU/L; lipase, 84 IU/L; creatine kinase, 2,155 IU/L; and lactate dehydrogenase, 2614 IU/L. Urinalysis revealed a proteinuria of +3, with five to nine erythrocytes and five to nine leukocytes per high-power field. Serum samples were tested for serodiagnosis of HFRS using an immunofluorescent antibody test (SD Bioline, Korea) for detection of IgG, IgM, and IgA antibodies to the hantavirus genus. Serologic tests were positive for Hantaan virus and negative for leptospirosis and tsutsugamushi. On his second day in hospital, the patient complained of worsening dyspnea with hemoptysis and wheezing in both lung fields. His oxygen saturation decreased to 66% according to pulse oximetry, and he was placed on a ventilator. A chest X-ray and portable bronchoscopy showed pulmonary hemorrhage in both lungs (Fig. 1A and B). The follow-up laboratory findings were suggestive of disseminated intravascular coagulation (DIC), as follows: fibrinogen, 525 mg/dL; fibrin degradation products, 71.9 g/mL; antithrombin III, 69.9%; D-dimer, 2129 g/L; prothrombin time, international normalized ratio of 1.13; and activated partial thromboplastin time, 83.1 seconds. He continued to receive ventilator care, antibiotics, platelet transfusions, and support for DIC as indicated. Unlike typical HFRS, there was no prominent shock phase (Fig. 2). His urine volume and pulmonary hemorrhage gradually improved (Fig. 3). He was discharged on Day 22 without complications.

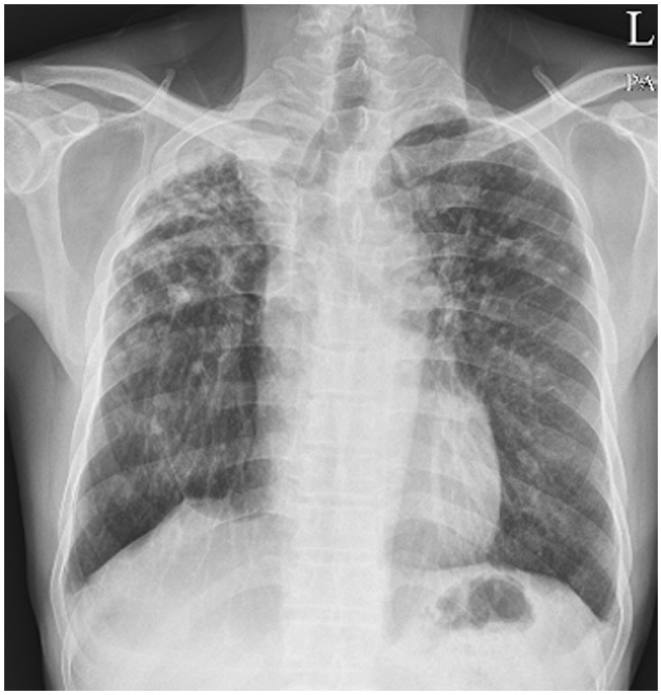

Figure 3. After adequate treatment, a chest X-ray demonstrated the absence of pulmonary hemorrhage.

Discussion

Hantaviruses are the causative agents of HFRS and HPS, and are widely distributed in Eurasia and North America. Hantaviruses are rodent-borne and transmitted to humans by direct contact with infected animals or their secretions, such as urine, feces, and saliva. Increased vascular permeability plays a general role in the pathogenesis of severe hantavirus infection. The clinical course can be extremely variable, and some infected patients are asymptomatic. Moreover, the manifestations and local distribution of the illness depend on the strain of the infecting virus [3–5]. HFRS occurs with infections by Hantaan and Dobrava viruses, while Sin Nombre and Andes viruses primarily induce HPS [1,6]. HFRS and HPS share some clinical features, but hemorrhage and renal failure are hallmarks of HFRS, while pulmonary problems are

distinctive signs and symptoms in patients with HPS. The mortality rate for patients with severe HFRS has decreased to $< 5\%$ with advanced supportive care. However, HPS can progress to a life-threatening condition more frequently than HFRS. Patients with HPS, after a prodromal phase similar to that of HFRS, very rapidly develop pulmonary edema and shock, which often requires mechanical ventilation and/or extracorporeal membrane oxygenation. The case fatality rate is approximately 35% [7]. The basis of lung vascular leakage during hantavirus infection, and ultimately HPS, is not well understood. The progression to HPS is likely to be a multifactorial process with contributions directly from virus replication and indirectly from the immune response induced by viral infection [8]. In this case, we did not recognize pulmonary hemorrhage during the prodromal phase of the illness. The prodromal phase was followed by cough and dyspnea, and progressed to bronchorrhea and pulmonary hemorrhage. However, after adequate ventilation and conservative treatment, the patient had a complete recovery. This is a rare case of HFRS caused by Hantaan virus that was manifest as unusual pulmonary hemorrhage.

Conflict of interest

None declared.

References

[1] Lee JS: Clinical features of hemorrhagic fever with renal syndrome in Korea. *Kidney Int. Suppl.* 35:S88–S93, 1991
[2] Kim MS, Lee SH, Park JW, Do J, Yoon KW: Hantavirus pulmonary syndrome with hemorrhagic fever with renal syndrome. *Korean J. Med.* 73:651–655, 2007
[3] Bugert JJ, Welzel TM, Zeier M, Darai G: Hantavirus infection – hemorrhagic fever in the Balkans? Potential nephrological hazards in the Kosovo war *Nephrol Dial Transplant* 14:1843–1844, 1999
[4] Glass GE, Watson AJ, LeDuc JW, Childs JE: Domestic cases of hemorrhagic fever with renal syndrome in the United States. *Nephron* 68:48–51, 1994
[5] Clement J, Colson P, McKenna P: Hantavirus pulmonary syndrome in New England and Europe. *N. Engl. J. Med.* 331:545–546, 1994
[6] Khan AS, Khabbaz RF, Armstrong LR, Holman RC, Bauer SP, Graber J, Strine T, Miller G, Reef S, Tappero J, Rollin PE, Nichol ST, Zaki SR, Bryan RT, Chapman LE, Peters CJ, Ksiazek TG: Hantavirus pulmonary syndrome: the first 100 US cases. *J. Infect. Dis.* 173: 1297–1303, 1996
[7] Terajima M, Hayasaka D, Maeda K, Ennis FA: Immunopathogenesis of hantavirus pulmonary syndrome and hemorrhagic fever with renal syndrome: do $CD8^+$ T cells trigger capillary leakage in viral hemorrhagic fevers? *Immunol Lett.* 113:117–120, 2007
[8] Macneil A, Nichol ST, Spiropoulou CF: Hantavirus pulmonary syndrome. *Virus. Res.* 162:138–147, 2011