

Hemorrhagic fever with renal syndrome with concurrent aortic dissection: a case report

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Case Report

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Abstract

Background

Hemorrhagic fever with renal syndrome (HFRS) is caused by hantaviruses presenting with high fever, hemorrhage, acute kidney injury. Microvascular injury and hemorrhage in mucus was often observed in patients with hantavirus infection. Infection with bacterial and virus related aortic aneurysm or dissection occurs sporadically. We present a previously unreported case of hemorrhagic fever with concurrent Stanford B aortic dissection.

Case presentation:

A 56-year-old man complained of high fever, generalized body ache, with decreased platelet counts of $10 \times 10^9/L$ and acute kidney injury. The ELISA test for Hantaan virus of IgM and IgG antibodies were both positive. During the convalescent period, he complained sudden onset acute chest pain radiating to the back and the CTA revealed an aortic dissection of the descending aorta extending to iliac artery. He was diagnosed with Hemorrhagic fever with renal syndrome and Stanford B aortic dissection. The patient recovered completely after surgery with other support treatments.

Conclusion

We present a case of HFRS complicated with aortic dissection, and no study has reported the association of HFRS with aortic disease. However, we suppose that hantavirus infection not only cause microvascular damage but may be risk factor for acute macrovascular detriment. A causal relationship has yet to be confirmed.

Background

Hemorrhagic fever with renal syndrome (HFRS) is caused by hantaviruses (such as Hantaan, Seoul and Puumala virus) which are carried by a specific rodent host species and transmitted through their saliva, urine, feces and blood [1]. In China, the hantaan virus and Seoul virus infection are two main pathogens for HFRS, with more than 11,000 cases reported annually [2]. The most commonly classic HFRS presents with high fever, loin or abdominal pain, nausea and vomiting, malaise, conjunctival hemorrhage and progressing to acute kidney injury. Hantavirus cardiopulmonary syndrome is another life-threatening clinical syndromes infected by Sin Nombre virus in the United States and Andes virus circulating in south America[3]. Since hantavirus primarily infects endothelial cells, it had been investigated that hantavirus infection induce the leakage of the vascular endothelia cells and present with pleural or perirenal effusion in patients[4]. The clinical course, from fever to abrupt hypotension with oliguria, can be extremely variable and some patients were asymptomatic.

AD is a lethal and critical disease, presenting with the separation of the aortic wall layers and subsequent formation of a false lumen [5]. The Stanford B aortic dissection is defined as the appearance of a false lumen at the segment distal to the left subclavian artery. Risk factors of AD include hypertension, genetic disorders and inflammation of the aortic wall, etc. [6]. Infected AD is a rare life threatening condition because of the possibility of rupture as well as perforation to surrounding organs. Although less common, infective aortic disease due to bacteria (such as staphylococcus, salmonella, mycobacteria) and virus (such as Zoster Virus,) have been reported [7–8]. The infection related inflammatory response in the vascular media may lead to aortic dilation and formation of aneurysm [9].

In this report, we present a case of HFRS with concurrent aortic dissection during the convalescent period. To our knowledge, the hantavirus infection could cause microvascular inflammation and endothelium damage [10], however, hemorrhagic fever complicated with aortic dissection was no report before, and a causal relationship has yet to be confirmed.

Case Presentation

In December 16, 2018, a previously healthy 56 year old man presented to our emergency department complaining of high fever (the highest recorded oral temperature 39.7°C), fatigue and generalized body ache for 3 days. The local clinic blood test showed an increased WBC ($11.1 \times 10^9 /L$) with dramatically decreased platelets ($36 \times 10^9/L$). He lived in rural area and worked in a place overrun with rats. On admission, his oral temperature was 38.0°C, respiratory rate 19/min, heart rate 78/min, blood pressure 129/86 mmHg. Physical examination found a poor general condition, petechiae in the oral and neck. His blood tests revealed as followed: leukocyte count $14.9 \times 10^9 /L$, hemoglobin 212 g/L, platelets $10 \times 10^9/L$, alanine aminotransferase 66 U/L, aspartate aminotransferase 108 U/L, lactic dehydrogenase 1079 IU/L, creatinine 187 $\mu\text{mol}/L$, C-reactive protein 33.3 mg/L (reference 0–5). The coagulation function test showed the prothrombin time 15.5 s (reference 11.5–14.5), the partial thromboplastin time 91.2 s. The clinical course and manifestations were summarized in Fig. 1. The laboratory results and reference range were listed in Table 1. The computed tomography scan of chest and abdomen showed pleural effusion, perinephric effusion extended to paracolic sulcus, slight peritoneal and pelvic effusion (Fig. 2A-D). Enzyme-linked immunosorbent assays (ELISA) of IgM and IgG antibodies for HFRS were both positive and the serotype was hantaan virus. Based on clinical symptoms and signs, along with his platelets count, creatinine level, urine volume changes, the patient was eventually diagnosed as HFRS. The treatment mainly includes transfusion of platelets and fresh frozen plasma, hemodialysis, antibacterial drug Piperacillin/Tazobactam empirically in dealing with abdomen effusion and other supportive therapies. His condition was recovered gradually after treatment.

On hospital day 10, he complained sudden onset acute chest pain radiating to the back when eating lunch. After consulting a cardiologist, he was sent for a computed tomography angiography (CTA) of the aorta. The CTA revealed an AD of the descending aorta extending to iliac artery with the left subclavian artery involved (Fig. 3A-D). On hospital day 26, when the platelets were recovered to normal level and the creatinine to 122 $\mu\text{mol}/L$, he received an angiography of aortic and surgery of thoracic endovascular aortic repair (Fig. 3.E, F). A week after operation, the patient was discharged and followed up as outpatient.

Table 1
Clinical Laboratory Results.

Measure	Hospital day									
	Reference range	Local clinic	1	3	6	8	12	14	24	33
WBC($\times 10^9$ /L)	2.5–9.5	11.1	14.9	26.4	10	7.6	10	6.8	9	8.5
PLT($\times 10^9$ /L)	125–350	36	10	18	41	84	125	186	417	384
Hb(g/L)	130–175	197	212	177	134	135	114	91	98	89
Creatinine(μ mol/L)	57–97		187	598	907	782	445	170	122	88
ALT (U/L)	9–50		66	51	50		36	55	91	40
AST (U/L)	15–40		108	102	88	55	69	61	86	22
LDH (U/L)	120–250		1079	1043	831	639	486	280	333	199
APTT (s)	29.2–41.2		81	54	46.4	42.6			44.9	

WBC: white blood cell; PLT: Platelets; Hb: hemoglobin; ALT:alanine aminotransferase; AST:aspartate aminotransferase; LDH: lactic dehydrogenase; APTT: partial thromboplastin time.

Discussion And Conclusion

Hantaviruses are negativesense singlestranded ribonucleic acids viruses, which can survive for more than ten days as a virion type at room temperature[11]. The exposure to aerosolized rodent excreta containing pathogenic virus is the main cause of human infection with hantaviruses. The classical manifestation of HFRS includes high fever, conjunctival hemorrhage, and gastrointestinal symptoms like abdominal pain, malaise, nausea and vomiting. Some patients develop severe oliguric acute kidney injury and need hemodialysis. Patients typically have abnormal laboratory values including a leukocytosis, thrombocytopenia, elevation of serum creatinine and lactate dehydrogenase. The diagnosis of hantavirus infection can be confirmed by serum specific antibody or viral RNA. We were not able to perform reverse transcription-polymerase chain reaction to make a molecular test because of condition limitations. But the clinical symptoms and signs, platelets count, creatinine level, urine volume changes, all indicated HFRS.

Increased vascular permeability appears to be a dramatic expression of this patient, which had pleural and perinephric effusion according to the CT scan (Fig. 2.). In patients, hantaviruses replicate primarily in the endothelium, which cause damage to vascular endothelium, tubular and interstitial, and further increasing the permeability [1]. The increased vesicular permeability is mediated in part by bradykinin and cytokines such as tumor necrosis factor and interleukin-6 [3]. All of these pathogenesis can increase the possibility of vascular inflammation, damage, and hemorrhage in HFRS.

Infection with virus or bacterial related aortic aneurysm or dissection were reported sporadically. Staphylococcus aureus and Salmonella species were reported to cause AD[5]. Virus infection such as herpes zoster, human immunodeficiency virus and varicella-zoster virus, can also lead to vascular dissection[12]. However, the exact mechanisms of infection related vascular dissection are still far from clear. Prior report suggested that virals might lead to inflammatory injury of the arterial wall that subsequently developed artery dissection[13]. During the recovery period of HFRS, our patient developed a sudden AD on day 10 in hospital. A multivariate analysis confirmed that the dissection was independently associated with a diagnosis of recent infection[9]. Besides, the hantavirus caused coagulation disorders and thrombocytopenia contribute the risk of AD too. For there was no hantavirus infection case with aortic complications reported, future study should attempt to investigate whether this concurrent is causal. Although the hantavirus may not a direct cause of aortic dissection, we suppose that this infection could lead to a damaged vessel wall, and may contribute to subsequent dissection. Further investigations with larger patient groups of the hantavirus infection associate data of dissected vessels are needed to support this hypothesis.

In conclusion, we present a rarely case of HFRS complicated with aortic dissection, and no study has reported the association of HFRS with aortic disease. However we can suppose that hantavirus infection not only lead to microvascular damage but may be risk factor for macrovascular detriment in HFRS patients. The causal relationship has yet to be confirmed and further accumulation of cases of aortic disease with hantavirus infection is necessary in the future.

Abbreviations

HFRS: Hemorrhagic fever with renal syndrome; AD: Aortic dissection; CTA: computed tomography angiography; ELISA: Enzyme-linked immunosorbent assays; IgM: Immunoglobulin M; IgG: Immunoglobulin G.

Declarations

Ethics approval and consent to participate: This study was approved by the Research Ethics Committee of the First Affiliated Hospital, College of Medicine, Zhejiang University.

Consent for publication: Written informed consent was obtained from the patient for publication of this case report in accordance with the Declaration of Helsinki.

Availability of data and materials The datasets supporting the conclusions of this article are included within the article.

Competing interests: The authors declare that they have no competing interests.

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Authors' contributions: Fengqi Qiu. wrote the first draft of the manuscript; Congcong Li. edit some sections of the manuscript. Jianya Zhou. contributed to manuscript revision, All authors read and approved the final manuscript.

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Figures

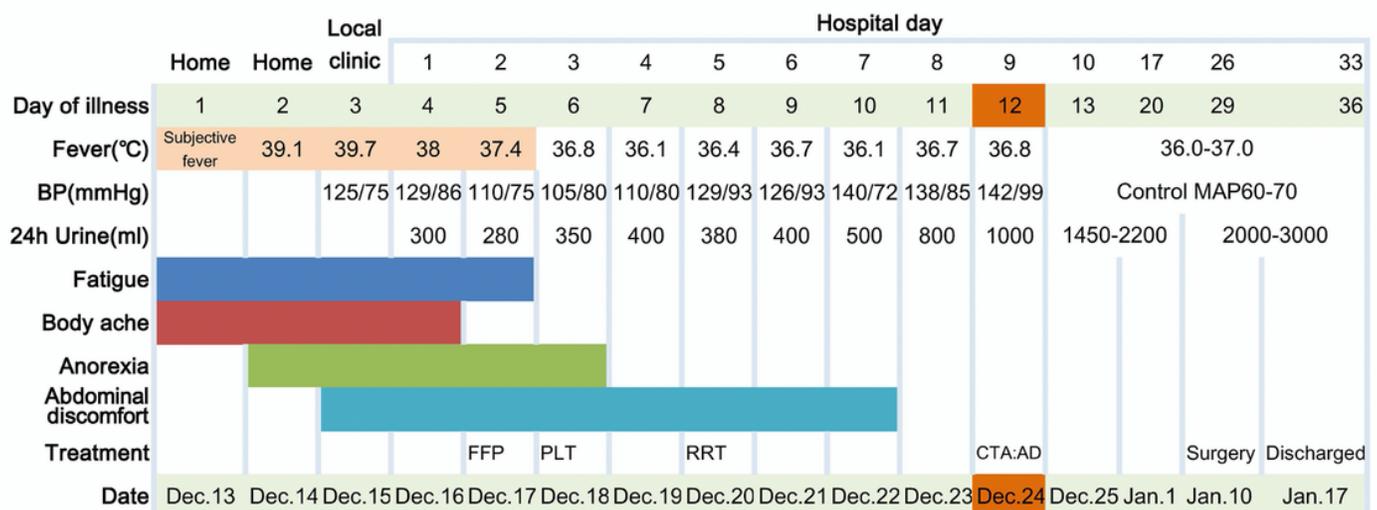


Figure 1

The patients' manifestation and main treatment according to day of illness and hospitalization, December 13, 2018 to January 17, 2019. BP, blood pressure, FFP, fresh frozen plasma, PLT, Platelets, RRT, renal replacement therapy, CTA, computed tomography angiography, AD, aortic dissection, MAP, mean atrial blood pressure.

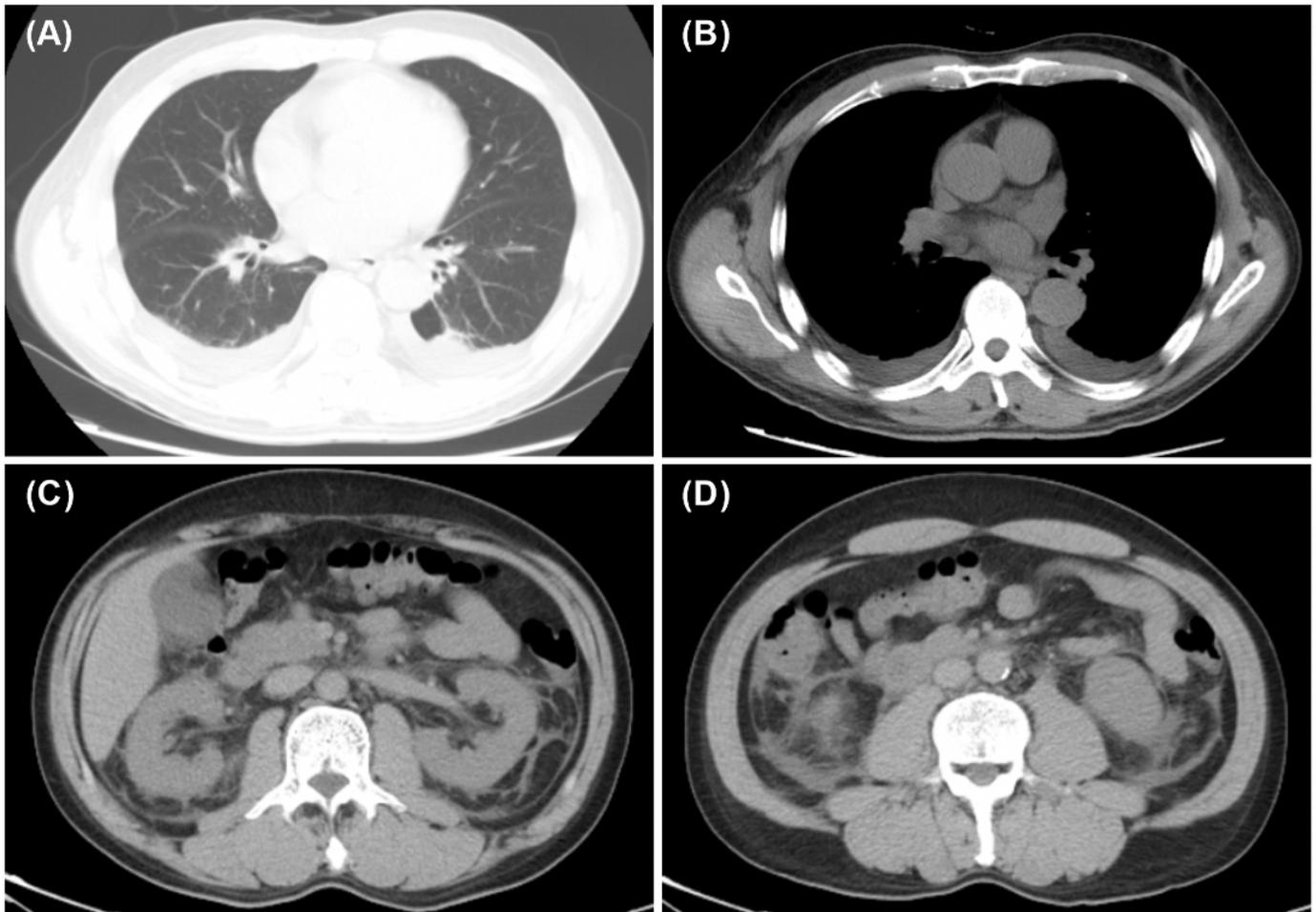


Figure 2

Computed tomography of the thorax and abdomen on hospital day 1 showing pleural effusion (A, B), perinephric effusion extended to paracolic sulcus, slight peritoneal and pelvic effusion (C, D).

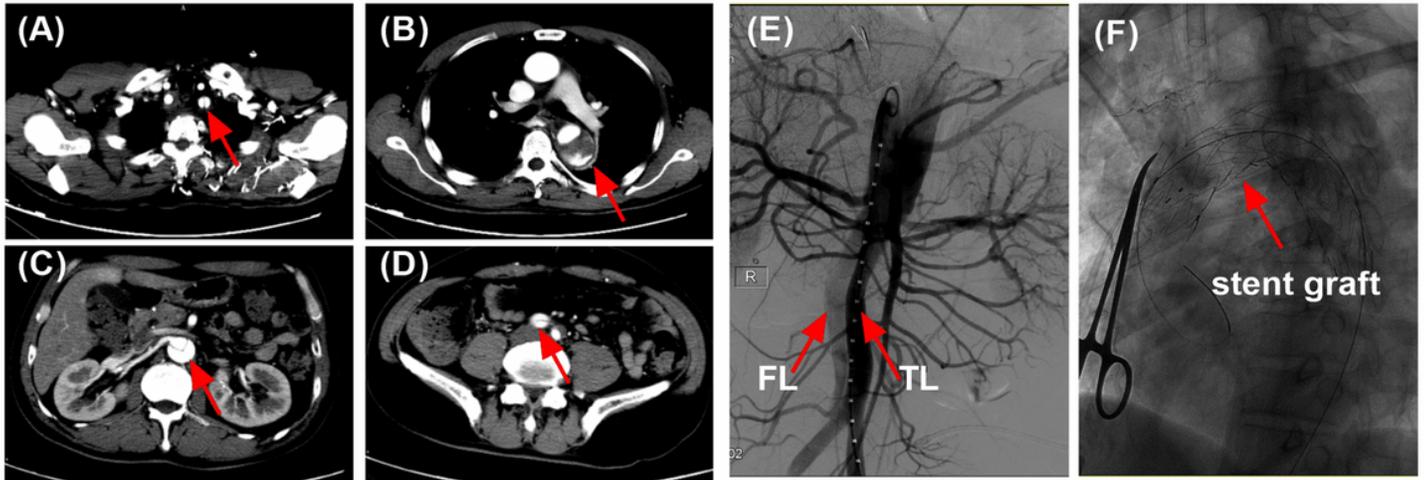


Figure 3

Computed tomography angiography of the aorta on hospital day 9 showed an aortic dissection involving the left subclavian artery(A), descending aorta (B, C), extending to iliac artery (D). Angiography of aortic during thoracic endovascular aortic repair surgery, showing false lumen and true lumen (E, red arrow). Stent graft was implanted into vascular (F, red arrow). FL, false lumen TL, true lumen.