Case Report

Hemorrhagic fever with renal syndrome and reversible splenial lesion syndrome

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ABSTRACT

تعد الحمى النزفية المصحوبة بالمتلازمة الكلوية (HFRS) ومتلازمة الآفة الطحالية القابلة للعكس من الحالات غير الشائعة النادرة نسبيًا. الحمى والنزيف وإصابة الكلى الحادة هي الأعراض السائدة التي يتم ملاحظتها بشكل متكرر في حالات HFRS. نستعرض في هذا التقرير حالة رجل في منتصف العمر تم إدخاله إلى المستشفى مصابًا بالحمى وأعراض عصبية حادة. وكانت أعراضه الرئيسية هي الدوخة المتكررة. لم يكشف التصوير المقطعي للجمجمة (CT) عن أي آفات واضحة، مثل نزيف الدماغ أو الاحتشاءات. أظهر الطحال من الجسم الثفني فرط الكثافة في التصوير بالرنين المغناطيسي للدماغ (MRI)، وهو ما يتماشى مع الملاحظات الشعاعية المميزة لمتلازمة الآفة الطحالية القابلة للعكس (RESLES). وكشفت التحليلات الإضافية أن عدد الصفائح الدموية لدى المريض قد انخفض إلى 7×10^9/لتر بينما كانت الأجسام المضادة للحمى النزفية إيجابية. في النهاية، قمنا بتشخيص إصابة المريض بمتلازمة HFRS وأظهر تحسنًا سريريًا بعد العلاج النشط.

Hemorrhagic fever with renal syndrome (HFRS) and reversible splenial lesion syndrome are both considered uncommon conditions relatively rare. Fever, hemorrhage, and acute kidney injury are the prevailing symptoms frequently observed in cases of HFRS. We describe a case of a middle-aged man who had been hospitalized with fever and acute neurological symptoms. His main symptom was recurrent dizziness. Cranial computed tomography (CT) did not reveal any obvious lesions, such as encephalorrhagia or infarctions. The splenium of corpus callosum showed hyperintensity on brain magnetic resonance imaging (MRI), which is in line with the characteristic radiographic observations of reversible splenial lesion syndrome (RESLES). Further analyses revealed that the patient's platelet counts had decreased to 7×10^9/L while hemorrhagic fever antibodies were positive. Eventually, the patient was diagnosed with HFRS and exhibited clinical improvements after active treatment.

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Hemorrhagic fever with renal syndrome is an acute zoonotic infectious disease caused by Hantavirus genera within the Bunyaviridae family. Hantan virus (HTNV) and the Seoul virus (SEOV) are the predominant causative agents of HFRS in China. The illness is characterized by symptoms such as fever, hemorrhage and renal impairments.[1,2] In some hemorrhagic fever patients, the early symptoms are atypical, with higher rates of missed diagnosis and misdiagnosis. In this case, we describe a case of patient diagnosed with HFRS coupled with reversible splenial lesion syndrome (RESLES).

Case Report. Patient information. A 58-year-old male patient arrived at out facility with a fever and dizziness 3 days. On the preceding day, the symptoms worsened, accompanied by slurred speech, muscle weakness with instability, and difficulty in walking. The patient denied having any prior medical conditions such as hypertension, dyslipidemia, epilepsia, or a history of smoking, alcohol consumption, or illicit drug use.

Clinical findings. The patient's blood pressure levels was measured at 121/85 mmHg, which falls within a normal range. Additionally, the neurological examination yielded normal results. Initial serum testing revealed normal white blood cell, apart from mild reductions in platelet counts (reference range: 100-300 mmol/L) and reduced potassium levels (3.07; reference range: 3.6-5.5 mmol/L). The IgG and IgM antibodies against epidemic Influenza A and B virus as well as hemorrhagic fever virus were negative. CSF detection and computed tomography (CT) of the head was normal.

Diagnostic assessment. Due to the neurological symptoms, the possibility of acute cerebral infarction was

Table 1 - Abnormal indicators of peripheral blood analysis.

Days	1	2	3	5	10	Normal range
WBC (× 10^9/L)	7.25	33.89	23.28	11.3	8.09	3.5-9.5
N (%)	89.9	74	78.6	84	78.1	50-70
PLT (×10^9/L)	87	7	13	28	98	100-300
CRP (mg/L)	62.34	72.38	68.16	50.44	157.76	0-10
PCT (ng/mL)	8.42	30.41	23.66	12.92	0.91	0-0.05
BNP (pg/ml)	374.84	2253.6	5832.9	6736.8	1869.3	0-125
Na^+ (mmol/L)	120.8	128	129.4	137	136	136-145
PT (sec)	14.2	13.6	13	15.2	13.3	10.4-14.5
D-Dimer (ng/mL)	13.86	1.15	1.88	2.85	5.85	0-0.5
Fibrinogen (g/L)	2.57	1.59	1.75	2.24	5.46	2-4
SCR (µmol/L)	-	294	369	213	421	58-110
BUN (mmol/L)	-	18.52	23.3	13.4	18.57	3.2-7.1
Plasma lactate (mmol/L)	3.26	4.83	1.2	1.1	0.7	0.7-2.1
K^+ (mmol/L)	3.07	3.44	3.75	3.5	3.2	3.5-5.5
ALT (U/L)	-	83	42	36	29	0-50
AST (U/L)	119	218	138	105	24	17-59

WBC - White blood cell count, N - Neutrophils, PLT - Platelet, CRP - C-reactive protein, PCT - Procalcitonin, BNP - N-terminal-pro-B-type natriuretic peptide, Na^+ - Blood sodium, PT - Plasma prothrombin time, SCR - Serum creatinine, BUN - Blood urea nitrogen, K^+ - Blood potassium, ALT - Alanine amino transferase, AST - Antarctic submillimeter telescope

Table 2 - Timeline table.

Date	Event
Day 1	Fever, dizziness
Day 3	Slurred speech, muscle weakness with instability, and difficulty in walking
Day 4	MRI showed hyperintensity in the splenium of the corpus callosum.
Day 5	Mild abnormal renal function
Day 6	Systemic inflammatory response severe thrombocytopenia
Day 16	Renal function recovery
Day 20	Discharge

considered. The next day, the patient was hospitalized at the neurology department. After hospitalization, his symptoms were progressive, including high fever (heat peak of 39.5°C),significant fatigue, shortness of breath, and depressed spirit. Brain magnetic resonance imaging (MRI) showed areas of high-signal-intensity on T2WI, FLAIR, and DWI (**Figure 1 A-E**). The observed hyperintensity in the splenium of the corpus callosum corresponded with the characteristic radiographic findings associated with RESLES. Procalcitonin levels were increased to 30.41 ng/ml, while his platelet counts

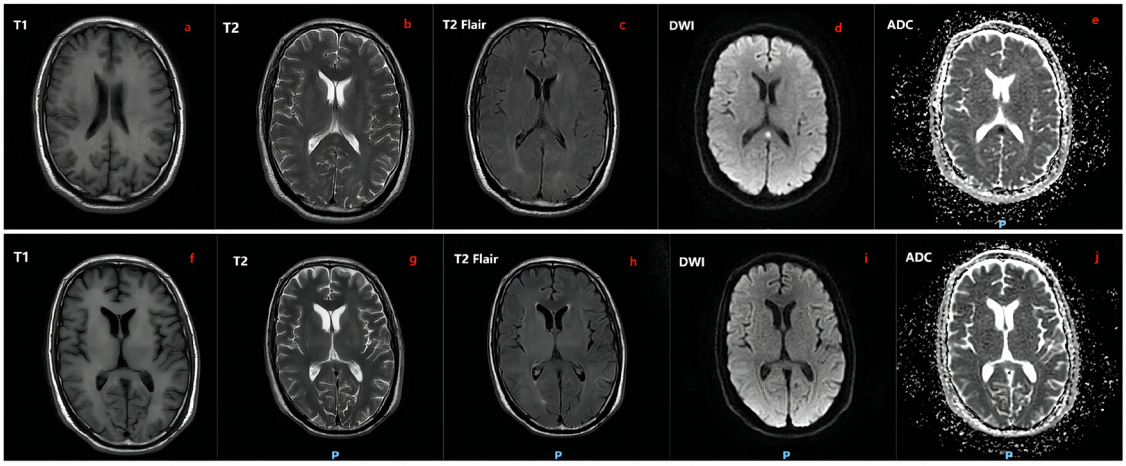

Figure 1 - On the day of admission, MRI (a-e) showed areas of high-signal-intensity on T2WI, FLAIR, and DWI. And after effective treatments, follow-up MRI (f-j) revealed significant regression of the lesion in SCC.

were significantly decreased to 7.0*10^9/L (**Table 1**). Re-examination of hemorrhagic fever antibodies revealed positive outcomes. Therefore, his diagnosis was confirmed as hemorrhagic fever virus infection complicated with reversible splenial lesion syndrome.

Therapeutic assessment. Considering the suspected cause of his condition and the results of laboratory tests, the patient received a comprehensive treatment regimen that included acyclovir, antibiotics, blood transfusion, and correction of electrolyte imbalance among other treatments.

Follow-up and outcomes. The patient experienced a rapid improvement in clinical symptoms, leading to his discharge on the 20th day after onset. Approximately 1 month after being discharged, the patient returned to the hospital's outpatient clinic for follow-up examination, which included a repeat of MRI. The MRI resuts revealed the complete resolution of the initial lesion (**Table 2, Figure 1 F-J**).

Discussion. We present a case of hemorrhagic fever highlighting typical imaging findings suggesting RESLES. This patient lacked a typical presentation of hemorrhagic fever at the first visit, except fever. Hemorrhagic fever with renal syndrome (HFRS) is a natural focus disease caused by Hantavirus infections. This condition has been observed to cause diffuse damage to micro-vessels throughout the body, destruction of vascular endothelial cells, increased permeability of capillaries and a decrease in platelet counts.[3] Human infections with Hantaviruses majorly occur through contact with rodent excreta, including urine, feces, or saliva harboring the virus.[4] In the present case, although he denied being bitten by mice, it is possible that he unknowingly came into contact with objects contaminated by virus. Acute kidney injury, increased vascular permeability, and coagulation abnormalities are typical manifestations during viral hemorrhagic fevers. The enhanced state of inflammation caused by hantavirus infections contributes to increased risk of stroke during acute HFRS. This patient had no typical presentations of hemorrhagic fevers at the first visit, except fever.

Reversible splenial lesion syndrome (RESLES) is an extremely uncommon clinical condition, and its precise cause remains unknown. Among the known causes of RESLES, the most common ones include infections, epilepsy, high-altitude cerebral oedema, as well as nutritional and metabolic factors including hypoglycaemia and hypernatraemia, systemic lupus erythematosus etc.,[5] Incidences of RESLES are closely associated with infections, particularly viral infections, such as measles, herpes virus,[6] Epstein-Barr virus, dengue virus, varicella-zoster virus, and adenovirus.[6] The RELES has diverse clinical features, including headaches, seizures, loss of consciousness, mental abnormalities, dizziness, obtundation and syncope.[7,8] Most patients have good prognostic outcomes. In our case, the patient was admitted to the hospital with symptoms of dizziness and fever, with increased levels of inflammatory indicators. The increase in inflammatory factors and inflammatory cells led to cytotoxic oedema, suggesting that RESLES stimulates the immune system and can increase the levels of a few inflammatory response factors.

Based on these findings, the author postulates that HFRS is a potential trigger factor for RESLES. This rare case brings attention the occurrence of RESLES as an atypical neurological manifestations of HFRS. However, additional large-scale studies are necessary to verify the RESLES-associated morbidity rates in HFRS patients. When patients present with fever and neurological symptoms, clinicians should consider HFRS, repeatedly check the hemorrhagic fever antibodies, and perform blood routine analyses to avoid treatment delay.

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