A child with an unusual complication of Crimean-Congo hemorrhagic fever: Hemorrhagic pleural effusion

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Crimean-Congo haemorrhagic fever (CCHF) is a tick-borne disease caused by Nairovirus group of the Bunyaviridae family. Infection is transmitted to humans by Hyalomma ticks or by direct contact with the blood or tissues of infected humans or viraemic livestock¹. CCHF virus has a wide geographic distribution, circulating in Africa, the Middle East, Asia, and Central and South-Eastern Europe². CCHF first emerged in Turkey in 2002, and the prevalence of the disease has been found to be increased³. Central Anatolia Region is endemic for the disease where sporadic cases or even outbreaks are being observed every year⁴–⁵. Clinical features usually include a rapid progression characterised by fever, malaise, nausea, vomiting, abdominal pain, myalgia, petechia and ecchymosis⁶, with a mortality rate of up to 30%⁷. Diarrhea, lymphadenopathy, hepatomegaly, acute appendicitis and acute renal failure have also been reported⁸–¹⁰. We report here a child with serohemorrhagic pleural effusion, an unusual complication of CCHF.

Case Report

A previously healthy 8-yr-old boy, living in the city Tokat (Central Anatolia Region), visited a pediatrician in the state hospital with complaints of fever (38–39°C) and cough for two days. During physical examination a tick was found on patients shoulder and removed carefully. The patient received ambulatory care (antibiotics and antipyretics) after laboratory tests were found normal. One day after, his fever increased (39–40°C) and vomitting was added to complaints. Repeated laboratory tests showed decrease in thrombocyte and white blood cell count. The patient was referred to our hospital on May 26, 2011. On admission to the clinic, the patient presented fever, cough and vomitting. On initial examination, his vital signs included a body temperature of 39°C, a pulse of 88 beats/min and a respiratory rate of 24 breaths/min. Thrombocytopenia was noted with a count of 41000/mm³. White blood count was normal (4540/mm³) but near to lower limit (4000/mm³) and hemoglobin level was 13.4 g/dl. Aspartate aminotranspherase (AST), alanin aminotranspherase (ALT), lactate dehydrogenase (LDH), and creatine phosphokinase (CPK) were increased with the levels of 503 IU/L (5–40 IU/L), 142 IU/L (5–54 IU/L), 1.202 IU/L (98–192 IU/L) and 287 IU/L (38–174 IU/L), respectively. Serum electrolytes, blood urea nitrogen, creatinine, bilirubins, total protein and albumin were normal on blood analysis. Urinanalysis was normal. Prothrombin time (PT), activated partial thromboplastin time (aPTT) and international normalized ratio (INR) were prolonged to 23.8 (11–14), 48.9 (25–40) and 1.51 (0.9–1.4) sec, respectively. Treatment was started with supportive therapy, intravenous antibiotics, oral ribavirin and antipyretics. Serological tests for hepatitis were negative. Serum sample was referred to the national reference laboratory of CCHF, virology laboratory, Communicable Diseases Research Center, Refik Saydam National Institute of Health, Ankara, Turkey. Fever and vomitting improved within two days but cough persisted.

Laboratory tests started to heal with the first day and they recovered fully on Day 6 of the treatment, except for formed elements of blood. Thrombocyte counts and white blood cell counts were <60000/mm³ (min. 32000/mm³) and <5000/mm³ (min 2700/dl) for the following nine days. On Day 3, the patient had worsened cough, respiratory distress and tachypnea. The oxygen saturation, arterial blood gas analysis and blood pressures were normal. Chest X-ray showed pleural effusion on the right side (Fig. 1). Thrombocytes were 41000/mm³ and aPTT was 73.6 sec. Hemoglobin decreased from 13 to 10.2 g/dl rapidly in 6 h. There were not any other focus of bleeding that could explain the decrease of hemoglobin. Thoracentesis was done. Pleural fluid showed plenty of erythrocytes; the glucose level was 73 mg/dl, LDH was 782 IU/L and protein was 3.5 g/dl. Fresh frozen plasma and antibiotherapy was continued. Fresh frozen plasma and
thrombocyte suspension were transfused in view of bleeding. Gram stain, acid-fast bacilli stain and bacterial cultures were negative. After four days with hemorrhage, dramatic clinical improvement and resolution of pleural effusion were observed and chest tube was removed when drainage stopped. He was in an endemic region of CCHF, and laboratory and clinical findings also supported a CCHF diagnosis. Definitive diagnosis of CCHF was confirmed by reverse transcription-PCR. At discharge (11 days after admission), hemoglobin, thrombocyte, white blood cell count, AST, ALT, PT and aPTT were 9.7 g/dl, 129000/mm³, 5880/mm³, 44 IU/L, 57 IU/L, 13 and 29.8 sec, respectively.

**DISCUSSION**

CCHF has four phases\(^{11}\). Incubation phase is usually 1–3 days after tick bite or five days after contact with livestock blood/tissue or human blood. Prehemorrhagic phase lasts 3–6 days with fever (39–41°C), rigor, severe headache, myalgia and abdominal pain. Hemorrhagic phase lasts 2–3 days with possibility of hemorrhagic manifestations of mucous membranes (especially oral and nasal) and skin. In rare cases, gastrointestinal, genitourinary, cerebral and pulmonary hemorrhage could occur. Death may ensue in these patients. After this period, convalescence phase starts and lasts for 15–20 days with weakness, nausea, poor appetite, headache, sweating, polyneuritis and occasional hair loss.

The pathogenesis of CCHF could not be defined completely for several reasons but viral hemorrhagic fevers have similar pathophysiologic, clinical and laboratory features. Infection in viral hemorrhagic fevers have a major effect on endothelium. Capillary fragility is common in viral hemorrhagic fevers\(^ {12}\). The tendency of bleeding in CCHF results from thrombocytopenia, disseminated intravascular coagulation, vascular endothelial injury and liver dysfunction\(^ {13}\). Although, pulmonary involvement and the pulmonary course of patients with CCHF are poorly established, pleural effusion, pneumonitis, hemoptysis and pulmonary hemorrhage have been reported with other viral hemorrhagic fevers. In a study, where chest radiographies of 108 CCHF patients were evaluated; 33 cases showed abnormal findings like infiltration, pleural thickening, hilar pathology, interstitial pathology and mediastinal pathology, but pleural effusion was not reported\(^ {14}\). In present case, serohemorrhagic pleural effusion developed during hemorrhagic phase concurrently with lower platelet count and longer PTT. Pleural effusion started to heal dramatically after tube drainage and resolved completely on Day 4. In literature, two cases with pleural effusion have been reported. Both were children and both were resolved spontaneously under supportive medications and ribavirin\(^ {15–16}\). We performed tube drainage and transfused thrombocyte suspension and fresh frozen plasma because of rapid decrease in hemoglobin levels and respiratory distress.

As a conclusion, although there is no clear reason of bleeding in pleural site, CCHF patients could show hem-

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**Fig. 1:** Chest radiography of the patient showing pleural effusion on the right side.

**Fig. 2:** Chest radiography after drainage tube was inserted to pleural site.
Hemorrhagic pleural effusion during the hemorrhagic phase. Clinicians must keep hemorrhagic pleural effusion possibility in mind, especially in the period of lowest platelet count and longest PTT, as the possibilities of skin and mucosal bleedings. Hemorrhagic pleural effusion recovers spontaneously but some cases might require surgical intervention.

REFERENCES


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