

Crimean-Congo Hemorrhagic Fever Accompanied by Acalculous Cholecystitis and Pancytopenia: A Rare Case

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To the Editor,

Crimean-Congo hemorrhagic fever (CCHF) is a tick-borne zoonotic disease caused by a highly pathogenic virus, with a mortality rate ranging from 10% to 40% (1). Contrary to the high mortality rates reported in other countries, the mortality rate in Türkiye has been observed to be approximately 5% (2). Outbreaks of CCHF have been observed in Türkiye during specific periods, with the first case reported in our country in 2002 (3).

Although most patients with CCHF exhibit symptoms such as myalgia, dizziness, arthralgia, photophobia, and diarrhea, bleeding manifestations—typically a hallmark of severe disease—may be delayed (4).

The CCHF virus induces direct endothelial damage, including apoptosis and increased capillary permeability mediated by various cytokines. This endothelial dysfunction activates the coagulation cascade and contributes to multiorgan injury via proinflammatory cytokines (5). CCHF has been shown to involve a wide range of tissues, including the adrenal glands, liver, spleen, brain, bone marrow, lymph nodes, lungs, muscles, kidneys, cervix, and vascular endothelial cells (6). Here, we present a case of Crimean-Congo hemorrhagic fever characterized by severe pancytopenia and acalculous cholecystitis—an uncommon manifestation of organ involvement and a rare complication.

A 38-year-old female patient presented with a 10-day history of fever, abdominal pain, and recurrent episodes of nausea and vomiting. She had no notable personal or family medical history, no history of medication use, and denied ingestion of unusual plants or mushrooms. The patient was involved in animal husbandry but reported no known tick exposure. On physical examination, the patient was alert and oriented. Tenderness was noted in the right upper quadrant of the abdomen. A petechial rash was observed on the body. No other pathological findings were detected.

Laboratory investigations revealed pancytopenia, markedly elevated hepatic enzymes, and mild coagulation abnormalities (Figure 1A). Peripheral blood smear revealed no morphologically atypical or malignant cells. Cytological findings were within normal hematologic limits, and platelet morphology and distribution were consistent with the CBC results.

The patient was monitored in the intensive care unit. Abdominal computed tomography (CT) revealed diffuse thickening of the gallbladder wall measuring 16 mm, accompanied by marked edema. Pericholedochal fluid accumulation was noted, and the gallbladder appeared hydropic. No calculi were observed within the gallbladder lumen or the extrahepatic biliary tree. The intrahepatic and extrahepatic bile ducts were of standard caliber.

These findings were consistent with acute acalculous cholecystitis. Splenic vertical length was increased, measuring 150 mm, and perihepatic free fluid was identified (Figure 1). Oral intake was discontinued, and empirical antimicrobial therapy with intravenous meropenem was initiated. The patient also received platelet transfusions and fresh frozen plasma.

In parallel with clinical suspicion for CCHF raised by the infectious diseases department, antiviral therapy with oral ribavirin was initiated (2000 mg loading dose, followed by 1000 mg four times daily for four days, then 500 mg four times daily for six days), alongside dexamethasone (16 mg intravenous once daily for three days). The diagnosis was confirmed by reverse transcription polymerase chain reaction (RT-PCR), with a cycle threshold (Ct) value of 34.32. At two-week follow-up post-treatment, the patient was asymptomatic and exhibited complete normalization of hematologic, hepatic, and coagulation parameters.

Crimean-Congo haemorrhagic fever can range from asymptomatic infection to severe haemorrhagic bleeding, with mortality rates reported to exceed 60% (7). Fatal infections are characterised by vascular dysfunction, disseminated intravascular coagulation, and multiple organ failure (8). Although tick-borne transmission is the primary route of infection, transmission can also occur through contact with virus-carrying animals, infected humans, and contaminated surfaces. In our case, the patient had no history of tick exposure, but was engaged in livestock farming in a rural area. Given the endemic setting and clinical presentation, early suspicion of CCHF was raised. The absence of atypical cells on peripheral smear, rapid hepatic deterioration despite antibiotics, and profound thrombocytopenia further supported the diagnosis, which RT-PCR later confirmed. Systems for predicting mortality in cases of CCHF are under study. Bakır et al. have demonstrated the feasibility of predicting disease progression and mortality in patients diagnosed with CCHF using the Severity Grading Score (SGS) system. They also revealed that mortality is exceptionally high in patients with a score of ≥ 9 points (9). Moreover, when compared with established systems such as SOFA (Sequential Organ Failure Assessment) and APACHE II (Acute Physiology and Chronic Health Evaluation II), SGS exhibited substantial prognostic value in mortality estimation (10). In our case, although the patient had an SGS score of 5—classified as intermediate risk—no mortality was observed, likely due to timely and appropriate therapeutic intervention. Although pancytopenia may result from various etiologies—including hematological malignancies, chronic liver disease, vitamin B12 deficiency, and rheumatological conditions—CCHF should be considered in the differential diagnosis, particularly in endemic regions during the spring and summer months. Abdominal imaging findings in CCHF are variable. In a study by Özmen et al., patients with platelet counts below $50 \times 10^9/L$ exhibited a significantly higher incidence of intra-abdominal free fluid (11). Similarly, Zıraman et al. reported hepatomegaly (25%), increased gallbladder wall thickness (21%), and splenomegaly (19%) as the most frequent ultrasound findings (12). These studies suggest a potential association between gallbladder wall thickening, intra-abdominal fluid accumulation, and disease severity. In our case, consistent with these observations, the patient presented with a platelet count $< 50 \times 10^9/L$, along with increased gallbladder wall thickness, splenomegaly, and perihepatic free fluid.

Acalculous cholecystitis, known to occur in the setting of various viral and bacterial infections, may complicate the clinical course by obscuring diagnosis and extending the duration of hospitalization (13). While earlier reports have described this condition as uncommon in patients with CCHF, more recent studies incorporating abdominal imaging suggest that its actual frequency may be higher than previously assumed (11,14). In a study by Guner et al., the emergence of acalculous cholecystitis and intra-abdominal abscesses in CCHF cases was attributed to widespread inflammatory activity and endothelial disruption secondary to a cytokine-driven immune cascade (15). Given the temporal alignment of clinical and imaging findings, and in light of reported pathophysiological mechanisms, the observed acalculous cholecystitis in our patient is more likely a complication of CCHF rather than an unrelated coexisting condition.

In summary, recognizing potential complications of CCHF and maintaining a high index of suspicion in patients presenting with cytopenias and abnormal abdominal imaging—particularly during the spring and summer months in endemic areas—may facilitate timely diagnosis. Early isolation and appropriate treatment in such cases have the potential to improve clinical outcomes and reduce the length of hospital stay.

Conflict of Interest The authors declare no conflict of interest.

Informed Consent Written informed consent was obtained from the patient for publication of this case report.

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Parameter	Patient Value	Reference Range
Hemoglobin	10.9 g/dL	11–15 g/dL
Leukocytes	$1.18 \times 10^9/L$	$4-10 \times 10^9/L$
Neutrophils	$0.67 \times 10^9/L$	$2-7 \times 10^9/L$
Platelets	$11 \times 10^9/L$	$150-450 \times 10^9/L$
APTT	41.7 sec	20–30 sec
PT	11.6 sec	10.4–13.6 sec
AST	866 U/L	0–31 U/L
ALT	330 U/L	0–45 U/L
GGT	880 U/L	0–49 U/L
LDH	1013 U/L	0–248 U/L
Ferritin	1291 µg/L	20–200 µg/L
Total Bilirubin	0.9 mg/dL	0.2–1.2 mg/dL
Direct Bilirubin	0.5 mg/dL	0–0.4 mg/dL

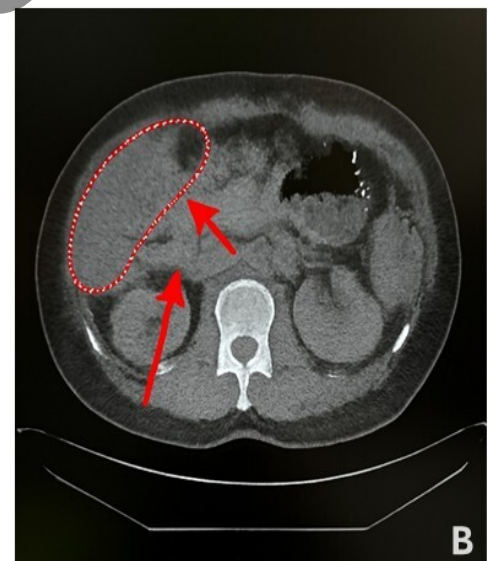


Figure 1: A. Hematological and biochemical parameters with reference intervals. **B.** CT Findings – Acalculous Cholecystitis in a Crimean-Congo Case Axial abdominal CT shows gallbladder wall thickening and pericholecystic fluid without visible calculi, consistent with acalculous cholecystitis. Surrounding fat stranding supports active inflammation. **Abbreviations:** ALT, alanine aminotransferase; APTT, activated partial thromboplastin time; AST, aspartate aminotransferase; FER, ferritin; GGT, gamma-glutamyl transferase; Hb, hemoglobin; LDH, lactate dehydrogenase; NEU, neutrophils; PLT, platelets; PT, prothrombin time; WBC, white blood cells.