

# Tropical Fever: Unveiling an Asymptomatic Case of Polycythemia Vera

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## ABSTRACT

We report a case of fulminant hepatic failure due to the Budd–Chiari syndrome following preservation with a tropical fever. A young lady came with fever, altered mental status, jaundice, and renal failure. Following tropical workup, it was diagnosed as a case of leptospirosis (WHO Faine's criteria) with multi-organ dysfunction. Despite adequate antimicrobial cover, she progressed to hepatic coma (hyperammonemia) and was noted to have worsening conjugated hyperbilirubinemia. Following history review and evaluation for other causes of hepatic failure, hepatic vein thrombosis was detected in addition to the presence of antibodies against *Leptospira* antigen. Further studies into the causes of thrombosis and persistent hemoconcentration despite aggressive fluid resuscitation led to the diagnosis of polycythemia vera (cytometric analysis). During her stay, she further worsened despite aggressive organ support including dialysis but she succumbed to gram-negative sepsis that occurred during her stay in ICU. This is an interesting and rare case of leptospirosis that unveiled a case of previously asymptomatic polycythemia vera.

**Keywords:** Budd–Chiari syndrome, Fulminant hepatic failure, Leptospirosis, Polycythemia vera, SPIRO.

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## INTRODUCTION

In tropical and subtropical regions of India, acute febrile illness is because of multiple infective pathogens and categorized as tropical fever which mandates investigations. A seasonal change due to vectors is common and usually points to a specific illness. Clinical suspicion and identification prior to reports or evaluation are based on a syndromic approach to the illness. Patients who require ICU care during the course of illness are likely to be sick and have higher morbidity and mortality. Late institution of therapies is another factor that contributes to the outcome. Due to overlapping symptoms among illnesses and in ICU patients who are sick, it is prudent to undertake a detailed history taking and have a stepwise approach to working up the causes based on the local prevalence of these illnesses.<sup>1</sup>

## CASE DESCRIPTION

A 19-year-old young Indian lady came to our tertiary care center with complaints of fever with rigor, jaundice, altered mentation, and renal failure. Following a fever workup and starting on antibiotics in the emergency department, she was admitted to the medical ward for further management. In view of the deteriorating conscious state, the patient was shifted to the ICU. Based on possible tropical fever presenting with jaundice, a leptospirosis evaluation was undertaken as part of initial fever testing and was noted to be positive. We reviewed her history as she continued to deteriorate despite optimizing antimicrobial agents. Her mother confessed to jaundice being present for a few weeks prior to the illness and that she was exposed to alternative therapies (ayurvedic medication) for the same as she was otherwise doing well. A further workup for intrahepatic and extrahepatic causes was initiated for rapidly progressing conjugated hyperbilirubinemia including Wilson's disease.<sup>2</sup>

Investigations noted a rapidly worsening conjugated hyperbilirubinemia and hyperammonemia with coagulopathy confirming fulminant hepatic failure (FHF). Investigations failed to detect viral hepatitis as a cause of the above. This led to a

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referral to the gastroenterologist with transplant expertise for an opinion as she fit the criteria for liver transplantation. The patient had persistent hemoconcentration beyond 1.5 days after continuous intravenous fluid therapy. A contrast-enhanced CT scan of the abdomen to evaluate the hepatobiliary system showed a congested large bowel with hepatic vein thrombosis and caudate lobe enlargement (acute Budd–Chiari syndrome [BCS]), with no evidence of cholestasis. An interventional radiologist was consulted but any invasive radiological intervention was deferred because of coexisting coagulopathy, renal failure requiring renal replacement therapy, and septic shock requiring high doses of vasopressors.

In view of hydration-resistant hemoconcentration, she underwent a phlebotomy until her hematocrit level is maintained at or below 45. On further evaluation and as per the hematologist's opinion, polycythemia vera (PV) was confirmed based on the flow cytometry analysis with two major criteria being met toward the WHO diagnostic criteria.<sup>3</sup>

Despite complete workup, pharmacotherapy, hemodialysis, and supportive care, her FHF progressively worsened. She was evaluated with a bedside Doppler of the hepatic vessels as well as sepsis. The Doppler did not show any further worsening of the hepatic and portal vessel morphology but blood cultures noted gram-negative organisms. In a low- to middle-income country healthcare setting, difficulty with transplant listing and concurrent gram-negative sepsis are the reasons she could not be referred for a liver transplant as rescue therapy.<sup>4,5</sup> Though *Klebsiella pneumoniae* bacteremia was addressed with appropriate antimicrobial agents (including carbapenem and polymyxin), sepsis overwhelmed the clinical state and she succumbed to the illness on day 8 following the admission.

## DISCUSSION

FHF fulfilling criteria for liver transplantation is associated with very high mortality. Identification of FHF is of prime importance as it allows for a systematic workup and in turn management. Rescue strategies like liver transplantation could reduce mortality to under 40% in people who otherwise have a near-fatal illness.

In our case, we were faced with a presentation similar to a tropical fever, and workup did present findings and investigations supportive of leptospirosis (modified Faine's criteria score: Total >25).<sup>6</sup>

This case highlights the need for further evaluation of FHF in patients with leptospirosis when the apparent remission of leptospirosis does not concur with worsening liver function. The disease course is generally mild to moderate and often complicated by liver failure.<sup>7</sup> Severity evaluation based on scoring systems (out patient department [OPD] Lepto score or systolic blood pressure  $\leq$  mmHg -1 Point, respiratory auscultation abnormalities -1 point, oliguria -1 point [SPiRO] score) does not include hepatic dysfunction or conscious state.<sup>8</sup> The patient was managed with ceftriaxone and doxycycline initially and is an appropriate line of management in severe cases.<sup>9</sup>

The patient was monitored in ICU awaiting a response but worsening of sensorium and liver dysfunction prompted extended workup which noted worsening coagulopathy as well as hyperammonemia, confirming the ruminant nature of liver dysfunction. Due to the disproportionate hyperbilirubinemia, patients were evaluated for hepatic and extrahepatic causes. Due to the absence of clear pathology on the bedside ultrasound of the hepatobiliary system, the patient underwent an extensive viral marker evaluation followed by a contrast-enhanced CT of the abdomen. Given the clinical scenario of resuscitation, refractory hemoconcentration, and hepatic dysfunction, a finding of acute hepatic vein thrombosis led us to be concerned about myeloproliferative disorders, and further workup confirmed a diagnosis of PV according to WHO criteria.<sup>10</sup> PV is the commonest cause of BCS after viral causes. PV is an uncommon myeloproliferative disorder in which the bone marrow makes too many red blood cells and overproduction of white blood cells and platelets.<sup>11</sup> Hepatic vein outflow obstruction secondary to thrombosis is associated with hepatic malignancies, PV, use of oral contraceptives, paroxysmal nocturnal hemoglobinuria, lupus antiphospholipid antibody syndrome during pregnancy, myeloproliferative disorders,<sup>12,13</sup> causes of hereditary thrombophilia,<sup>14</sup> and sometimes herbal medications. The prevalence of PV in all diagnosed cases of BCS is around 40%.<sup>15</sup> Portal vein thrombosis in the absence of liver cirrhosis

and local malignancy<sup>16</sup> is less frequently encountered and shows an etiological overlap with primary BCS evidence suggests that the western population has a higher proportion of hepatic vein thrombosis compared to the Indian/Southeast Asian population where inferior vena cava thrombosis is more common.<sup>17</sup>

Sepsis in patients who are suffering from acute liver failure (ALF) (fulminant) is common and it is more likely to be gram-negative organisms. Current guidance of ALF management confirms a low threshold to initiate antimicrobial agents for patients with worsening sensorium, development of severe metabolic acidosis or new organ dysfunction, and/or suspicion of infection. The patient was managed with a broad-spectrum cover including polymyxin for an XDR *Klebsiella* bloodstream infection.<sup>18</sup>

## CONCLUSION

Progressive liver failure after adequate antimicrobial treatment in leptospirosis mandates the need for further evaluation of history and investigations to rule out other potential causes. Early diagnosis and timely therapy can reduce mortality. The clinical condition and biochemical analysis may not be obvious of the underlying disease at initial presentation. Along with all potential infective causes of progressive hepatic dysfunction, BCS should always be suspected in any case of polycythemia and fluid resuscitation-resistant hemoconcentration. A detailed history, clinical examination, and full workup are needed in all atypical presentations and rapid progression of common illnesses to early diagnosis of underlying illnesses and in turn prompt the management of both.

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