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T Cell Prolymphocytic Leukemia: A Rare Cause of Acute Liver Failure

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Acute liver failure is commonly defined as the development of hepatic encephalopathy within 8 weeks of the onset of jaundice in a person without underlying liver disease (1). It affects approximately 2000 persons per year in the United States (2). Until recently, viral hepatitis was the most common cause of acute liver failure, but it has now been replaced by acetaminophen toxicity and idiosyncratic drug reactions as the number one cause (2).

Malignancy is an uncommon etiology of acute liver failure rarely considered in the differential diagnosis (1, 3). The diagnosis is made at autopsy in a majority of cases. Most cases of liver failure secondary to malignancy that have been described in the literature to date are due to metastatic tumor or lymphoma. We describe the case of a 58-year-old man who developed acute liver failure due to T-cell prolymphocytic leukemia. Only seven adult cases of acute liver failure secondary to leukemia have previously been reported in the literature (4–7), and to our knowledge this is the first case report of acute liver failure due to T-cell prolymphocytic leukemia.

CASE REPORT

A 58-year-old white man presented to the emergency room with a 2-week history of abdominal pain, nausea, vomiting, and diarrhea. These symptoms were associated with poor oral intake and fever. He had been diagnosed with T-cell prolymphocytic leukemia 2 years prior to admission on the basis of a peripheral blood smear showing typical morphology of blood lymphocytes (medium-sized peripheral blood prolymphocytes, approximately twice the size of a small lymphocyte, with immature-appearing nuclear chromatin, a single, prominent vesicular nucleolus, and scant to moderate cytoplasm) and a bone marrow aspirate showing infiltration by similar cells. Prolymphocytes comprised >55% of the cells in the blood and bone marrow. Phenotypically, these were T cells positive for CD4/CD8 and lack of CD 34. The patient was treated with chemotherapy, which included mitoxantrine, pentostatin, fludarabine, and alemtuzumab (human CD 52 antibody). His last treatment was 15 months prior to presentation, and he had been in remission since. The patient's medical history was significant for hypertension, coronary artery disease, prior cerebro-vascular accident, and gastroesophageal reflux disease. He had no underlying history of liver disease. He denied any alcohol or illicit drug use. Medications on admission included bupropion, esomeprazole, and trandolapril.

Pertinent physical examination findings included scleral icterus, macular–papular rash on the upper extremities, and right upper quadrant abdominal tenderness. Liver span was normal. Laboratory tests on admission were remarkable for cholestasis (Table 1). Tests for other etiologies of liver disease such as drugs, viral infections, and autoimmune disorders were negative (Table 2). Radiological imaging studies including CT of the abdomen and pelvis were unremarkable except for mild splenomegaly. An endoscopic retrograde cholangiopancreaticogram (ERCP) was performed and showed a normal nondilated biliary duct.

The patient developed hepatic encephalopathy on hospital day 18, with continued worsening of his liver enzymes. A transjugular liver biopsy was performed and showed extensive infiltration of the liver parenchyma with lymphocytes consistent with recurrence of T-cell prolymphocytic leukemia (Figure 1). Lymphocyte cell surface markers for the liver biopsy were not performed. Chemotherapy with alemtuzumab was started. The patient's condition continued to deteriorate, and he developed multiorgan failure. He died on hospital day 21.

DISCUSSION

Leukemia is a hematologic neoplasm that usually presents with widespread involvement of the bone marrow

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TABLE 1. LABORATORY DATA

	18 mo prior to admission	*12 moprior to admission*	*On admission*	*Hospital day 6*	*Hospital day 12*	*Hospital day 18*
Total bilirubin	0.5	0.6	4.7	6.5	21.6	30.9
γ-Glutamyl transferase (GGT)	348	474	570	536	440	714
Alkaline phosphatase	145	289	357	348	403	636
Aspartate transaminase (AST)	74	38	104	77	141	82
Alanine transaminase (ALT)		41	224	105	84	33
Lactate dehydrogenase (LDH)	240	265	232	238	579	766
Prothrombin time (PT)	18	12.4	17.6	17.6	17.9	16.4
Partial thromboplastin time (PTT)		27.7	30.9	37.7	43.5	56.5
International normalized ratio (INR)	1.5	0.9	1.4	1.5	1.5	1.4
Creatinine	1.0	1.2	0.9	0.9	1.8	4.4
Lactate			1.0			

Note. Normal ranges: total bilirubin, 0.1–1.2 mg/dL; AST, 10–40 IU/L; ALT, 5–40 IU/L; GGT, 5–70 IU/L; alkaline phosphatase, 40–120 IU/L; LDH, 100–250 IU/L; PT, 11.5–14.7 sec; PTT, 23–36.9; INR, 1.0; lactate, 1–3.

and is typically accompanied by the presence of large numbers of tumor cells in the peripheral blood. Leukemia and lymphoma account for approximately 8.1% of newly diagnosed cancers each year (8). Hepatic involvement by leukemia is fairly common, occurring in 80–100% of cases in chronic leukemia and 60–70% of cases in acute leukemia (9). However, it rarely presents as acute liver failure, and patients infrequently die from liver complications.

It is important to identify the cause of liver failure in patients with leukemia to treat correctable etiologies. The differential diagnoses of liver failure in these patients include infection, chemotherapy complications, drug toxicity, radiation injury, and diffuse infiltration of the liver. This case is unique in that it is the only reported instance of acute liver failure secondary to diffuse hepatic infiltration in a patient with T-cell prolymphocytic leukemia.

TABLE 2. LABORATORY WORKUP

Laboratory test	*Result*
Antimitochondrial antibody	Negative
Anti-nuclear antibody	Negative
Anti-smooth muscle antibody	Negative
Complement levels	Negative
Hepatitis serologies*	Negative
Human immunodeficiency virus	Negative
Cytomegalovirus	Negative
Human simplex virus I & II	Negative
Epstein Barr virus	Negative
Parvovirus B19 antibody	Negative
Syphilis serology (VDRL)	Negative
Acetaminophen level	Negative
Urine drug screen	Negative

*Hepatitis A antibody (IgM and total), hepatitis B surface antigen, hepatitis B core antibody (IgM and total), hepatitis C antibody and hepatitis C RNA by PCR (qualitative).

T-cell prolymphocytic leukemia is a rare, well-defined entity usually seen in patients over the age of 50, and it has a male predominance (10). It is characterized by elevated white blood-cell counts, hepatosplenomegaly, poor response to therapy, and poor survival. T-cell prolymphocytic leukemia represents only 2% of cases of small lymphocytic leukemias in adults. The pattern of hepatic infiltration varies among the different types of leukemias (9). T-cell prolymphocytic leukemia commonly affects the sinusoids as well as the portal triads. Laboratory studies typically indicate a pattern of cholestasis as seen in this patient, thought to be secondary to extensive hepatic infiltration. In our case, the liver biopsy was delayed while further laboratory workup (see Table 2) was being awaited, but it is unlikely to have changed the clinical outcome given the poor response to therapy and poor survival seen in patients with T-cell prolymphocytic leukemia (10). In diffuse leukemic infiltration of the liver, mortality is almost 100%. This patient continued to deteriorate despite being started on chemotherapy with alemtuzmab. He died 3 weeks after presentation.

In summary, it is very common to see hepatic involvement by leukemia, but it rarely presents as acute liver failure. The common causes of acute liver failure must first be excluded. When no other cause can be identified, malignant infiltration should be considered in the differential diagnosis, and a liver biopsy performed to confirm this diagnosis. A limited number of adult cases of acute liver failure due to leukemia have been described in the literature, and this is the first reported case of acute liver failure due to T-cell prolymphocytic leukemia.

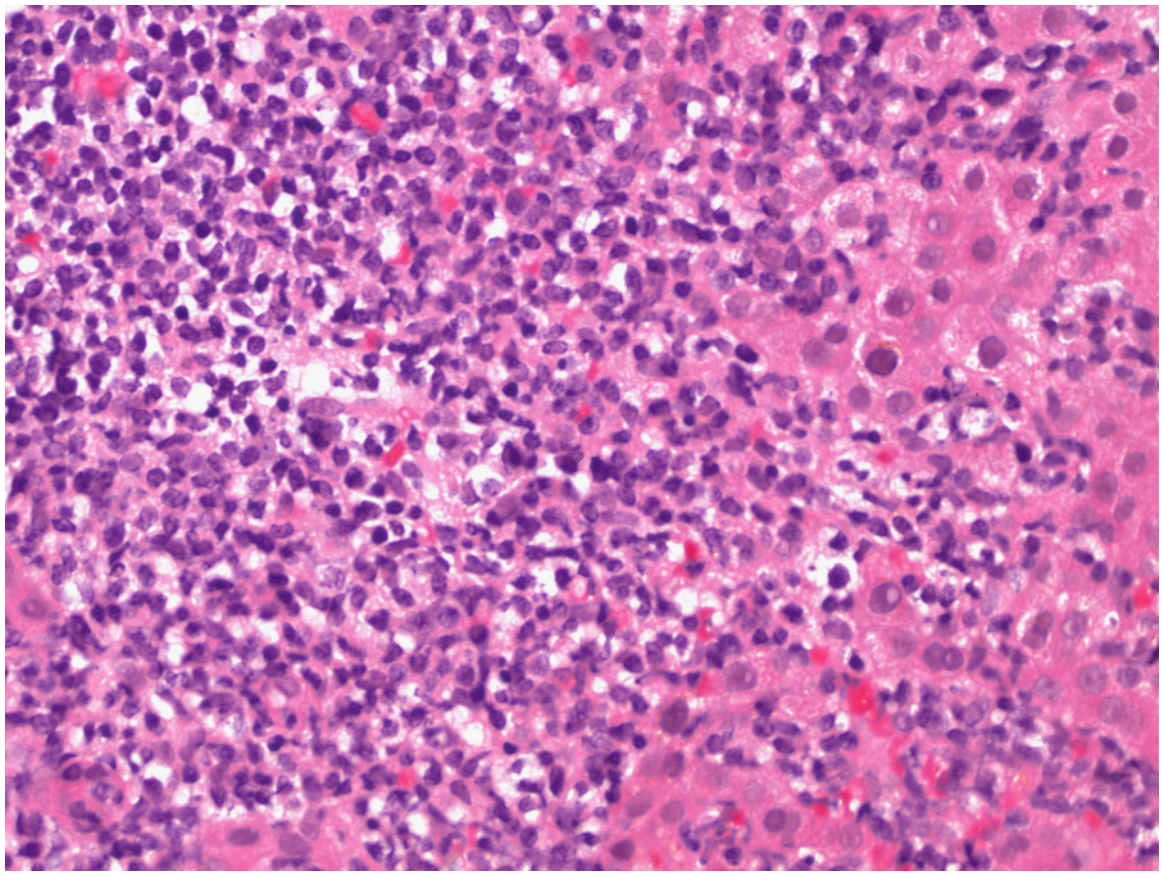

Fig 1. Liver biopsy specimen showing extensive infiltration of liver parenchyma with lymphocytes. (Hematoxylin & eosin; original magnification, ×400.)

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