CASE REPORT

Diffuse large B-cell lymphoma causing acute liver failure: a rare case of survival

Devika Kapuria,¹ Kristen Strasser,² Abdulraheem Qasem²¹Department of Internal Medicine, University of Missouri Kansas City, Kansas City, Missouri, USA²Department of Hematology and Oncology, University of Missouri Kansas City, Kansas City, Missouri, USA

Correspondence to

Dr Devika Kapuria,
kapuriad@umkc.edu

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SUMMARY

Acute liver failure is a rare but life-threatening illness with an incidence of 2–8 per million population. The most common causes of acute liver failure include drug ingestion and viral hepatitis followed by ischaemic hepatocellular injury and, less commonly, malignancy. Our patient presented with acute liver failure, which was found to be secondary to hepatic infiltration by diffuse large B-cell lymphoma. He received early treatment and has been in remission for more than a year after his initial presentation. To the best of our knowledge, our patient is the second reported survivor of acute liver failure caused by malignant hepatic infiltration by diffuse large B-cell lymphoma.

BACKGROUND

Acute liver failure (ALF) is a rare but life-threatening illness with an incidence of 2–8 per million population,¹ with common causes being drug-induced liver injury, viral hepatitis and, very rarely, malignancy. It is defined as ‘evidence of coagulation abnormality, usually an international normalised ratio (INR) of >1.5 and any degree of mental retardation in a patient without pre-existing cirrhosis and with an illness of <26 weeks’ duration’.² Acetaminophen poisoning is the leading cause of acute liver failure in the developed world,³ followed by viral hepatitis (12%),^{2–3} Wilson’s disease (2–3%),⁴ autoimmune hepatitis, ischaemic hepatocellular injury and rarely malignant infiltration.³

Prompt recognition of acute liver failure and early diagnosis is vital in the management of patients. ALF as the manifestation of malignant hepatic infiltration by lymphoma is extremely rare, and the only chance at survival these patients have is a low threshold of suspicion and early initiation of therapy.⁵ Our case holds special interest as the patient developed acute liver failure 3 days into hospitalisation, by which time we were able to get a liver biopsy while he was stable, and reach the diagnosis of lymphoma around the same time he went into ALF, prompting immediate treatment, which most likely saved his life.

In a case series performed over 18 years, 17 out of 18 patients with ALF due to malignant infiltration died of multiorgan failure within 6 days of hospital admission.⁶

CASE PRESENTATION

Our patient was a 57-year-old African-American man, with no significant medical history other than alcohol use, who presented to the emergency

department with 3 weeks of left upper quadrant (LUQ) abdominal pain with bloating, constipation, darkening of urine and melena. Physical examination showed scleral icterus with dry and jaundiced oral mucosa, diffuse abdominal pain, especially in LUQ, with distension, palpable liver with firm/round margin 5 cm below the costal margin and splenomegaly. CT of the abdomen and pelvis showed hepatomegaly and splenomegaly with innumerable spherical hypodensities in the liver, with an indeterminate left lower lobe 1.3 cm pulmonary nodule (figure 1). CT of the chest showed a borderline enlarged right hilar lymph node with heterogeneous left thyroid mass and left thyroid nodule. The patient underwent ultrasound-guided liver biopsy the next day. He also had an MR cholangiopancreatography, which showed mild intrahepatic biliary duct dilation due to invasion of ducts by metastatic hepatic masses and compression of proximal common bile duct due to a large hepatic mass. Bone scan was negative.

Five days after admission, the patient became more somnolent and subsequently went into acute hepatic failure with encephalopathy, with an INR of 3 (table 1). His biopsy results came back the next day showing diffuse large B-cell lymphoma. Cytogenetic analysis showed high-grade NHL Ki-67 100% likely DLBCL vs Double Hit vs Burkitt’s lymphoma (figures 2–5). The patient was treated with steroids and one dose of rituximab. After 3 days, his liver function tests (LFT’s) began trending down with an improvement in his mental status. Subsequent bone marrow biopsy and lumbar puncture ruled out bone marrow and brain involvement. On day 7 of hospitalisation, he was started on cycle one of EPOCH-R (etoposide, doxorubicin, cyclophosphamide, vincristine, prednisone and

Figure 1 CT scan showing heterogeneous opacities in the liver.

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Table 1 Serum liver function tests during patient's admission

	Bilirubin (T/D/I) mg/dL	ALP (U)	AST (U)	ALT (U)	LDH (U)	Ammonia (µg/dL)
Admission	1.4/0.8/0.6	314	204	83	219	32
Day 5	15.9/9.6/6.3	168	1441	485	2067	71
Discharge	4.5/2.3/2.2	273	73	119	100	NA

ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate aminotransferase; LDH, lactate dehydrogenase; NA, not applicable.

rituximab) chemotherapy.⁷ He was discharged home after cycle one with improvement in his LFT's and in his general condition. He subsequently underwent another five cycles of EPOCH-R chemo with intrathecal prophylaxis. A repeat CT of his abdomen showed significant resolution of his liver masses. (figure 6).

A positron emission tomography scan carried out 6 months after the patient's discharge showed complete remission.

DIFFERENTIAL DIAGNOSIS

We initially thought the patient had hepatic and pulmonary metastases from a solid tumour most likely originating from his thyroid. Also, given his history of alcohol use, we also thought he could be suffering from encephalopathy due to decompensated alcoholic cirrhosis.

OUTCOME AND FOLLOW-UP

The patient completed six cycles of DA-EPOCH in February 2014. He also received intrathecal methotrexate prophylaxis. Given his high IPI score, he was referred to a bone marrow transplant centre for consideration of high-dose therapy and autologous bone marrow transplant, but he declined.

As of now, there has been no evidence of recurrence of lymphoma. The patient continues follow-up with oncology every 3 months. He reports a good functional status and denies any problems.

DISCUSSION

Haematological malignancies are the most common cause for malignant hepatic infiltration, however, ALF due to the same was observed in only 0.44% of cases of liver failure in one of the largest single-centre studies undertaken.⁶ There has also

Figure 2 H&E stain showing lymphoma cells at ×10.

Figure 3 H&E stain showing lymphoma cells at ×100.

Figure 4 CD 20 stain at ×150.

Figure 5 CD 3 stain at ×150.

been a report of ALF as a manifestation of relapsing non-Hodgkin's lymphoma where prior knowledge of the malignancy helped in initiating early chemotherapy and enabling survival.⁸ Another reported case is of hepatic lymphoma causing ALF in a patient who underwent liver transplantation.⁹

Figure 6 CT scan showing resolution of opacities 3 months later.

Diagnosis, as mentioned above, is often challenging due to the absence of a primary malignancy, acute instability of the patient precluding a liver biopsy and a lack of awareness.

Prodromal symptoms may be seen in some patients in the accompaniment of lymphadenopathy, but most often the

Learning points

- ▶ Acute liver failure is a rare but life-threatening illness, with prompt evaluation for cause and initiation of treatment being key to preventing mortality.
- ▶ Acute liver failure due to malignant infiltration is very rare, however, it needs to be kept in mind for any patient presenting with acute liver failure.
- ▶ In absence of radiological or physical findings and no evidence of another cause, liver biopsy early in the course of hospitalisation is essential.
- ▶ Peripheral lymphadenopathy and presence of prodromal symptoms are indicators of malignant infiltration.

presentation is similar to that in other, more usual causes. Very often, the diagnosis is too late and the patient is too unstable to initiate chemotherapy.⁵ Although orthotopic liver transplantation is the only life-saving therapy for all end-stage liver diseases, malignant metastatic lymphoma is considered a contraindication to liver transplantation.

Death in these patients generally occurs due to ALF leading to multiorgan failure. The mechanism of liver failure is thought to be due to infiltration of small intrahepatic bile ducts leading to cholangitis, ischaemic injury and duct necrosis.¹⁰

Competing interests None declared.

Patient consent Obtained.

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