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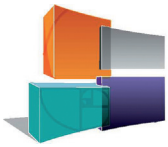

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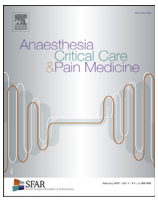

Letter to the Editor

T-cell lymphoma with secondary hemophagocytic lymphohistiocytosis as a rare cause of acute liver failure
T-cell lymphoma as a cause of acute liver failure

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Acute liver failure (ALF) is a life-threatening condition characterised by rapidly progressive liver dysfunction (whose signs are jaundice, coagulopathy and encephalopathy) occurring in patients without pre-existing liver disease. The main aetiology of ALF in western countries is acetaminophen overdose. Early recognition of the cause is crucial in order to initiate targeted treatment. The global management of acute liver failure is based on intravenous administration of N-acetylcysteine and organ failure support. The sickest patients may need liver transplantation, which have favourable long-term results in this setting.

A thirty eight-year-old female patient with no particular history other than recurrent genital herpes was admitted to intensive care for acute liver failure. She complained of abdominal pain with fever between 39 and 40 °C for the past week. She self-treated with paracetamol for a week (total dose: 14 grams). In the emergency department, physical examination showed stable haemodynamics, normal consciousness, diffuse abdominal pain, mild jaundice, hepatomegaly and multiple oral and genital vesicles. Blood tests revealed elevation of transaminases at 30 times the upper limit of normal, hyperbilirubinemia (84 μmol/L), normal coagulation and kidney function tests. The etiological assessment found negative HAV, HBV, and HEV serology. Gamma globulin levels were normal and autoantibody testing was negative. The abdominal ultrasound showed isolated splenomegaly. The patient was then admitted to a medical ward and a treatment with intravenous N-acetylcysteine, Acyclovir and Ceftriaxone was started. Two days after the admission, worsening of liver function, appearance of tachycardia (120 bpm), arterial hypotension (85/54 mm/Hg) and persistence of high fever motivated the transfer of the patient to our intensive care unit with a suspected diagnosis of herpetic acute liver failure.

Laboratory values on admission are summarised in Table 1. Rapidly, the patient developed encephalopathy and circulatory failure and was listed for emergency liver transplantation. During the surgery a liver biopsy was performed and revealed an infiltration of portal areas by malignant cells, contraindicating liver transplantation. The procedure was stopped and the patient died a few hours later.

The definitive histopathological analysis confirmed diffuse portal infiltration with large pleomorphic T cell lymphoma with a marked EBV staining, complicated with major intrasinusoidal hemophagocytosis. The result of the EBV PCR showed an intense replication (6.86 logUI/mL) while HSV PCR remained negative.

In case of ALF associated with fever, Herpes Simplex Virus (HSV) hepatitis must be suspected since a specific treatment (i.e. acivlovir) should be started without delay because of a very poor spontaneous outcome [1,2]. Most of the time, it occurs in an immunocompromised patient. It can be secondary to a primary infection or viral reactivation. Classically, clinical and biological features include plateau hyperthermia at 39–40 °C, transaminase elevation above 100 times the upper limit of normal, leukopenia and thrombocytopenia. Jaundice and vesicles are often missing. The diagnosis relies on HSV PCR or on histological examination of the liver (diffuse hepatocytes necrosis and intranuclear inclusions).

However, clinicians must be aware of other rare causes of ALF with fever, including Hemophagocytic Lymphohystiocytosis (HLH) and tumour infiltrations. Its diagnosis requires five criteria from those summarised in Table 2 [3].

The diagnosis of certainty remains histological, with the visualisation of hemophagocytosis on a bone marrow, lymph node, spleen, skin or liver sample. However, the hemophagocytosis images may be lacking, rendering diagnosis even more difficult. In addition, images of hemophagocytosis are not specific, and can be found in case of massive transfusion or acute viral or bacterial infection.

The main causes of HLH (which can be associated) are tumours and infections. Herpes viruses account for more than 60% of the infectious etiologies. EBV infection is found to be the cause of HLH in 30% of the cases. Tumoral causes include non-Hodgkin's malignant lymphoma in particular T- or NK-cell lymphomas [4].

Tumour infiltrations are a rare aetiology of acute liver failure (estimated incidence between 0.44 and 1.4%). Acute hepatic failure is related to the infiltration of tumour cells into the sinusoidal capillaries, resulting in anoxia of the hepatocytes. Haematological diseases are more frequent but solid tumours (e.g. breast adenocarcinoma, small cell bronchial cancer, melanoma and undifferentiated digestive carcinomas) may also be involved. Liver failure frequently leads to the discovery of the tumoral disease, but it can also occur when the diagnosis of cancer is already known.

The clinical presentation combines abdominal pain, ascites and jaundice. Thrombocytopenia is almost constant and more pronounced in cases of hematologic malignancies. Imaging can be normal. The presence of hepatomegaly (very frequent) should alert the clinician, since there are few differential diagnoses of acute liver failure associated with hepatomegaly. The prognosis is quasi-systematically fatal [5].

Tumour infiltration of the liver is a rare cause of acute liver failure but should not be ignored as they contraindicate transplantation. Evolution is quasi-systematically fatal. The

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Table 1
Biological data at ICU admission.

Biochemistry	Blood gas	Hematology
Na + 129 mmol/L	pH 7.41	Leukocytes 1.2 g/L
K + 3.2 mmol/L	PaCO2 27 mmHg	Neutrophils 74%
Cl − 103 mmol/L	PaO2 106 mmHg	Haemoglobin 9.2 g/dL
Protides 41 g/L	CO2 total 17 mmol/L	Platelets 45 g/L
Blood urea nitrogen 4.4 mmol/L	Lactates 2.58 mmol/L	Liver exams
Serum creatinine 57 μmol/L	Hemostasis	SGOT 889 UI/L
Ca + 1.53 mmol/L	Prothrombin rate 26%	SGPT 476 UI/L
Ph 0.5 mmol/L	TCA ratio 4.84	Alkaline phosphatase 321 UI/L
Troponin < 5 ng/mL	Fibrinogen 1.39 g/L	Gamma GT 226 UI/L
Triglycerides 2.29 mmol/L (N 0.50–1.70 mmol/L)	Factor V 36%	Total serum bilirubin T 174 μmol/L
Ferritin 35185 μg/L (N = 20 à 200 μg/L)	Factor II 36%	Conjugated serum bilirubin 128 μmol/L

Table 2
Diagnosis criteria of Hemophagocytic Lymphohystiocytosis.

Features	Cut off
Fever	
Splenomegaly	
Cytopenia	≥ 2 cell lines
Haemoglobin	< 9 g/dL
Platelets	< 100 g/L
Neutrophils	< 1 g/L
Hyperferritinemia	> 500 μg/L
Hypertriglyceridémia or	> 3 mmol/L
Hypofibrinogenemia	< 1.5 g/L
Elevated soluble CD25	> 2400 U/mL
Hemophagocytosis	Bone marrow or other tissues
Reduced or absent NK cytotoxicity	

elements that should suggest the diagnosis are the presence of hepatomegaly, abdominal pain and blood cell count abnormalities. Associated with HLH, it can mimic viral hepatitis, in particular herpes simplex virus hepatitis. Clinicians should keep in mind this rare cause of acute liver failure, and perform a liver biopsy if unusual signs are present to avoid needless transplantation.

Disclosure of interest

The authors declare that they have no competing interest.

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