

Jaundice with severe leucocytosis

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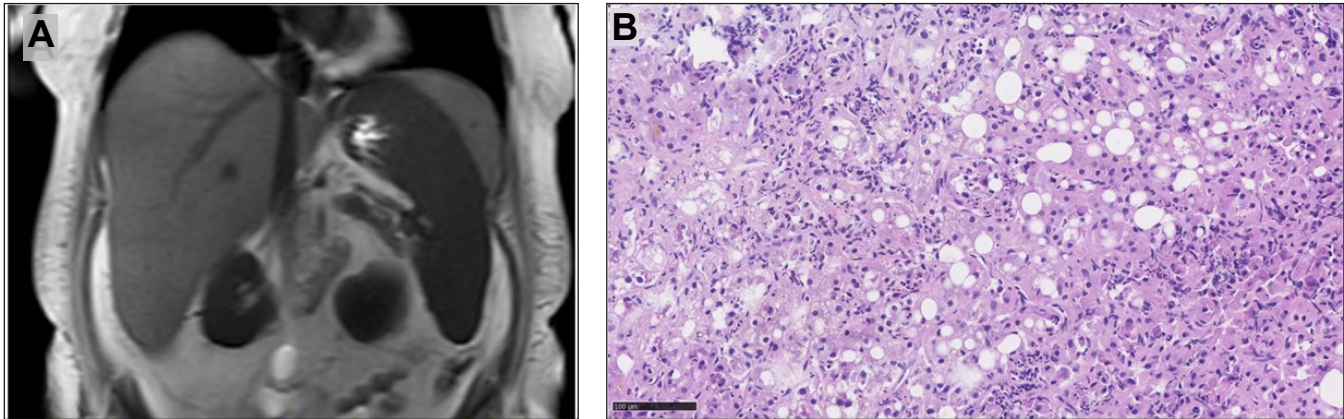


Fig. 1. MRI showing significant hepatosplenomegaly and histology showing altered liver architecture. (A) MRI showing significant hepatosplenomegaly without biliary dilatation. (B) On histology, the architecture of the liver appears altered, with a significant inflammatory infiltrate and moderate macrovesicular steatosis.

Description

A 36-year-old Hispanic woman was admitted to the emergency department with jaundice, abdominal pain and fatigue. The patient reported daily alcohol consumption (70 units per week). Physical examination revealed jaundice, hepatosplenomegaly, high BMI (30 kg/m²) and significant bilateral oedema of the lower limbs. Complete blood count showed a severe leucocytosis with neutrophilia (white blood cell count at 48,000/μl including 85% neutrophils) associated with bicytopenia (haemoglobin at 4.3 g/dl and platelet count at 87,000/μl). Liver tests indicated cholestasis (gamma-glutamyltransferase 573 U/L [<60 U/L] and alkaline phosphatase 300 U/L [40–130 U/L]) with total bilirubin of 11.6 mg/dl (direct 9.6 mg/dl [<1.2 mg/dl]), aspartate aminotransferase of 75 U/L [13–35 U/L], normal alanine aminotransferase and low albumin of 26 g/L [34–52 g/L]. C-reactive protein was elevated at 143 mg/L [<5 mg/dl]. Coagulation tests showed a prolonged prothrombin time of 18 seconds [9.3–14 seconds] and an elevated international normalised ratio (1.6). Blood triglycerides were increased to 264 mg/dl. Abdominal imaging revealed hyperechoic hepatomegaly at 28 cm and splenomegaly at 20 cm (Fig. 1A). Common causes of chronic liver disease (viral hepatitis, autoimmune) were excluded. A similar episode occurred 3 years earlier. A transvenous liver biopsy was performed (Fig. 1B).

What is your diagnosis?

- Chronic neutrophilic leukaemia.
- Severe alcohol-related steatohepatitis.
- Drug-induced liver injury.
- Sepsis complicating MetALD cirrhosis.

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Diagnosis and outcome

A liver biopsy was performed to exclude a haematological disease due to the extremely high level of leucocytes. Liver biopsy showed severe neutrophilic and lobular inflammation, moderate macrovesicular steatosis, satellitosis and prominent Mallory-Denk bodies, consistent with alcohol-related steatohepatitis (Fig. 2A).² Masson blue trichrome staining revealed significant pericellular fibrosis without cirrhosis (Fig. 2B). The hepatic venous pressure gradient was slightly increased (7 mmHg), which contrasted with the pronounced splenomegaly. Bone marrow biopsy did not indicate any leukaemia or myeloproliferative neoplasm and the cytogenetic/molecular tests did not reveal any clonal abnormality or mutation (*i.e.* BCR/ABL, JAK2V617F and CSF3R negative).

Surprisingly, 3 years earlier, the patient had a similar first episode (anaemia with severe leucocytosis, impaired liver function, hepatosplenomegaly and similar results at the liver biopsy). At this time, she denied any alcohol consumption. As the bone marrow biopsy showed a rich marrow with megakaryocytes and toxic granulations, an atypical myeloproliferative disorder was suspected and a treatment with hydroxyurea was started with a good improvement on white blood cell levels and liver tests. The treatment was stopped after 1 month because of worsened anaemia and thrombocytopenia. The liver tests and spleen size were back to normal after 5 months and the patient was lost of follow-up until the second episode. At the time of the second episode, the patient finally indicated that she also consumed alcohol before the first episode.

In this second episode, due to biopsy-proven severe alcohol-related steatohepatitis (with a Maddrey discriminant function of 37) oral methylprednisolone was started. With

corticosteroid treatment, white blood cells rose to 93,700/ μ l. However, treatment was interrupted after 7 days due to an unfavourable Lille's score. The evolution was slowly favourable with cessation of alcohol consumption, nutritional support, albumin supplements and diuretic and insulin treatment (due to the development of corticosteroid-induced diabetes). The patient was hospitalised for a total of 1 month. The total leucocyte and bilirubin count normalized after 2 months' follow-up. A total weight loss of 12 kg was noted due to the disappearance of fluid retention. Currently, after 1 year, the patient is asymptomatic and maintains abstinence from alcohol.

Severe alcohol-related steatohepatitis with leukemoid reaction

Alcohol-related hepatitis is commonly associated with leucocytosis (15,000–18,000 cells/ μ l). However, severe leucocytosis is rare and presents a diagnostic dilemma. Leukemoid reaction is defined as persistent neutrophilic leucocytosis above 40,000–50,000 cells/ μ l when the cause is not leukaemia (which it is important to exclude) but is rather linked to events outside the bone marrow, such as severe infections (tuberculosis, shigellosis, ...), intoxications, malignancies, severe haemorrhage, or acute haemolysis.¹ Leukemoid reaction is rarely found in alcohol-related hepatitis.³ One hypothesis concerning the pathophysiology of this phenomenon could involve the release of pro-inflammatory cytokines and granulocyte colony-stimulating factor by damaged hepatocytes in order to stimulate liver cell regeneration. However, of the 21 cases we found in the literature, only 6 survived. This case is the first reporting its possible recurrence.

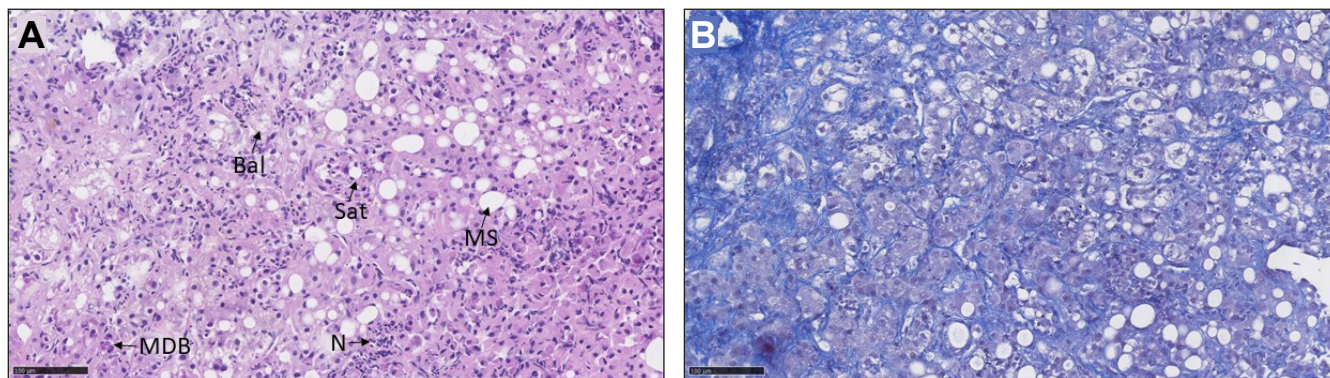


Fig. 2. High-magnification liver biopsy stained with H&E and Masson blue trichrome. (A,B) The high-magnification liver biopsy stained with H&E (A) and Masson blue trichrome (B) shows macrovesicular steatosis (MS). The large lipid vacuole pushes the nucleus to the periphery of the cell. The inflammatory infiltrate consists mainly of neutrophils with the nucleus divided into three parts (N). Images of satellitosis are also present (Sat). Mallory Denk bodies are also visible with intracytoplasmic eosinophilic condensation (MDB). Ballooned cells with clarified cytoplasm and a granular image around the nucleus still in a central position (Bal) provide further evidence for the diagnosis of alcohol-related steatohepatitis. On Masson trichrome staining, significant pericellular fibrosis, without cirrhosis, is observed.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Please refer to the accompanying ICMJE disclosure forms for further details.

Authors' contributions

Drafting of the manuscript: SH and NL; critical revision and approval of the final manuscript: SH, PB, PT, VH, NL.

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The patient gave her written and signed consent for the publication of this case report.

Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jhep.2023.10.014>.

References

- [1] Sakka V, Tsiodras S, Giamarellos-Bourboulis EJ, Giamarellou H. An update on the etiology and diagnostic evaluation of a leukemoid reaction. *Eur J Intern Med* 2006;17:394–398. <https://doi.org/10.1016/j.ejim.2006.04.004>.
- [2] Lanthier N, Spahr L. Letter: the value of quality liver biopsy before initiation of corticosteroids for severe alcoholic hepatitis. *Aliment Pharmacol Ther* 2022;55:889–890. <https://doi.org/10.1111/apt.16835>.
- [3] Morales AM, Hashimoto LA, Mokhtee D. Alcoholic hepatitis with leukemoid reaction after surgery. *J Gastrointest Surg* 2006;10:83–85. <https://doi.org/10.1016/j.gassur.2005.07.006>.