



Short communication

Acute liver failure and misdiagnosis: Do not forget viral hepatitis E

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ARTICLE INFO

Article history:

Available online 11 July 2018

Keywords:

Acute liver failure
Hepatitis E

Hepatitis A, D, and E viruses contribute to highly fulminant viral infections and subsequent acute liver failure. Viral hepatitis A (HAV) and E (HEV) infections have been mostly observed in low sanitary and socioeconomic conditions. The main sources of HEV are infected swine meat and contaminated drinking water via faecal-oral transmission. HEV-related acute liver failure is often lethal in the absence of targeted therapy. Moreover, diagnosis is often delayed, leading to worsened outcome and excluding potential liver transplantation consideration.

We report the case of a 78 year-old man, living in the south of France, W.H.O 1 status, with past medical history of obesity (body mass index = 34 kg/m²), Carpentier's mitral repair surgery, atrial fibrillation treated with coumadin and amiodarone, and uncomplicated medically treated sigmoid diverticulosis (normal colonoscopy one year ago).

The patient was admitted to the emergency department (day 1) after consulting his general practitioner for asthenia, fever, abdominal pain, jaundice and discoloured stools, evolving for a week. Physical examination found no sign of peritonitis, circulatory or respiratory failure, no altered consciousness neither delirium. Laboratory tests showed: hyperleukocytosis = 16.8 G/L, haemoglobin = 12.8 g/dL, platelet count = 227 G/L, kaliemia = 5.0 mmol/L, serum creatinine level = 75 µmol/L, C-reactive protein = 25 mg/L, massive cytolysis (aspartate aminotransferase (AST) = 5534 UI/L, alanine aminotransferase (ALT) = 6591 UI/L) and severe liver failure (prothrombin time (PT) < 10%, total plasma bilirubin level = 228 µmol/L, Fig. 1). The liver ultrasound found an alithiasic cholecystitis. The patient was admitted to the surgical ward and

treated with intravenous ceftriaxone therapy associated with the patient's usual treatment (digoxin and cordarone).

On day 2, the patient developed confusion, in the context of urinary retention and overload haematuria. A urine catheter was inserted and treatment with oral sodium polystyrene sulfonates and intravenous furosemide was induced as kaliemia rose up to 5.9 mmol/L.

On day 3, the mental state worsened, physical examination found a Glasgow Coma Scale = 3 associated with oliguria (< 250 mL in 12 h). Blood samples showed: KDIGO 2 acute kidney injury with serum creatinine level = 158 µmol/L, kaliemia = 5.9 mmol/L, decrease in liver enzymes but persisting liver failure (478 UI/L AST and 2306 UI/L ALT, Factor V = 22%, Fig. 1) along with balanced metabolic acidosis (pH = 7.44, arterial lactate level = 9.9 mmol/L). Orotracheal intubation was performed. The patient was given intravenous fresh frozen plasma and vitamin K. Ceftriaxone was switched to piperacillin-tazobactam. Brain and abdominal CT scans did not show any cerebral bleeding or oedema, any signs of acute or chronic hepatic, biliary tract and gall bladder abnormalities.

The patient was transferred to the ICU on day 3 (SOFA score = 17, SAPS2 score = 94). Considered as brain injured, the patient was monitored by Glasgow Coma Scale, Behaviour Pain Scale, invasive blood pressure, temperature, hourly urine output, daily transcranial Doppler, PaO₂/FiO₂ ratio, routine biochemistry and haematology tests. Trans-cranial Doppler remained normal along the ICU stay (IP < 1.4, diastolic velocities > 20 cm/s).

Local liver transplant intensive care unit advice was sought, ruling out super-emergency liver transplantation indication, due to multiple organ failure, patient age and history of cardiac surgery. Considering the hypothesis of evolving peritonitis, amikacin was added to on-going piperacillin-tazobactam course. Intravenous N-acetylcysteine was also started. Recent history found no consumption

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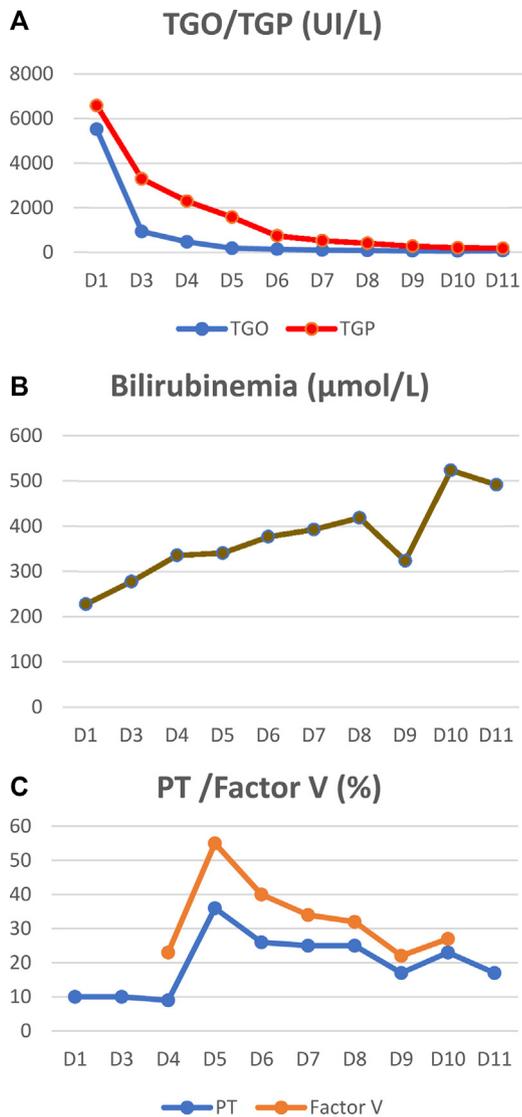


Fig. 1. Evolution over time from day 1 (D1) to day 11 (D11) of TGO/TGP (A), total bilirubinemia (B) and PT/Factor V (C).

of hepatotoxic food, i.e. amanita. A, B, C hepatitis viruses, HIV, CMV, EBV screenings were all negative. Plasmatic acetaminophen, cooper, ceruloplasmin, iron and transferrin concentrations were normal. There was no history of alcohol consumption or recently introduced hepatotoxic medication (except for ceftriaxone 1 g q.d. since the admission in the emergency department). However, a new family meeting revealed that the patient used to drink his own well water in the backcountry, as well as the presence of boars' faeces nearby his house and the well.

On day 5, another abdominal CT scan was performed, showing no signs of peritonitis. Positives HEV IgM antibodies came back leading to immediately initiating intravenous ribavirine with rifaximine. Blood cultures, urine culture, pulmonary samples were negatives.

On day 11, multiple organ failure worsened with: persistent grade 3 hepatic encephalopathy after all sedative agents have been ceased, refractory shock, anuria, acute liver failure (PT = 16%, bilirubinemia = 508 µmol/L, Fig. 1) leading to the patient death despite rescue extracorporeal liver support (Molecular Adsorbents Recirculating System (MARS)).

The European Association for the Study of the Liver (EASL) describes acute liver failure as "an acute abnormality of liver blood tests in an individual without underlying chronic liver disease associated with development of a coagulopathy of liver aetiology, and clinically apparent altered level of consciousness due to hepatic encephalopathy" resulting in high mortality [1].

Viral hepatitis is the first aetiology of acute liver failure [2] in France, and the first known aetiology of liver transplantation in Europe [3]. Precise diagnosis is recommended [1] to establish the need for transplantation, and stage the prognosis, which seem poorer in elderly patients, as in the present patient.

Although often diagnosed in patients travelling in Asia or Africa, some studies [4–6] showed that autochthonous hepatitis E was endemic in Western Europe.

According to the literature, between 9 and 22% of hepatitis E acute liver failure were first diagnosed as drug-induced liver injury [7,8] underlining the fact that a complete and structured assessment of medical history can be difficult, but absolutely necessary, looking for recent porcine contact or travel in endemic regions.

N-acetylcystein, considered as the main treatment improving prognosis should be initiated early in any acute liver failure, even in non-paracetamol related intoxication or overdose [9,10].

In this severe HEV infection, ribavirine has been initiated as it has been proposed as a potential rescue therapy for acute or chronic hepatitis E infection [11,12].

In conclusion, this case report highlights three major messages:

- a systematic and extended screening of the most commons aetiologies of acute liver failure (paracetamol overdose or misuse, others drugs reaction, hepatitis viruses) must not be delayed or shortened because of clinical suspicion, i.e. alcohol consumption forejudge or recent use of paracetamol at standard dosing regimens;
- early discussion with a transplant unit should be encouraged to avoid useless long-lasting bridges therapies in the context of acute liver failure;
- even if HEV infection is a rare cause of acute liver failure, risk factors of HEV exposure should be sought during past medical history examination.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial or not for profit sectors.

Disclosure of interest

The authors declare that they have no competing interest.

Références

- [1] Wendon J, et al. EASL Clinical Practical Guidelines on the management of acute (fulminant) liver failure. *J Hepatol* 2017;vol. 66(No. 5) [p. 1047–1081].
- [2] Ichai P, et al. Patients with acute liver failure listed for superurgent liver transplantation in France: reevaluation of the Clichy-Villejuif criteria. *Liver Transpl* 2015;vol. 21(No. 4) [p. 512–523].
- [3] Germani G, et al. Liver transplantation for acute liver failure in Europe: outcomes over 20 years from the ELTR database. *J Hepatol* 2012;vol. 57(No. 2) [p. 288–296].
- [4] Mansuy JM, et al. Acute hepatitis E in south-west France over a 5-year period. *J Clin Virol* 2009;vol. 44(No. 1) [p. 74–77].
- [5] Dalton HR, Bendall R, Ijaz S, Banks M. Hepatitis E: an emerging infection in developed countries. *Lancet Infect Dis* 2008;vol. 8(No. 11) [p. 698–709].
- [6] Rein DB, Stevens GA, Theaker J, Wittenborn JS, Wiersma ST. The global burden of hepatitis E virus genotypes 1 and 2 in 2005. *Hepatology* 2012;vol. 55(No. 4) [p. 988–997].

- [7] Dalton HR, et al. The role of hepatitis E virus testing in drug-induced liver injury. *Aliment Pharmacol Ther* 2007;(No. 10) [p. 1429–1435].
- [8] Crossan CL, et al. Hepatitis E virus in patients with acute severe liver injury. *World J Hepatol* 2014;vol. 6(No. 6) [p. 426–434].
- [9] Nguyen-Khac E, et al. Glucocorticoids plus N-Acetylcysteine in severe alcoholic hepatitis. *N Engl J Med* 2011;vol. 365(No. 19) [p. 1781–1789].
- [10] Mumtaz K, et al. Role of N-acetylcysteine in adults with non-acetaminophen-induced acute liver failure in a center without the facility of liver transplantation. *Hepatol Int* 2009;vol. 3(No. 4) [p. 563–570].
- [11] Haboubi HNY, Diyar R, Benton A, Ch'ng CL. A case of acute hepatitis E infection in a patient with non-hodgkin lymphoma treated successfully with ribavirin. *Case Rep Gastrointest Med* 2017;vol. 2017:11.
- [12] Waldenström J, Castedal M, Konar J, Karason K, Lagging M, Norder H. Chronic hepatitis E infection with an emerging virus strain in a heart transplant recipient successfully treated with ribavirin: a case report. *J Med Case Rep* 2015;vol. 9(No. 1):11.