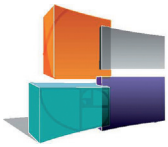
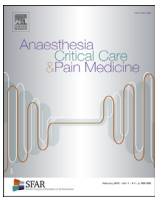
Anaesth Crit Care Pain Med 38 (2019) 9–10



SFAR
Société Française d'Anesthésie et de Réanimation



Editorial

Acute liver failure: Running fast between the traps

ARTICLE INFO

Keywords:
Acute liver failure
Hepatitis
Liver transplantation

Acute liver failure (ALF) is a critical condition characterised by a rapidly progressive liver dysfunction (usually assessed by a prothrombin rate lower than 50%) occurring in patients without previous history of liver disease. Initial features of coagulopathy and jaundice (respectively reflecting alterations of hepatic synthesis and clearance) are quickly followed by worsening of neurological status (defining former fulminant hepatitis) and can rapidly lead to death from intracranial hypertension or multiple organ failure (MOF) [1,2]. Despite significant improvement of management, ALF burden remains high without liver transplantation (LT). The outcome of ALF has been improved with emergency LT (70% of one-year survival) but it remains significantly poorer than the prognosis of LT in patients with cirrhosis (85% of one-year survival) [3,4].

These patients are usually admitted in acute care settings for the management of organ failures [2,5]. Given the frequent suspicion of sepsis, prompt initiation of empirical antibiotic (targeting gram-negative bacilli) is often required. Intravenous N-acetyl-cysteine (NAC) must be widely and rapidly administrated, whatever the suspected aetiology, because it may slow down liver dysfunction and promote liver regeneration while having a good safety profile.

Beside these first line treatments, the search for aetiology must be quickly initiated, as it is an important indicator for prognosis and treatment strategy. Determination of ALF aetiology requires medical history of the patient (recent or ancient), biology, imaging, and only rarely histology of liver. Indeed, the obligation to choose transjugular access limits the use of liver biopsy as initial approach in the context of ALF.

The diagnostic approach should be driven by the early recognition of the few aetiologies for whom a specific treatment is available (Table 1). The aetiological diagnostic also helps recognising patients that will not survive with medical treatment alone and that are likely to benefit for emergency LT. This assessment, initiated at the site of first presentation, should involve a specialist centre where LT is available to discuss the transfer of the patient at the earliest opportunity. Finally, some aetiologies should not be ignored as they contraindicate transplantation (Table 1). However, in case of rapid worsening of patient's status, decision to perform emergency LT can sometimes be taken only on the basis of neurological status and liver failure, even in the absence of known aetiology.

This issue of Anaesthesia, Critical Care and Pain Medicine reports three clinical cases [6–8] which highlight usual pitfalls and difficulties for the etiological diagnosis of ALF and the referral to emergency LT. Altogether, these cases nicely illustrate the main dilemma of LT in the context of ALF: early transplantation before the patient becomes too sick and on demand transplantation allowing potential liver recovering and thus avoiding futile LT.

Guillotin et al. [6] describe the case of a woman who developed ALF caused by Herpes Simplex Virus (HSV) hepatitis. This case highlights the unreliability of HSV serology and the potential paucity of clinical signs suggesting HSV diagnostic at the time of ALF. Rather, positive diagnostic of HSV was lately obtained with positive serum PCR and immunostaining of post-mortem liver biopsies. As HSV is a rare but severe cause of ALF, early pre-emptive therapy targeting this virus should be discussed and administered as early as non-specific treatments (NAC and wide spectrum antibiotics), in cases of suspicion of HSV or in cases of ALF of unknown origin without waiting for virological confirmation.

Laumon et al. [7] report a case of ALF due to Hepatitis E virus (HEV) where the patient was probably contaminated through water soiled by animal excrements. In this case, evolution toward ALF and MOF was rapid and occurred before positive result of HEV serology was known. HEV infection must be systematically searched at the onset of ALF, as antiviral therapy with ribavirin can be discussed. In this case, emergency LT was ruled out after discussion with the specialised centre, due to age, medical history with cardiac disease and severity of MOF, leading to high probability of death despite LT.

Finally, Chouik et al. [8] report a case of ALF rapidly worsening despite acyclovir in a patient with both history and clinical signs of HSV infection. The onset of MOF led to the decision to perform LT without confirmation of the HSV diagnosis and a liver biopsy performed at the beginning of the surgery pointed out a malignant infiltration of the liver that unfortunately led to contra-indicate LT. This case highlights the facts than unusual clinical and biological features must lead to question initial diagnostic and therapy, and that histology can bring definitive answers and major changes in therapeutic options.

In conclusion, ALF remains a critical condition, which requires early identification of hepatic or extra-hepatic organ failures and

https://doi.org/10.1016/j.accpm.2018.12.012

Table 1
Specific laboratory analyses and treatments for acute liver failure.

Aetiology	Laboratory analyses	Treatment
Paracetamol-related	Paracetamol serum level	N Acetyl-cysteine
Non-Paracetamol-related		N Acetyl-cysteine
HSV or VZV related	Anti-HSV IgM (herpes simplex virus types 1 and 2); HSV and VZV PCR	Acyclovir
HBV related	HBsAg, anti-HBc IgM (HBV DNA), delta if positive for HBsAg	Lamivudine
HEV related	Anti-HEV IgM	Ribavirin to be discussed
Hypoxic hepatitis	Echocardiography	None LT not indicated
Primary Budd-Chiari syndrome	Hepatic echo-Doppler	Anticoagulation TIPS if anticoagulation failure
Autoimmune	Antinuclear antibodies, antimitochondrial antibodies, anti-LKM antibodies, smooth muscle antibodies, hypergammaglobulinemia	Corticosteroids to be discussed
Wilson's disease	Serum caeruloplasmin, serum and urinary copper	D-penicillamine
Pregnancy-related	Abdominal Doppler ultrasound	Delivery
Lymphoma	Hepatic echo-doppler ± liver biopsy	Chemotherapy LT contraindicated

HBV: Hepatitis B virus; HSV: Herpes simplex virus; VZV: Varicella Zoster virus; HEV: Hepatitis E virus; PCR Polymerase-chain reaction; LT: Liver Transplantation; TIPS: Transjugular intrahepatic portosystemic shunt.

rapid aetiological diagnosis to adapt the treatment strategy. Prompt management of organ failures and initiation of specific treatments such as N-acetyl-cysteine and acyclovir (in cases of HSV suspicion) are of particular importance. The need for LT must also be quickly assessed as patient's condition can rapidly worsen while waiting for a graft. During this race against time, the multidisciplinary team must keep focused on the fact that some patients might not be eligible to LT due to aetiology of ALF (e. g. ischaemic hepatitis or malignancy) or too severe medical conditions.

Disclosure of interest

The authors declare that they have no competing interest.

References

[1] Bernal W, Wendon J. Acute liver failure. N Engl J Med 2013;369(26):2525–34.
[2] E.A.S.L.. Clinical Practical Guidelines on the management of acute (fulminant) liver failure. J Hepatol 2017;66:1047–81.
[3] Germani G, Theocharidou E, Adam R, Karam V, Wendon J, O'Grady J, et al. Liver transplantation for acute liver failure in Europe: outcomes over 20 years from the ELTR database. J Hepatol 2012;57(2):288–96.
[4] Agence de la Biomédecine. Rapport annuel; 2017, https://www.agence-biomedecine.fr/annexes/bilan2017/accueil.htm; 2017 [Accessed december 12 2018].
[5] Weiss E, Paugam-Burtz C, Jaber S. Shock Etiologies and Fluid Management in Liver Failure. Semin Respir Crit Care Med 2018;39(5):538–45.
[6] Guillotin V, De Guillebon S, Bui N, Sazio C, Boyer A. Herpes simplex virus: a rare but treatable cause of fulminant hepatitis. Anaesth Crit Care Pain Med 2019;38(1):77–8.
[7] Laumon T, Dietrich H, Muller L, Roger C. Acute liver failure and misdiagnosis: do not forget viral hepatitis E. Anaesth Crit Care Pain Med 2019;38(1):73–5.
[8] Chouik Y, Blaise L, Hachouf M, Giabicani M, Roux O. 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. Anaesth Crit Care Pain Med 2019;38(1):79–80.

Jean-Marc Delay[a], Audrey de Jong[a],
Catherine Paugam-Burtz[b], Emmanuel Weiss[b,*]
[a]*Department of Anaesthesiology and Critical Care, Saint-Eloi Hospital, Montpellier University Hospital, Montpellier, France*
[b]*Department of Anaesthesiology and Critical Care, Hôpitaux Universitaires Paris Nord Val de Seine, Hôpital Beaujon, Paris, France*

*Corresponding author: Beaujon Hospital, 100 bld du general Leclerc, 92110 Clichy, France
E-mail address: jm-delay@chu-montpellier.fr (J.-M. Delay).