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Drug-induced hepatitis: Etiological profile and therapeutic management

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Abstract

Drug-induced hepatotoxicity is one of the main forms of iatrogenic pathology, which is often under-diagnosed. Numerous drugs are implicated and can cause hepatic damage reproducing the whole spectrum of non-iatrogenic liver pathology, ranging from a simple transient disturbance of the liver balance to fulminant, life-threatening hepatitis. We report here our experience with a series of 194 patients who presented with drug-induced hepatitis, reviewing the data in the literature.

Keywords: Hepatotoxicity; Drugs; Jaundice; Cytolysis; Monitoring enzymes

1. Introduction

Drug-induced hepatotoxicity is one of the main forms of iatrogenic pathology, which is often under-diagnosed. Numerous drugs are implicated and can cause hepatic damage reproducing the whole spectrum of non-iatrogenic liver pathology, ranging from a simple transient disturbance of the liver balance to fulminant, life-threatening hepatitis. The aim of our work is to study the etiological profile and therapeutic management of drug-induced hepatitis.

2. Materials and methods

This is a retrospective descriptive monocentric study from January 2010 to August 2023 of patients with drug-induced hepatitis in the "Médecine B" Hepato-Gastro-Enterology and Proctology Department at CHU IIbn Sina, Rabat.

Diagnosis was based on the elimination of infectious, immunological and toxic causes of hepatitis. For all patients, viral serologies for hepatotropic viruses and a pharmacovigilance investigation were carried out before concluding that the cause was drug-induced.

3. Results

194 patients were included in our study, with a mean age of 44.2 years, ranging from 23 to 84 years. Female predominance was observed, with 110 women (56.7%) versus 84 men (43.2%), i.e. a sex ratio F/H of 1.3.

In 59 cases (30.4%), liver damage was discovered by chance during a biological check-up. In the other cases, clinical manifestations were dominated by jaundice in 112 patients (57.7%), followed by asthenia in 42 patients (21.6%), pruritus in 35 cases (18%) and fever in 17 cases (8.7%). Liver function tests showed cytolysis in 97 cases (50%), mixed disease in 74 patients (38.1%), and cholestasis in 23 patients (11.8%). The time to onset of clinical or laboratory signs

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of hepatotoxicity ranged from 03 days to 09 months. Severe acute hepatitis occurred in 70 cases (36%), including 48 cases (24.7%) of fulminant hepatitis. In all cases, viral serologies and autoimmune tests were negative. Liver biopsy was consistent with drug-induced hepatitis in 35 cases (18%). The main drugs implicated were anti-tuberculosis drugs in 110 cases (56.7%), followed by immunosuppressants, particularly azathioprine in 44 cases (22.6%), then paracetamol in 23 cases (11.8%), antidepressants in 6 cases (3%), and non-steroidal anti-inflammatory drugs (NSAIDs) in 3 cases (1.5%). Other drugs less frequently associated with liver dysfunction included allopurinol, fluconazole, synthetic antithyroid drugs, antiepileptics (Carbamazepine), hypolipidemics, ciprofloxacin, anti-TNF drugs (Adalimumab), and anti-angiotensin drugs: 1 case each (0.5%).

Discontinuation of the treatment in question was considered in all patients. Patients with fulminant acute hepatitis were managed in intensive care, and N-acetylcysteine was introduced in patients admitted for paracetamol-induced hepatitis. The outcome was favorable in 160 patients (82.4%), while 34 (17.5%) died of severe hepatocellular failure.

4. Discussion

The liver is a metabolic organ playing an essential role in the biotransformation and elimination of drugs (1). For this reason, drugs are an important and frequent cause of liver damage. These lesions can be of any kind, ranging from a simple elevation of liver enzymes to the patient's death. Acute drug-induced hepatitis is the most frequent complication of drug-induced iatrogenesis, and is the most common cause of acute hepatitis after the age of 50 (2). Asymptomatic forms are the most common, and are generally detected by abnormal liver tests such as serum aminotransferases and alkaline phosphatases, or by non-specific symptoms such as asthenia, nausea or vomiting (3).

The incidence of drug-induced liver damage is estimated at 14 to 19 cases per 100,000 people (4) (5). Although the most common presentation is asymptomatic elevation of liver enzymes, this condition is the most frequent cause of acute liver failure in most Western countries (over 50% of cases) (4). Drug-induced liver damage, which may be associated with overdose or therapeutic dose, results either from direct hepatotoxicity intrinsic to a drug, or from idiosyncratic (unpredictable) hepatotoxicity (6).

If liver damage is suspected on questioning, the first step is a clinical examination, followed by an ultrasound scan. This is followed by more or less specific liver tests and other imaging techniques. Finally, if necessary, a biopsy or cytopuncture is performed (3).

Establishing a reliable chronological link between exposure and the onset of disease is crucial. The typical latency period is 1 to 5 days for direct hepatotoxicity, and 5 to 90 days for idiosyncratic hepatotoxicity (4). It should be noted, however, that idiosyncratic hepatotoxicity may appear earlier if exposure has already occurred (5). The pattern of hepatic enzyme elevation may be cytolytic, cholestatic or mixed; however, no pattern of elevation can be precisely associated with specific drugs.

Drug-induced liver damage can be particularly difficult to distinguish from autoimmune hepatitis, since antibodies detected in the latter may also be detectable in drug-induced liver damage (5). The Roussel Uclaf Causality Assessment Method (RUCAM) clinical decision-making tool can help determine the likelihood of drug-induced liver damage (5).

Typically, liver enzyme levels fall within days or weeks; less than 10% of patients will still have chronic impairment 1 year later (7). If there is a sharp rise in liver enzymes (alanine aminotransferase ≥ 5× or alkaline phosphatase ≥ 2×, and total bilirubin ≥ 2× the upper limit of the normal range (5)) or clinical signs of liver failure, or if no improvement is seen within the expected timeframe, it would be indicated to conduct further investigations (e.g. liver biopsy) to explore other causes of liver damage or possible complications (5).

The first course of treatment is immediate discontinuation of the drug suspected of causing hepatotoxicity. No therapy can slow or halt the development of severe hepatocellular failure, and only liver transplantation can be effective. The most important measure is to monitor the enzymes ALAT, ASAT and PAL, particularly for drugs known to be hepatotoxic, in order to prevent any liver problems. This should be done systematically when a patient complains of asthenia, nausea, abdominal pain or fever, enabling the drug to be discontinued to avoid liver damage (3). Antidotes are available for certain drugs, such as N-acetylcysteine (NAC) for paracetamol. In the most serious cases, when liver damage is irreversible, the only treatment is liver transplantation.

5. Conclusion

Drug-induced hepatitis is a delicate condition, given its polymorphic presentation and the diversity of potentially hepatotoxic drugs prescribed. Diagnosis is based on the elimination of other possible causes of liver dysfunction, a suggestive or compatible chronology between the administration of the drug and the onset of hepatitis, and a favorable evolution after discontinuation of the drug. Prevention requires compliance with prescribing rules, early detection of signs of therapeutic intolerance and rigorous monitoring of progress under treatment.

Compliance with ethical standards

Statement of informed consent

All authors contributed to the conduct of this work. All authors also declare that they have read and approved the final version of the manuscript.

References

[1] GUENARD, H. Physiologie humaine. s.l. Pradel, 2009. ISBN: 978-2-913996-76-2.

[2] MALLAT, A. Hépatites médicamenteuses: diagnostic et prise en charge. s.l: Masson, 1999.

[3] J-P. BENHAMOU, S. ERLINGER. Maladies du foie et des voies biliaires. s.l.: Flammarion, 2000. ISBN: 2-257-13471-0.

[4] 4. Hoofnagle JH, Björnsson ES. Drug-induced liver injury — types and phenotypes. N Engl J Med 2019; 381:264–73.

[5] European Association for the Study of the Liver. EASL clinical practice guidelines: drug-induced liver injury. J Hepatol 2019;70: 1222–61.

[6] Kumachev A, Wu PE. Atteinte hépatique médicamenteuse. CMAJ. 2021 May 17;193(20): E746-E747. French. doi: 10.1503/cmaj.202026-f. PMID: 34001555

[7] David S, Hamilton JP. Drug-induced liver injury. US Gastroenterol Hepatol Rev 2010; 6:73–80