Albendazole Induced Recurrent Acute Toxic Hepatitis: A Case Report

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Abstract

Introduction : **Drug induced acute toxic hepatitis can be idiosyncratic. Albendazole, a widely used broad spectrum antiparasitic drug is generally accepted as a safe drug. It may cause asymptomatic transient liver enzyme abnormalities but acute toxic hepatitis is very rare. Case Report : Herein, we present the case of 47 year old woman with recurrent acute toxic hepatitis after a single intake of albendazole in 2010 and 2014. The patient was presented with symptoms and findings of anorexia, vomiting and jaundice. For diagnosis, other acute hepatitis etiologies were excluded. Roussel Uclaf Causality Assessment Method (RUCAM) score was calculated and found to be 10, which meant highly probable drug hepatotoxicity. Within 2 months, all pathological findings came to normal.**

Result : **There are a few reported cases of albendazole induced toxic hepatitis, but at adults, there is no known recurrent acute toxic hepatitis due to albendazole at this certainty according to RUCAM score.**

Conclusion : **Physicians should be aware of this rare and potentially fatal adverse effect of albendazole.** (Acta gastroenterol. belg., **2017**, 80, **309-311**).

Key words : Albendazole, recurrent, toxic, hepatitis.

Introduction

Drug induced liver injury (DILI) can be idiosyncratic or dose dependent. Idiosyncratic DILI develops independently of drug dose, or route or duration, of administration (1). Clinically, idiosyncratic DILI may take many forms, varying from asymptomatic, often self-limiting, and transient elevation in liver biochemical tests to jaundice and severe life threatening acute liver failure and rarely to chronic liver disease (2).

Albendazole is a widely used broad spectrum anti-helminthic drug. It is generally accepted as a safe drug and in some countries sold as over the counter. It may cause transient liver enzyme abnormalities especially after prolonged administration but significant hepatotoxicity is very rare (3, 4). Herein, we presented the case of albendazole induced recurrent acute toxic hepatitis in different years after a single dose. Although there are a few reports of albendazol induced toxic hepatitis, there is no known recurrent acute toxic hepatitis at adults requiring hospitalisation at this certainty according to Roussel Uclaf Causality Assessment Method of the Council for International Organizations of Medical Sciences (RUCAM/CIOMS) scale.

Case report

A 47 year old woman was accepted to our Gastro-enterology Unit with the diagnosis of acute hepatitis of unknown etiology. She had symptoms of vomiting and anorexia for 4 days. About 10 days ago, she received a single dose of 400 mg albendazol for empirical treatment of suspicious gastrointestinal parasitosis prescribed by a doctor. There was no history of any other drug, alcohol, herbs, herbal remedies or suspicious hypotensive attack causing ischemic hepatitis. She didn't have any other remarkable past medical history except for cholecystectomy and a probable diagnosis of albendazole induced toxic hepatitis 4 years ago. On admission to our unit, only pathological physical examination finding was jaundice. Laboratory investigations showed a normal complete blood cell count expect for eosinophilia %8, ALT 1332 IU/L, AST 710 IU/L, ALP 159 IU/L, GGT 71 IU/L, total biluribin 4,3 mg/dL (direct 2,8 / indirect 1,5 mg/dL), LDH 542 IU/L, INR 1,2, aPTT 32 sn , total protein 6,8 g/dL, albumin 3,8 g/dL. Abdominal ultrasonography was normal. Knowing the patient history of albendazole hepatotoxicity, pre-diagnosis of DILI was made. But because DILI is a diagnosis of exclusion, possible causes of acute hepatitis were investigated. Most possible causes of acute viral hepatitis etiologies (hepatitis A, B, C, E, CMV, EBV and HSV), autoimmune liver diseases and metabolic liver diseases (Wilson disease, hemochromatosis, and alfa-1 antitrypsin deficiency) were excluded with appropriate tests. A liver biopsy was done which showed eosinophilic portal inflammation and hepatitis with portal and lobular necroinflammatory activity (Fig 1). By the end of 1 month, transaminase levels decreased more than %50. Then RUCAM score was calculated and found 10, which meant highly probable DILI. Approximately 2 months later, all laboratory findings were normal. The laboratory results of the patient on admissions to our unit and changes during follow-up in 2010 and 2014 are presented in table I and figure 2 below.

Discussion

We presented a patient with recurrent toxic hepatitis due to albendazole usage. In the history of patient,

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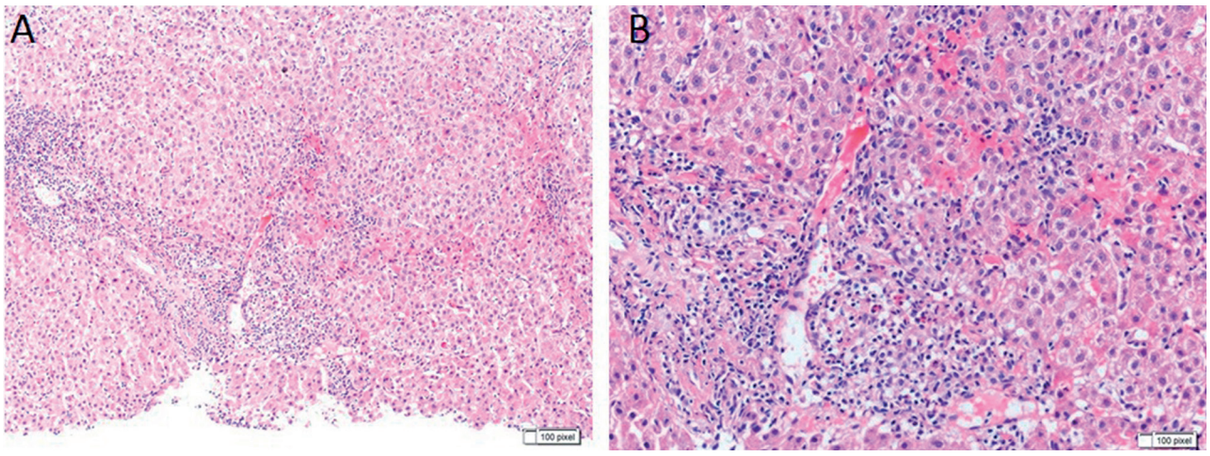

Fig. 1.

Table 1. — Major laboratory results of the patient on admissions in 2010 and 2014.

Parameters	2010	2014	Normal values
AST (IU/L)	1120	710	5-34
ALT (IU/L)	1562	1332	0-55
ALP (IU/L)	189	159	40-150
GGT (IU/L)	127	71	9-64
T.Bil (mg/dL)	6,4	4,3	0,2-1,2
D. Bil (mg/dL)	4,6	2,8	0-0,5
LDH (IU/L)	665	542	125-243
INR	1,3	1,2	0,8-1,2
aPTT (sn)	33	32	28-35
Total Protein (g/dL)	7,1	6,8	6,4-8,3
Albumin (g/dL)	4,0	3,8	3,5-5

there was a probable diagnosis of albendazole induced toxic hepatitis in 2010. Because there was no history compatible with other causes of acute hepatitis and knowing that she had taken albendazole 10 days ago, we considered albendazole induced toxic hepatitis initially. In order to confirm the diagnosis, the other causes of acute hepatitis should be excluded. So we investigated common causes of viral hepatitis, autoimmune hepatitis and metabolic causes of hepatitis and found negative for all of these diseases. A liver biopsy was done which was compatible with toxic hepatitis. We applied RUCAM/CIOMS scale to our case and found a score of 10, which meant highly probable toxic hepatitis. All pathological laboratory results decreased more than %50 within one month and came to normal within 2 months without any treatment.

RUCAM/CIOMS scale is determined by a score based on 7 criteria, including temporal relationship, clinical course (response after withdrawal of drug), risk factors, concomitant drugs, exclusion of other non-drug etiologies, likelihood of a reaction based on package labeling, and rechallenge. Possible results are : 'highly probable', 'probable', 'possible', 'unlikely' or 'excluded'

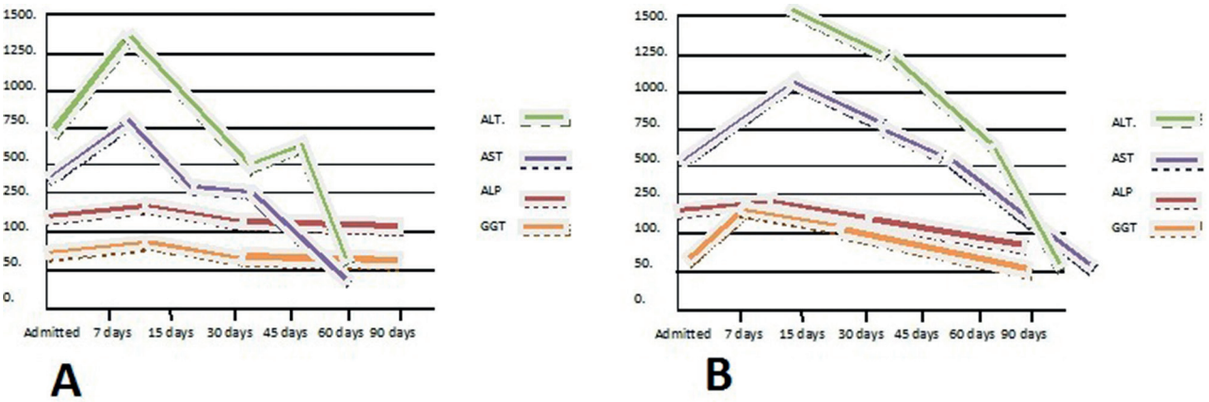

Fig.2.

based on the total score obtained. Although rechallenge with a potential causative drug to establish a diagnosis is one of criteria in the RUCAM/CIOMS scale, it is not advised and may be contraindicated from an ethical viewpoint (5,6). But in our case, an unintentional and accidental use of albendazole caused second episode of hepatotoxicity and was accepted as rechallenge of the drug when we were calculating RUCAM score. We used RUCAM causality assestment form from http ://www. livertox.nih.gov web adres.

Although albendazole is mainly metabolized in the liver, liver enzyme elevations are rarely reported. In most reported cases, these elevations have been mild or moderate after prolonged administration and have improved after discontinuation of treatment (6). In a meta-analysis performed in patients treated with benzimidazoles (albendazole and mebendazole), showed that only 13 of 1681 patients (%0, 7), developed mild and transient elevated liver enzyme levels (7). However, reports of albendazole induced severe liver toxicity are very rare. In the medical literature , there are a few reports of albendazol induced toxic hepatitis (3,4,6,8) and two cases of recurrent toxic hepatitis due to albendazole at pediatric age group (9,10) but there is no reported albendazole induced recurrent acute hepatitis at adults requiring hospitalization at this certainty according to RUCAM/CIOMs scale. In our case, not from a prolonged use but after a single dose of albendazole intake, toxic hepatitis had developed.

Drug induced toxic hepatitis or DILI is defined as serum ALT ≥ 5 times elevation of upper limit of normal (ULN) or ALP elevation ≥ 2 times ULN or ALT ≥ 3 ULN with elevation of bilirubin to ≥ 2 ULN. Hepatitic or cholestatic types of liver injury are defined by using R value (R = ALT ULN/ALP ULN) ; R ≥ 5 is suggestive of hepatocellular injury while R < 2 is suggestive of cholestatic injury and R value in between 2 and 5 is suggestive of mixed type of liver injury (11). Liver injury is likely to be more severe in hepatocellular type than in cholestatic/mixed type and elevated bilirubin levels in hepatocellular type indicates serious liver injury (5). R was found greater than 5 in our case. As seen in our case and other cases in medical literature, albendazole induced severe toxic hepatitis usually seems to be idiosyncratic and hepatocelluar type of liver injury with elevated bilirubin levels.

When our case is examined deeply, it was found that the onset of clinical symptoms was more rapid (2 days vs 6 days), the levels of liver enzymes and biluribins were higher and the time for the liver enzymes and bilurubin levels coming to normal (3 months vs 2 months) was longer at first episode in 2010 compared to second episode in 2014. When examined together with medical literature, we had a thought that toxic hepatitis due to albendazole seems to develop more quickly and more severe at younger ages and at first episodes. According to RUCAM scale, age older than 55 is a risk factor for DILI but all reported cases of albendazole induced toxic hepatitis in medical literature are younger than 55 years old.

We and patient didn't remember too much whether she was informed or not about albendazole hepatotoxicity 4 years ago. Our case might go to fulminant hepatitis, luckily she didn't. So it is very important to inform patients about the drugs causing toxic hepatitis. Also patients should be informed with generic name of drug and must be given written all commercial marks of the drug that causing toxic hepatitis.

Conclusion

DILI should be considered at patients with unknown acute hepatitis. Albendazole is a widely used and generally accepted as a safe antiparasitic drug. Rarely, it may cause acute toxic hepatitis. Physicians should be aware of this rare and potentially fatal adverse effect. Patients who have had a diagnosis of drug induced toxic hepatitis should be well informed about the drug causing hepatotoxicity.

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