Acute toxic hepatitis induced by a herbal medicine : Anchusa Boraginaceae

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Abstract

Backgraound and Aim : **Herbal treatments are becoming increasingly popular in many countries. Anchusa Boraginaceae (also called Tort plant and beef tongue) is commonly used as a herbal medicine in Elazıg region as diuretic and in the treatment of ulcers, and it is stated that this has no adverse effect. We report a case of acute hepatitis associated with long time use of high doses of Anchusa Boraginaceae.**

Case : **A 43-year-old male patient is drinking water of Anchusa Boraginaceae that is boiling for 14 days to dissolve the stones in the gallbladder. He had no medical history and did not take any other drugs or toxins. Two weeks later ; he admitted with developed tea colored like urine and yellowing of the body. Three weeks later; he was referred to the our department from the epicenter. Blood tests showed aspartate aminotransferase : 37 U/L, alanine aminotransferase : 66 U/L, gama glutamyl transferase : 23 U/L, total bilirubin : 16.9 mg/dL, direct bilirubin : 12 mg/dL, and INR : 1.3 Viral and autoimmune hepatitis were eliminated. Upper abdominal ultrasound was normal. After the herbal medicine was stopped on admission, the patient's laboratory tests didn't recover. Then; the support treatment was performed. The clinical and the laboratory values returned to normal after 2 months after the acute episode.**

Conclusions : **The consumption of herbal medicines containing Anchusa Boraginaceae can induce toxic hepatitis. Recovery can be complete after discontinuation. This case report highlights the risk and lytic effect on gallstone associated with Anchusa Boraginaceae.**
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Keywords*:* Toxic hepatitis, Anchusa Boraginaceae, jaundice

Introduction

Acute hepatitis is a condition caused by several reasons such as viruses, toxins, alcohol and metabolic disorders, which progresses with hepatic cell necrosis and inflammation of the liver. Ischemic hepatitis and autoimmune hepatitis are also among causes of acute hepatitis (1). It is observed that toxic events in the liver related to use of herbal products become increasingly common in recent years (2).

Toxic hepatitis comprises a wide clinical spectrum that presents with clinical conditions ranging from mild biochemical abnormalities to acute hepatic failure. It has been reported that many herbal drugs have hepatotoxic effect. Data on hepatotoxic adverse effects of these products which contain several biologically active compounds are limited. However, it is warranted that these agents should be taken into consideration as an etiological factor in unexplained liver damage (3). In recent years, herbal products have been increasingly used due to many reasons and idea that they are beneficial in several disorders. In particular, there are toxic pyrrolizidine alkaloids (PA) in 3% of the world flowering plants.The most important plant family containing the tumorigenic pyrrolizidine alkaloids is Boraginacea. It may cause acute or chronic toxicity (4).Anchusa Boraginaceae(AB) is a plant covered by stiff, bristly hairs which naturally grows in Europe, Africa, East Asia as well as Elazığ province in our country (Fig. 1). This plant is used as diuretic, anti-ulcer and to increase sweating (5). By this manuscript, we aimed to present a case with acute toxic hepatitis following use of the herbal product, namely Anchusa Boraginaceae, for the lytic effect on gallstone.

Fig. 1. — Anchusa Boraginaceae plant provided by the patient.

Case report

A 43-years old man presented to our facility with jaundice. The patient who had a history of chronic disorder reported that he presented to another facility

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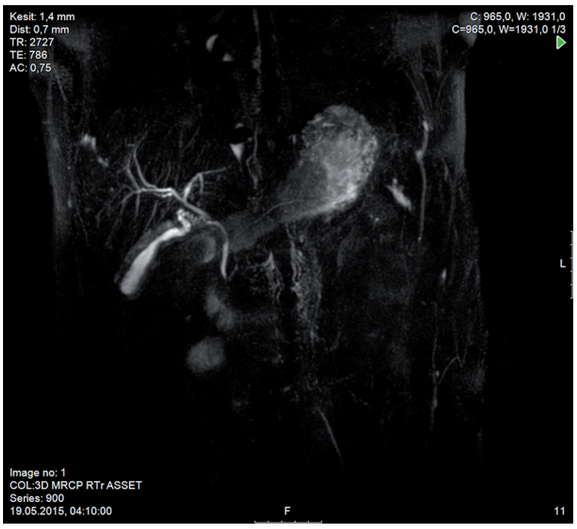

Fig. 2. — MRCP image of patient.

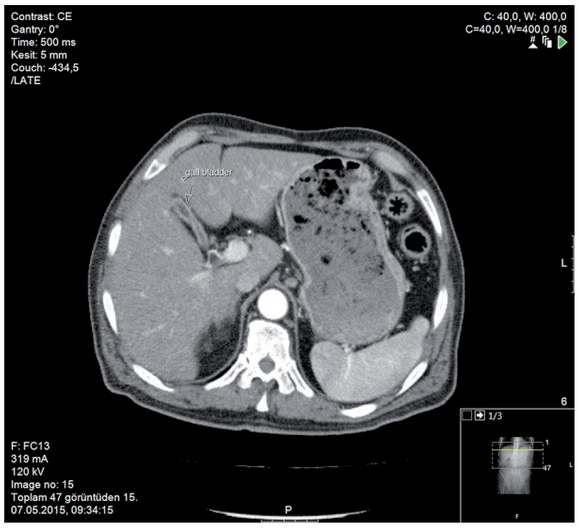

Fig. 3. — Abdominal CT scan image of patient.

with abdominal pain on right side and nausea 4 months ago, and that a gallstone (12 mm in size) was detected on sonography. Again, it was found out that a gallstone (10 mm in size) was detected on sonography 3 months ago while the diameter of common bile duct was reported as 11 mm on the same evaluation. Surgery was offered to the patient, but he declined to undergo surgery. The patient cited that he heard about AB, a plant commonly found around Elazığ province, which is implied to have lytic effect on gallstone; thus, he drank the water obtained by boiling the plant over 14 days. Thereafter, he underwent sonography 2 months ago, which revealed a lack of stone in gallbladder and normal common bile duct with minimal pericholecystic fluid. However, the patient had had following laboratory results during that period : bilirubin, 4.1 mg/dL, AST, 71 ; ALT, 139 ; ALP, 266 and GGT, 154 U/L. Nausea, fatigue and increased jaundice became apparent; thus, biochemical tests and imaging studies were performed in that facility. No abnormal finding was detected on MR cholangiography. Abdominal MR imaging was reported as normal (Fig. 2). Again, markers for hepatitis, CMV, EBV, Parvovirus, HSV, Rubella, Toxoplasmosis and Brucellosis were reported to be negative. Thus, the patient was admitted to the facility where evaluations were performed, and he was discharged after scheduling control visits as he had stable course. During control visits, bilirubin level reached up to 8 mg/dL. The patient presented to our clinic due to increased jaundice. The following results were found in biochemical evaluation performed at presentation: bilirubin, 16.9 mg/dL; direct bilirubin, 12 mg/dL, AST, 37 U/L; ALT, 66 U/L; GGT, 23 U/L and INR, 1.3. Markers for hepatitis, hepatitis B DNA, auto-immune test battery, iron, iron binding capacity, ferritin and ceruloplasmin were found to be normal in our facility. Hepatobiliary sonography, abdomen computed tomography and magnetic resonance imaging was reported to be normal (Fig. 3, 4). In the liver biopsy

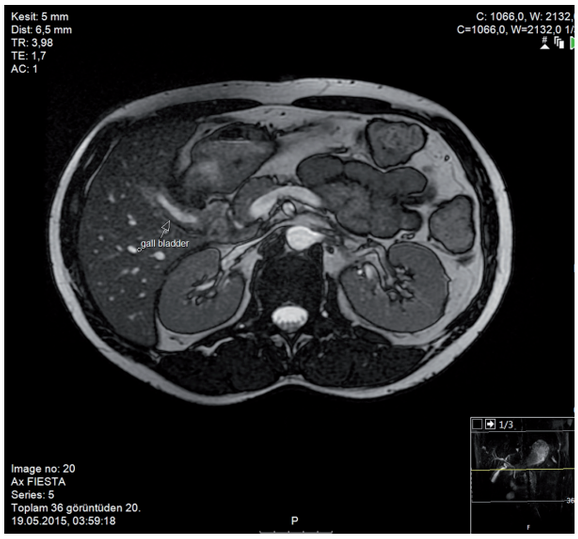

Fig. 4. — Magnetic Resonance Imaging of patient.

was reported portal inflammation, feathery degeneration and canalicular cholestasis (Fig. 5, 6). Plasmapheresis was performed over 3 consecutive days as he had a progressive increase in bilirubin levels. The patient was given acetylcysteine, ursodeoxycholic acid and vitamin E. After plasmapheresis, bilirubin began to decline during follow-up. The patient was discharged after 2 weeks by scheduling outpatient controls. At discharge, total bilirubin, AST and ALT were 4.3 mg/dL, 34 U/L and 62 U/L, respectively. In the control visit on month one, total bilirubin, AST and ALT were found to be 1.1 mg/dL, 23 U/L and 37 U/L, respectively (Table 1).

Discussion

Hepatotoxicity can be commonly encountered as the liver is the main organ where many drugs and chemical substances are metabolized. In addition, it is also known

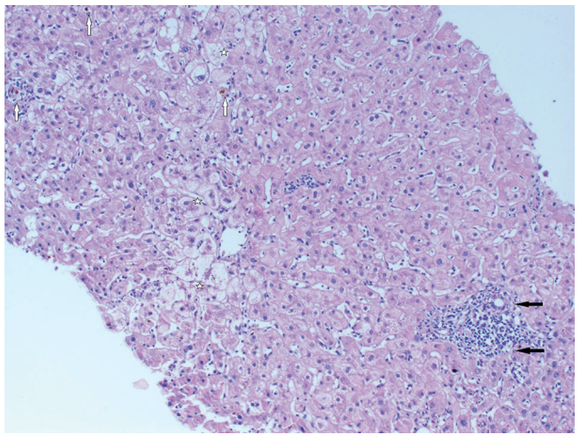

Fig. 5. — Biopsy of the case shows portal inflammation (black arrows), feathery degeneration (asterisks) and canalicular cholestasis (white arrows). H&E x 100.

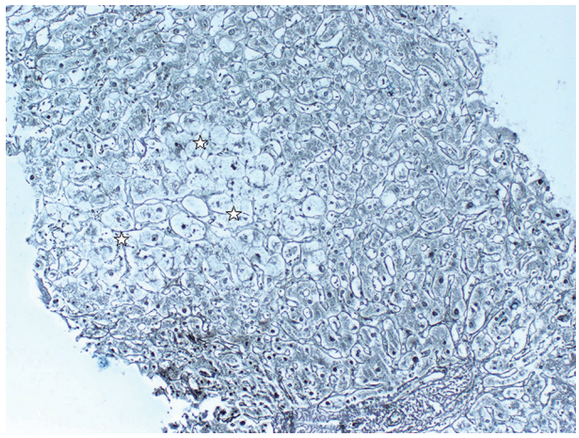

Fig. 6. — Collapse of reticulin fibers at the feathery degeneration and cholestasis area (asterisks). Reticulin stain x 100.

Table 1. — **Liver function test results for patient**

	AST(U/L)	ALT(U/L)	ALP(U/L)	GGT(U/L)	TBLB(mg/dL)	LDH(U/L)	ALB(g/dL)	INR(%)
Admit	71(5-40)	139(5-40)	266(30-120)	154(0-55)	16.9(0.0-1.1)	177(120-246)	3.1(3.5-5,3)	1.3(0.8-1.2)
2 weeks later	34	62	202	88	4.3	155	3.3	1.1
Final	23	37	181	23	1.1	149	4.4	0.97

AST = aspartate aminotransferase ; ALT = alanine aminotransferase ; ALP = Alkaline phosphatase ; GGT = γ-glutamyltransferase ; TBLB = Total bilirubin ; LDH = lactate dehydrogenase ; ALB=Albumin. The values given in parentheses are the reference range.

that a certain substance can exert different effects in different individuals (6). Today, there is a substantial risk associated with the use of many herbal substances regarding toxicity due to either lack of knowledge about potential side effects and drug interactions or insufficient evidence for effectiveness. The toxicity caused by plants can appear either after several months in some cases or within hours and days in others. Acute toxicity of PA can lead massive hepatotoxicity with hemorrhagic necrosis. In long-term use, it can lead venous occlusion, progressive portal hypertension resulting hepatic failure, fatty degeneration, liver cirrhosis through inhibition of mitosis, nodular hyperplasia and adenoma or carcinoma. It is well known that PA is natural hepatotoxin that is present in thousands of plants worldwide (7, 8). History of toxic substances exposure, lack of underlying pathology, recovery of clinical and laboratory findings after withdrawal of toxic substance and relapse after re-exposure is rather more important than clinical presentation to establish diagnosis (9). In addition, liver biopsy can be performed for differential diagnosis of other hepatic lesions in particular. However, consistency between clinical and pathological findings is warranted for a diagnosis. No liver biopsy was performed in our patient. However, toxic hepatitis was considered in our case based on the findings that time to liver damage after exposure to AB was 2 weeks and delayed regression of laboratory findings after withdrawal of plant.

Although exact incidence of herbal toxic hepatitis is unknown since patients tend to hide or not to cite herbal product used, it is estimated that plants account for 20% of all toxic hepatitis cases (10). In our case, it was clearly cited that the herbal product was used for lysis of gallstones. However, the patient had a sonography result reporting gallstone before ingestion of a toxic substance but no image was present.

The mainstay of treatment in herbal hepatotoxicity relies on withdrawal of herbal product. Early diagnosis of toxicity is important for both early assessment of acute liver failure and follow-up. Although corticosteroids play role in the treatment of patients with hypersensitivity reaction, it has been failing to show benefit in majority of toxic hepatitis (11). Serial biochemical tests are used to monitor patients. Recovery is anticipated after withdrawal of toxic exposure in most patients. The increased bilirubin level indicates poor prognosis. In advanced cases, supportive therapy is required ; in case of acute liver failure, liver transplantation could be required and even death can occur (12). In our case, plasmapheresis was performed over 3 consecutive days due to persistent increase in bilirubin levels but no corticosteroid was used.

In conclusion, long-term and excessive use of AB can cause hepatotoxicity. However, full recovery can be achieved when it is promptly withdrawn. It is thought that herbal products can always be used safely as they are natural; however, it should be kept in mind that herbal products can be toxic as well as being therapeutic. Further case reports and studies are needed to establish safety of herbal products and to elucidate the lytic effect of this plant on gallstone in particular.

Conflict of Interest

All authors declare that no conflict of interest

Informed Consent

It was recevied the informed consent form the patient.

Funding Information

There are no Funding Sources in this case report

Abbreviations

PA : Pyrrolizidine alkaloids, AB : Anchusa Boraginaceae

References

1. KARSEN H., ÇALIŞIR C., DUYGU F., *et al.* Zayıflama Çayı Kullanımına Bağlı Gelişen Akut Hepatit : Bir Olgu Sunumu.
2. BROULAC-SAGE P., BALABAUD C. Toxic and drug induced disorders of the liver. Surgical Pathology of the GI tract, Liver, Biliary tract and Pancreas, *Philadelphia Saunders*, 2004, 833-61.
3. SHAD J.A., CHINN C.G., BRANN O.S. Acute hepatitis after ingestion of herbs. *Southern medical journal*, 1999, **92** (11) : 1095-7.
4. FU P.P., YANG Y.-C., XIA Q., *et al.* Pyrrolizidine alkaloids-tumorigenic components in Chinese herbal medicines and dietary supplements. *Journal of Food and Drug Analysis*, 2002, **10** (4) : 198-211.
5. ÇAKILCIOĞLU U., TÜRKOĞLU İ., KÜRŞAT M. Harput (Elazığ) ve çevresinin etnobotanik özellikleri. Doğu Anadolu Bölgesi Araştırmaları, Fırat Üniversitesi, Elazığ. 2007.
6. JAESCHKE H., MCGILL M.R., RAMACHANDRAN A. Oxidant stress, mitochondria, and cell death mechanisms in drug-induced liver injury : lessons learned from acetaminophen hepatotoxicity. *Drug metabolism reviews*, 2012, **44** (1) : 88-106.
7. GAO H., LI N., WANG J.Y., *et al.* Definitive diagnosis of hepatic sinusoidal obstruction syndrome induced by pyrrolizidine alkaloids. *Journal of digestive diseases*, 2012, **13** (1) : 33-9.
8. ROEDER E. Medicinal plants in Europe containing pyrrolizidine alkaloids. *Pharmazie*, 1995, **50** (2) : 83-98.
9. NAVARRO V.J., LUCENA M.I. Hepatotoxicity induced by herbal and dietary supplements. 2014.
10. Navarro V.J., Barnhart H., Bonkovsky H.L., *et al.* Liver injury from herbals and dietary supplements in the US Drug-Induced Liver Injury Network. *Hepatology*, 2014, **60** (4) : 1399-408.
11. O'GRADY J.G., ALEXANDER G., HAYLLAR K.M., *et al.* Early indicators of prognosis in fulminant hepatic failure. *Gastroenterology*, 1989, **97** (2) : 439-45.
12. BJÖRNSSON E. Drug-induced liver injury : Hy's rule revisited. *Clinical Pharmacology & Therapeutics*, 2006, **79** (6) : 521-8.