CASE REPORT

Liver failure associated with mahogany seed extract consumption

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SUMMARY

A 45-year-old woman presented to the emergency department with jaundice of 2 weeks' duration. This was associated with mahogany seed extract (Skyfruit supplement) consumption for 6 months prior to admission. Examination was normal apart from scleral icterus and grade 2 encephalopathy. Liver function tests showed a hepatocellular pattern of derangement: alanine transaminase, 1267 U/L (10–36); aspartate transaminase, 1255 U/L (10–30); alkaline phosphatase, 124 U/L (22–104); bilirubin, 258 µmol/L (3–21) with a prolonged prothrombin time of 16.8 s (9.2–11.0). Viral hepatitis work-up was largely unremarkable and liver biopsy showed moderate inflammatory infiltrates (mostly lymphocytic with scattered eosinophils) in the periportal region and lobule with bridging necrosis, favouring drug-induced liver injury. Withdrawal of the drug resulted in normalisation of liver function.

BACKGROUND

Drug-induced liver injury (DILI) carries an estimated incidence of 13.9 ± 2.4 cases per 100 000 persons.¹ It is associated with significant morbidity and mortality, accounting for 11% of the cases of acute liver failure² and 15% of all liver transplants performed in the USA annually.³ Herbal and dietary supplements (HDSs) have also been implicated in the development of DILI. A prospective study performed in Singapore found that 55% of DILIs were attributed to traditional Chinese herbs and 16% caused by Malay alternative medications.⁴ Despite increasing use of HDSs globally, the adverse effects associated with their use are under-reported and poorly understood.⁵

CASE PRESENTATION

A 45-year-old Indian woman presented to the emergency department with jaundice and tea-coloured urine of 2 weeks' duration. This was associated with malaise, lethargy and anorexia. Following specific query, she reported consumption of mahogany seed extracts over the past 6 months. She denied chronic alcohol ingestion, intravenous drug use and high-risk sexual activity. Her medical history was only significant for depression. She was not on any chronic medications and did not have significant paracetamol use. Examination was only significant for grade 2 encephalopathy (associated with asterixis). Vital signs were normal and she had no stigmata of chronic liver disease. Abdominal examination was unremarkable.

INVESTIGATIONS

Laboratory tests revealed a predominantly hepatocellular pattern of deranged liver function tests: alanine transaminase, 1267 U/L (10–36); aspartate transaminase, 1255 U/L (10–30); alkaline phosphatase, 124 (22–104) U/L; bilirubin, 258 µmol/L (3–21) with a prolonged prothrombin time of 16.8 s (9.2–11.0). Based on this pattern of liver biochemistry, the primary differentials were viral hepatitis, and toxic and ischaemic liver injury. Subsequent work-up was thus aimed towards excluding these differentials.

White cell count was normal with no eosinophilia and renal function was preserved. Hepatotropic viral screen (hepatitis A, B, C, E) was negative. Non-hepatotropic viral serology demonstrated a weakly positive human herpes virus 6 PCR (<3.04 log), but was otherwise negative for herpes simplex virus (1 and 2), cytomegalovirus, Epstein-Barr virus, parvovirus 19, *Varicella zoster* virus and HIV. Paracetamol levels were not raised at <5 mg/L. Autoimmune work-up was weakly positive for anti-nuclear antibodies ($>1/800$), although IgG levels, anti-smooth muscle antibodies, anti-liver/kidney microsomal type 1 and mitochondrial M2 antibodies levels were negative. Caeruloplasmin levels were within range (28.5 mg/dL). Serum ammonia was 70 µmol/L.

CT liver demonstrated normal appearance of the liver and biliary tract, as well as patency of the hepatic artery, vein and portal vein. No neurological imaging was done in view of the absence of focal neurological signs.

Transjugular liver biopsy showed moderate periportal and lobular inflammation. The infiltrate was composed mostly of lymphocytes with some scattered eosinophils and only rare plasma cells. Bridging necrosis was seen and this was highlighted on the Chromotrope Aniline Blue stain (figure 1). There was no evidence of macrovesicular steatosis, canalicular cholestasis or viral inclusions.

Collectively, these findings were consistent with a diagnosis of DILI. Her Roussel Uclaf Causality Assessment Method score on admission was 7.

OUTCOME AND FOLLOW-UP

Drug withdrawal and supportive treatment were instated and the patient was monitored for signs of worsening liver failure.

The patient was reviewed by the institution's liver transplant team on day 3 of admission. The Model for End Stage Liver Disease score was 24 at the time

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Figure 1 Liver biopsy photomicrographs. (A) H&E-stained photomicrograph demonstrating bridging necrosis (low-power view). (B) Corresponding area on the Chromotrope Aniline Blue stain with the collagen in the area of necrosis highlighted in blue (low-power view). (C) H&E-stained photomicrograph demonstrating periportal inflammation (medium-power view). (D) H&E-stained photomicrograph demonstrating scattered eosinophils within the inflammatory infiltrate (high-power view). Portal tracts indicated by red asterisk.

of their review and she did not fulfil the King's College Hospital Criteria for transplantation (non-paracetamol induced). Resolution of encephalopathy was observed with a corresponding improvement in liver function tests. As such, their recommendation was to continue with supportive treatment.

The patient was eventually discharged 10 days after admission with close outpatient follow-up. Complete normalisation of the liver biochemistry was achieved within 75 days (figures 2 and 3).

DISCUSSION

Mahogany seed extract is produced by the *Swietenia mahagoni* tree, which natively occurs in Southern Florida and the Caribbean. It was first introduced to Asia in the late 1990s as a source

of timber, and soon after became widely used also as a natural remedy for many ailments.⁶ While there is some evidence to support its antimicrobial, antidiabetic and antitumour activities, the majority of the data is based on animal studies,⁷ which do not accurately predict human reactions. To date, there has been no human study on the efficacy and adverse reactions associated with mahogany seed extract consumption.

DILI secondary to HDS use poses a greater diagnostic challenge as compared with conventional medications. Diagnostic algorithms that have been designed for DILI secondary to conventional medications are not validated for use in the setting of DILI secondary to HDS.⁸ This is because HDS products often vary in their contents and concentrations, making standardisation of

Figure 2 Trend of serum alanine transaminase (U/L) and total bilirubin (μmol/L) against time. Arrow in black indicates time of presentation.

Figure 3 Trend of prothrombin time (s) against time. Arrow in black indicates time of presentation.

causality assessments nearly impossible. Secondly, the diagnosis of DILI relies heavily on the availability of well-documented reports of liver injury associated with a particular drug use. The lack of adequate literature surrounding HDS use makes the diagnosis much more difficult to make.

In this particular case, the diagnosis of mahogany seed extract-induced liver injury was made based on a combination of history and examination findings, judicious use of investigations and normalisation of liver function tests following withdrawal of the drug. Without increased recognition of their adverse effects, HDS-associated DILI will remain a diagnostic challenge.

In conclusion, this report represents the first documented case of mahogany seed extract-induced liver injury. It caused a predominantly hepatocellular pattern of liver injury, which resolved 75 days following cessation of its use. This highlights the need for increased clinician awareness of the potential hepatotoxicity of this commonly consumed herbal remedy.

Learning points

- Detailed history and dosage of supplemental drug is essential in all cases of liver failure.
- Drug-induced liver injury should be diagnosed after all viruses and other aetiologies have been excluded.
- Mahogany seed extracts, which are commonly consumed as health supplements, can cause hepatotoxicity resulting in liver failure.

Contributors All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated sufficiently in the production of this manuscript to take public responsibility for its content. RK was responsible for the conception and design of this manuscript. VY, TTJY, TL and RK acquired, analysed and reported the data presented in this manuscript. VY drafted the paper. Final revisions to the manuscript were made by TTJY, TL and RK.

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