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HALOTHANE INDUCED HEPATITIS: CASE REPORT
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SUMMARY

Halothane as a cause of hepatitis is rare and may be overlooked when evaluating a patient with sudden onset jaundice. A 34-year-old lady, a nurse, presented to the liver clinic with sudden onset non - pruritic jaundice. Viral and collagen serological tests were all normal, malaria and sickling tests were negative, but transaminases were elevated. She reported inadvertent exposure to halothane in surgical theatre where she works. She improved on conservative management, then had a re-exposure to halothane after three weeks and developed a similar clinical picture, which improved on conservative management. In an area endemic of malaria, hepatitis and haemolysing conditions like sickle cell anaemia, the diagnosis of halothane hepatitis requires high index of suspicion. The mechanism of halothane-induced hepatic damage in this patient is very likely idiosyncratic. This is because of the modest dose at first exposure and more severe clinical picture at re-exposure.

INTRODUCTION

Halothane is an inhaled anaesthetic agent. Rarely, it causes hepatitis with jaundice, low-grade fever and malaise(1). Hepatitis is rare on first exposure and common on re-exposure with elevated serum transaminases in both cases. It is common in young (≤ 40 years), obese, females. Most of the patients, up to 80%, improve on conservative management(2).

Drug-induced hepatitis may manifest with a wide range of symptoms from insignificant activation of enzymes (AST, ALT) with asthenic syndrome to severe disease with jaundice(3).

CASE REPORT

A thirty three year old female, nurse, married, Para 2+0, last delivery 2002 November, obese with BMI of 31kg/m^2, no morbidity, unremarkable medication history and had no known liver disease. She was previously well till she was posted to surgical theatre from paediatric ward. Within one week in theatre, she developed deep jaundice, lowgrade fever (37.9°C), no pruritus or abdominal pains, and mild averseness to food, low-grade headache, and normal stool colour. There was no history of blood transfusion, tattoos, hepatitis or jaundice within the family. The fever was noted within five days in theatre, (two days prior to development of jaundice) and routine tests to evaluate the fever were non-revealing i.e. (Blood slide for malaria - negative, widal test - negative, urinalysis - normal, haemogram - normal). Sickling test was negative. The patient declined liver biopsy. She was investigated and managed conservatively. She improved within three weeks. Liver ultrasound showed a normal liver and gall bladder achogenicity and no other abnormality detected in the abdomen.

Table 1

The biochemical, virological and immunological parameters were as follows

	First Episode	Second Episode
AST (LU/L) 0-40	230	317
ALT (U/L) 0-36	170	251
ALP (U/L) 0-360	290	271
HBsAg	Negative	Negative
HAV- IgM + IgG	Negative	Negative
HBcAb	Negative	Negative
HCV antigen	Negative	Negative
HCV Antibody	Negative	Negative
B.S tor Mps	Negative	Negative
ANA	Negative	Negative
ASMA	Negative	Negative
PTI/INR	1.7	2.0
RBS (mmol/L)	4.7	5.3
HIV	Negative	Negative
Sicking test	Negative	Negative

ANA=anti-nuclear antigen, HAV=Hepatitis A virus, AT=Alanine transaminase, HCV=Hepatitis C virus, AST=Aspartate transaminase, BS=Blood slide, ALP= Alkaline Phosphatase, MPs=Malarial parasites, RBS=Random blood sugar; ASMA=anti-smooth muscle antibodies

She was given supportive treatment of low protein diet (0.6mg/kg Bwt.), low fat diet, bed rest and high carbohydrate diet, with the assistance of the nutritionist. Jaundice cleared within thirteen days and she resumed duties in theatre in the next three days. Within four days of resuming duties, she developed a similar

clinical picture of jaundice and fever but the fever was higher at 39.3°C. She was investigated as shown above and the blood tests done had results that were unrevealing. With supportive management, she improved within two weeks, transferred to outpatient department and there was no recurrence. She has been reviewed at the liver clinic on four occasions (three months apart). She has fully recovered.

DISCUSSION

The clinical syndrome of halothane hepatitis is rare but characteristic when there is inadvertent exposure to halothane, like the above case. Liver injury occurs within one to ten days (1,2). First exposures are typically associated with mild ALT/AST elevations while re-exposure leads to higher transaminases(3,4). It may be dose-independent or idiosyncratic drug reaction and this particular case typifies this clinical symptomatology. Indeed, most drug induced liver disorders are idiosyncratic and not dose related(5). The frequency of developing hepatitis after the first exposure is low, 1/10,000 persons but increases after two or more (≥2) exposures to 15/10,000 persons(1,4,6). Fever occurs within three to four days, while jaundice is within twenty one days (mean of nine days). The liver is normal in size, swollen, tender or reduced in size secondary to necrosis(4,6). Predisposing factors are female gender and obesity like this case. Usually there is no alcohol intake. Other risk factors are pre-existing liver disease, age ≤ 40 years and genetic factors but it is more severe in age > 40 years old. The condition is rare in children(7). Obesity as a risk factor causes increased storage of halothane or induction of hepatic enzyme CYPZEl(7,9).

This patient was obese with a BMI of 31kg/m^2. This could be the obvious risk factor in the development of halothane hepatitis in her. Two thirds of cases occur in persons with a history of previous reactions leading to hepatitis and repeated exposure to halothane in 28 days, in young to middle aged obese women(2,4,8). This patient did develop a more severe hepatitis in the second exposure.

Diagnosis rests on history taking and exclusion of other causes of liver diseases. It is worth noting that 2% of cases of jaundice (hospitalised patients) and 25% of cases of fulminant hepatitis are drug induced(10). The importance of drug history in a patient with jaundice is therefore very important.

Mortality in halothane-induced hepatotoxity is 10-80% and worse with re-exposure. Poor prognostic factors include bilirubin >200 µmol/l, early onset of symptoms and signs and prolonged prothrombian time/ INR (2,6,7). Most cases resolve within 5-14 days from onset of fever and jaundice with complete recovery. This compares well with this case, which resolved in 10 days.

Moderate to severe cases are successfully managed conservatively through supportive care, however, there are few very severe cases that have required orthotopic liver transplant(2,8).

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