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Ischaemic Hepatitis in an Elderly Woman

J K H Lim, K B Yap

ABSTRACT

An elderly woman presented with very high levels of transaminases and lactic dehydrogenase in her liver function tests. Viral and drug-induced hepatitis were considered unlikely because of the absence of risk factors. Sepsis was suspected and antibiotic treatment was started with clinical improvement. A retrospective diagnosis of ischaemic hepatitis due to septicaemia was made. Markedly raised liver transaminases need not always be drug-induced or viral-related, especially in the elderly. It could be ischaemic in origin and the serious underlying condition needs to be sought and treated urgently.

Keywords: sepsis, aged, ischaemic hepatitis, liver function tests

INTRODUCTION

The older literature suggested that viral hepatitis was common in elderly patients. In one series, acute fulminant hepatitis was more common in the elderly population[1]. However, these reports preceded the current developments in serological testing. A more recent study[2] of patients with viral hepatitis found only 4 of 159 patients (2.5%) were aged 65 or older, suggesting that viral hepatitis is infrequent in the elderly population. In particular, acute viral hepatitis B is rare in the older patient[3]. When faced with an ill elderly patient with raised liver transaminases, other important causes such as drug-induced hepatitis, sepsis or ischaemic hepatitis should be considered. The entity of ischaemic hepatitis is not well described in standard internal medicine reference texts. We report an elderly patient with ischaemic hepatitis to highlight this entity.

CASE REPORT

A 75-year-old woman with a past history of hypertension presented to hospital with a one-week history of being unwell with nausea and loss of appetite. On admission, she was noted to be lethargic. Her temperature was 36.8°C, pulse was 90/min and respiratory rate was 20/min. Her blood pressure was 160/105 mmHg. There was no pallor, jaundice or oedema. Examination of the cardiorespiratory systems and abdomen was normal. She had no skin rashes and the joints were normal.

The initial clinical diagnosis was "sepsis of undetermined source – probably urinary tract or hepatobiliary infection". She was started on intravenous ceftriaxone.

Her initial leucocyte count was normal. The chest X-ray showed normal lung fields. The ECG revealed sinus tachycardia. Urine microscopy was normal. The results of other tests are shown in Tables I and II. The serum D-dimer and soluble fibrin monomer tested positive on day 3.

On the third day of hospitalisation, she was noted to be drowsy and tachynoeic. Her toes were cold and dusky. Her blood pressure was 130/80 mmHg and the pulse was 110/min. Urgent ultrasound scan of the hepatobiliary system was normal. She was subsequently sent to the intensive care unit for monitoring. The blood culture grew coagulase-negative *Staphylococci* on day 4 in all the four specimens sent. The hepatitis A, B and C markers were negative. She was kept on cloxacillin for 2 weeks and made a gradual recovery. We were not able to localise the source of the infection after repeated clinical examination. A bone scan and an echocardiogram performed during the second week of hospitalisation did not reveal any abnormalities. She developed dry gangrene at the tips of her toes at the end of the second week of hospital stay.

DISCUSSION

Our patient only had an elevated heart rate and respiratory rate to suggest the diagnosis of sepsis[4] on initial presentation. The presenting clinical history was non-specific and there was no leucocytosis, fever or any detectable focus of infection on admission to hospital. Atypical presentation of sepsis is well known in the elderly[5,6]. Although the patient had a history of hypertension, she had defaulted treatment for several months and did not consume any medication recently. Drug-induced hepatitis was therefore unlikely.

The initial liver function tests showed a marked rise in serum transaminases and lactic dehydrogenase levels. However, an initial diagnosis of viral hepatitis was not considered to be likely because of the lack of risk factors or exposure in this patient. If viral hepatitis had been diagnosed because of the presence of marked transaminitis, the outcome would have been fatal since

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Table I – Haematologic laboratory values

Variable	On admission	Day 3 of admission
Haemoglobin (g/dL)	11.4	13.8
White-cell count (per mm^3)	6,280	19,110
Differential (%)		
Neutrophils	81	49
Platelet count (per mm^3)	106,000	51,000
Prothrombin time (seconds)	25.9 (control 11.6)	40.7 (control 22.6)
Activated thromboplastin time (seconds)	34.5 (control 11.3)	54.7 (control 26.6)

Table II – Blood chemical values

Variable	Admission	Day 3	Day 5	Day 20
Urea (mmol/L)	14.9	27.2		
Sodium (mmol/L)	148	142		
Potassium (mmol/L)	4.4	5.0		
Chloride (mmol/L)	118	114		
Creatinine (umol/L)	227	378		
Total protein (g/L)	60	61	57	61
Albumin (g/L)	36	33	32	30
Bilirubin, total (mmol/L)	32	153	27	7
Alkaline phosphatase (U/L)	84	117	90	112
Alanine aminotransferase (U/L)	2282	2222	796	31
Aspartate aminotransferase (U/L)	5236	1704	298	58
Lactic dehydrogenase (U/L)	4039	-	616	814

Table III – Proposed criteria for ischaemic hepatitis

- Exclusion of other causes eg. viral and drug-induced
- An appropriate clinical setting, usually an acute fall in cardiac output at the time of onset
- Hepatitic liver function tests especially the presence of markedly elevated LDH
- Liver transaminases reach peak levels within 24 to 48 hours and resolution is also relatively rapid

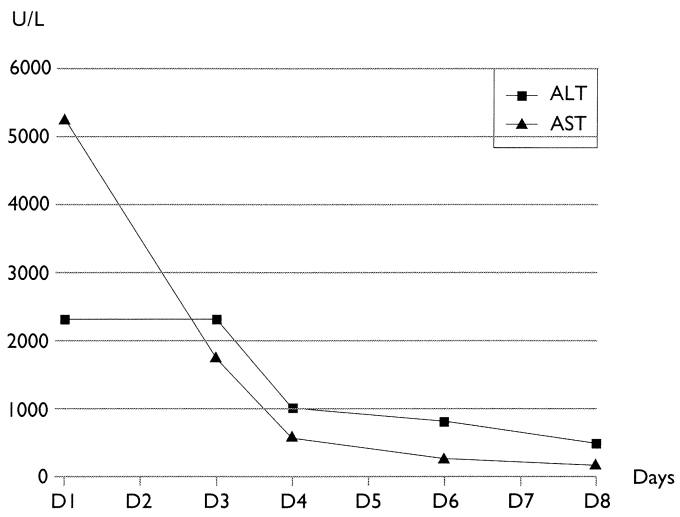

Fig 1 – Trend of liver function tests

she would not have received antibiotics. Her subsequent clinical course proved that she had septicaemia.

The marked rise in transaminases and lactic dehydrogenase levels in our patient can be attributed to the presence of ischaemic hepatitis based on the criteria proposed by Gibson and Dudley[7] (Table III). The essential pathological feature of this condition is centrilobular hepatocyte necrosis with little or no inflammatory response. This diagnosis was made retrospectively in our patient based on the subsequent pattern of recovery in her liver transaminases and lactic dehydrogenase profile.

The alanine aminotransferase (ALT), aspartate aminotransferase (AST) and lactic dehydrogenase (LDH) levels were initially markedly raised in our patient. The time course of the elevation in the transaminases was also characteristic: the levels typically reached peak levels within 24 to 48 hours of the ischaemic episode and resolution was relatively rapid. Fig 1 shows the time course of the levels of transaminases in our patient. Liver biopsy was not performed in our patient because she was ill and was not likely to tolerate the procedure well. We wish to emphasise that hypotension need not be a "must" criteria for the diagnosis of ischaemic hepatitis, although it is common. In Gibson and Dudley's series[7], hypotension was only documented in 5 out of their 17 patients. Although the majority of their patients had a cardiovascular cause to account for the liver injury, one patient had a diagnosis of volvulus while another had dehydration.

Ischaemic hepatitis is not a rare condition but this entity is not well documented in standard medical textbooks. The topic was not listed in the subject index of the three latest editions of internal medicine textbooks available locally: Harrison's Principles of Internal Medicine, Oxford Textbook of Medicine and Cecil Textbook of Medicine. The latest edition of an intensive care manual[8] had a one paragraph description of the topic. There have also been very few papers on this subject in the recent English medical literature. A Medline search over the last five years only yielded case reports in the non-English literature[9-11].

The clinical significance of ischaemic hepatitis lies in the fact that it occurs secondary to another serious condition, usually hypotension. Unless the clinician is aware of the entity, the underlying condition may be missed or ignored because of the apparent diagnosis of "viral" hepatitis. The first few reports of this condition was made in the early 1960s. Logan, Mowry and Judge[12] reported 3 patients with cardiac failure simulating viral hepatitis. The serum level of aspartate aminotransferase in each instance exceeded 1,000 unit. In two of these cases, a clinical diagnosis of viral hepatitis was made antemortem but autopsy in all three cases showed only centrilobular necrosis of the liver. Bynum, Boitnott and Maddrey[13] reported seven patients with cardiovascular disease with clinical episodes and marked transaminase elevations that suggested viral hepatitis, but all had morphologic evidence (from liver biopsy or autopsy specimens) that

documented centrilobular necrosis (ischaemic hepatitis) with no evidence of viral or drug injury. In their report, they emphasised that liver congestion alone, no matter how severe or prolonged, seems to do little if any damage to the liver. Centrilobular necrosis or ischaemic hepatitis appears to result from failure of hepatic perfusion (with or without preceding hypotension) and presents with clinical and laboratory features that suggest viral hepatitis.

Ischaemic hepatitis requires no specific treatment other than management of the underlying illness. It is not an uncommon complication of reversible hypotension. The prognosis is dependent on the disease that caused it, rather than the subsequent hepatic dysfunction. It usually runs a benign, self-limiting course and may be differentiated from viral hepatitis on clinical and biochemical criteria alone.

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