Lesson of the Week

Paracetamol overdose as a cause of non-A, non-B hepatitis

C L S LEEN, P D WELSBY

The term non-A, non-B hepatitis is usually applied to cases of apparent viral hepatitis which cannot be attributed to infection with hepatitis A virus, hepatitis B virus, Epstein-Barr virus, cytomegalovirus, or any other known virus. We describe three patients referred to our infectious diseases unit with a diagnosis of viral hepatitis. Each had taken a paracetamol overdose, and two had initially concealed their overdose. These patients illustrate the importance of careful, and on occasion probing history taking associated with a high index of suspicion, especially when there is a possibility of drug ingestion as a cause of jaundice.

Case reports

Case 1—A 16 year old kitchen maid presented to her general practitioner with a three day history of vomiting. The general practitioner found her to be jaundiced but not particularly unwell. She denied relevant exposure to risk factors for hepatitis A or B. Blood tests confirmed that she had a hepatitis (bilirubin concentration 43 $\mu\text{mol/l}$ (2.5 mg/100 ml), alanine aminotransferase activity 5390 U/l, alkaline phosphatase activity 19 U/l) but serological studies, including tests for hepatitis A virus, hepatitis B virus, Epstein-Barr virus, and cytomegalovirus, gave negative results. The general practitioner therefore referred her as an outpatient to the infectious diseases unit, where she admitted that she had taken 20 paracetamol tablets after a family argument. She had made a complete recovery.

Case 2—A 25 year old man was admitted with a two day history of abrupt onset of vomiting and severe abdominal pain. A flatmate had suffered a brief episode of vomiting four days previously. On repeated direct questioning he denied taking any drugs; he specifically denied paracetamol overdose. On examination he was mildly jaundiced, very anxious, and hyperventilating. Physical findings were otherwise normal, apart from generalised abdominal pain and voluntary abdominal rigidity. Initial investigations confirmed an acute hepatitis (alanine aminotransferase activity 13 450 U/l). On admission he was in established renal failure with a serum creatinine concentration of 1468 $\mu\text{mol/l}$ (16.6 mg/100 ml). No paracetamol or paracetamol metabolites were detected in blood or urine. Two days later, when his condition was critical with both hepatic and renal failure, he admitted taking 24 Veganin (paracetamol 250 mg, aspirin 250 mg, codeine phosphate 6.8 mg), 20 Panadeine Co (paracetamol 500 mg, codeine phosphate 8 mg), and 26 paracetamol. He had started vomiting immediately after the overdose and had continued to vomit thereafter. In retrospect, the vomiting immediately after the overdose probably saved his life. He made a full recovery.

Covert paracetamol overdose as a cause of non-A, non-B hepatotoxicity is probably quite common and is easily overlooked

Case 3—Five weeks after his return from a holiday in Thailand a 34 year old taxi driver was admitted with a two day history of anorexia, nausea, and vomiting. The general practitioner had noted jaundice and could not exclude a viral hepatitis. On examination the patient was jaundiced and showed early signs of hepatic encephalopathy, with slow mentation and vagueness of expression. He thought that he had taken an overdose of some 100 paracetamol tablets about one week previously because he had been feeling depressed. (In fact, he had probably taken the paracetamol overdose later than that.) On admission he was anuric, and results of relevant blood and urine tests were in keeping with acute renal failure. Malaria, which may present with this clinical picture, was excluded by repeated staining of blood films. Bilirubin concentration was 397 $\mu\text{mol/l}$ (23.2 mg/100 ml), alanine aminotransferase activity 1835 U/l, alkaline phosphatase activity 239 U/l, and his prothrombin ratio, which had been 1.4, increased subsequently. Despite vigorous supportive treatment he deteriorated, and he died of hepatic coma with renal failure and pneumonia as contributory causes.

Comment

At present there is no generally acceptable serological marker for the putative agents of non-A, non-B hepatitis, and a diagnosis of non-A, non-B hepatitis is therefore one of exclusion.¹⁻³ Very large doses of paracetamol taken in suicide attempts cause acute hepatic necrosis,⁴⁻⁷ and even small amounts may cause severe illness. The clinical and biochemical features of paracetamol induced liver damage may thus be indistinguishable from those of viral hepatitis and it is inevitable that some cases of acute hepatitis will be ascribed to non-A, non-B hepatitis unless a careful drug history excludes drug induced hepatitis. Moderate to severe hepatic necrosis due to both paracetamol and viral hepatitis may be accompanied by hypoglycaemia, metabolic acidosis, disseminated intravascular coagulation, encephalopathy, and acute renal failure.

The importance of excluding drug overdosage in jaundiced patients cannot be overemphasised. Firstly, a positive history of drug overdosage and its temporal relation to the onset of symptoms will avoid the performance of expensive and unnecessary serological tests for viruses. Secondly, patients who survive paracetamol induced hepatic necrosis do not develop chronic liver disease,⁸ unlike patients with non-A, non-B hepatitis, in whom the incidence of subsequent liver disease may be high^{9 10}; later reports,^{11 12} however, suggested that most patients with non-A, non-B hepatitis will have a relatively benign chronic persistent hepatitis unless their disease was related to transfusion with

Infectious Diseases Unit, City Hospital, Edinburgh EH10 5SB

C L S LEEN, MRCP, registrar

P D WELSBY, MRCP, consultant physician

Correspondence to: Dr P D Welsby.

blood or blood products. Thirdly, patients with concealed paracetamol overdose may present late and evidence of overdose may not be found on routine screening of blood and urine. Fourthly, patients may not receive psychiatric assessment if they successfully conceal their overdose. Finally, identification of concealed paracetamol overdose will prevent these patients being entered into various studies as sufferers from non-A, non-B hepatitis.

Although the results of liver function tests for viral hepatitis and paracetamol induced hepatic necrosis may be indistinguishable, the magnitude of the rise in alanine aminotransferase activity in some patients shortly after the onset of paracetamol induced hepatitis may provide a very valuable differentiating feature. For example, in our case 2 the activity of the enzyme (13 450 U/l) was far in excess of values seen in hepatitis A, hepatitis B, or cytomegalovirus or Epstein-Barr virus related hepatitis. In a study including 69 jaundiced patients with hepatitis admitted to the infectious disease unit in 1981¹³ the maximum alanine aminotransferase activity recorded in patients with proved viral hepatitis was 5300 U/l (mean 2122 U/l, SD 1565 U/l).

In conclusion we emphasise the importance of obtaining a reliable history of drug ingestion in any patient presenting with jaundice, particularly as paracetamol induced liver necrosis carries a good prognosis once the patient has survived the acute episode. Unfortunately, it may well be that patients with concealed paracetamol overdoses usually present more than 10 hours after the overdose, when it is too late for antidotes to have any chance of success.

References

- 1 Blumberg BS. Non-A, non-B hepatitis. *Ann Intern Med* 1977;87:111-3.
- 2 Alter MJ, Purcell RM, Holland PV. Clinical and serological analysis of transfusion associated hepatitis. *Lancet* 1975;ii:838-41.
- 3 Dienstag JL, Alaama A, Mosely JW, Redeker AG, Purcell RM. Etiology of sporadic hepatitis B surface antigen negative hepatitis. *Ann Intern Med* 1977;87:1-6.
- 4 Davidson DGD, Eastham WN. Acute liver necrosis following overdosage of paracetamol. *Br Med J* 1966;ii:497-8.
- 5 Prescott LF, Roscoe P, Wright N, Brown SS. Plasma paracetamol half-life and hepatic necrosis in patients with paracetamol overdosage. *Lancet* 1971;i:519-22.
- 6 Proudfoot AT, Wright N. Acute paracetamol poisoning. *Br Med J* 1970;iii:557-8.
- 7 Clark R, Borirakchanyavat V, Davidson AR, Thompson RPH, Widdop B, Goulding R. Hepatic damage and death from overdose of paracetamol. *Lancet* 1973;i:66-9.
- 8 Portmann B, Talbot IC, Day DW, Davidson AR, Murray-Lyon IM, Williams R. Histopathological changes in the liver following a paracetamol overdose: correlation with clinical and biochemical parameters. *J Pathol* 1975;117:169-80.
- 9 Galbraith RM, Portman B, Eddleston ALWF, Williams R, Gower PE. Chronic liver disease developing after an outbreak of HBsAg negative hepatitis in a haemodialysis unit. *Lancet* 1975;ii:886-90.
- 10 Knowdell RG, Conrad ME, Ishak KG. Development of chronic liver disease after acute non-A non-B post-transfusion hepatitis. *Gastroenterology* 1977;72:902-9.
- 11 Rakela J, Redeker AG. Chronic liver disease after acute non-A non-B viral hepatitis. *Gastroenterology* 1979;77:1200-2.
- 12 Norkrans G. Clinical, epidemiological and prognostic aspects of hepatitis A, B, and non-A non-B. *Scand J Infect Dis* 1978;suppl 17:1-44.
- 13 Leen CLS, Welsby PD. The differentiation between medical and surgical jaundice. *Practitioner* (in press).

(Accepted 6 July 1983)

MATERIA NON MEDICA

Labrathon

This year saw the first Labrador winter games, which were held in and around Goose Bay. The highlight was the first ever Labrathon—a marathon peculiar to Labrador. The event was held on a bay of Lake Melville, on top of the lake since the ice was between two and three feet thick and was covered by a layer of snow eighteen inches or so deep. The contestants were those found to be the fittest and ablest to complete the course, and they came from small communities and tiny settlements up and down coastal Labrador, each community pooling its resources to send contestants to the games.

The competitors set off in heats to complete the five kilometre course on snowshoes. At the start each loaded up a komatik (a long flat sled) with the items required during the event and then set off pulling this to the first stop. There they built a fire—no mean task on snow and with a cold wind blowing—and boiled a kettle of snow. They also shot at a target from standing. Then after repacking the komatik they raced to the second post, where they erected a traditional tent from the packed equipment and shot at a target from a kneeling position. After repacking the tent and komatik they snowshoed to the third stop. There they each set and camouflaged a bear trap before springing it. Then each dug a hole through the ice for fishing, an arduous task with traditional tools. After that they again loaded up their komatiks and the rush was on for the finishing post.

Points were awarded for each part of the course, highest points going for accuracy in shooting. Some of the contestants candidly admitted afterwards that they would have gone hungry if they had been shooting for the pot. The contest was monitored not only by the officials awarding scores but also by a medical team who travelled with the contestants by skidoo drawn komatik. This was necessary because of the many possibilities for injury; these obviously included gunshots, fire, and injury from the traps—which could take off a hand—and also fatigue, snow blindness, and the cold. It was not just the contestants who were at risk but some of the onlookers who skidooed in for a closer look. The temperature was about -20°C but dropped rapidly to -35°C as the wind blew across the bare expanse of the icy lake.

In future years this one event will be a way of ensuring that at least some of the traditional skills and methods are not completely lost with

increasing mechanisation. The Labrathon is a reflection of a way of life that has persisted for years and should continue to do so, since the harsh conditions of the land and the climate ensure survival of only the fittest.—PENELOPE A BROOM, general practitioner, Goose Bay, Labrador.

Attila the hen

There can now be few of us who fail to realise the central place of *Ovis aries* in the economy of the Falkland Islands. Sheep outnumber the islanders by 350 to one, and their mark is everywhere: in countryside and in conversation one is never far from them. The outsider soon develops a familiarity with their care, their products, and their future. One learns the statistics of sheep—the total numbers, the tons of wool per year, the fact that the great shearing sheds of Goose Green process 100 000 sheep each summer. These black sheds are reputedly the sixth largest in the world; once second, they have been surpassed by giant sheds in Australia, where Falkland shearing teams often work, and in Russia, where they don't.

It follows that mutton is a staple of the island diet (it is known locally as "365," most people claiming to be served it in some form every day of the year). Equally unsurprisingly, woollen bobble hats and pullovers are almost a uniform, and knitting a natural accomplishment. It is perhaps even acceptable that much mutton is fed to the local pigs, who thrive on it. To find that chunks of mutton are the favourite bait for mullet, and that splendid sea trout take it avidly, begins to stretch one's sense of the proper order of things. The final dislocation comes with the discovery that the *hens* are fed largely on mutton. Every hen run on the islands is a charnel house of mutton bones, picked white and clean; joints and rib cages and great gobbets of purplish meat are savaged by Rhode Island Red and White Wyandotte, scarlet in beak and claw. They strut boldly up to one, casting speculative eyes on any exposed flesh; they sidle round behind to cut off any retreat; they have none of the dizzy panic of our foolish fowl at home. When a sheep wanders near the run the hens eye it brazenly and squawk raucously. The sheep look uneasy and edge away. Their plaintiff bleatings, whirling down the eternal winds, mingle with the harsh cackling of their unlikely persecutors.—M D CONROY, general practitioner, Tidworth, Hants.