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Veno-occlusive disease of the liver secondary to ingestion of comfrey

There is currently considerable interest in alternative medicine and herbal remedies. These treatments are not without risk, however, as illustrated by the following case.

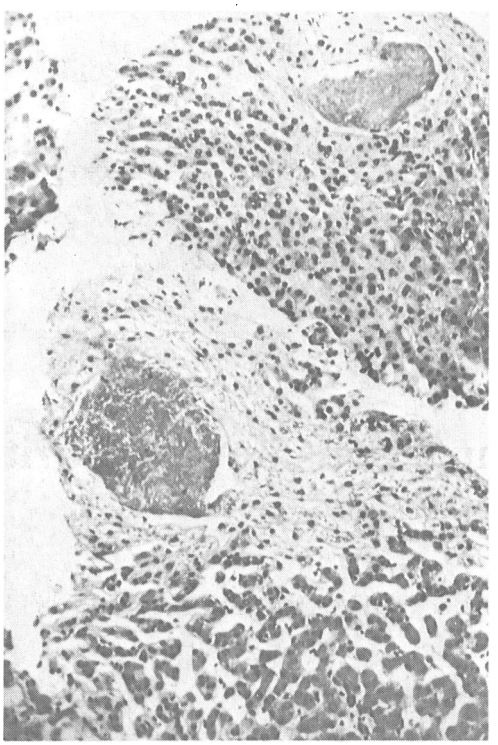
Case report

A 13 year old boy was admitted in July 1986 for investigation of hepatomegaly and ascites. Three years earlier Crohn's disease had been diagnosed from radiographs showing consistent changes in the terminal ileum and colon and from histological studies of the colon. He was treated with prednisolone and sulphasalazine with benefit. At his parents' request these drugs were discontinued and he was treated with acupuncture and comfrey root, prescribed by a naturopath. Up to 1986 he had been regularly given a herbal tea containing comfrey leaf. The exact quantities of leaves given and frequency of administration are unknown. An exacerbation of his inflammatory bowel disease in 1984 required a further course of prednisolone. In June 1986 he presented with fatigue, diarrhoea, and weight loss and a few weeks later developed fever, abdominal pain, and swelling. He was taking prednisolone and sulphasalazine. He had never taken azathioprine.

On examination he had ascites and tender hepatomegaly but no dehydration, jaundice, or heart failure and no stigmata of chronic liver disease. Sigmoidoscopy showed mildly inflamed, cobblestoned mucosa. He had mild iron deficiency anaemia (haemoglobin 117 g/l) and raised serum bilirubin concentration (26 mmol/l, normal <17) and aspartate aminotransferase activity (87 IU/l; normal 6-35). Serum albumin was low at 27 g/l. The results of the following tests were normal: urea, electrolytes, serum globulin, alkaline phosphatase, complement, plasma viscosity, full coagulation screen, autoantibody profile, and acid haemolysis. Hepatitis B surface antigen and antibodies to hepatitis A were absent as were Epstein-Barr virus and cytomegalovirus. Ascitic fluid protein concentration was 27 g/l. The inferior vena cava and major hepatic veins were patent on Doppler ultrasound and percutaneous phlebography. Percutaneous liver biopsy showed the thrombotic variant of hepatic veno-occlusive disease (figure).[1] He was treated with spironolactone, salt restriction, and bed rest with a good response. His bowel disease remained relatively inactive with treatment with prednisolone and sulphasalazine; at the time of writing he was back at school and tolerably well on his medication.

Comment

Known or suspected causes of hepatic veno-occlusive disease are systemic lupus erythematosus, alcoholic hepatitis, immune deficiency, azathioprine (in renal transplant recipients), radiotherapy, chemotherapy (especially in bone marrow transplant recipients), and pyrrolizidine alkaloids.[2] These alkaloids are present in a wide variety of plant species, and those of the genera *Heliotropium*, *Senecio*, and *Crotalaria* are particularly toxic.[3] Ingestion of plants containing alkaloids in "bush" or herbal teas or as food contaminants is responsible for appreciable numbers of cases world wide.[3] Only two cases of hepatic veno-occlusive disease as a result of pyrrolizidine alkaloid ingestion have been described in Britain, however, and both patients had ingested imported herbal teas. We think that the only possible causal factor for hepatic veno-occlusive disease in our patient was comfrey, which he had regularly ingested for two to three years; major hepatic vein thrombosis but not veno-occlusive disease has been described in patients with colitis.[1] The common comfrey, *Symphytum officinale*, a native British plant, contains at least nine potentially hepatotoxic pyrrolizidine alkaloids in its leaves and roots.[3] These alkaloids are less toxic than those in other plants—for example, senecios—which may explain why only a few cases of hepatic veno-occlusive disease caused by ingestion of comfrey are known (G Nicholson and C C J Culvenor, personal communications) and only one has been published.[4] This second published case is the first to result from a native British plant. The prognosis for our patient remains uncertain for although about half of Jamaican patients with acute hepatic veno-occlusive disease recovered completely, the remainder died or developed cirrhosis.[5] Malnutrition and poor health may be risk factors in Jamaica so our patient may have been susceptible to hepatic veno-occlusive disease from comfrey because of his underlying inflammatory bowel disease.[5]



Two freshly thrombosed centrilobular veins in liver biopsy with intimal thickening, sinusoidal distension, and loss of centrilobular hepatocytes. Haematoxylin and eosin.

This report serves as a reminder that herbal as well as orthodox medications may have serious side effects.

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