Letters to the Editor

Fluid leak from an iliac crest in a biopsy site

Sir,

A 50 year old man presented to a surgeon with a 4 month history of epigastric pain and loss of weight. The only clinical finding was a small right pleural effusion. Cytology showed no malignant cells. His albumin was low – 7 g/l. An ultrasound of the epigastric region and a computed tomography scan both showed a huge mass of nodes in the coeliac axis region. He underwent a laparotomy and a small amount of ascitic fluid was noted, gland biopsies were taken which revealed a diffuse high-grade non-Hodgkin lymphoma. Further investigation included an iliac crest trephine biopsy which proved to be normal.

The biopsy site did not heal and 500 ml per day of fluid began to leak. The fluid contained abundant neutrophils, but no malignant cells and probably represented lymph with much fluid transudate because of his low albumin. He was seen by an oncologist after the fluid leak occurred and culture of the bone marrow site yielded *Streptococcus faecalis* and *Staphylococcus aureus* phage type 29. He received appropriate antibiotics and intravenous chemotherapy for his lymphoma. His albumin gradually increased without the need for additional transfusions and the leak ceased after 4 weeks chemotherapy.

When he attained complete remission he developed a left pleural effusion but the fluid yielded no malignant cells. Culture grew *Staphylococcus aureus* phage type 29 identical to the organism previously affecting the bone marrow puncture site. The empyema required daily aspiration and instillation of flucloxacillin into the pleural cavity. Chemotherapy was resumed and completed. He remains fully fit and in complete remission 40 months later.

As far as we know, fluid leak from an iliac crest trephine biopsy site has not been previously recorded. In a fit of enthusiasm to investigate the patient as fully as possibly before referring for a specialist opinion, the marrow examination had been requested, but due attention had not been paid to the very low serum albumin. This proved to be a case of 'more haste, less speed', for there was some difficulty treating the initially infected leak site and the subsequent left empyema was, presumably, a metastatic phenomenon, as the same organism was cultured.

Ironically, none of this need ever have happened, for the state of his high-grade non-Hodgkin lymphoma was such that he would have been treated with chemotherapy from the outset and a bone marrow examination would not have been requested.

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Cholestatic jaundice associated with danazol therapy

Sir,

The association of elevated liver enzymes with danazol therapy is infrequent and cholestatic jaundice has been reported in only one patient before the following case to the best of our knowledge.

A 55 year old man was diagnosed as having immune-mediated thrombocytopenia purpura in July 1988. He was treated initially with prednisolone 60 mg daily with a brief transient rise in the platelet count. A trial of azathioprine of 100 mg daily gave no response. Finally, he underwent splenectomy in October 1988. The spleen was normal in size and the platelet count, which was $12 \times 10^9/l$, did not improve remarkably after splenectomy. In view of the unresponsiveness of the disease he was started on danazol 600 mg daily and the thrombocytopenia responded with platelet counts going up to $50 \times 10^9/l$ within 4 weeks of therapy.

Treatment with danazol was continued for 4 months when the patient noticed jaundice and was investigated. Liver profile, which was normal prior to therapy revealed a bilirubin of $284 \mu\text{mol/l}$, direct 133 and indirect 149. His gamma glutamate transferase was 90 IU/l (3–50), serum glutamic pyruvic transaminase 35 IU/l (0–55) and alkaline phosphatase was 316 IU/l (28–124). There was no evidence of haemolysis and serology for hepatitis A, B and C and antimitochondrial antibodies and antinuclear antibodies was negative. A computed tomography scan of the liver was normal with no dilatation of the collecting system. In view of this picture of intrahepatic cholestasis, danazol was stopped and prednisolone was restarted. Liver biopsy was not done because of severe thrombocytopenia. The patient's jaundice improved progressively and liver function returned to normal after 6 weeks with a platelet count of $25 \times 10^9/l$, which fortunately has not dropped any further.

Danazol is a synthetic anabolic steroidal, isoxazol, which is an impeded androgen with a reduced capacity of masculinization. Mild but transient elevations of aspartate transaminase and alkaline phosphatase have been reported in less than 0.4% of patients receiving danazol therapy.¹ Pearson and Zimmermann reported four patients who had biochemical evidence of liver dysfunction and one patient with jaundice after taking danazol.² The mechanism of this androgenic steroid-related hepatocellular injury is unknown. However, steroids that have been modified by an additional alkyl group in the configuration at position 17 regularly result in sodium sulphobromophthalein (Bromsulphalein) retention if given in sufficiently large doses and in some instances these compounds may produce cholestasis.^{3,4} Reports of danazol producing cholestatic jaundice are rare and the effect is likely to be related to its similarity to C-17 alkylated anabolic steroids. Our patient developed severe cholestatic jaundice related to danazol therapy but the jaundice resolved within 6 weeks of stoppage of treat-