Clostridium tetani, however, have been found in up to 40% of samples of human faces. Another of our patients developed postoperative tetanus, which was attributed to self-contamination, after removal of a tumour of the buttock. Since rubber-band ligation of haemorrhoids produces an avascular area, and since this is in contact with a potential source of Clostridium tetani, the tetanus in this case may reasonably be attributed to the operation. Certainly the time relationship fits in with the incubation period of tetanus.


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Primary biliary cirrhosis after long-term practolol administration

Oculocutaneous syndrome, sclerosing peritonitis, and pulmonary fibrosis may result from practolol treatment1 but liver disease has not been implicated as an adverse effect. We have recently seen two patients with oculocutaneous lesions typical of practolol sensitivity who also had clinical and laboratory features of primary biliary cirrhosis (PBC, primary non-suppurative destructive cholangitis).

Case reports

A 76-year-old man developed pruritus after four years’ continuous treatment with practolol 300 mg daily for angina of effort. He had an eczematous rash with palmar erythema; dryness of the eyes was confirmed by Schirmer filter paper testing. Smooth, non-tender hepatoepigaly was noted. The following measurements were made: serum bilirubin 25 μmol/l (1.5 mg/100 ml) (normal 1.7–17 μmol/l, 0.1–1.0 mg/100 ml)), alkaline phosphatase (liver isoenzyme) 405 IU/l (normal 20–90), serum aspartate transaminase (SGOT) 12 IU/l (normal 4–20), serum albumin 36 g/l, serum total globulin 40 g/l, serum IgM 2.2 g/l (0.7–2.0), IgG 11.6 g/l (9.5–16.5). Hepatitis B antigen was absent. Antinuclear factor was present (titre 1/80) as was smooth muscle antibody (1/20) and mitochondrial antibody (1/80). Liver scan and histological examination of a needle biopsy specimen confirmed the presence of cirrhosis.

He remained well after practolol was stopped, but liver function tests showed persisting cholestasis. The development of cervical lymphadenopathy two years later, however, led to the diagnosis of nodular sclerosing Hodgkin’s lymphoma. Despite radiotherapy he died after six months. Patent bile ducts were found at necropsy, and histology of tissue obtained a few minutes after death confirmed advanced cirrhosis with proliferating bile ducts and lymphocyte aggregates consistent with primary biliary cirrhosis. Staining with orcin and ruban acid showed hepatocytic metalloprotein complex as found in PBC. Typical sclerosing peritonitis affecting the jejunum was also present.

A 57-year-old man was treated with practolol 300 mg/day for angina. After seven months he developed a psoriasiform rash and two months later he complained of dryness of the eyes. Liver function was not tested until 16 months after discontinuing the drug. Findings were: serum bilirubin concentration 50 μmol/l (3.0 mg/100 ml), alkaline phosphatase concentration 144 IU/l, and SGOT 15 IU/l. Serum protein and immunoglobulins were normal as were autoantibody tests except mitochondrial antibody, which was positive to a titre of 1/160. A needle biopsy specimen of the liver showed normal lobular architecture, but near bile ducts were large epithelioid granulomata with surrounding lymphocytes (fig).

Comment

These patients conform to the usual diagnostic criteria for primary biliary cirrhosis,1 including cholestasis, a high mitochondrial antibody titre, and consistent liver histology. Chronic liver disease after drug administration usually resembles active chronic hepatitis. Only three cases of abnormal liver function after practolol administration have been reported to the Committee on Safety of Medicines in the United Kingdom, but the details are incomplete and difficult to interpret. Autoantibody abnormalities, however, are recognised with practolol rashes. Thus the serum in five of out of 18 patients was reported positive for antinuclear factor but none of them had mitochondrial antibody.1 A relationship between practolol and chronic hepatobiliary disease seemed likely but the presence of PBC-like histology and mitochondrial antibody in patients taking practolol could also have been fortuitous. We have therefore tried to calculate the probability of men with PBC being exposed to practolol. By making several assumptions, an estimate of the figure may be obtained from the number of prescriptions for practolol and the number of certified deaths from PBC a year. Two cases of PBC exposed to practolol in the northern region gives a much greater overall incidence than would be expected from annual prescription and mortality data. We therefore think that the association between PBC and practolol in our two cases was probably not fortuitous.

5. Committee on Safety of Medicines, personal communication.

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Malignant disease presenting as Addison’s disease

Primary adrenal hypofunction—Addison’s disease—is uncommon. Autoimmune destruction of the adrenals is now the commonest cause, other causes being due to metastatic carcinoma and tuberculosis. Vieweg et al1 reviewed the published work and found only eight cases of Addison’s disease associated with malignancy in which the diagnosis had been confirmed by the results of ACTH and cortisol estimations. It must be unusual for malignant infiltration of the adrenals to produce Addison’s disease when there is no other evidence of malignant disease. Two such cases are described.

Case histories

Case I—A 75-year-old man presented in 1975 with prostatism. His medical history included tuberculosis at the age of 15; partial gastrectomy for duodenal ulcer in 1944; and syncopal attacks due to cardiac arrhythmias in 1966. In the six months after prostatectomy for benign prostatic hypertrophy, he...