MEDICAL MEMORANDA

Cholestatic Jaundice due to Methyldopa

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The occurrence of hepatitis in patients taking methyldopa was first described over 10 years ago (Gillespie *et al.*, 1962). Though the degree of bile retention in published case reports varies considerably (Tysell and Knauer, 1971) the clinical picture described is generally indistinguishable from viral hepatitis. When the following patient was seen drug-induced jaundice was suspected but as we could find no documented case of cholestatic jaundice attributable to methyldopa laparotomy was undertaken. It is, however, apparent that methyldopa should be included among drugs that can produce "pure" cholestatic jaundice (Toghill *et al.*, 1974).

Case Report

A 51-year-old woman, a university lecturer, had been known to have hypertension for a number of years. On 23 May 1973 methyldopa 250 mg thrice daily with two tablets of Navidrex-K (containing cyclopenthiiazide 0.25 mg/tablet) was begun but discontinued after 10 days.

On 19 October the drugs were restarted at the same dosage. In early December the patient noticed generalized pruritus followed some days later by the appearance of dark urine, pale stools, and frank jaundice with some vague heartburn but no anorexia, nausea, fever, or general ill health. The drugs were stopped on 20 December, when she was first seen. Careful questioning elicited no history of excessive alcohol intake, injections, or exposure to other drugs either prescribed or bought over the counter such as laxatives.

On examination on 20 December she was found to be jaundiced with a just palpable, non-tender liver and a blood pressure of 180/110 mm Hg. There was no fever, the spleen and gall bladder were not palpable, and there were no signs of hepatocellular dysfunction or hypertensive vascular disease.

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Investigations were: haemoglobin 13.3 g/100 ml; W.B.C. 6,800/mm³; film, "no eosinophilia"; platelets 237,000/mm³; E.S.R. 10 mm in first hour; direct Coombs test result negative; prothrombin time and control 15 sec; serum bilirubin 11.3 mg/100 ml; alkaline phosphatase 13.0 K.A.U./100 ml; SGOT 33 IU/l. (normal <20); LDH 274 IU/l. (normal <230); cholesterol 255 mg/100 ml; total proteins 7.4 g (albumin 4.0 g)/100 ml; electrophoretic strip, γ -globulin raised; urine, bile present, urobilinogen in normal amounts; immunofluorescence, no anti-smooth-muscle or antimitochondrial antibodies; tests for presence of HBsAg, L.E. cells, and A.N.F. negative; chest x-ray picture, E.C.G., barium-meal examination, urine culture and microscopy, blood urea, and electrolytes all normal.

On 27 December the serum bilirubin was 18 mg and on 3 January 1974 23.4 mg/100 ml, LDH 343 IU/l., SGOT 30 IU/l., and alkaline phosphatase 16.0 K.A.U./100 ml. On 10 January the serum bilirubin was 20 mg/100 ml.

At laparotomy on 16 January the liver and extrahepatic bile ducts looked normal; the spleen was not enlarged. Wedge biopsy of the liver showed cholestasis but no abnormality of liver cell morphology or any evidence of cellular infiltration.

The patient made an uneventful recovery and the jaundice gradually receded. On 31 January the serum bilirubin was 10.7 mg, on 14 February 5.4 mg, and on 21 March 1.1 mg/100 ml with normal liver enzymes and no bile in the urine.

Comment

Paton (1969) mentioned a case of cholestatic jaundice attributed to methyldopa but could give no further details (A. Paton, personal communication). The occurrence of jaundice in the present case with a second course of methyldopa suggests an immunological mechanism. Lymphocyte transformation tests carried out postoperatively, however, gave negative results with the drug (Dr. E. S. K. Assem); blood eosinophilia was not found preoperatively but two weeks after the laparotomy the W.B.C. was 6,800/mm³ with 7% eosinophils. Eosinophilia may prove to be a pointer to methyldopa-induced cholestasis.

Though the patient's jaundice deepened after withdrawal of the drug it was probably about to remit at the time of the laparotomy. Knowledge that methyldopa can produce cholestatic jaundice might have prevented the laparotomy. This experience and the cases of cholestatic jaundice reported by Toghill *et al.* (1974) should be borne in mind by clinicians faced with deeply jaundiced patients without clinical or biochemical features of hepatitis who have taken methyldopa.

References

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