Chlorpromazine and other psychotropic drugs with definite antidopaminergic properties should be considered among the possible causes of idiopathic oedema.

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Hepatic adenomas induced by norethisterone in patients receiving renal dialysis

The association between using oral contraceptives long term and developing hepatic adenomas is known,^{1,2} but there has been only one report of such lesions occurring in a patient with end stage renal failure who had received oestrogens and norethisterone.³ Dysfunctional uterine bleeding may be severe in patients receiving dialysis, contributes to their anaemia, may be exacerbated by anticoagulation during haemodialysis, and is difficult to treat. Continuous high dose norethisterone (up to 30 mg/day) has been used successfully, though breakthrough bleeding often occurs if the dose is reduced. We report the development of hepatic adenomas in two patients receiving dialysis who were treated with high dose norethisterone.

Case reports

CASE 1

A 33 year old woman had been treated for end stage renal failure by continuous ambulatory peritoneal dialysis for five years. Intermittent intraperitoneal bleeding due to retrograde menstruation had led to the peritoneal catheter blocking on several occasions, so menstruation had been suppressed by norethisterone 10 mg twice daily, which she had taken continuously for four years.

On the day of admission she developed acute epigastric pain and abdominal distension and the dialysate became heavily bloodstained. She was clinically shocked but resuscitated with blood transfusion, and bleeding stopped after 48 hours. Ultrasonography showed a mass in the left lobe of the liver. Computed tomography confirmed this to be a tumour measuring 12.5×8.0 cm and replacing most of the left lobe (figure). Two other lesions, both about 1.5 cm in diameter, were seen in the right lobe. Selective angiography confirmed that the lesion in the left lobe was hypovascular consistent with extensive necrosis. Serum α fetoprotein concentration was not increased.

After laparotomy and left hepatectomy histological examination showed a typical hepatic adenoma with no evidence of carcinoma. Postoperatively she was treated by haemodialysis and then peritoneal dialysis after one month. She was subsequently well although she did not menstruate despite withdrawal of norethisterone. Computed tomography after six months showed that the two remaining lesions had disappeared.

CASE 2

A 23 year old woman had been treated by haemodialysis for two years. Heavy uterine bleeding had become debilitating, and after serious gynaecological disease had been excluded the bleeding was suppressed with norethisterone 10 mg thrice daily.

She presented three years later with fever, neutrophilia, erythrocyte sedimentation rate 155 mm in the first hour, and abnormal results of liver function tests. Abdominal ultrasonography showed multiple intrahepatic lucencies. Computed

Abdominal computed tomogram in case 1 showing large tumour, with central necrosis and surrounding areas of haemorrhage, replacing most of left lobe of liver.

tomography showed several masses containing areas of calcification in both hepatic lobes, the appearances suggesting a multifocal liver tumour. Histological examination of a biopsy specimen showed hepatic adenoma but no malignancy.

She died three months later from a cardiac arrhythmia. Permission for necropsy was refused.

Comment

This is the first report of hepatic adenomas developing during treatment with norethisterone alone. The women had received continuous high dose norethisterone for three and four years respectively, and in both, unusually, the adenomas were multiple. The risk of adenomas increases with duration of contraceptive treatment and high oestrogen dosage,^{1,2} but the effects of different doses of progestogen are not known.²

Both women had end stage renal failure requiring dialysis, and data on progestogen metabolism in such patients are few.⁴ As the drug is normally excreted in the urine, however,³ high concentrations of norethisterone and its conjugate metabolites may have accumulated in our patients. These cases show the need for caution in using norethisterone in patients with renal impairment, and modification of recommended doses may be necessary.

Hepatic adenomas may remain undiagnosed until quite large¹ and may present suddenly with lifethreatening complications. Regular ultrasonography should lead to their early detection in patients at high risk.

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