a new chemotherapeutic agent, VP 16/213 (etoposide). The patient remained clinically well 12 months after embolisation. In case 2 AFP concentrations continued to fall steadily over a total of 10 months to a value 3% of that at presentation, and the tumour diameter, as shown by ultrasonography, decreased by 31% overall. The epigastric mass became impalpable and the serum alkaline phosphatase concentration only slightly raised (115 IU/l as compared with 690 IU/l previously).

PATIENT WITH BENIGN ADENOMA (case 3)

Hepatic arteriography showed a well-circumscribed and highly vascular tumour in this patient. Complete occlusion of its arterial supply by embolisation was shown arteriographically (fig 3). Within 24 hours the patient developed nausea and vomiting and some upper abdominal pain lasting about a week. Subsequent recovery was delayed by the development of an abscess cavity, but after surgical drainage she improved rapidly. Repeat hepatic arteriography at four weeks confirmed that the distal portion of the main hepatic artery was still occluded, and follow-up at 12 months, including isotope scanning, showed no evidence of any remaining adenoma.

Discussion

The changes in serum AFP concentration leave no doubt that the objective of reducing viable tumour size was achieved in the two cases of hepatocellular carcinoma. Changes in AFP concentration are proportional to changes in viable tumour cell mass.⁴ Although the shrinkage in overall tumour size was small, as estimated by ultrasonography, the central echogenicity that developed would also be consistent with the production of tumour necrosis.

Embolisation has obvious advantages for the patient, since surgery is avoided and greater devascularisation is almost certainly achieved than with surgical ligation. Moreover, selective embolisation of individual tumours is possible, as in our two patients with hepatoma, in neither of whom would hepatic artery ligation have been feasible because of cirrhosis in the first and a portal vein block in the second. The pain after the procedure may be quite severe, though may be controlled with pethidine, and may occur partly because the liver capsule is affected by more peripheral embolisation. The abscess in the

patient in case 3, who underwent embolisation first, may have formed because prophylactic antibiotics were omitted; the eventual outcome was, nevertheless, highly satisfactory. Other reported complications, which did not occur in our patients, are inadvertent embolisation of normal structures and passage of emboli into the lungs through arteriovenous shunts.⁵

Tumour embolisation, as with surgical ligation, should be regarded as only the first step in managing hepatocellular carcinoma and as a means of reducing appreciably the viable tumour mass before chemotherapy. The effect of embolisation and the timing of chemotherapy may be well assessed by serial measurement of serum AFP concentrations. Although pain was not a prominent feature in our cases, embolisation may alleviate it considerably.^{6,7} Embolisation has also been used for metastatic endocrine-hormone-secreting tumours in the liver, such as carcinoids and glucagonomas,⁸ reducing the circulating hormone concentrations considerably. In patients with benign liver tumours, as in case 3, embolisation may be used as the primary and definitive treatment. These tumours may regress after oral contraceptives have been withdrawn, but in patients in whom they do not or in whom complications such as intraperitoneal haemorrhage or pain occur, more active treatment measures become necessary. The alternative procedure to embolisation—namely, surgical resection—is by comparison a major undertaking.

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SHORT REPORTS

Emboli from a prosthetic heart valve during postmenopausal oestrogen therapy

While the possible thromboembolic complications of oestrogen-containing oral contraceptives have received wide publicity,¹ the risks of similar complications during oestrogen therapy for control of menopausal symptoms may be overlooked. We report a case of multiple systemic emboli occurring during oestrogen therapy in a patient with a prosthetic mitral valve.

Case report

A 52-year-old postmenopausal woman with rheumatic heart disease had undergone mitral valve replacement with a Starr-Edwards prosthesis in 1971, after the development of severe mitral regurgitation through a previously inserted fascia lata valve. Recovery was uncomplicated. At regular follow-up visits over the next seven years she remained in atrial fibrillation with no evidence of dysfunction of the valve prosthesis or of cardiac failure. Her only symptom was mild exertional dyspnoea. She was maintained throughout on digoxin 0.25 mg daily, frusemide 40 mg daily with potassium supplements, and supervised anticoagulation with phenindione.

During 1978 she developed recurrent urinary tract infections and was referred to a urologist. As the urinary infections were attributed to postmenopausal atrophic changes she was given conjugated equine oestrogens (Premarin) 0.625 mg twice daily. Several days later she experienced a sudden transient episode of imbalance, lasting a few seconds. Over the next five weeks she suffered several similar episodes and two clear episodes of transient monocular visual loss (amaurosis fugax) in the left eye. On 15 February 1979 a small arterial embolus was clearly visible in the left retina on ophthalmoscopy. There were no other new cardiovascular signs. In particular there was no carotid bruit and no clinical evidence of infective endocarditis. Her haemoglobin level and white cell count were normal, and the erythrocyte sedimentation rate was 4 mm in the first hour. Prothrombin times measured on 9 and 23 January and 13 February had all been more than twice the control times and were comparable to levels recorded during the previous year.

Oestrogens were discontinued, and dipyridamole (Persantin) 100 mg thrice daily started. The patient stopped taking this drug after five days, however, because of headache, which persisted despite a reduction in dose. Two months later she had experienced no further embolic symptoms and the valve prosthesis continued to function normally.

Comment

The clear temporal relationship between the ingestion of oestrogen and the occurrence of transient cerebral ischaemic attacks in this case leaves little doubt that oestrogen therapy precipitated these

attacks. Oestrogens may increase the plasma concentrations of some of the coagulation factors with shortening of the prothrombin time. Toy *et al*² found this effect with synthetic oestrogens but not with "natural" oestrogen (oestriol succinate). Thus it is improbable that this mechanism was responsible for thromboembolic episodes in our patient. The oestrogen preparation she was taking was a naturally occurring one (conjugated equine oestrogen), and the patient's prothrombin times remained within the therapeutic range, at levels similar to those maintained in the past without embolic symptoms.

An increase in platelet adhesiveness, which can be shown during oestrogen therapy,³ was probably responsible for the appearance of embolic phenomena in our patient. The importance of platelets in the genesis of emboli from prosthetic heart valves is further illustrated by reports that patients being treated with dipyridamole in addition to oral anticoagulants derive greater protection from non-fatal thromboembolism than those taking anticoagulants alone.⁴

In an extensive review of reports on oestrogen treatment in post-menopausal women, Shoemaker *et al*⁵ concluded that there was no proved risk of thromboembolic disease on such treatment. While this may be true for most women, it does not necessarily apply in those with an additional predisposing factor, such as a prosthetic heart valve. Our case illustrates the potential risks of oestrogen therapy in patients with valve prostheses. Anticoagulation with warfarin or phenindione alone should not be considered to protect these patients adequately against thromboembolic complications of oestrogen treatment. Non-essential oestrogen administration should be avoided in all patients with prosthetic heart valves.

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¹ *Sunday Times*, 9 October 1977, p 44.

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Blindness after treatment for malignant hypertension

Patients with untreated malignant hypertension are at risk of developing encephalopathy, renal failure, and cardiac failure and require urgent correction of blood pressure. Rapid reduction of hypertension, however, has been associated with cerebral and myocardial infarction.^{1 2} We report on two patients who became blind after treatment for malignant hypertension.

Case reports

Case 1—A 30-year-old Caucasian housewife presented with a three-week history of blurring of vision of the left eye, two weeks' morning nausea and vomiting, and three days' haematuria. She had no history of hypertension and was taking no medication. She smoked five cigarettes daily. She had a sinus tachycardia of 124/min, blood pressure of 270/175 mm Hg, and clinical and electrocardiographic features of left ventricular hypertrophy. Fundoscopy showed grade IV hypertensive retinopathy, and visual acuity was decreased in the left eye. After admission to hospital she received methyldopa 500 mg by mouth six-hourly (figure). The next day she was confused and drowsy but there were no new focal neurological signs. Methyldopa was withdrawn and propranolol 80 mg eight-hourly and Moduretic two tablets daily given. Thirty-six hours after admission her conscious level was normal but she complained of total loss of vision and hallucinations. The pupils were bilaterally dilated and unresponsive to light. Fundal appearances were unchanged. Dexamethasone 4 mg six-hourly was given from the fourth day without measurable benefit. The only other neurological abnormality was transient urinary retention 40 hours after admission. The patient has

remained blind despite good blood-pressure control, and bilateral optic atrophy has developed.

Case 2—A 32-year-old Caucasian woman presented with two weeks' blurring of vision. For four days before admission she had received tetracycline 250 mg six-hourly for a probable urinary tract infection. Four years previously she had failed to attend for treatment for mild hypertension (160/105 mm Hg). She was not taking an oral contraceptive. She smoked 15 cigarettes daily. She had a sinus tachycardia of 120/min, blood pressure of 250/170 mm Hg, and clinical and electrocardiographic signs of left ventricular hypertrophy. A chest x-ray film showed cardiac enlargement. Grade IV hypertensive retinopathy was present, and visual acuity was slightly decreased bilaterally. She was treated with diazoxide 300 mg given as an intravenous bolus, frusemide 80 mg intravenously, and atenolol 100 mg by mouth. Her blood pressure fell to 90/70 mm Hg within 10 minutes but rose to 120/70 mm Hg after immediate administration of intravenous saline (figure). She

Changes in blood pressure with treatment in both patients, showing when blindness first developed.

complained of blindness in both eyes and developed dilated pupils unresponsive to light. The fundal appearances did not change. The only other neurological defect was urinary retention, which developed on the day of admission and required catheterisation for two weeks. Blindness has persisted despite satisfactory blood pressure control, and bilateral optic atrophy has developed.

Further disease—In both patients renal function improved after correction of hypertension (case 1: creatinine clearance 13 ml/min rising to 33 ml/min by six weeks; case 2: serum creatinine concentration 275 μ mol/l (3.1 mg/100 ml) falling to 160 μ mol/l (1.8 mg/100 ml) after two weeks). The patient in case 2 had a partially treated urinary tract infection but there was no other evidence of primary renal, endocrine, or collagen disease in either patient. A cerebral computerised tomographic (CAT) scan was normal in case 1, and an isotope brain scan was normal in case 2.

Comment

We have found no published reports of blindness after treatment for malignant hypertension. Both our patients were young, active women who presented with visual impairment but none of the usual features of hypertensive encephalopathy. The predominant neurological damage was confined to the visual pathways and probably localised to the optic nerves. This site is suggested by the pupillary changes, fundal appearances, and normal CAT scan (case 1) and brain scan (case 2). The optic nerves are susceptible to ischaemic damage in temporal arteritis and arteriosclerosis.^{3 4} In our patients ischaemia presumably resulted from a fall in perfusion pressure in tissue with a high interstitial pressure due to oedema. The complications of treating malignant hypertension^{1 2} are usually attributed to a precipitate fall in blood pressure. Blindness occurred in case 1 despite the correction of hypertension being carried out over 24 hours, suggesting that blood pressure should be reduced even more slowly or that additional measures, such as the early use of dexamethasone, are required to prevent this devastating complication.

¹ Kumar, G K, *et al*, *Journal of the American Medical Association*, 1976, **235**, 275.