responded promptly to treatment with digoxin and diuretics and reverted to sinus rhythm though left bundle-branch block persisted. Both thyroxine and imipramine were discontinued as possible aggravating factors, and she was discharged on digoxin 0.25 mg/day.

She remained well for several months but then developed the signs and symptoms of hypothyroidism, which was confirmed by thyroid function tests. Thyroxine 0.3 mg/day was restarted and the digoxin stopped. Despite a good clinical response to thyroxine she remained depressed and was again treated with imipramine 25 mg three times a day. Soon afterwards her episodes of palpitation recurred and on 1 August 1973 she was readmitted with acute heart failure. The E.C.G. showed supraventricular tachycardia (rate 150/min) with left bundle-branch block. After treatment with digoxin and diuretics the pulmonary oedema cleared and sinus rhythm was restored. She was discharged taking quinidine as a prophylactic measure in addition to digoxin and thyroxine, but soon after going home imipramine was added by her practitioner. When seen a month later she continued to complain of palpitations and an E.C.G. showed frequent ectopics and a short run of supraventricular tachycardia. The relationship between treatment with imipramine and her arrhythmia finally became apparent and the drug was discontinued. Since then she remained well and an E.C.G. taken three months later showed that the left bundle-branch block had resolved, the only residual abnormality being lateral S-T changes related to her digoxin treatment. There was no radiological or clinical evidence of cardiac disease.

Comment

Though the potential hazards of the tricyclic antidepressants have been recognized for over 10 years (Kristiansen, 1961) the results of two recent retrospective surveys have conflicted (Coull *et al.*, 1970; Boston Collaborative Drug Surveillance Program, 1972). The Boston Collaborative Drug Surveillance Survey (1972) found no higher incidence of arrhythmias in patients on these drugs than in the rest of the hospital population. Nevertheless, there are enough reports of patients with supraventricular tachycardia (Alexander and Nino, 1969), atrial fibrillation (Rosen, 1960; Moorhead and Knox, 1965), bundle-

branch block (Alexander and Nino, 1969), and ventricular tachycardia (Scollins *et al.*, 1972) to suggest that arrhythmias can be caused by tricyclic therapy, particularly when, as in our case, the arrhythmias resolves on stopping treatment.

The relationship between the tricyclic drugs and heart failure is less clear. In previous case reports (Cossa *et al.*, 1960; Alexander and Nino, 1969; Luke, 1971) there has been evidence of underlying heart disease or patients have been receiving large doses of phenothiazines at the same time. In our patient underlying heart disease could not be excluded with certainty but the complete resolution of both the heart failure and the E.C.G. abnormality strongly support the causative role of imipramine. In theory some interaction between imipramine and thyroxine may have occurred, as suggested with guanethidine in another case (Williams, 1971). Thyroxine is known to sensitize tissues to the effects of circulating catecholamines (Harrison, 1964), which may be increased during treatment with psychotropic drugs (Carlsson *et al.*, 1966). Tricyclic antidepressants should therefore be prescribed with caution to patients already taking thyroxine.

We thank Dr. W. Whitaker for permission to report the details of this patient under his care.

Requests for reprints should be sent to Dr. C. Davidson.

References

- Alexander, C. S., and Nino, A. (1969). *American Heart Journal*, 78, 757.
- Boston Collaborative Drug Surveillance Program (1972). *Lancet*, 1, 529.
- Carlsson, C., *et al.* (1966). *Lancet*, 1, 1208.
- Cossa, P., Gasaix, M., and Darcourt, G. (1960). *Annales médico-psychologiques*, 118, 314.
- Coull, D. C., *et al.* (1970). *Lancet*, 2, 590.
- Harrison, T. S. (1964). *Physiological Reviews*, 44, 161.
- Kristiansen, E. S. (1961). *Acta Psychiatrica Scandinavica*, 36, 427.
- Luke, C. M. (1971). *New Zealand Medical Journal*, 74, 345.
- Moorhead, C. N., Knox, S. J. (1965). *American Journal of Psychiatry*, 122, 216.
- Rosen, B. P. (1960). *Journal of the Mount Sinai Hospital*, 27, 609.
- Scollins, M. J., Robinson, D. S., Niles, A. (1972). *Lancet*, 2, 1202.
- Williams, R. F. (1971). *Annals of Internal Medicine*, 74, 395.

Transvenous Biopsy of Carcinoma of Bronchus Causing Superior Vena Caval Obstruction

P. ARMSTRONG, D. F. HAYES, P. J. RICHARDSON

British Medical Journal, 1975, 1, 662-663

A histological diagnosis in patients presenting with superior mediastinal obstruction of suspected neoplastic origin may be difficult to establish. We recently encountered just such a patient from whom we obtained tissue with a transvenous endomyocardial bioprobe introduced percutaneously.

Case Report

A 66-year-old white woman presented in September 1969 complaining of backache, breathlessness, flatulence, and swelling of the face.

King's College Hospital, London SE5 9RS

P. ARMSTRONG, M.B., F.F.R., Consultant Radiologist

D. F. HAYES, M.B., M.R.C.P., Research Assistant, Chest Unit

P. J. RICHARDSON, M.B., M.R.C.P., Research Fellow, Department of Cardiology

She had previously had a hysterectomy for a benign lesion and had suffered for some years from depression. She smoked 15 cigarettes a day. She was on prednisone 2 mg on alternate days for late onset asthma.

The chest x-ray film showed slight elevation of the right hemidiaphragm and enlargement of the superior mediastinum in the right paratracheal region compatible with lymph node enlargement. She developed obvious superior vena caval obstruction and became very distressed. Bronchoscopy was carried out and no intraluminal lesion was seen but the roof of the right upper lobe bronchus bulged inwards due to an external mass. A biopsy of this area was performed. While awaiting the results of histological analysis, in view of the rapidly progressive obstruction which was almost certainly due to malignant disease, radiotherapy with ⁶⁰Co was started on 2 November 1969. She was given a mid-point dose of 3600 rads over 27 days to the mediastinum with great relief of symptoms. Histological analysis proved unhelpful and a definite diagnosis was never arrived at.

The patient was seen several times over the next few years and in 1972 was investigated for a peripheral neuropathy, which was thought to be related to the mediastinal malignancy. On 24 July 1974 she was again admitted with a recurrence of the superior vena caval obstruction. She also had profound bilateral posterior column impairment.

The chest x-ray film showed a raised right hemidiaphragm which on fluoroscopy was shown to be paralysed. Apart from bullae in the right upper lobe no other abnormality was present. There was no evidence of a superior mediastinal mass.

A superior venacavagram on 2 August 1974 showed an obstruction of the superior vena cava due to a spherical intraluminal filling defect which was apparently attached to its left wall at the level of

the junction of the azygos vein and the superior vena cava (see photograph).

Superior venacavagram showing round intraluminal filling defect in superior vena cava causing obstruction. Inset shows tip and jaws of biopsy catheter.

We thought that bronchoscopy would be unhelpful and as a histological diagnosis was desirable to guide future management a biopsy of the obstructing lesion was carried out using an endomyocardial biptome.

PROCEDURE

The biptome (Richardson, 1974) was introduced via a Desilet (Vigon) 7F sheath after percutaneous puncture of the right femoral vein in the groin under local anaesthetic. The catheter biptome was passed through the right atrium into the superior vena cava. Under fluoroscopic control it was easy to tell when the biptome had reached the lesion since the catheter curved slightly without advancement of the tip. Two biopsy specimens were taken.

From the specimen a histological diagnosis of oat cell carcinoma was made. This was treated with 20 mg of mustine intravenously and prednisone by mouth, with rapid relief of the obstruction.

Comment

It was technically easy to obtain tissue from the obstructing mass in the superior vena cava in this patient and the procedure caused her almost no discomfort; it was clearly important in her subsequent management. The alternative technique of medias-tinoscopy and direct biopsy might have presented problems with bleeding owing to the presence of superior vena caval obstruction. We decided to approach the lesion from below so that if by mischance a small perforation of the superior vena cava were to occur it would not be subjected to the raised venous pressure above the obstruction. We also felt that it would be much easier to localize the lesion by the feel of the catheter if the path to the area were straight. Certainly, we had no problems with localization, and the force on the catheter tip was minimal.

This technique may prove to be useful in those patients with superior vena caval obstruction in whom superior venacavagraphy shows an intraluminal mass, suggesting that the tumour has grown through the wall of the vein and is therefore amenable to biopsy using forceps which only obtain a very small and superficial sample.

The patient was admitted under the care of Dr. P. Hugh-Jones.

Reference

Richardson, P. J. (1974). *Lancet*, 1, 660.

Porphyria Variegata Provoked by Contraceptive Pill

CLARE J. FOWLER, JOANNA M. WARD

British Medical Journal, 1975, 1, 663-664

Combined oestrogen-progesterone oral contraceptives are known to produce neuropsychiatric and abdominal symptoms in acute intermittent porphyria (Zimmerman *et al.*, 1966). This is thought to be due to the induction of δ -aminolaevulinate synthetase (*British Medical Journal*, 1972). The activity of this enzyme is increased in all forms of inherited porphyria, and, though this is probably not the primary biochemical lesion, oestrogens would tend to compound the existing defect.

In porphyria variegata oestrogens do not apparently provoke acute attacks, but four cases have been reported in which the "pill" produced cutaneous symptoms associated with liver damage (Eales, 1963; Dean, 1965; Baxter and Permowicz, 1967; McKenzie and Acharya, 1972). We present a further case.

The patient, with undiagnosed porphyria variegata, took an oral contraceptive and two months later developed a light-sensitive bullous eruption followed by cholestatic jaundice. The case illustrates a probable mechanism for the photosensitivity.

Case History

A 26-year-old Irish woman of previous good health took Minilyn (0.5 mg ethinyloestradiol and 2.5 mg lynoestrenol) for three weeks in June 1973. At the end of this course she developed acute swelling and itching of the face and hands followed by blistering. The lesions subsided but recurred at the end of a second course in July. On that occasion the lesions persisted and worsened over the next month though she took no further tablets. In the middle of August she became jaundiced and two weeks later was admitted to hospital for investigation.

She had no past history of jaundice, skin fragility, or photosensitivity. On admission she was jaundiced and had a widespread erythematous rash on all light-exposed areas. She had oedema of the eyelids and multiple bullae of varying size—some haemorrhagic—on the hands, arms, face, and legs. All other systems were normal. Liver function tests (see table) suggested a cholestatic jaundice. All investigations to exclude other forms of liver disease gave normal results. Liver biopsy showed normal architecture with cholestasis and some hyperplasia of the Kupffer cells, appearances compatible with "pill" administration. Skin biopsy showed a subepidermal bulla with patchy epidermal spongiosis. Superficial vessels stained weakly with periodic-acid Schiff. There was a marked increase in urinary

Central Middlesex Hospital, London NW10 7NS

CLARE J. FOWLER, M.B., B.S., House Physician

JOANNA M. WARD, M.B., M.R.C.P., Senior Registrar in Dermatology