Pulmonary hypertension after lung irradiation in infancy

Irradiation of the lung may lead to several complications including pneumonitis, pulmonary fibrosis, pleural effusion, and pneumothorax. The development of pulmonary hypertension is less well known and was not recorded in either of two recent reviews of the complications of radiotherapy.^{1,2} We report a case here.

Case report

A 14-year-old girl presented with an 18-month history of syncope and mild dyspnoea on effort. At the age of 7 months a neuroblastoma arising from the left of the thoracic spine had been resected. Histology had shown severe cystic degeneration of the tumour. Postoperatively, irradiation had been given by linear accelerator in 55 exposures over eight weeks (tumour dose 3500 rads, given dose 2041 rads to the posterior mediastinum; given dose 2372 rads to the anterior mediastinum). A further 200 rads had been given to the left lower chest for a presumed metastasis arising in the scar area. She had remained well until the onset of syncope at the age of 12 years.

On examination she was small (height 153 cm, weight 40 kg) with underdevelopment of the left side of the chest and the left breast. There was no cyanosis or finger clubbing. Blood pressure was 120/70 mm Hg. Jugular venous pressure was raised to the angle of the jaw. There was a left parasternal heave of right ventricular hypertrophy. The pulmonary second sound

Pulmonary arteriogram: right pulmonary artery and branches are normal; left pulmonary artery is small, with severe reduction in number and size of its branches.

was accentuated. There were signs of functional tricuspid regurgitation, with a soft pansystolic murmur at the left sternal edge increasing on inspiration together with a third heart sound. The liver was enlarged 3 cm below the subcostal margin and was slightly pulsatile. There was no peripheral oedema. Breath sounds were normal.

An electrocardiogram showed sinus rhythm, an axis of $+150^\circ$, right atrial enlargement, and right ventricular hypertrophy with a tall R wave in V1 of 20 mm, and the amplitude of the S wave equal to that of the R wave in V6 (9 mm). Chest x-ray examination showed underdevelopment of the left side of the chest with mild crowding of the ribs and slight kyphoscoliosis convex to the left. The cardiothoracic ratio was 48%. The lung fields on each side seemed normal and there was no fibrosis. An echocardiogram showed an enlarged right ventricle of 3 cm diameter but was otherwise normal.

Lung function tests showed a restrictive pattern with a diminished transfer factor of 10.1 (predicted 22.0) ml/min/mm Hg. At cardiac catheterisation the pressures were (mm Hg): right atrium $a=15$, $x=10$, $v=15$, $y=7$, mean $=12$; right ventricle 70/16; and pulmonary artery 70/30. Systemic arterial pressure was 95/70 mm Hg. A satisfactory wedge pressure was not obtainable. There was no intracardiac shunt on oximetry. Systemic saturation was 100%. Blood gas tensions were normal. Haemoglobin concentration was 15.4 g/dl. A pulmonary arteriogram (figure) showed a normal right pulmonary artery but the branches to the left were small, spidery, and hypoplastic. The

pulmonary veins from the left lung were underdeveloped. Follow-through to the left side of the heart and aorta was normal, and there was no evidence of a ventricular septal defect.

Comment

The pulmonary vasculature is sensitive to irradiation and, if the dose is sufficient, reduced perfusion on lung scans, pneumonitis, and late pulmonary fibrosis seen on chest x-ray films may develop.³ Irradiation in infancy also inhibits the proliferation of alveoli and pulmonary vasculature and considerably reduces the subsequent size of the lung and chest wall.⁴ Both these mechanisms were probably acting to produce the late development of pulmonary hypertension in this patient.

Information on the x-ray fields used in this case was not available, but the dose of irradiation was high and protracted over an unusually long period. The outcome emphasises that every attempt should be made, especially in children, to keep the dose and field of therapeutic irradiation to a minimum.

We thank Dr L Arthur, consultant paediatrician, Derby Children's Hospital, who referred this patient, and Dr N Nicol, consultant radiotherapist, Leicester Royal Infirmary, for advice on the radiotherapy aspects of the case.

Requests for reprints should be sent to Dr P J B Hubner.

¹ Gross NJ. Pulmonary effects of radiation therapy. *Ann Intern Med* 1977; **86**:81-92.

² Strickland P. Complications of radiotherapy. *Br J Hosp Med* 1980;**23**: 552-61.

³ Goldman SM, Freeman LM, Ghossein NA, Sanfilippo LJ. Effects of thoracic irradiation on pulmonary arterial perfusion in man. *Radiology* 1969;**93**:289-96.

⁴ Wohl MEB, Griscom NT, Traggis DG, Jaffe N. Effects of therapeutic irradiation delivered in early childhood upon subsequent lung function. *Pediatrics* 1975;**55**:507-16.

(Accepted 18 August 1981)

Department of Cardiology, Groby Road Hospital, Leicester LE3 9QE

P BUTLER, MB, MRCP, senior house officer (present appointment: registrar in diagnostic radiology, Manchester AHA(T))

P CHAHAL, MB, MRCP, senior house officer (present appointment: registrar, Department of medicine, Hammersmith Hospital, London W12 0HS)

N M HUDSON, MB, FRCR, consultant radiologist

P J B HUBNER, MB, MRCP, consultant cardiologist

Peripheral oedema in patients treated with isosorbide dinitrate

Isosorbide dinitrate is widely used to treat angina and increasingly to manage congestive cardiac failure.¹ Reported side effects are headache, flushing, and postural hypotension.² I report three cases which suggest that it may also cause peripheral oedema.

Case reports

Case 1—A 74-year-old man with a history of myocardial infarction was admitted with central chest pain. There was clinical and radiographic evidence of left heart failure but his jugular venous pressure was normal and there was no peripheral oedema. Electrocardiograms showed sinus rhythm and acute ischaemia. Cardiac enzyme activities and tests of renal and hepatic function were normal. He was treated with bumetanide 1 mg daily and isosorbide dinitrate 10 mg three times daily. Chest pain did not recur. Signs of left heart failure resolved in 24 hours and a chest x-ray film three days later was normal. Six days after admission bilateral pitting ankle oedema was noted; jugular venous pressure was normal and there was no clinical evidence of left heart failure. Echocardiography showed normal right and left ventricular dimensions. The electrocardiogram was unchanged. Bumetanide 1 mg daily was continued and isosorbide withdrawn; the ankle oedema resolved within 36 hours. Isosorbide was reintroduced when he was fully ambulant; the oedema did not recur.

Case 2—A 69-year-old man was admitted with central chest pain. There was clinical and radiographic evidence of left heart failure but the jugular venous pressure was normal and he had no peripheral oedema. Electrocardiograms showed sinus rhythm and anterior subendocardial infarction. Cardiac enzyme activities were raised and renal and hepatic function normal. He

was treated with frusemide 80 mg daily and isosorbide dinitrate 10 mg four times daily. Later he developed a chest infection and episodes of supra-ventricular tachycardia, which were suppressed with verapamil 80 mg three times a day. He was symptom free 14 days after admission, the radiographic signs of left heart failure had resolved, and he was mobilised. Five days later gross bilateral ankle oedema was noted. Jugular venous pressure was normal and the chest x-ray film and electrocardiogram were unchanged. Frusemide and verapamil were continued in the same dosage and isosorbide withdrawn. The ankle oedema resolved within 48 hours without accompanying weight loss. Isosorbide was reintroduced when he was fully ambulant: the oedema did not recur.

Case 3—A 61-year-old man with ischaemic heart disease and congestive cardiac failure was admitted for reassessment. He had basal crepitations, raised jugular venous pressure, enlargement of the liver, and bilateral ankle oedema. An electrocardiogram showed atrial fibrillation and previous anterior myocardial infarction. There was radiographic evidence of cardiomegaly and pulmonary venous congestion. Liver function tests were abnormal. Serum albumin, urea, and creatinine concentrations were normal. Treatment with digoxin, bumetanide, spironolactone, and isosorbide dinitrate 20 mg three times a day was continued. He was not confined to bed. Weight and ankle circumference were measured serially. Isosorbide was withdrawn after seven days. Over the next week, while symptoms and weight were unchanged, the ankle oedema decreased. Isosorbide was reintroduced. The oedema reaccumulated over the following week and his weight remained unchanged.

Comment

There is strong evidence that isosorbide dinitrate caused the peripheral oedema in cases 1 and 2 and aggravated it in case 3. On the basis of these and similar cases I suggest that peripheral oedema is a fairly common side effect of isosorbide dinitrate and that failure to recognise this may lead to inappropriate diuretic treatment.

Isosorbide dinitrate causes venous dilatation with resulting venous pooling and diminished venous return.³ Peripheral oedema is thus an easily explicable side effect, and it is surprising that it has not been reported previously.

My observations suggest that isosorbide-induced oedema is most likely to occur in semi-ambulant patients. Case 3 raises the possibility that hepatic dysfunction with impaired degradation of the drug may be an additional predisposing factor.

¹ Franciosa JA, Cohn JN. Sustained hemodynamic effects without tolerance during long-term isosorbide dinitrate treatment of chronic left ventricular failure. *Am J Cardiol* 1980;**45**:648-54.

² Anonymous. Drugs used in the treatment of diseases of the cardiovascular system. In: Wade A, ed. *British National Formulary*. London: British Medical Association and Pharmaceutical Press, 1981:71.

³ Gray R, Chatterjee K, Vyden JK, Ganz W, Forrester JS, Swan HJC. Hemodynamic and metabolic effects of isosorbide dinitrate in chronic congestive cardiac failure. *Am Heart J* 1975;**90**:346-52.

(Accepted 19 August 1981)

Monklands District General Hospital, Airdrie, Lanarkshire ML6 6JS
J CHRISTINE RODGER, MD, FRCPGLAS, consultant physician

Hyperkalaemic cardiac arrhythmia caused by potassium citrate mixture

We report a case of severe hyperkalaemia after ingestion of potassium citrate mixture BP.

Case report

An 83-year-old woman presented to the casualty department after collapsing at home. She was unable to give a clear history and on examination looked pale and dyspnoeic. Peripheral pulses were poor and heart rate was regular at 40/min. Blood pressure was 100 mm Hg by palpation. Jugular venous pressure was normal, and there was no oedema. Auscultation disclosed a pansystolic murmur at the apex and crepitations at both lung bases. She had suprapubic abdominal tenderness. There were no abnormal neurological signs. Electrocardiography showed a junctional bradycardia with absent P waves (figure). A temporary transvenous endocardial pacing wire was inserted, after which her clinical state improved and she was able to give a history.

She had been well until one week before admission, when she had developed urinary frequency, haematuria, and dysuria. She had purchased and ingested indeterminate large volumes of potassium citrate mixture BP. Immediately before admission her urinary frequency had worsened and she had become faint and dizzy.

Initial investigations showed sodium 137 mmol(mEq)/l, potassium 8.7 mmol(mEq)/l, urea 6.0 mmol/l (36.0 mg/100 ml), chloride 102 mmol(mEq)/l, carbon dioxide 26 mmol(mEq)/l, and creatinine 0.11 mmol/l (1.2 mg/100 ml). A midstream urine specimen showed over 100 leucocytes/mm³ and no bacterial growth. Chest radiography disclosed no abnormalities. Serum potassium concentration reverted to normal after the administration of glucose and insulin and thereafter remained within the normal range. Urinary symptoms responded to a course of ampicillin. Further investigations showed: creatinine

Rhythm strip (a) on admission and (b) 12 hours later, when serum potassium concentration normal.

clearance 37 ml/minute, urinary sodium 49 mmol(mEq)/l, urinary potassium 38 mmol(mEq)/l, urinary aldosterone 16 nmol (5.8 µg)/24 hours (normal 10-55 nmol (3.6-19.8 µg)/24 hours), and plasma aldosterone 200 pmol/l (7.2 ng/100 ml) (normal 100-500 pmol/l (3.6-18.0 ng/100 ml)). Serial cardiac enzyme activities were normal, and a Synacthen test gave normal results.

Comment

Severe hyperkalaemia may cause life-threatening cardiac arrhythmias. As the extracellular potassium concentration rises characteristic changes occur in the electrocardiogram. Initially these are peaked T waves (serum potassium concentration 6-8 mmol(mEq)/l) and then atrial asystole and complete heart block before bizarre QRS complexes, ventricular fibrillation, and standstill occur (serum potassium concentration over 8 mmol(mEq)/l). Such bradyarrhythmias may be managed by temporary cardiac pacing¹ while the hyperkalaemia is corrected.

Hyperkalaemia is usually seen complicating acute or chronic renal failure, but in patients with normal renal function it is most commonly drug induced²—such drugs include potassium supplements and potassium-sparing diuretics—or due to hyporeninaemic hypoaldosteronism.³ We believe that the transient hyperkalaemia in this patient was caused by the excessive ingestion of potassium citrate mixture BP. This is used to alkalise the urine in urinary tract infections and contains 28 mmol(mEq) potassium/10 ml dose. The recommended dose is up to 40 ml daily. Hyperkalaemic ventricular fibrillation has been reported after ingestion of small amounts of potassium salts (40-60 mmol(mEq)/l) in patients with good renal function.⁴ Potassium citrate mixture BP has a high concentration of potassium and may be hazardous to those who handle the ion poorly.

We are concerned that this potentially dangerous mixture may be purchased over the counter from any retail chemist.

We thank Professor J M Evanson for permission to report this case.

¹ Rosenberg AS, Furman S, Escher DJW, Lister J. Emergency cardiac pacing in hyperkalemia. *Arch Intern Med* 1970;**126**:658-9.

² Lawson DH. Adverse reactions to potassium chloride. *Q J Med* 1974;**43**:433-40.

³ Tan SY, Burton M. Hyporeninemic hypoaldosteronism. *Arch Intern Med* 1981;**141**:30-3.

⁴ Hultgren HN, Swenson R, Wettach G. Cardiac arrest due to oral potassium administration. *Am J Med* 1975;**58**:139-42.

(Accepted 7 August 1981)

Professorial Medical Unit, University Hospital of South Manchester, Manchester M20 8LR

J J BROWNING, MB, CHB, house officer (now at department of anatomy, University of Bristol)

K S CHANNER, BSC, MRCP, senior house officer (present appointment: registrar in neurology, Bristol Royal Infirmary)