Postgraduate Medical Journal (September 1978) **54**, 633–636.

Hypocalcaemic cardiac failure

D. P. BRENTON*
M.D., M.R.C.P.

J. GONZALES†
M.D.

A. B. POLLARD‡
M.D., F.R.C.P.

**Department of Human Metabolism, University College Hospital Medical School, London WC1; †Colegio Mayor Fonseca, Salamanca; ‡Essex County Hospital, Colchester*

Summary

A 35-year-old patient who presented with recurrent chest infection, pulmonary oedema and cardiac failure was found to be grossly hypocalcaemic owing to previously undiagnosed hypoparathyroidism. The cardiac failure was not easily relieved by digoxin and diuretics but it quickly responded when the plasma calcium was restored to normal with dihydrotachysterol. With dihydrotachysterol as sole treatment for more than 2·5 years he had normal exercise tolerance and no features of cardiac failure.

Introduction

Congestive cardiac failure is not well recognized as a complication of hypoparathyroidism although the ECG changes of hypocalcaemia are well known. In their early review, Bronsky *et al.* (1958) recorded cardiac failure in four out of fifty published cases of idiopathic hypoparathyroidism. More recently, in neonates, the association between oedema, hypomagnesaemia and hypocalcaemia has been noted (Chiswick, 1971, 1972) and others (Troughton and Singh, 1972) have attributed oedema to cardiac failure secondary to hypocalcaemia in this age group. In older children cardiomegaly in association with hypoparathyroidism was noted by Antebi *et al.* (1966), cardiac size becoming normal during treatment with vitamin D_2 and calcium gluconate. More dramatic results were described by Aryanpur, Farhoudi and Zangeneh (1974) in a 14-year-old girl with hypoparathyroidism whose cardiomegaly and frank congestive failure responded to intravenous calcium and vitamin D. Cardiac complications of hypoparathyroidism may however occur in adult life. Three of the four patients in the review of Bronsky *et al.* (1958) were adults, but each may have had some other contributing factor for their cardiac failure. The patient reported here is an adult with the monilia hypoparathyroid syndrome whose profound hypocalcaemia was complicated by congestive cardiac failure.

Case history

The patient was a 35-year-old unmarried man who presented in December 1974 with shortness of breath, productive cough and fever. He was admitted to the Essex County Hospital where he appeared ill and dyspnoeic. The relevant physical findings were as follows. Temperature 37·6°. Pulse 100/min, regular. BP 160/110 mmHg. Coarse crepitations throughout both lungs. Liver palpable two fingers, but no elevation of jugular vein pressure (JVP). The relevant investigations were: WBC $13{\cdot}3 \times 10^9$/l with 76% polymorphs, scattered bronchopneumonic changes throughout both lung fields radiologically and a prolonged QT interval in the ECG. The patient remained intermittently breathless after adequate antibiotic treatment and one week after admission pulmonary oedema was diagnosed clinically and radiologically (Fig. 1). There was oedema of both feet and sacrum, the liver was palpable two fingers below the costal margin and the JVP was elevated by 3–4 cm. He improved on furosemide 40 mg b.d. and slow-K. He was discharged one week later while still on his diuretic treatment.

During out-patient follow-up he continued to have mild ankle oedema and oral monilia was noted. On 21 February 1975 he was admitted with dyspnoea, slight cyanosis and carpopedal spasm. A history of recent muscle cramps and episodes of tetany was obtained, and it was known that he had been maintained for many years on phenobarbital 30 mg b.d. and phenytoin 100 mg/day because of two grand mal seizures at the ages of 17 and 22 years. It was later learned that his second dentition had been completely lost during his early teenage years. The relevant clinical findings were, temperature 37·2°C, pulse 120/min and regular, respirations 40/min and BP 140/90 mmHg. The JVP was raised 3 cm, there was slight pitting oedema of the ankles, and coarse rales in both lung fields with a pleural friction rub over the left lower chest anteriorly. The Chvostek sign was negative, but papilloedema was considered to be present and there were no cataracts. Apparent finger clubbing was later identified as swelling due to chronic monilial paronychia. A diagnosis of hypoparathyroidism, congestive cardiac failure and bronchopneumonia

0032–5473/78/0900–0633 $02.00

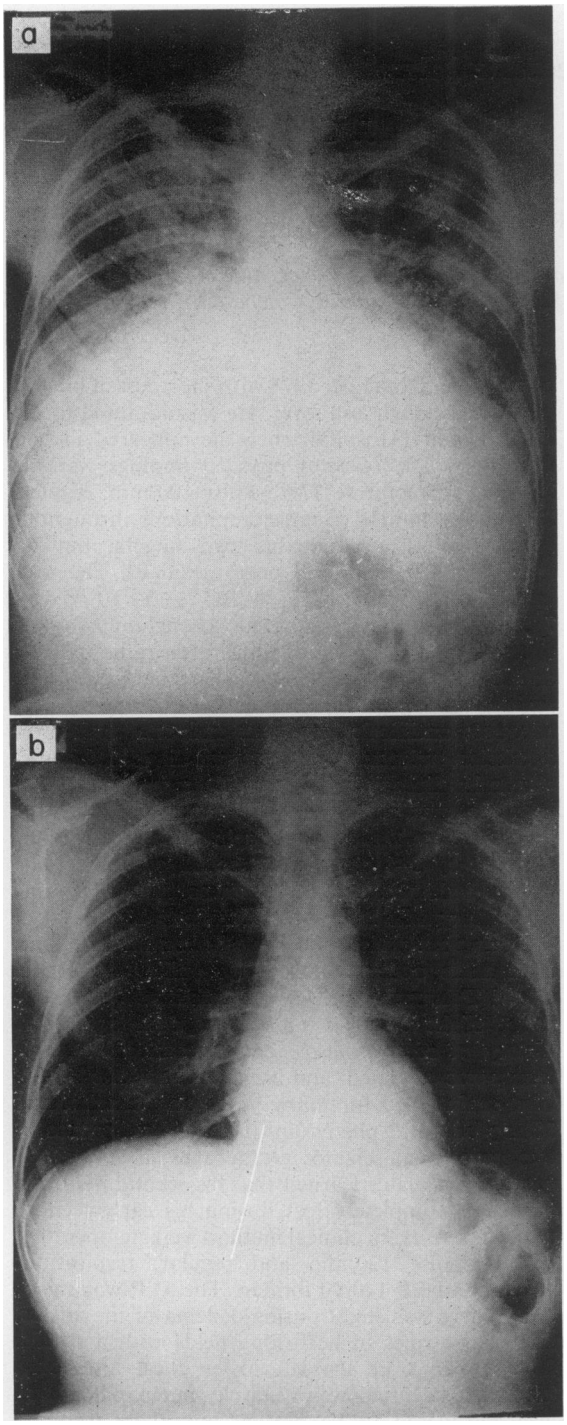

FIG. 1. Chest X-rays (a) December 1974. Acute pulmonary oedema during hypocalcaemia. (b) June 1975. Several months after plasma calcium restored to normal. No digoxin or diuretic therapy for 4 months.

was made. The chest X-ray showed bilateral pleural effusions and pulmonary congestion. The plasma calcium was 1mmol/l, phosphorus 3·65 mmol/l, total serum proteins 77 g/l and albumin 37 g/l. He was treated with ampicillin, flucloxacillin, furosemide and vitamin D_2 1·25 mg t.d.s. His episodes of tetany were relieved by i.v. calcium gluconate which he required frequently. One week after admission he was acutely dyspnoeic, and digoxin was added to his treatment. He was transferred to University College Hospital, London, on 1st March 1975. Examination revealed a sick-looking edentulous man with florid oral monilia and chronic monilial paronychia. There was extensive bilateral ankle oedema, bilateral basal crepitations, hepatomegaly (four fingers) and a slightly raised jugular venous pressure. The papilloedema had subsided. He was afebrile with a pulse of 80/min and a BP of 120/80 mmHg. Chest X-ray had considerably improved and showed a right-sided pleural reaction. X-rays of the skeleton showed nothing abnormal. Bilateral phlebograms of the legs revealed no evidence of peripheral venous thrombosis. There were prolonged QT intervals in the ECG and evidence of left ventricular hypertrophy. The plasma calcium was 1·55 mmol/l (SG of plasma 1028, normal 2·20–2·58), phosphorus 1·74 mmol/l (normal 0·6–1·5), and alkaline phosphatase 9 KAu./100 ml (normal 4–12). Other results were as follows:

Haematological: Hb 12·2 g/dl, WBC $12·2 \times 10^9$/l, ESR 50 mm, plasma iron 22·2 μmol/l (normal 7–45), RBC folate 269 μg/l (normal 140–650), serum B_{12} 700 ng/l (normal 150–950).

Plasma biochemistry: Urea 3·98 mmol/l (normal 2·7–8·4), Na 137, K 4·2, Cl 91, HCO_3 24 mmol/l, creatinine 141·4 μmol/l (normal 53–124), urate 110 μmol/l (normal 170–500), bilirubin 12·0 μmol/l (normal 3–17), PGOT 11 i.u./l (normal 1–12), serum albumin 37 g/l, globulins 48 g/l.

24hr urines: 24 hr urinary calcium 9·03 mmol/d (normal), and total hydroxyproline 0·39 mmol/d (normal).

Renal function tests: Urine pH fell to 5·5 six hours after a standard ammonium chloride test. No aminoaciduria, glycosuria or proteinuria was present.

Endocrine tests: Plasma T_4 117 μmol/l (normal 70–160), T_3 resin uptake 95% of normal. Plasma cortisol 331 nmol/l (midnight), 469 nmol/l (9·00 a.m.) (normal 170–720) rising to 1242 nmol/l 30 min after 0·25 mg of synacthen given i.m. Plasma ACTH 87 pg/ml (normal 9–80). Plasma PTH no hormone detectable by standard radioimmunoassay (normal values in this assay varied from 0 to 0·5 ng/ml).

Gastrointestinal function: Faecal fats 31·7 mmol/d and 21·1 mmol/d (normal 11–18).

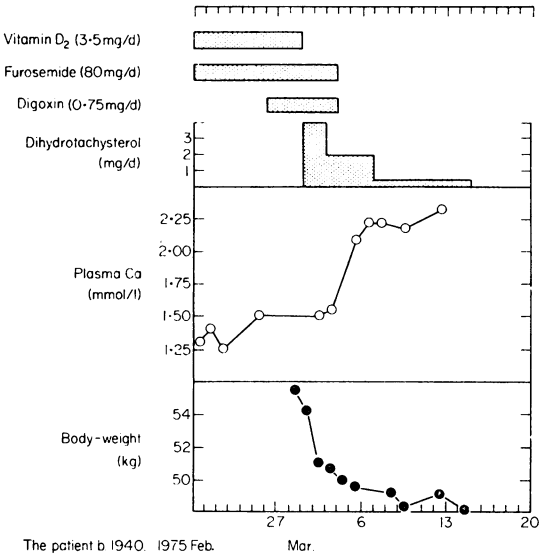

FIG. 2. Rising plasma calcium during DHT treatment with loss of weight due to loss of oedema which did not recur after stopping diuretics and digoxin.

On admission to UCH the vitamin D_2 was stopped and replaced with dihydrotachysterol (DHT) 2 mg b.d., the dose being reduced in stages. His subsequent progress is illustrated in Fig. 2. The digoxin and diuretics were stopped when the plasma calcium was nearly normal and have never subsequently been required since there has been no recurrence of the oedema or other clinical features of congestive cardiac failure. He was discharged on DHT 0·5 mg/d and nystatin for his oral monilia. He was asked gradually to decrease his dose of anticonvulsants which were finally discontinued in June 1975. He has remained well and in full time work, being last seen in the Outpatient Clinic in August 1977.

Discussion

The main purpose of this report is to emphasize the association of cardiac failure with severe hypocalcaemia and hypoparathyroidism. It has been known for many years that cardiac contraction depends upon the presence of extracellular calcium ions (Mines, 1913). A review of the present evidence concerning the role of calcium ions has been made by Nayler (1975). Briefly, it is believed that membrane depolarization results in a sudden increase in the intracellular availability of calcium ions. The ions interact with the regulatory proteins troponin and tropomyosin allowing the actin to activate myosin ATPase. Under these conditions ATP hydrolysis occurs at a sufficiently rapid rate to provide energy for the activation of the cross-bridges linking adjacent actin and myosin filaments. It is suggested that the cardiac failure in the patient described here was directly due to the profound hypocalcaemia impairing myocardial contractility.

Cardiac failure in this patient only occurred after many years of hypoparathyroidism. The chronicity is indicated by the early loss of his second dentition, a known feature of hypoparathyroidism, and the seizures in his earlier life, presumably also due to hypoparathyroidism. The monilial paronychia was chronic and had been present for many years. His long-standing anticonvulsant treatment may have contributed to his profound hypocalcaemia since such drugs may cause vitamin D deficiency (Richens and Rowe, 1970; Dent *et al.*, 1970). His myocardium, therefore, was probably subjected to years of severe hypocalcaemia. The patient of Aryanpur *et al.* (1974) had also taken phenobarbital and phenytoin and presented with a serum calcium of 3·5 mg/100 ml (0·88 mmol/l). After allowing for the serum albumin of 28 g/l in this patient the calcium would correct to about 1·3 mmol/l, a value similar to that in the patient reported here when he first presented. The patient of Antebi *et al.* (1966) suffered severe and frequent seizures from 1 year of age and presented with profoundly low plasma calcium values of 3·6–4·6 mg/100 ml (0·9–1·2 mmol/l). Anticonvulsant treatment was not mentioned in this account nor any plasma protein values with which to correct the calcium measurements.

The patient described here suffers from the monilia–hypoparathyroid syndrome (see Rimoin and Schimke, 1971, for discussion). His cardiac failure with oedema required energetic treatment with digoxin and diuretics until the plasma calcium values began to approach normal which resulted in rapid improvement. There has been no recurrence of any of the signs of congestive cardiac failure in the 2·5 years since the calcium values were restored to normal. Restoration of normal calcium values therefore cures the cardiac abnormalities of hypoparathyroidism just as it cures the seizures and other neuropsychiatric abnormalities. It does not, however, cure the monilia which many would regard as evidence of an underlying immunological disorder.

The present patient (like other patients with hypoparathyroidism) did not suffer any gross weakness of skeletal muscle whatever the impairment of his cardiac muscle. The situation contrasts with that seen in vitamin D deficency where skeletal muscle weakness may be prominent. Plasma calcium values are not usually as low in vitamin D deficient patients as in the hypoparathyroid patients with cardiac failure, and cardiac failure has not been described as a feature of vitamin D deficiency. There is evidence that vitamin D deficiency results in disordered intracellular calcium metabolism in skeletal muscle

since uptake of calcium into sarcoplasmic vesicles is reduced in vitamin D deficient animals (Curry *et al.*, 1974). It would seem that the normal function of skeletal muscle is more sensitive to lack of vitamin D and that of cardiac muscle more sensitive to very low extracellular calcium concentrations.

There was no evidence of adrenal cortical deficiency in this patient which is commonly found in the monilia–hypoparathyroid syndrome. Several other interesting metabolic abnormalities were found, however, including the hypouricaemia which reversed during treatment and was unexplained. The very mild steatorrhoea might have been secondary to the hypocalcaemia (Dent and Friedman, 1964) but repeat measurements of the faecal fats have not been made to see if the abnormality has reversed now the plasma calcium is normal.

References

ANTEBI, L., BOUCHARD, R., GUEDENEY, J., PERLES, C. & WEILL, J. (1966) Cardiomegaly due to chronic hypocalcemia. *Pediatrics*, **38**, 909.

ARYANPUR, I., FARHOUDI, A. & ZANGENEH, F. (1974) Congestive heart failure secondary to hypoparathyroidism. *American Journal of Diseases of Children*, **127**, 738.

BRONSKY, D., KUSHNER, D.S., DUBIN, A. & SNAPPER, I. (1958) Idiopathic hypoparathyroidism and pseudohypoparathyroidism: Case reports and review of the literature. *Medicine*, **37**, 317.

CHISWICK, M.L. (1971) Association of oedema and hypomagnesaemia with hypocalcaemic tetany of the newborn. *British Medical Journal*, **3**, 15.

CHISWICK, M.L. (1972) Heart failure and neonatal hypocalcaemia. *British Medical Journal*, **4**, 364.

CURRY, O.B., BASTEN, J.F., FRANCIS, M.J. & SMITH, R. (1974) Calcium uptake by sarcoplasmic reticulum of muscle from vitamin D deficient rabbits. *Nature*, **249**, 83.

DENT, C.E. & FRIEDMAN, M. (1964) A comparison between AT 10 and pure dihydrotachysterol in controlling hypoparathyroidism. *Lancet*, **ii**, 164.

DENT, C.E., RICHENS, A., ROWE, D.J.F. & STAMP, T.C.B. (1970) Osteomalacia with longterm anticonvulsant therapy. *British Medical Journal*, **4**, 69.

MINES, G.R. (1913) On functional analysis by the action of electrolytes. *Journal of Physiology*, **46**, 185.

NAYLER, WINIFRED G. (1975) The ionic basis of contractility, relaxation and cardiac failure. In: *Modern Trends in Cardiology*. (Ed. by Oliver, M.F.). pp. 154–181. Butterworths, London.

RICHENS, A. & ROWE, D.J.F. (1970) Disturbance of calcium metabolism by anticonvulsant drugs. *British Medical Journal*, **4**, 73.

RIMOIN, D.L. & SCHIMKE, N. (1971) Hypoparathyroidism, adrenal cortical insufficiency and moniliasis. In: *Genetic Disorders of the Endocrine Glands*, p. 84. C. V. Mosby Co., St Louis.

TROUGHTON, O. & SINGH, S.P. (1972) Heart failure and neonatal hypocalcaemia. *British Medical Journal*, **4**, 76.