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Hypocalcaemic chorea secondary to malabsorption

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Summary

A patient presented with chorea and a recent history of Crohn's disease. Investigation revealed the cause of the chorea to be hypocalcaemia secondary to malabsorption. So far as is known there has been no previous report of hypocalcaemic chorea due to malabsorption.

Introduction

There are many causes of chorea, or choreoathetoid movements, including familial, endocrine, infective, vascular, drug-induced and metabolic. A variety of metabolic causes has been reported which includes hepatic disease (Victor, Adams and Cole, 1965), hypomagnesaemia (Randall, Rossmeisl and Bleifer, 1959), hypernatraemia (Sparacio, Anziska and Schutta, 1976), and hypocalcaemia (Simpson, 1952; McKinney, 1962).

In all but one of the previous reports of hypocalcaemia producing chorea, the hypocalcaemia has been a result of hypoparathyroidism, either idiopathic (Simpson, 1952), postoperative (Frame, 1965), or pseudo-hypoparathyroidism (MacGregor and Whitehead, 1954), the chorea being proportionately more common in the idiopathic variety (McKinney, 1962). In that one report, the chorea followed hypocalcaemia in a case of drug-induced osteomalacia during the treatment of epilepsy (Hosking *et al.*, 1975). However, chorea has not been reported following hypocalcaemia due to any other cause.

Despite the fact that steatorrhoea is a relatively common disorder and that low serum calcium levels occur in up to 60% of such patients (Losowsky, Walker and Kelleher, 1974), chorea has not so far been reported in association with this condition.

A patient is now reported who presented with chorea due to hypocalcaemia which was caused by malabsorption as a result of extensive small bowel disease.

Case report

A 58-year-old housewife had a past history of rheumatic chorea at the age of 18 years, and of an episode of paroxysmal atrial fibrillation at the age of 55 years. Six months before she was admitted to St James's Hospital she had been investigated for weight loss (32 kg in 1 year), abdominal pain and diarrhoea. Laparotomy had shown 18 skip lesions, typical of Crohn's disease, throughout the small bowel, producing 4 areas of local obstruction which were by-passed by a single anastomosis, since clearly no other surgical treatment was appropriate. Thereafter she had remained weak, her diarrhoea had persisted, but her weight had been steady. She was taking digoxin and cyclopenthiazide, but no other medication.

She presented to the authors, 20 weeks after operation, complaining of the gradual onset, over 3 days, of difficulties with articulation and coordination, together with constant writhing movements, more marked on the left side. There were no other neurological symptoms. She also complained of diarrhoea, bowel action being up to 10 times/day, the stool being described as pale and offensive.

On examination she had gross clubbing of the fingers and toes, and bilateral ankle oedema, but there was no evidence of cardiovascular or respiratory disease. There were mild, generalized abdominal distension and normal bowel sounds. Neurologically comprehension was good but articulation was poor owing to involuntary movements of the tongue. There was marked facial grimacing with bilateral limb chorea and hypotonia, choreiform movements being more evident on the left. There were no other neurological signs; Chvostek's and Trousseau's signs were negative.

Initial investigations showed (normal values in parentheses): ESR 33 mm in the first hour; Hb 10 g/dl; WBC count $9{\cdot}9 \times 10^9$/l; platelets 405×10^9/l; blood film normal. Sodium 135 mmol/l (135–145); potassium 2·5 mmol/l (3·6–5); chloride 102 mmol/l (98–107); bicarbonate 28·9 mmol/l (21–28); urea 3·7 mmol/l (2·5–7·1); creatinine 94 mmol/l (50–140); albumin 14 g/l (37–49); calcium 1·05 mmol/l (2·25–

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2·60); 'adjusted' calcium (Payne *et al.*, 1973) 1·70 mmol/l (2·25–2·60); phosphate 0·93 mmol/l (0·8–1·3); alkaline phosphatase 14·8 KAu. (4–13); magnesium 0·3 mmol/l (0·7–1·0).

Correction of the serum potassium and magnesium over the next 7 days did not produce any improvement in the neurological signs; her movements, in fact, became more marked. Her diarrhoea persisted with frequent, loose, watery, pale stools.

Other abnormal results during the first week were: Prothrombin time 17 s (control 12 s); urinary calcium 0·16 mmol/24 hr (normal 1·25–9·0). The following investigations gave normal results: Blood sugar; lipids; serum bilirubin; ALT; thyroid function tests; ANF; DNA-binding; serum folate; red cell folate; serum B_{12}; serum levels of vitamins A and E; leucocyte vitamin C; blood cultures; WR; ASO titre; urinalysis and urine culture; urinary nicotinamide; plain X-rays of chest and skull; ECG; EEG.

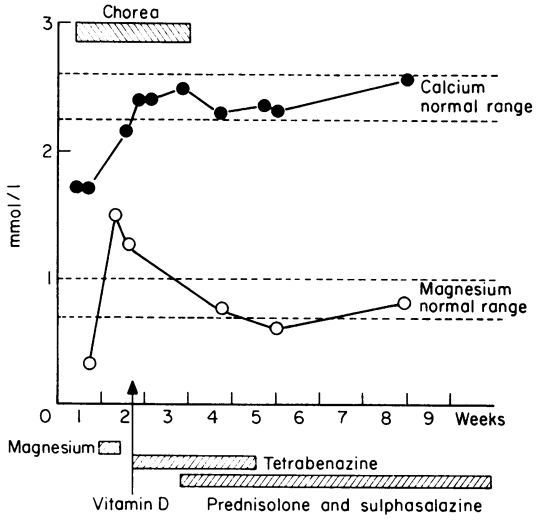

FIG. 1. Showing the relationship of chorea to adjusted serum calcium during the time of observation in hospital. ●——● Adjusted serum calcium; ○——○ serum magnesium.

At this stage she was given one i.m. dose of 300 000 u. of vitamin D (Fig. 1) on the presumption that the low serum calcium was the cause of the chorea. At the same time tetrabenazine (100 mg daily) was introduced, because the continued involuntary movements had led to a state of near exhaustion. Over the next 2 weeks the neurological signs improved to such an extent that there remained only the occasional grimace and choreiform movement and the patient was beginning to walk on her own and had started knitting. It was possible to withdraw the tetrabenazine. In the meantime, the Crohn's disease was being treated with sulphasalazine (4 g/daily) and prednisolone (40 mg/day). Further investigation during the period of improvement included urinary indican 97·4 mg/day and 218 mg/day (normal < 100 mg/day), a small bowel enema demonstrated changes typical of Crohn's disease, jejunal biopsy was normal and a smear for *Giardia* was negative.

After 5 weeks in hospital, the patient was discharged home. Over the next 8 months she remained well, her diarrhoea was well controlled, she had only the occasional facial grimace and choreiform movement of the hands. She was able to lead a normal life.

At 8 months, a faecal fat measurement was 7·7 g/day and cerebral computerized axial tomography (CAT) and psychometric testing were normal.

She continues well, after a further 9 months, taking prednisolone (2·5 mg/day); sulphasalazine (1·5 g/day) and spironolactone (100 mg/day). She has not required any further vitamin D. Her serum magnesium has been maintained without supplements. Parathyroid hormone estimation, while she was normocalcaemic, at 13 months after presentation, was 0·2 ng/ml (normal < 1·0 ng/ml).

Discussion

There are several possibilities which could account for the chorea in this patient.

In view of the absence of family history, normal psychometry one year after presentation and the normal appearance on CAT scanning, Huntington's chorea seems unlikely.

The previous history of rheumatic chorea suggests the possibility of a recurrence (Aron, Freeman and Carter, 1965). However, 80% of such recurrences are within 2 years and recurrences are usually associated with pregnancy, intercurrent illness, or periods of emotional stress (Lessof, 1958). Forty years had elapsed since this patient had Sydenham's chorea, and there had been no recurrence during periods of intercurrent illness or pregnancy. ASO titre was normal and there were no stigmata of rheumatic infection. It is therefore unlikely that this was a recurrence of rheumatic chorea. The previous history of such chorea, however, does raise the possibility of residual damage to the basal nuclei rendering the patient liable to extra-pyramidal symptoms in the presence of some other precipitating factor such as hypocalcaemia.

A vascular cause can be effectively excluded. Investigation revealed no evidence of polycythaemia rubra vera (Gautier-Smith and Prankerd, 1967), or a collagen vascular disease (Donaldson and Espiner, 1971). The bilaterality of the chorea and absence of hemiplegia or sensory disturbance render an acute

vascular event unlikely, the lesion in such cases being in the posterior part of the lateral nucleus of the thalamus and anterior to the pulvinar (Déjerine, 1926).

No endocrine abnormality was found and there was no history of ingestion of any drugs such as phenothiazines associated with movement disorder (Singer and Wong, 1970).

Several authors (Randall *et al.*, 1959; Smith, Hammarsten and Eliel, 1960; Fishman, 1965) have commented on chorea as an occasional manifestation of hypomagnesaemia. In all those reports there have been other neurological features, namely confusion, delirium, muscle twitching and generalized convulsions. Correction of the serum magnesium in these patients has led to a dramatic improvement in their chorea. Indeed Fishman (1965) considers the administration of magnesium as a therapeutic test. Not only did the present patient fail to improve with normalization of the serum magnesium, but also the other usual neurological accompaniments of hypomagnesaemia were absent. On admission, the patient was not only hypomagnesaemic but also hypocalcaemic. The serum magnesium was corrected before commencing other therapy but the involuntary movements did not improve. It therefore seems likely that the chorea in this patient was due to hypocalcaemia.

The association of chorea with hypocalcaemia was first described by Simpson (1952), the cause of the hypocalcaemia being idiopathic hypoparathyroidism. Since then there have been several reports of this association (Sparacio *et al.*, 1976; Fonseca and Calverley, 1967; Muenter and Whisnant, 1968). Other neurological manifestations of hypocalcaemia, namely tetany, epilepsy, mental retardation and papilloedema, have also been reported (Sugar, 1953). The peripheral neurological complication, tetany, is commonly seen whatever the cause of hypocalcaemia. However, the central neurological complication of chorea has been reported only when the hypocalcaemia was a consequence of hypoparathyroidism (Simpson, 1952; Frame, 1965; MacGregor and Whitehead, 1954), or anti-convulsant therapy (Hosking *et al.*, 1975). The parathyroid hormone estimation, during convalescence when the patient was normocalcaemic, was normal which does not exclude hypoparathyroidism but makes it unlikely. In addition, there are several reasons for rejecting hypoparathyroidism in this patient: (1) the biochemical results, a low serum phosphate and, initially, 2 raised values of alkaline phosphatase, both suggest malabsorption as the cause of hypocalcaemia; (2) patients usually present with idiopathic hypoparathyroidism at an earlier age; (3) there were no ectodermal features of hypoparathyroidism; (4) there had been no surgery to the neck; (5) the normal serum calcium has been maintained without vitamin D for 17 months; (6) X-rays of the hands suggest secondary hyperparathyroidism. The hypocalcaemia, in this patient, would therefore appear to be due to malabsorption as a result of Crohn's disease.

In patients with hypocalcaemia due to malabsorption, replacement with vitamin D and calcium supplements is required. It is well recognized that resistance to this therapy may be due to magnesium deficiency and indeed the serum calcium can be increased by replacing the magnesium alone (Petersen, 1963; Heaton and Fourman, 1965). In this patient the serum calcium was already increasing after magnesium supplements, before vitamin D was given.

The mechanism by which hypocalcaemia produces extrapyramidal symptoms is not known. Initially it was thought to be due to deposition of calcium in the basal ganglia. However, this is not invariably the case (Sparacio *et al.*, 1976) and CAT scanning of the patient failed to show calcium in the basal ganglia which might have been missed by conventional radiology (Klawans, Lupton and Simon, 1976).

Some authors report the persistence of chorea in a proportion of cases even when the serum calcium has returned to normal (Frame, 1965; Muenter and Whisnant, 1968). In this case the occasional choreiform movement persisted for several months after the serum calcium was normal.

The lack of previous reports of chorea or extrapyramidal movements caused by hypocalcaemia due to malabsorption may be an indication that the degree of hypocalcaemia and its duration are not usually as severe as in hypoparathyroidism. Possibly a contributory factor in the present case was residual damage to the extrapyramidal system through previous rheumatic chorea rendering the patient susceptible to the CNS effects of hypocalcaemia.

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