she did not respond satisfactorily to oral chloroquine, on day 7 (2 July) she was given a free combination of pyrimethamine 75 mg and sulfadoxine 1500 mg. On day 8 the parasite density had fallen to $0{\cdot}18 \times 10^9$/l. Subsequent blood smears taken until day 63 remained negative for *P falciparum* trophozoites.

Comment

The results of the two in vitro macrotests showed that schizonts formed up to the last chloroquine concentration tested of 3·0 μmol/l; schizont formation was completely inhibited at a mefloquine concentration of 0·25 μmol/l. Thus the strain of *P falciparum* was resistant to chloroquine but sensitive to mefloquine. The in vivo results show that this was a case of type II resistance (World Health Organisation classification), successfully treated with a combination of pyrimethamine and sulfadoxine.

Detailed results of our work on the sensitivity of *P falciparum* to chloroquine and mefloquine in Zambia will be published later. The chloroquine resistant strain is in continuous culture, and further work is being done on it.

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Idiopathic hypoparathyroidism associated with stable untreated myelofibrosis

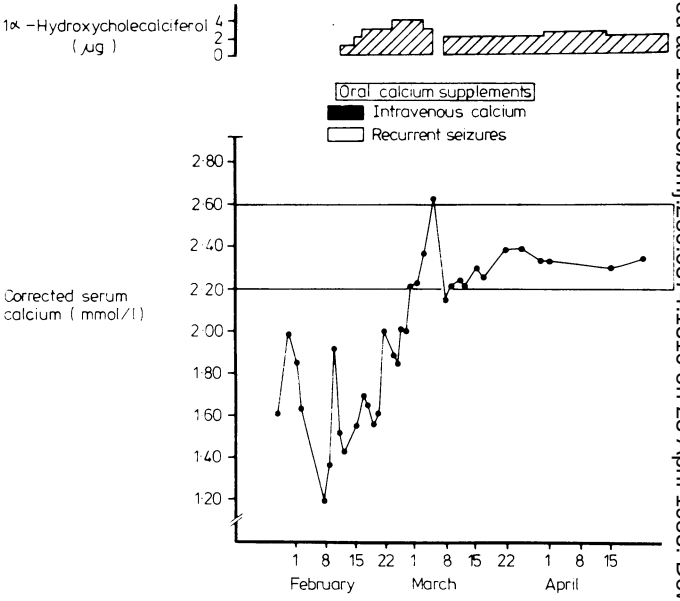
Idiopathic hypoparathyroidism is rare and characteristically occurs in young people in association with other endocrine conditions.[1] An acute form has been described in elderly patients,[2] but more recently hypocalcaemia and hypoparathyroidism have been recognised in association with chemotherapy for both haematological malignancies[3] and solid tumours.[4] The chemotherapy has been the presumed cause, but the neoplasm itself may predispose to hypoparathyroidism.

We describe a patient with untreated myelofibrosis who developed hypoparathyroidism associated with profound hypocalcaemia and recurrent major convulsions.

Case report

A 77 year old woman with stable chronic renal failure, serum creatinine concentration 200-230 μmol/l (2·3-2·6 mg/100 ml), and a six year history of myelofibrosis was admitted to hospital for routine blood transfusion. Her myeloproliferative state had been managed conservatively, and she had not received either chemotherapy or radiotherapy. On admission, apart from obvious anaemia, her condition was satisfactory but she had multiple painful gouty tophi in both hands. Biochemical investigation confirmed her usual degree of renal impairment but showed hyperuricaemia, the plasma urate concentration being 0·83 mmol/l (14 mg/100 ml) (normal 0·12-0·45 mmol/l (2·0-7·6 mg/100 ml)). She was mildly hypocalcaemic, with serum calcium concentration (corrected for albumin) 2·06 mmol/l (8 mg/100 ml). Despite her poor renal function serum phosphate concentration and alkaline phosphatase activity were normal. Haemoglobin concentration was 6·4 g/dl. Three units of packed cells were transfused and allopurinol 100 mg/day started. Her initial progress was satisfactory, and she was discharged home, taking allopurinol, after five days.

She was admitted six days later (8 February; figure) after a major convulsion at home associated with blurred vision and mental confusion. She was drowsy and confused, and Trousseau's and Chvostek's signs were present. Serum biochemistry showed no appreciable change in renal function, but she had profound hypocalcaemia: corrected calcium concentration was 1·16 mmol/l (4·6 mg/100 ml), phosphate concentration 2·09 mmol/l (6·5 mg/100 ml), and alkaline phosphatase activity 58 IU/l, while the serum magnesium concentration, also corrected for albumin, was 0·7 mmol/l (1·7 mg/100 ml) (normal 0·7-1·1 mmol/l (1·7-2·7 mg/100 ml).) She had recurrent major convulsions, which were successfully treated with repeated injections of intravenous calcium gluconate (10% w/v). No parathyroid hormone was detectable by radioimmunoassay.



Corrected serum calcium concentration and forms of replacement treatment given.
Conversion: SI to traditional units—Calcium: 1 mmol/l ≈ 4 mg/100 ml.

Over the next eight days she needed large quantities of intravenous calcium (figure) and was also given oral calcium supplements. In addition, oral 1α-hydroxycholecalciferol 1 μg daily was started. Her general condition improved, and the corrected serum calcium concentration rose to 2·14 mmol/l (8·6 mg/100 ml). The dose of 1α-hydroxycholecalciferol was stabilised at 2 μg daily, at which point the corrected serum calcium concentration was 2·22 mmol/l (8·9 mg/100 ml). Her mental state had returned to normal, and she had no further convulsions.

Another predominant symptom was diarrhoea. Stool cultures and tests for malabsorption yielded negative results, as did barium studies of the alimentary tract. Diarrhoea is a recognised feature of hypocalcaemia[5] and in this case resolved when the serum calcium concentration was restored to normal.

At discharge from hospital she had no symptoms and was taking 2 μg 1α-hydroxycholecalciferol daily and a normal diet without calcium supplements. Her corrected serum calcium concentration was 2·28 mmol/l (9·1 mg/100 ml).

Comment

This patient suffered recurrent major convulsions associated with hypocalcaemia, which was subsequently corrected by oral 1α-hydroxycholecalciferol. The aetiology of her hypoparathyroidism was unclear. An age related decline in parathyroid function may occur, and this patient and two other cases[2] may represent extreme examples. Acute idiopathic hypoparathyroidism has been reported in patients with leukaemia treated with cytotoxic agents[3] and in patients with breast cancer treated with chemotherapy.[4] Our patient had never received any chemotherapeutic agents. Freedman *et al*[3] postulated that low

magnesium concentrations may play a part in hyposecretion of parathyroid hormone, but our patient had consistently normal concentrations.

Stress, in the form of serious underlying illness, may contribute to the development of hypoparathyroidism; our patient had a complex medical history. In retrospect she was found to have had a low serum calcium concentration before her first admission to hospital and may have had subclinical hypoparathyroidism then. We recommend that the serum calcium concentration be checked promptly in any elderly patient after an unexplained convulsion.

We thank Dr B F Allam, consultant clinical biochemist at this hospital, for his invaluable help and guidance with this case.

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Chlorpropamide-alcohol flushing and coronary heart disease in non-insulin dependent diabetics

Chlorpropamide-alcohol flushing in non-insulin dependent diabetics[1] and its relation to diabetic complications is a subject of much interest and dispute. Barnett and Pyke[2] and Jerntorp and Almér[3] suggested that non-insulin dependent diabetics with a positive chlorpropamide-alcohol flushing test result have a diminished risk of large vessel disease. In the following study, however, we could not find any association between a positive reaction in the test and protection from coronary heart disease.

Patients, methods, and results

We examined 36 non-insulin dependent diabetics originally identified in 1979-81 in a study of 138 newly diagnosed diabetics aged 45-64 years who were representative of the diabetic population of Kuopio, Finland. In the original study population 23 diabetics had a history of myocardial infarction verified at hospital or electrocardiographic abnormalities diagnostic of previous myocardial infarction (Minnesota code 1·1-1·2) and 21 diabetics were free of coronary heart disease by strict criteria (absence of chest pain by Rose cardiovascular questionnaire and normal electrocardiogram). These two groups of diabetics were invited to participate in this study and, finally, 20 diabetics with previous myocardial infarction (coronary heart disease group) and 16 diabetics free of coronary heart disease took part. The coronary heart disease group comprised nine men and 11 women, and the other group 10 men and six women. Of all 36 patients, 27 were being treated with diet, seven with sulphonylureas, and two with metformin.

The chlorpropamide-alcohol flushing test was performed in a room kept at a constant 20-22°C. Patients were given 40 ml of sherry 12 hours after 250 mg of chlorpropamide. Temperature of the face was measured by a digital thermometer with a resolution of 0·1°C. Facial warmth, flushing, or burning of the face were regarded as subjective evidence of a positive reaction. An increase of over 1°C in skin temperature 30 minutes after the sherry was taken as objective evidence of a positive reaction.

Plasma insulin concentration was determined by radioimmunoassay (Novo, Denmark) before and one and two hours after a 75 g oral glucose load. Serum total cholesterol and triglyceride concentrations were estimated by enzymatic methods. Serum high density lipoprotein cholesterol was determined from supernatant after precipitation by dextran sulphate and magnesium chloride. Serum chlorpropamide concentration was measured by high performance liquid chromatography.[4] The χ^2 test and Student's two tailed t test were used for statistical analyses.

Of the 16 diabetics without coronary heart disease and the 20 with a history of heart disease, four and six, respectively, gave subjective evidence of flushing (difference not statistically significant). Objective evidence of flushing was obtained in six patients in each group (difference not significant). Use of other criteria for a rise in skin temperature (increase of 1·5°C or more 30 minutes after sherry or a maximal increase of 2°C or more, or both; and a maximal temperature rise of over 1°C) also showed no statistically significant difference in the prevalence of chlorpropamide-alcohol flushing between the groups.

Comparison of subjects with and without evidence of flushing showed no statistically significant differences in age, relative weight, serum concentrations of cholesterol, high density lipoprotein cholesterol, and triglycerides, plasma insulin concentration, or serum chlorpropamide concentration. The table summarises these results. In the coronary heart disease group flushers had lower high density lipoprotein cholesterol concentrations than had the non-flushers ($p < 0·005$).

Comment

Our results did not confirm reports[2,3] of an association between chlorpropamide-alcohol flushing and a diminished risk of large vessel disease. Contradictory results may be explained by differences in the selection and treatment of diabetics, by differences in the definition of large vessel complications studied, and by different criteria used to define a positive reaction in the chlorpropamide-alcohol flushing test.

The test was carried out in two groups of non-insulin dependent diabetics who had been included in a larger population based survey. The presence or absence of coronary heart disease was determined by strict criteria. None of the diabetics was receiving chlorpropamide as maintenance treatment. Long term chlorpropamide increases the proportion of patients giving positive reactions in the test[5] and is thus a confounding factor in studies correlating chlorpropamide-alcohol flushing with small vessel or large vessel complications.

Our results do not support the view that non-insulin dependent diabetics giving positive reactions in the chlorpropamide-alcohol flushing test have a diminished risk of large vessel disease.

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Relative weight, concentrations of high density lipoprotein cholesterol, plasma insulin values during oral glucose tolerance test, and serum chlorpropamide concentrations in flusher and non-flusher diabetics without and with coronary heart disease. Values are means ± SEM

	Relative weight (%)	High density lipoprotein cholesterol (mmol/l)	Plasma insulin after oral glucose (mU/l)			Serum chlorpropamide (mg/l)
			0 h	1 h	2 h	
Diabetics without coronary heart disease						
Non-flushers (n = 10)	133·8 ± 9·6	1·17 ± 0·08	23·1 ± 6·8	58·8 ± 16·4	61·0 ± 13·9	25·5 ± 1·8
Flushers (n = 6)	139·0 ± 11·6	1·17 ± 0·18	18·8 ± 7·6	50·3 ± 21·6	44·3 ± 19·0	21·9 ± 2·1
Diabetics with coronary heart disease						
Non-flushers (n = 14)	145·2 ± 7·7	1·07 ± 0·08	28·8 ± 3·7	65·6 ± 10·4	65·1 ± 10·4	23·8 ± 0·8
Flushers (n = 6)	128·8 ± 5·6	0·76 ± 0·06	30·5 ± 5·7	64·5 ± 9·2	58·5 ± 10·1	22·2 ± 1·6
All diabetics						
Non-flushers (n = 24)	140·5 ± 6·1	1·11 ± 0·05	26·4 ± 3·6	62·8 ± 9·3	63·4 ± 8·4	24·5 ± 0·9
Flushers (n = 12)	133·9 ± 6·6	0·96 ± 0·11	24·7 ± 5·1	57·4 ± 11·9	51·9 ± 10·9	22·1 ± 1·3

Conversion: SI to traditional units—High density lipoprotein cholesterol: 1 mmol/l ≈ 38·6 mg/100 ml.