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Osteomalacia in presence of "normal" serum 25-hydroxycholecalciferol concentration

Measurement of serum 25-hydroxycholecalciferol (25-OHD) concentration is commonly thought to be of value in diagnosing osteomalacia, especially in doubtful cases.¹ Preece *et al*² measured 25-OHD concentrations in patients with unequivocal osteomalacia and in no case was the concentration greater than 9 nmol/l (3.5 ng/ml). Undetectable serum concentrations of 25-OHD have, however, been shown to occur in elderly subjects in whom osteomalacia had been excluded on histological, biochemical, and radiological criteria.³ We now report two cases of osteomalacia, diagnosed histologically, in which serum 25-OHD concentrations were close to the mean in elderly patients.

Case reports

CASE 1

A 74-year-old woman presented with a two-week history of aches and pains across the chest and increasing lassitude and fatigue. She had been housebound for many years because of a nervous disposition and had been taking pentobarbitone sodium regularly at night. Investigations showed serum calcium concentration, corrected for albumin and globulin,⁴ 1.06 mmol/l (4.2 mg/100 ml) (normal range for elderly women 1.22-1.66 mmol/l (4.9-6.7 mg/100 ml)), serum phosphate 0.58 mmol/l (1.8 mg/100 ml) (normal range for elderly women 0.80-1.30 mmol/l (2.5-4.0 mg/100 ml)), and alkaline phosphatase 156 IU/l (normal range 30-130 IU/l). Urea, electrolyte, and creatinine concentrations were within the normal range and there was no history of chronic renal disease. Radiography of the chest, spine, pelvis, and upper femora showed thin bones but no Looser's zones. Serum 25-OHD concentration measured five days after admission was 26 nmol/l (10.3 ng/ml). Histological examination of a bone biopsy specimen showed osteoid seams covering most of the bony surface with up to five bright lines.

CASE 2

An 87-year-old woman presented with loss of appetite for six months and weakness of the legs for two months. Two weeks before presentation she had suffered two bad falls, after one of which she had developed pain in the jaw. She had been virtually housebound for the past three years because of her age, her dependent personality, and living up 15 stairs. Examination showed a bruise on the right side of the neck and tenderness posteriorly over the right ribs. Radiography showed a fracture through the ramus of the right jaw, multiple rib fractures, and symmetrical lesions on the medial aspects of both upper femora that had some of the features of Looser's zones.

Investigations showed corrected serum calcium concentration 1.28 mmol/l (5.1 mg/100 ml), phosphate 0.89 mmol/l (2.8 mg/100 ml), and alkaline phosphatase 269 IU/l. Urea, electrolyte, and creatinine concentrations were within the normal range and there was no history of chronic renal disease. Biochemical findings were not strongly suggestive of osteomalacia as calcium and phosphate concentrations were in the lower normal range, and the alkaline phosphatase activity may have been raised as a result of the multiple fractures. In view of the clinical and radiological features, however, serum 25-OHD concentration was measured and a bone biopsy performed. Serum 25-OHD concentration on the day after admission was 15 nmol/l (6 ng/ml). Histological examination of the bone biopsy specimen showed osteoid seams covering most of the bony surface with up to six bright lines.

Comment

The mean serum 25-OHD concentration in elderly women is 18 nmol/l (7.1 ng/ml),⁵ and concentrations in both our patients were close to this. Our results, combined with those in the patients without osteomalacia in whom serum 25-OHD was undetectable,³ show that this measurement does not help either in making or excluding the diagnosis. As 25-OHD is not the active hormone this conclusion is not unexpected. Further work needs to be done to see whether measurement of the active hormone, 1:25 dihydrocholecalciferol, is more useful.

We thank Professor I Macintyre's laboratory for the 25-OHD measurements.

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Crohn's disease presenting as recurrent pulmonary oedema

Hypoproteinaemia is a well-recognised complication of Crohn's disease,¹ especially when the disease is widespread, but the presentation of Crohn's disease as oedema from hypoproteinaemia is uncommon. Steinfeld *et al*² reported hypoalbuminaemia in nine out of 23 patients with Crohn's disease. Of 120 patients with Crohn's disease attending our gastroenterology clinic, 22 had hypoalbuminaemia (<35 g/l) at diagnosis, of whom seven had oedema as one of the presenting symptoms.

We report on one of these patients, who presented with recurrent pulmonary oedema caused by hypoalbuminaemia, subsequently found to be due to small-intestinal Crohn's disease.

Case report

A 29-year-old man was admitted as an emergency in October 1974 after a week of acute dyspnoea, which had been waking him from sleep. His medical history included spinal tuberculosis at the age of 2 years, which had required several orthopaedic operations and left him with a residual spastic paraparesis and a dislike of both hospitals and doctors. He had had diarrhoea for one year, diagnosed as "colitis" by his general practitioner and treated with sulphasalazine (Salazopyrin), and recent vomiting and loss of weight. He was emaciated, with kyphoscoliosis, clubbing, pitting ankle oedema, and bilateral basal crepitations but no evidence of heart disease. Investigations showed normal blood count and plasma viscosity, urea and electrolyte concentrations, and cardiac enzyme activities. Chest radiography showed diffuse opacities throughout both lung fields, consistent with pulmonary oedema. This was thought to be due to heart failure of uncertain cause and was treated with frusemide with appreciable improvement. He declined further investigations and was discharged from hospital, only to be readmitted a few weeks later with similar symptoms. Chest radiography again showed opacities in both lung fields, most distinct in the lower zones. As before he refused further investigations and remained well until April 1975, when he required readmission. At this time he complained of loose stools and on examination had gross ankle oedema. Serum albumin concentration was 24 g/l and total protein 47 g/l. Chest radiography showed no active lung lesion.

Two months later further investigations showed haemoglobin concentration 11.3 g/dl, mean cell haemoglobin concentration 30 g/dl (30%), plasma viscosity 1.28 mPa s (1.28 cP), total protein concentration 36 g/l, albumin 20 g/l, and calcium 1.85 mmol/l (7.4 mg/100 ml). Small-bowel barium studies

showed diffuse small-bowel abnormality with signs of malabsorption and areas of narrowing. Rectal biopsy specimens showed granulomas but no tubercle bacilli. Guinea-pig inoculations for mycobacteria were negative. Crohn's disease with presumed bacterial overgrowth was diagnosed, and his condition improved with oral tetracycline, prednisolone, and azathioprine. He required small-bowel resection in September 1979 for subacute obstruction and subsequently remained well. The histology of the resected specimen was consistent with the diagnosis of Crohn's disease.

Comment

This patient initially presented with pulmonary and peripheral oedema due to hypoproteinaemia secondary to widespread Crohn's disease. Pulmonary oedema due to hypoproteinaemia is extremely uncommon, though the mechanism of production is probably the same as that causing peripheral oedema from hypoproteinaemia: a reduction of plasma proteins leads to a lowered plasma colloid osmotic pressure, which then disturbs the balance of fluid distribution between the intravascular and extravascular compartments, resulting in increased fluid in the interstitial space. Studies in dogs³ have shown that when plasma protein is removed by plasmapheresis pulmonary oedema may be induced at progressively lower left atrial pressures.

As far as we are aware, this is the only reported case of Crohn's disease presenting as pulmonary oedema, itself an uncommon presentation of hypoproteinaemia.

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Importance of symptoms after highly selective vagotomy

Highly selective vagotomy has been studied for just over a decade as a surgical treatment for duodenal ulceration. Good results have been widely reported, and controlled trials have shown improvements compared with truncal or selective vagotomy and drainage¹ and truncal vagotomy and antrectomy.² Recurrent ulcer and other persistent abdominal symptoms are, however, still present in 20-25% of patients. Some of these residual symptoms may not be related to duodenal ulceration, and in an attempt to clarify this possibility we compared patients' symptoms after highly selective vagotomy and after inguinal herniorrhaphy.

Patients, methods, and results

Ninety-one patients with chronic duodenal ulceration were treated with highly selective vagotomy by one surgeon (JRS) between November 1973 and March 1980. The operation was that described by Johnston and Wilkinson but modified by the use of tantalum clips instead of ligatures to secure the neurovascular bundles to the lesser curve of the stomach.³ All the patients were requested to attend a special follow-up interview at which a list of questions were asked concerning 11 symptoms—namely, abdominal pain, epigastric fullness, flatulence, nausea, food vomiting, bile vomiting, dysphagia, heartburn, early dumping, late dumping, and diarrhoea—and their frequency (daily, weekly, monthly, or more than monthly). Sixty-five patients who had undergone an operation for inguinal hernia during 1979-80 were also asked to attend the hospital on the same day. The interviewer was unaware of which operation the patient had undergone. All patients were warned that the interviewer would ask questions that might seem

unrelated to their operation but that they should answer as accurately as possible. A standard questionnaire was sent to those who were unable to attend for interview. The ranking of patients was carried out using the modified Visick classification²: (1) no symptoms; (2) mild symptoms; (3) moderate symptoms; and (4) recurrent or bad symptoms; and this was completed before the operation code was broken.

Almost 80% of both groups were followed up and assessed. Four late deaths occurred after highly selective vagotomy, which were not related to ulcer disease. Additional procedures were performed in 28 patients at the time of highly selective vagotomy: dilatation of the pylorus (21 patients), cholecystectomy (four), splenectomy (two), and closure of duodenal perforation (one). Age and sex distributions of the patients in the two groups were comparable. No significant differences were found between the patients who had undergone highly selective vagotomy and those who had undergone herniorrhaphy (table). After highly selective vagotomy three patients (3.3%) subsequently developed recurrent ulcers.

Symptomatic results by Visick classification. Figures are numbers (%) of patients

	Visick classification			
	1	2	3	4
Highly selective vagotomy (n = 66)	38 (57)	15 (23)	7 (11)	6 (9)
Hernia (n = 51)	32 (62)	11 (22)	6 (12)	2 (4)

Comment

Highly selective vagotomy evolved in an attempt to reduce the incidence of symptoms that may follow truncal vagotomy with a drainage procedure. By denervating only the proximal acid-secreting part of the stomach the distal stomach and pylorus retain their normal activity so that gastric emptying is not disturbed. A drainage procedure with its attendant problems of dumping and bile reflux is then not needed. Although many reports have affirmed the effectiveness of the operation, the incidence of recurrence of ulcer, which has been as high as 12% in one series, has been a cause for concern. Surgical technique appears to be all important, however, and surgeons who have had considerable experience with the operation can achieve much lower recurrence rates. None the less, recurrence would appear to be more likely after this operation than after vagotomy and pyloroplasty. The low recurrence rate in our series may be due in part to the fairly short period of follow-up, but such low rates are not particularly unusual.

The importance of symptoms after any operation may depend on the attitudes of the interviewer and the patient. Heartburn and indigestion are common in the general population.⁴ Kennedy *et al*⁵ found no difference in the Visick classification of symptoms between patients after highly selective vagotomy and patients with no known gastrointestinal disease and who had not undergone operation, though none of his controls were classified as grade 3 or 4. Our study has shown that patients are symptomatically no worse after a hernia operation than those after highly selective vagotomy. Thus a success rate of over 80% should not be asked for operations for duodenal ulcer as long as an incidence of recurrence in the region of 10% is acceptable.

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