Association between prolonged dietary vitamin D deficiency and autonomous hyperparathyroidism

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We describe two Asian women with dietary osteomalacia whose parathyroid overactivity persisted despite treatment with vitamin D.

Case reports

CASE 1

A 33 year old vegetarian Indian woman, who had lived in Britain for nine years, presented with a two year history of bone pain. For six weeks she had difficulty in climbing stairs. There was tenderness over the spine and right lower ribs.

The results of tests of renal and intestinal function were normal. Her albumin concentration was 36 g/l; calcium 2.48 mmol/l; phosphate 0.4 mmol/l (normal 0.8-1.45); alkaline phosphatase 840 IU/l (normal <100); and 25-hydroxy vitamin D 8 nmol/l (normal 20-100). Skeletal x ray pictures were normal. An isotopic bone scan showed increased uptake in the hips, thoracic spine, and ribs. Dietary osteomalacia was diagnosed. In November 1983 she started taking oral ergocalciferol. Her symptoms improved rapidly, and her alkaline phosphatase activity fell to normal over 16 months (figure). Her plasma calcium concen-

tration, however, rose to 2.88 mmol/l, and her phosphate concentration remained low. In May 1984 ergocalciferol was stopped. Her normal plasma 25-hydroxyvitamin D concentration (30 nmol/l) excluded vitamin D toxicity. Her serum parathyroid hormone concentration was raised at 0.84 µg/l (normal <0.55). A thallium-technetium subtraction scan showed increased uptake in the region of the right lower parathyroid.

In December 1984 her enlarged right lower parathyroid was removed. Histological examination showed an adenoma. The patient subsequently remained well, and recent tests yielded normal results.

CASE 2

A 45 year old Kenyan Asian woman, a non-vegetarian who had lived in Britain for 18 years, presented with an 18 month history of bone pain and difficulty in climbing stairs. She had a waddling gait, proximal muscle weakness, and thoracic spine tenderness.

The results of tests of renal and intestinal function were normal. Her albumin concentration was 38 g/l; calcium 2.60 mmol/l; phosphate 0.62 mmol/l; alkaline phosphatase 1300 IU/l; and 25-hydroxyvitamin D 3 nmol/l. Skeletal x ray pictures showed phalangeal subperiosteal erosions and resorption at the ends of the clavicles but no Looser's zones. Histological examination of the iliac bone showed osteomalacia with hyperparathyroidism. In April 1982 she started taking ergocalciferol. Three months later her symptoms had resolved: calcium concentration was 2.89 mmol/l; phosphate 1.22 mmol/l; and alkaline phosphatase 297 IU/l (figure).

In December 1983 her calcium concentration was 2.71 mmol/l, phosphate 0.55 mmol/l, alkaline phosphatase 118 IU/l, serum 25-hydroxyvitamin D 39 nmol/l, and serum parathyroid hormone 0.65 µg/l. Histological examination of the bone showed that the osteomalacia had resolved, but mild hyperparathyroidism remained. A thallium-technetium subtraction scan showed increased uptake in the region of the left lower parathyroid. In October 1986 the gland was removed; histological examination showed an adenoma.

Comment

Autonomous parathyroid overactivity occurs in patients with chronic renal failure¹ and in prolonged malabsorption,² diagnoses that were excluded in our patients. Both patients, however, gave a history of inadequate dietary intake of vitamin D and calcium. The coexistence of osteomalacia and autonomous hyperparathyroidism may be explained by (a) prolonged dietary vitamin D deficiency leading to parathyroid overactivity or (b) primary hyperparathyroidism in which hypercalcaemia either was masked by osteomalacia or caused increased metabolism and excretion of vitamin D.

When osteomalacia caused by vitamin D deficiency is treated the parathyroids usually return to normal. In our patients there was persistent hypercalcaemia that was not due to vitamin D toxicity. Autonomous parathyroid activity should be suspected in Asians with osteomalacia if restoration of plasma 25-hydroxyvitamin D and calcium concentrations to normal does not bring about a rapid fall in serum parathyroid hormone concentration.³ Our findings in our two patients, who were hypercalcaemic for one and three years, support this observation.

We recommend that Asians with dietary osteomalacia, once they have been treated adequately with ergocalciferol, should be seen every six months and discharged only if the plasma calcium and phosphate

Biochemical changes in two Asian women presenting with dietary osteomalacia. Arrows indicate parathyroidectomy

concentrations and alkaline phosphatase activity remain normal. Our policy is to give vegetarian Asians with osteomalacia 3000 units (75 µg) of vitamin D₂ syrup once a month for life.

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Use of endoscopy in patients with dyspepsia

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Dyspepsia may be an early symptom of a serious illness, such as peptic ulceration, cholelithiasis, or gastric carcinoma. Many patients with dyspepsia are examined by upper gastrointestinal endoscopy, but organic lesions are not found in up to one third. There is little evidence to show that endoscopy is helpful,

Sensitivity, specificity, and positive and negative predictive values of various investigations used to diagnose active on chronic gastritis associated with Campylobacter pylori in 107 patients

	Endoscopy		Culture		Rapid urease test		IgG >504*		IgA >205*	
	Positive	Negative	Positive	Negative	Positive	Negative	Yes	No	Yes	No
Histological diagnosis of gastritis:										
Positive	23	39	51	11	58	4	56	6	35	27
Negative	21	24		45		45	2	43	10	35
Sensitivity (%)		37		82		94		90		56
Specificity (%)		53		100		100		96		78
Positive predictive value (%)		52		100		100		97		78
Negative predictive value (%)		38		80		92		88		56

*Optical density at 450 nm.

though a histological examination often shows the presence of gastritis.

A strong association between the presence of *Campylobacter pylori* in the gastric mucosa and histologically confirmed type B gastritis is well recognised.¹ It is not clear how commonly gastritis associated with *C pylori* occurs in dyspepsia without ulceration and whether the presence of *C pylori* results in different symptoms. We therefore carried out a prospective study of patients with dyspepsia to try to determine this. We also compared the sensitivity and specificity of endoscopic examination with those of histological examination, rapid urease tests,² serological tests, and culture to determine whether endoscopy and antral biopsies are useful.

Patients, methods, and results

We studied 107 consecutive patients with dyspeptic symptoms, whose endoscopy showed either no abnormality or minor inflammatory features in the antrum (usually patchy erythema). One of us (DV) asked the patients whether they had epigastric pain, nausea, heartburn, halitosis, and postprandial bloating. At endoscopy four antral biopsy specimens were taken from each patient for histological examination. Rapid urease activity was tested, samples were cultured, and serum immunoglobulin concentrations were measured.^{1,3} Histological evidence of *C pylori* was taken as confirmation of the presence of the organism. The sensitivity, specificity, and positive and negative predictive values were calculated for each test compared with histological examination. In addition concentrations in the patients positive and negative for *C pylori*

on histological examination were compared with the *t* test after logarithmic transformation.

The most common symptoms experienced by the patients were postprandial bloating with nausea (68), epigastric pain (18), and halitosis and heartburn (21). Sixty two of the patients showed histological evidence of active on chronic gastritis; all of these also had *C pylori* on microscopy, and *C pylori* was cultured in 51 cases. The remaining 45 patients had normal histological features without evidence of gastritis or *C pylori*. Normal endoscopic findings were obtained in 63 of the 107 patients, while 39 were found to have patchy erythema and five superficial erosions. The table shows the sensitivity, specificity, and positive and negative predictive values of endoscopy and the other

investigations assessed when compared with the histological findings. IgG concentrations had a high sensitivity and specificity.

Comment

We found that 58% of patients with dyspepsia without ulceration had gastritis on histological examination even though in many of them the mucosa appeared normal at endoscopy. In all cases the gastritis was associated with *C pylori*. The main symptom experienced by the patients was postprandial bloating, which was present in 73% (45/62) of those with gastritis and 51% (23/45) of those without gastritis. Serological testing for *C pylori* is useful in screening a population at risk,⁴ to monitor the response to treatment,⁵ and perhaps to investigate patients with dyspepsia before endoscopy. Our data showed that endoscopy had a lower sensitivity and specificity than all the other tests used. We conclude that endoscopy is unhelpful in patients with dyspepsia if endoscopic biopsy specimens are not taken routinely.

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