ing sarcoidosis is in deciding when to treat. Since the disease may remit spontaneously and since steroids may cause significant side-effects, treatment is usually started only if there is an indication of interference with the function of a vital organ (lungs, kidneys, eyes, heart, or central nervous system). Because of severe dyspnoea and cough, the present case was treated with high-dose oral corticosteroids. He improved dramatically within 3 months and has been free of complications for 2 years.

Final diagnosis

Bronchial obstruction due to endobronchial sarcoidosis.

Learning points

- although obstructive ventilatory defects rarely occur in the early stage of pulmonary sarcoidosis, endobronchial sarcoidosis must be considered in a young patient presenting with clinical features of bronchial obstruction, when no evidence of other common cause of airway obstruction can be found
- corticosteroids are still an effective and safe treatment for this disorder

Box 2

Keywords: sarcoidosis; corticosteroids; pulmonary obstruction

1 Fanburg BL. Sarcoidosis. In: Wyngaarden JB, Smith LH, Bennett JC. eds. *Cecil Textbook of medicine*, 19th edn. Philadelphia: WB Saunders, 1992; pp 430–5.
2 Levinson RS, Metzger LF, Stanly NW, *et al*. Airway function in sarcoidosis. *Am J Med* 1977;**62**:51–9.
3 Stjernberg N, Thunell M. Pulmonary function in patients with endobronchial sarcoidosis. *Acta Med Scand* 1984;**215**: 121–6.
4 Hadfield JW, Page RL, Flower CDR, Stark JE. Localized airway narrowing in sarcoidosis. *Thorax* 1982;**37**:443–7.
5 Corsello BF, Lohaus GH, Funahashi A. Endobronchial mass lesion due to sarcoidosis: complete resolution with corticosteroids. *Thorax* 1983;**38**:157–8.
6 Crystal RG. Sarcoidosis. In: Fauci AS, Braunwald E, Isselbacher KJ, *et al*, eds. *Harrison's Principles of internal medicine*, 14th edn. McGraw-Hill, 1998; pp 1822–928.

Masked hypercalcaemia

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A 29-year-old man presented with a 6-month history of steatorrhoea and a weight loss of 5 kg over 2 months. Endoscopy showed ulcers in the descending duodenum. Fasting serum gastrin was 427 ng/l (normal range less than 100 ng/l). Basal gastric acid secretion was 42.8 mmol/h (normal less than 15 mmol/h). No abnormality was found on abdominal computed tomography (CT) scan. The patient also complained of proximal muscle weakness and rib pain. On examination he had Harrison's sulci and lower rib tenderness. Biochemical measurements are shown in the table.

Table Serum biochemistry

	At presentation	*Post-vitamin D supplementation*	*Post- para- thyroidectomy*	*Reference range*
Ionised Ca (mmol/l)	1.24	1.49	1.25	1.19–1.35
PTH (pmol/l)	87.3	42.1	7.64	0.2–5.5
Phosphate (mmol/l)	0.5	0.79	1.14	0.8–1.4
25(OH)D (nmol/l)	<5.0	53.2	17	<50
Osteocalcin (ng/ml)	—	152	3	8.8–14.8
Ur DPD (nmol/mmol Cr)	—	39.5	5	3.1–5.6

Ur DPD = urinary free deoxypyridinoline

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Questions

1 What was the most likely diagnosis in this patient ?
2 Why did the patient have steatorrhoea ?
3 What other conditions did this patient have and can you explain the reasons for this?
4 What syndrome did the patient have ?

Answers

QUESTION 1
This patient had Zollinger-Ellison syndrome (ZES), namely hypergastrinaemia from a gastrin- secreting tumour or tumours. The presence of peptic ulcers in the second part of the duodenum is almost pathognomonic of this condition. The elevated basal gastric acid secretion and circulating gastrin levels confirmed this diagnosis. Failure to demonstrate a discrete tumour in the pancreas or duodenal wall on CT scan is a common problem as many tumours are very small and some patients have multiple microtumours scattered throughout the pancreas and duodenal wall.

QUESTION 2
The excessive acid production denatures digestive enzymes in the duodenum, including pancreatic lipase. This causes fat malabsorption.

QUESTION 3
The clinical features of proximal muscle weakness and rib pain in conjunction with severe hypovitaminosis D and markedly elevated parathyroid hormone (PTH) level are consistent with severe vitamin D deficiency that has resulted in osteomalacia and secondary hyperparathyroidism.[1] Vitamin D is fat soluble. ZES causes fat malabsorption and malabsorption of fat-soluble vitamins such as vitamin D. In addition, steatorrhoea diminishes calcium absorption.

QUESTION 4
The combination of ZES and hyperparathyroidism with parathyroid gland hyperplasia suggests that the patient had multiple endocrine neoplasia type 1 (MEN type 1).

Treatment

He was treated with a proton pump inhibitor and a high dose of parenteral vitamin D (30 000 IU calciferol weekly). After one month of therapy, serum 25-hydroxyvitamin D (25(OH)D) concentration had increased to within the normal range at 53.2 nmol/l. Then hypercalcaemia was noted. Serum PTH concentration had decreased but was still elevated (table). There are two possible explanations for the hypercalcaemia. The patient could have had coexisting primary hyperparathyroidism (PHPT), either sporadic or as part of the MEN syndrome. The other possibility is that he had tertiary 'autonomous' hyperparathyroidism due to longstanding secondary hyperparathyroidism which was a consequence of chronic malabsorption.

A total parathyroidectomy was performed and part of a gland was autotransplanted to a sternomastoid muscle. Histological examination showed hyperplasia in all four glands. After surgery, serum ionised calcium concentration returned to normal and serum PTH concentration was only mildly elevated (table).

Hyperplasia of parathyroid glands in patients with MEN type 1 is a result of expansion of multiple-cell clones, whereas in sporadic PHPT the parathyroid adenoma results from activation of a single cell clone.[2] The diagnosis of MEN type 1 requires the presence of tumours in two or more of the three principal organs affected (parathyroid, pancreatic islet (gastrinoma, insulinoma), and anterior pituitary (most commonly prolactinoma)). Some patients have ZES alone at diagnosis while others have both ZES and PHPT.[3] PHPT is the most common manifestation, occurring in 80–100% of cases.

Learning points

- patients with ZES may have a coexisting primary hyperparathyroidism as part of a MEN type 1 syndrome. However, they may not have hypercalcaemia initially and the primary hyperparathyroidism will only become unmasked after the ZES-related vitamin D and calcium malabsorption and hypovitaminosis D are corrected
- the diagnosis of MEN 1 requires the presence of tumours in two or more of the three principal organs affected (parathyroid, pancreatic islet and anterior pituitary)
- patients with hypothyroidism or hypovitaminosis D from nutritional deficiency, malabsorption syndromes or drug-induced alterations in vitamin D metabolism, may also have masked autonomous primary (or tertiary) hyperparathyroidism. Frank hypercalcaemia only develops when the hypovitaminosis D or hypothyroidism is corrected

Discussion

This patient with MEN type 1, presented with osteomalacia. Vitamin D and calcium malabsorption were caused by steatorrhoea due to ZES. Following correction of the steatorrhoea and hypovitaminosis D, the PTH concentration fell but remained above normal. The patient developed symptomatic hypercalcaemia because an underlying hyperparathyroidism became unmasked after vitamin D replenishment. This hyperparathyroidism could have been caused by a coexisting PHPT or by tertiary hyperparathyroidism due to longstanding secondary hyperparathyroidism in response to the vitamin D deficiency. Since this patient has many features of MEN type 1, PHPT is the most likely explanation.

The following is the most probable mechanism by which ZES can mask coexisting hyperparathyroidism. Hypergastrinaemia stimulates excess gastric acid production which denatures intestinal digestive enzymes, giving rise to malabsorption of vitamin D and calcium. PTH secretion increases to restore calcium levels to the normal range. This phenomenon of hypovitaminosis D leading to secondary hyperparathyroidism in malabsorptive disorders has been well documented.[4] Following correction of the hypovitaminosis D, hypercalcaemia developed. If the elevated serum PTH concentration had been caused by hypovitaminosis D alone, PTH would have been expected to return to normal. However,

PTH remained significantly elevated, which was consistent with coexisting primary hyperparathyroidism.

Any cause of fat malabsorption with associated hypovitaminosis D can mask primary hyperparathyroidism. Reported examples include coeliac disease[5] and jejunoileal bypass surgery for obesity.[6] Primary hyperparathyroidism can also be masked by hypovitaminosis D arising from nutritional deficiency.[7 8] It can also be masked by alterations in vitamin D metabolism induced by some medications, such as isoniazid, rifampicin and phenytoin.[9 10] Primary hyperparathyroidism has also been masked byhypothyroidism[11]; the mechanism is unclear but hypovitaminosis D is not implicated.

Final diagnosis

Multiple endocrine neoplasia type 1 consisting of Zollinger-Ellison syndrome and primary hyperparathyroidism which was initially masked by vitamin D and calcium malabsorption due to Zollinger-Ellison syndrome.

Keywords: endocrine neoplasia; hypovitaminosis D; hyperparathyroidism; Zollinger-Ellison syndrome

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1 McKenna MJ, Freaney R, Casey OH, Towers RP, Muldowney FP. Osteoporosis and osteomalacia: Evaluation of a diagnostic index. *J Clin Pathol* 1983;**36**:245–52.
2 Brandi ML, Auerbach GD, Fitzpatick LA, *et al*. Parathyroid mitogenic activity in plasma from patients with familial multiple endocrine neoplasia type 1. *N Engl J Med* 1986;**314**:1287–93.
3 Benya RV, Metz DC, Venzon DJ, *et al*. Zollinger-Ellison syndrome can be the initial endocrine manifestation in patients with multiple endocrine neoplasia type 1. *Am J Med* 1994;**97**:436–44.
4 Keaveny AP, Freaney R, McKenna MJ, Masterson J, O'Donoghue DP. Bone remodeling indices and secondary hyperparathyroidism in celiac disease. *Am J Gastroenterol* 1996;**91**:1226–31.
5 Bertoli A, Di Daniele N, Troisi A, Lauro R. A woman with bone pain, fractures and malabsorption. *Lancet* 1996;**347**: 300.
6 Taylor HC, Teitelbaum SL, Lambert PW. Symptomatic osteomalacia after jejunoileal bypass surgery in a patient with primary hyperparathyroidism. *Gastroenterology* 1983; **85**:735–42.
7 Vaishnava H, Rizvi SNA. Primary hyperparathyroidism associated with nutritional osteomalacia. *Am J Med* 1969;**46**:640–4.
8 Woodhouse NJY, Doyle FH, Joplin GF. Vitamin D deficiency and primary hyperparathryoidism. *Lancet* 197;**ii**: 283–6.
9 Kovacs CS, Jones G, Yendt ER. Primary hyperparathryoidism masked by antituberculous therapy-induced vitamin D deficiency. *Clin Endocrinol* 1994;**41**:831–6.
10 Dent CE, Jones PE, Mullan DP. Masked primary (or tertiary) hyperparathyroidism. *Lancet* 1975;**i**:1161–4.
11 Lever EG. Primary hyperparathryoidism masked by hypothyroidism. *Am J Med* 1983;**74**:144–7.