phosphataemia may have contributed to the relatively acute onset of cardiomyopathy in the patient reported.¹

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Dr Levy replies as follows:

'Dr Larner is entirely correct to point out the importance of hypophosphataemia as a cause of significant muscle dysfunction, and not simply in patients receiving parenteral nutrition. Our patient repeatedly had an entirely normal serum phosphate concentration.

The take-home message is that patients receiving parenteral nutrition, even for short periods, which contain *apparently* adequate levels of vitamins, inorganic salts and trace elements, may still become biochemically deficient and manifest clinical signs and symptoms thereof.'

Oesophageal carcinoma presenting as isolated malignant hypercalcaemia

Sir,

Occult malignancy may present as hypercalcaemia and increased levels of parathyroid hormone-related protein (PTHrp), as recently reported in the Journal by Hutchesson *et al.*¹ Only six patients with oesophageal carcinoma presenting as hypercalcaemia have been reported. Only one patient had no local obstructing symptoms or bone metastasis, and serum parathyroid hormone was found to be mildly elevated.² We report a patient with squamous cell carcinoma of the oesophagus (SCCE) and no obstructing symptoms, presenting as malignant hypercalcaemia, with intact parathyroid hormone (iPTH) suppressed, and increased PTHrp.

A 56 year old man was admitted in June 1991 for acute hypercalcaemia. He had had surgery for duodenal ulcer and cholelithiasis in 1988 and 1989, when serum calcium was 2.1 mmol/l (normal range (NR) 2.1–2.6), and albumin 40 g/l. In the 15 days prior to admission asthenia, anorexia, weight loss, polyuria, polydipsia and altered level of consciousness progressively developed. Investigations disclosed metabolic alkalosis, total serum calcium,

3.69 mmol/l, total serum proteins 75 g/l, phosphorus 0.8 mmol/l. The serum iPTH was <0.3 pmol/l (NR 37–80). Serum PTHrp was determined by competitive radioimmunoanalysis using specific antibody against fragment 1–40 of human PTHrp, INCSTAR, USA and was 11.2 (range in normocalcaemic controls 0.99–7.39). Skeletal X-ray films were normal. Despite rehydration, total serum calcium reached 4.65 mmol/l. Calcitonin, steroids and intravenous biphosphonates were initiated, but no response was observed.

As neck ultrasound disclosed a round-shaped lesion, exploratory surgery was performed. A normal thyroid and scattered lymph nodes were found along the internal jugular chain. Biopsy of three parathyroids showed no abnormalities. Histological examination of one lymph node revealed metastasis of undifferentiated carcinoma. After surgery, hypercalcaemia persisted refractory to treatment and the patient finally died. Necropsy revealed a SCCE of the distal portion of the oesophagus, and metastasis to bone, liver and lungs.

PTHrp plays an important role in the humoral hypercalcaemia of malignancy of SCCE. Tachimori *et al.*³ have studied 11 SCCE tumour extracts obtained from patients with hypercalcaemia and all had detectable immunoreactive PTHrp. Northern blot hybridization for PTHrp mRNA revealed the expression of two bands which undergo hybridization. The incidence of hypercalcaemia in SCCE ranges between 16 and 56%,⁴ but in almost all cases local obstructing symptoms are present in our patient. Rapidly progressive dissemination involved the skeleton. However, hypercalcaemia in SCCE is rarely caused by bone metastasis⁴ and the presence of bone metastasis does not rule out the possibility of humoral hypercalcaemia of malignancy.³ PTHrp causes hypercalcaemia, activating preformed osteoclasts and inhibiting renal phosphate reabsorption.⁵ Patients with SCCE and hypercalcaemia have lower overall survival rates even in those cases without clinical evidence of bone metastases (survival rate, 9.1% at the 24th month in comparison with 37.8% in those SCCE without hypercalcaemia).⁶ This poor survival could be related to dedifferentiation of carcinoma cells.

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