Lesson of the week

Hypercalcaemia in cancer

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Malignancy associated hypercalcaemia may be due to primary hyperparathyroidism—testing the serum parathyroid hormone should be considered

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The commonest cause of hypercalcaemia in hospitalised patients is malignancy, so the tendency is to presume that hypercalcaemia in a patient with cancer is related to malignancy. This may not be the case, however.

Case reports

Case 1

A 50 year old woman underwent a wide local excision and axillary node clearance for breast cancer in July 1999. She received postoperative chemo-radiotherapy and made a good recovery. A year later she presented with fatigue and distal paraesthesia. Her adjusted serum calcium concentration was 2.69 mmol/l (normal range 2.2–2.6). She was investigated for metastatic breast cancer, including a bone scan, and was advised that her cancer had recurred. Four months later, she remained anxious but well; her serum calcium was 2.71 mmol/l, and a paired serum parathyroid hormone concentration of 10.9 pmol/l (normal range 1.1–7.5) confirmed primary hyperparathyroidism. After careful follow-up, a left lower pole parathyroid adenoma was removed. The patient's postoperative calcium concentration was in the normal range (2.57 mmol/l).

Case 2

An 81 year old woman had locally advanced breast cancer diagnosed in November 1993. She was treated with tamoxifen, as poor cardiac function precluded more aggressive treatment. She had a history of thyrotoxicosis, which had been treated by partial thyroidectomy in 1959. In March 2000 she presented with back pain and was found to be hypercalcaemic (adjusted serum calcium 3.15 mmol/l). This was attributed to her breast cancer, and she, too, had a bone scan and was advised that her breast cancer had probably spread. Three months later, she remained relatively well despite a serum calcium concentration of 3.08 mmol/l. A paired parathyroid hormone assay of 28.4 pmol/l confirmed primary hyperparathyroidism. She became more symptomatic from the hypercalcaemia, and in August 2000 neck exploration revealed only a small residual thyroid nodule. Her overall condition deteriorated, and she died in May 2001 from cardiac disease.

Case 3

A 56 year old man had carcinoma of the prostate diagnosed in 1999. A year later he presented with generalised symptoms and was found to be hypercalcaemic (adjusted serum calcium 4.18 mmol/l). Two bone scans failed to show any evidence of metastases, but he was referred to the palliative care team. Shortly after, his serum prostate specific antigen concentration was found to be within the normal range, and his serum parathyroid hormone concentration was 87.8 pmol/l. An infusion of disodium pamidronate initially controlled the hypercalcaemia (concentration fell to 2.46 mmol/l after one week), but it recurred after a month and the patient underwent a successful parathyroidectomy (postoperative calcium 2.43 mmol/l).

Discussion

We describe three patients presenting with primary hyperparathyroidism in the presence of active or recently diagnosed cancers. All three were erroneously advised that their cancer had become metastatic. Earlier recognition of the true cause of the hypercalcaemia might have avoided unnecessary distress. The correct diagnosis might have been overlooked entirely.

Concomitant hypercalcaemia of malignancy and primary hyperparathyroidism has been well recorded; the best estimate of the rate of the two conditions co-presenting is 15%, but this is probably an overestimate because of selection bias.¹ The commonest primary malignancies where the two conditions coexist are cancers of the colon, breast, and lymphoma.² Primary hyperparathyroidism may be linked with breast cancer as part of the spectrum of type 1 multiple endocrine neoplasia.^{3 4} Another possible link is radiotherapy used to treat breast cancer, which can cause development of primary hyperparathyroidism.⁵

Parathyroidectomy usually cures primary hyperparathyroidism, and minimally invasive techniques make surgery a real option even for patients with significant co-morbidity. When surgery is not possible drug treatment (bisphosphonates, parathyroid hormone inhibitors) may be effective.⁶ Making a diagnosis of primary hyperparathyroidism is straightforward, but relies on measuring parathyroid hormone; other rheological indices (including the level of hypercalcaemia) are not discriminatory.⁷

Survival for hypercalcaemic patients with concomitant hyperparathyroidism and malignancy is measured in years, whereas for those with hypercalcaemia due to malignancy alone it is measured in months.¹ Consequently, measuring parathyroid hormone concentration estimation is essential in patients with malignancy and hypercalcaemia when bone secondaries are not evident.

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