HYPERCALCAEMIA: A finding not to be taken too lightly

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INTRODUCTION

Many conditions are associated with hypercalcaemia: primary hyperparathyroidism, advanced secondary hyperparathyroidism, milk alkali syndrome, vitamin D intoxication, thiazide diuretic treatment, malignancy with or without bone metastases, and immobilisation. Primary hyperparathyroidism (pHPT) is the most common cause in ambulatory adult patients, but malignancy in hospitalised patients.[1]

Primary hyperparathyroidism is characterised by excessive bone resorption, pain and tenderness of bones, spontaneous fractures, nephrolithiasis, hypercalcaemia, hypophosphataemia, and an elevated intact serum parathormone level in more than 90 % of patients. pHPT may be the result of hyperplasia of all the parathyroid glands, but in approximately 80 % - 85 % of patients a single adenoma (neoplasia) of one of the glands is the cause. In hypercalcaemia of malignancy the PTH level may be normal but is usually decreased. Factors associated with hypercalcaemia include neosynthesis of a parathyroid hormone-related protein (PTH-rP) activating parathormone receptors, increased production of 1,25-dihydroxyvitamin D (in sarcoidosis), and increased production of interleukin-6.[2-7] Currently surgery is the only effective treatment for pHPT. To differentiate between a neoplastic adenoma and hyperplastic glands, bilateral exploration of all the glands was the preferred approach – cure rates > 95 %. However, as > 80 % of cases is caused by a single adenoma, together with improvement in preoperative localisation techniques, and complete endoscopic techniques, minimal invasive procedures are increasingly being used.[2]

Radioscintigraphic imaging of the parathyroids is one of the procedures used to localise the site of adenomas. Currently ^{99m}Tc-sestamibi is the radioactive agent of choice. Scintigraphy identifies about 100 % of adenomas 1000 – 1500 mg in size, > 90 % of adenomas ≥ 500 mg in size, and most of adenomas 300 – 500 mg in size. Other factors that may affect radiotracer uptake are significant P-glycoprotein expression in adenomas, cell cycle phases, mitochondrial density, and proliferative activity of the cells. The ability of radioscintigraphic techniques to localise hyperplastic parathyroids is disappointing.[8-13]

CASE REPORT

A physically fit road-running 44-year-old white woman with a history of excellent health until 10 months ago, started to lose weight, followed by tiredness two months later and widespread muskuloskeletal aching. On clinical examination she was underweight with diffuse muskuloskeletal tenderness. Her S-calcium level was 3·45 mmol/L (normal range 2·20 – 2·55), her plasma PTH level 19.3 ng/L (normal range 7·0 – 53·0), and her S-creatinine level 137 umol/L. A tentative diagnosis of a parathyroid adenoma was made, and she was referred for preoperative scintigraphic localisation of parathyroid pathology. A delayed imaging dual-phase ^{99m}Tc-sestamibi radioscintigraphic study was done and whole-body images acquired. No parathyroids were visualised and the thyroid was cool. However, the tracer accumulated diffusely and intensely in the

skeleton and bone marrow and a tentative diagnosis of multiple myeloma was made **(See Figure 1, 2 & 3)**. Bone marrow biopsy, cytology, a positive U-Bence-Jones protein, and her therapeutic response supported the diagnosis.

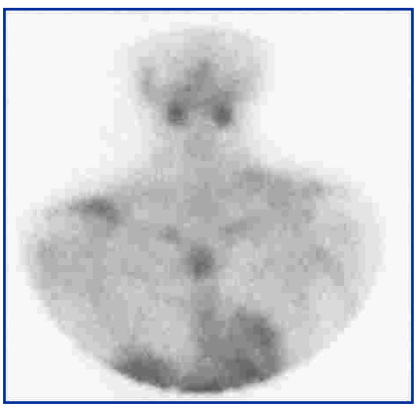
DISCUSSION

Hypercalcaemia is a relative frequent phenomenon in many malignant disorders. Many patients with mild hypercalcaemia may be asymptomatic and the condition is discovered accidentally. In high levels of hypercalcaemia of long duration anorexia, abdominal pain with vomiting, constipation and nephrolithiasis are common. If severe, muscular weakness and emotional instability may occur. Various patterns of ^{99m}Tc-sestamibi uptake in the bone marrow of multiple myeloma patients have been reported: normal (negative), focal, diffuse and combined focal and diffuse. A hypothesis has even been formulated, claiming that bone marrow uptake in myeloma patients is an *indicator* of myeloma activity .Diffuse and/or focal ^{99m}Tc-sestamibi uptake in the bone marrow is almost diagnostic of multiple myeloma.[14]

CONCLUSION

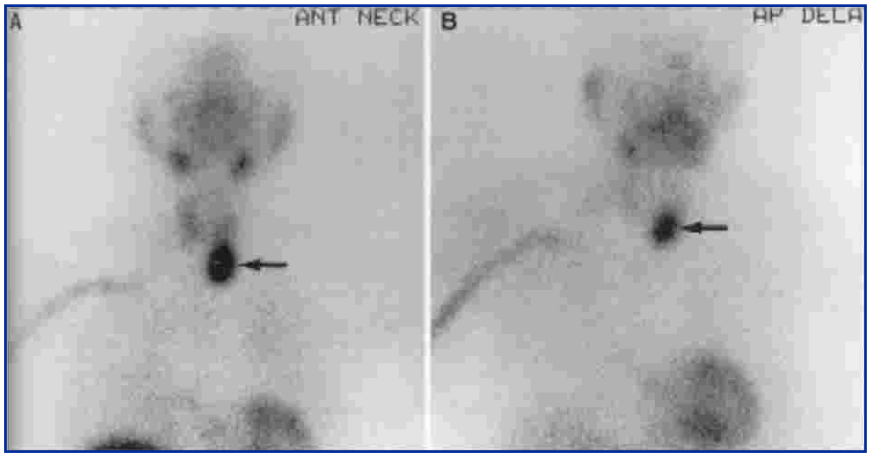
Although hypercalcemia is a relative frequent clinical phenomenon with an etiologic basis that varies from benign to devastating, it remains too often undiagnosed in medical practise because it is taken too lightly.

Figure 1:



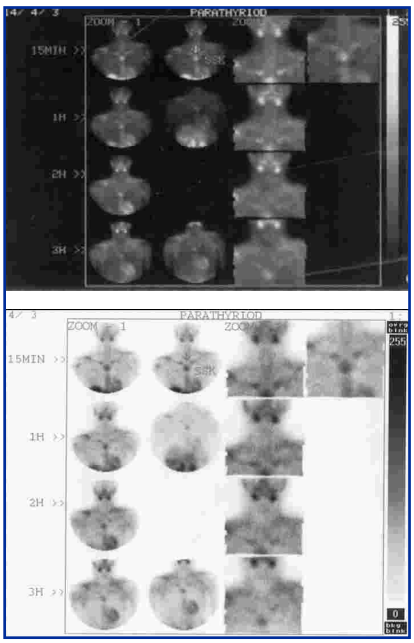
Practically no concentration of radiotracer in thyroid and parathyroid

Figure 2:



Dual-phase sestamibi parathyroid scan demonstrate an adenoma in the left inferior parathyroid gland (arrows). Normal background accumulation noted.

Figure 3:



Diffuse focal concentration of isotope in bone marrow, highly suggestive of myeloma

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