

Simultaneous Presentation of Metastatic Cancer and Primary Hyperparathyroidism – A Case Series

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Abstract The objective of our two case reports is to increase awareness of the simultaneous occurrence of primary hyperparathyroidism and malignancy in patients that presents with hypercalcaemia. This report reviews the case reports from the history, investigation, treatment and outcome for these two patients. A literature review of the association between malignancy and primary hyperparathyroidism was also performed. Both patients had metastatic cancer and primary hyperparathyroidism but died within months of diagnosis despite treatment for their primary malignancy. This serves as a reminder that these two separate diagnoses do exist, though it did not alter the outcome of our patients. However, we propose that in patients with malignancy who presents with hypercalcaemia and non-suppressed PTH level, further workup should be instigated to rule out primary hyperparathyroidism as surgical option is potentially curative for the latter.

Keywords: primary hyperparathyroidism, metastatic cancer, hypercalcaemia

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1. Introduction

Primary hyperparathyroidism is a common endocrine disorder. Its prevalence has been estimated at 3 in 1000 in the general population and as high as 21 in 1000 in postmenopausal women. [1] 85% of patients with primary hyperparathyroidism are due to a single parathyroid adenoma, 14% due to parathyroid hyperplasia and less than 1% due to carcinoma.

Although primary hyperparathyroidism is considered a benign condition, it has been linked with various malignancies. Dent and Watson [2] reported the first case where a patient presented with both primary carcinoma of the cervix and primary hyperparathyroidism due to parathyroid adenoma. Subsequently Palmer et al [3] reported an excess risk of malignancy in over 4000 patients in the Swedish Cancer Registry (1960-1981) who had undergone surgery for primary hyperparathyroidism. Using the same data from the Swedish Cancer Registry (1958-1997), Michels et al [4] found an observed association between hyperparathyroidism and subsequent breast cancer, although mechanism of its association remains unclear.

We report two cases where both patients presented with simultaneous diagnosis of primary hyperparathyroidism and metastatic cancer. The first case demonstrates the already known association with breast cancer with the second case involving oesophageal malignancy which has not been reported. However, in both of the cases, a cause

of their primary hyperparathyroidism was not identified as they were too unwell for further radiological imaging to identify the presence of the parathyroid adenoma and they eventually died from their primary malignancy.

2. Case 1

A 53 year old woman, with a history of right sided breast cancer presented as an emergency due to general deterioration and was found to have hypercalcaemia. She had undergone mastectomy, completed six cycles of chemotherapy and 25 fraction of radiotherapy ten months prior to admission.

Blood test revealed an adjusted calcium of 5.54nmol/L (NR 2.10-2.55nmol/L), PTH related peptide (PTHrp) of > 60pmol/L (NR 0.0-1.8pmol/L), unsuppressed PTH 34 ng/L (15-65 ng/L) and Vitamin D of 78nmol/L (NR 50-200). Further investigation included bone scan which did not show bony metastasis and an abdominal ultrasound revealing liver metastasis. Her calcium level had improved with intravenous fluids and bisphosphonate therapy, but had remained elevated at 3.67nmol/L. However, she had continued to deteriorate clinically and died during this admission.

3. Case 2

A 52 year old lady was admitted to the hospital with a two week history of right scapula pain, reduced appetite

and weight loss. Blood test revealed an adjusted calcium of 3.99 nmol/L (NR 2.1-2.55 nmol/L), PTH of 147 ng/L (NR 15-65ng/L), PTHrp of 4.3 pmol/L (NR 0.0-1.8 pmol/L), and normal myeloma screen. Normal 25-OH vitamin D levels and renal functions excluded the possible secondary PTH elevation.

CT scan of trunk showed evidence of lung and liver metastasis but the site of primary carcinoma could not be identified. Bone scan did not reveal any bony lesion. Liver biopsy confirmed metastatic carcinoma with possible lung or gastrointestinal tract as a primary site. She subsequently underwent an upper gastrointestinal tract endoscopy which confirmed squamous cell cancer on oesophageal biopsy.

Hypercalcaemia initially responded well to intravenous fluid and bisphosphonate therapy and she was discharged home after noticeable clinical and biochemical improvement. Her calcium had remained within normal range for about 3 weeks. She was readmitted with symptomatic hypercalcaemia at 3.32nmol/L. However, her hypercalcaemia during the second admission remained elevated and resistant to further fluids and bisphosphonate therapy. A trial of chemotherapy did not make any difference to her hypercalcaemia and two months after her initial diagnosis, she was admitted to hospice and eventually died.

4. Discussion

The knowledge that primary hyperparathyroidism is linked to subsequent risk of malignancy is not new. These studies (Palmer et al. 1988, Michels et al. 2004, Backlund et al. 2005, Nilsson et al. 2007) identified patients who had undergone surgery for primary hyperparathyroidism from the Swedish Cancer Registry at different intervals and were followed up for a period of time. Palmer et al [3] found a one point six increase relative risk of developing malignancy in this patient group compared to the general population. 20 years later, Nilsson et al [5] also found an increased risk of malignancy after surgery for hyperparathyroidism, in both sexes, all age group and persisted beyond 15 years after surgery. Backlund et al [6] found an increased risk of primary central nervous system (CNS) tumour and Michels et al [4] observed an association between hyperparathyroidism and subsequent breast cancer. However, not all studies had found similar associations. Hickey et al [7] did not find an interrelationship between malignancies and primary hyperparathyroidism, although the population studied included all patients with primary hyperparathyroidism, including those who did not have surgery and the population group studied were much smaller.

Breast cancer has been associated with primary hyperparathyroidism more than the other malignancies. Nilsson et al [5] and Michels et al [4] found an increased risk of breast cancer after parathyroid surgery. Even in the study by Hickey et al [7] who found no interrelationship between malignancy and primary hyperparathyroidism, breast cancer was still more frequent in patients with parathyroid adenoma. Fierabracci's [8] group had found an increase incidence of primary hyperparathyroidism in patients with known breast cancer in their study. Although the exact pathogenesis is unclear, it has been attributed to be the possibility of common etiological pathways shared

by the two conditions. Since then, multiple cases where patients presented with hypercalcaemia due to both primary hyperparathyroidism and breast cancer have been reported [9,10].

Hypercalcaemia is a poor prognostic indicator in patients with malignant disease. [11] The treatment for primary hyperparathyroidism however, is potentially curative with surgery. As primary hyperparathyroidism and malignancy may co-exist, further workup for primary hyperparathyroidism is indeed warranted in patients with malignancy and non-suppressed PTH. In contrast, in patients with metastatic disease, as seen in both of our patients, primary hyperparathyroidism is mere an interesting observation and it does not influence the course of patient's treatment and outcome. Both of our patients had died within the first few months of diagnosis despite aggressive treatment for their primary malignancy.

5. Conclusion

There is clear association between primary hyperparathyroidism and malignancy based on published studies. Due to the different outcome and management between metastatic disease and primary hyperparathyroidism, we advise routine measurement of serum PTH to rule out primary hyperparathyroidism in all patients with malignancy who presents with hypercalcaemia.

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