https://doi.org/10.17576/JSA.2016.0602.12

Case Report

Parathyroid Hormone Secreting Metaplastic Breast Carcinoma: A Case Report of Paraneoplastic Syndrome

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Abstract

Paraneoplastic syndrome (PNS) is a distant neurological manifestation of an underlying tumour. Humoral hypercalcaemia of malignancy is a form of paraneoplastic syndrome where there is an increased in calcium levels. In this article we report a 48 year old lady, with no known medical illness and presented with symptomatic hypercalcaemia. She presented to our institution complaining of a fungating and ulcerating mass over the right breast, measuring 11 X 15 cm and associated with gradual paraxial body weakness. Further investigations revealed the lesion to be an invasive breast carcinoma with metaplastic features. Computed tomography (CT) scan showed a locally advanced breast carcinoma with right axillary node metastasis, without evidence of distant metastasis. Serum calcium, i-PTH together with SPECT has confirmed the patient to have a humoral hypercalcaemia malignancy with elevated ectopic parathyroid hormone level. Bone scan did not reveal any evidence of metastasis. High volume intake and loop diuretics were employed in the management of hypercalcaemia, which was eventually resolved following mastectomy with axillary clearance of the ipsilateral side. Currently she's she is under oncologist's follow up for further management.

Keywords: Breast carcinoma, hypercalcaemia, hyperparathyroidism, paraneoplastic syndrome

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Date of submission: 9 Aug, 2016 Date of acceptance: 17 Oct, 2016

Introduction

It was recognised in the past century that some tumours can lead to a group of signs and symptoms that are not related to a direct hematological, lymphatic or compression by the cancer growth. This was attributed to rather humoral (hormonal and peptide) secretions from the cancer cells or in other cases by immune responses against the tumour itself (1). Collectively, those signs and symptoms were referred to as Paraneoplastic syndrome (PNS). Nearly all of the PNS cases are associated with breast, ovarian, lung or lymphatic cancers (2). Patients with paraneoplastic syndrome may have neurological, endocrine, mucocutaneous or even hematological manifestations.

About 8% of cancer patients have associated paraneoplastic syndrome. In some occasions, cancer patients present with paraneoplastic manifestations prior to detection of the tumour, such symptoms when detected may raise the suspicion for occult cancer. Humoral hypercalcaemia of malignancy (HHM) is a common paraneoplastic condition, which occur in 20% of paraneoplastic patients (3). Most of these patients present with or have an underlying breast cancer, lung cancer or multiple myeloma. Hypercalcaemia maybe attributed to several mechanisms, including; first,

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release of parathyroid hormone-related protein (PTHrP) (4,5) which accounts for the majority of the cases reported; second, an ectopic parathyroid hormone (PTH) secreting tumour which is a rare condition and last but not least due to 1 a-hydroxylase activity tumour that produce 1,25-dihydroxyvitamin D and bone metastasis and skeletal osteolysis tumour s (6). This case highlighted an example of PNS presented with hypercalcaemia, in a patient with locally advanced breast cancer.

Case Report

A 48-year-woman, with no underlying medical illness, had a previous history of Total Abdominal Hysterectomy Bilateral Salpingo Oophorectomy (TAHBSO) due to uterine fibroid at the age of 45. The patient first noticed a right breast lump over the last two years but unfortunately she did not seek any professional medical advice but resorted to traditional medicine and therapy. The lump gradually grew in size during those two years. She also had weight loss together with reduced in appetite along with generalized body weakness.

She only presented to us in July 2015 with a fungating and ulcerating right breast mass measuring around 11 X 15 cm. The wedge biopsy of the lesion reported as invasive carcinoma with metaplastic features. Immunohistochemical studies of the biopsy proven the malignant cells to be positive for Estrogen Receptor (ER) with 10% positivity and strong intensity, and negative for Progesterone Receptor (PR) and (human epidermal growth factor receptor 2(HER2) CT staging did not show any distant metastases and she was advised for neoadjuvant chemotherapy. She refused chemotherapy and decided to take only tamoxifen. She was lost to follow up and presented at a different hospital with progressive body weakness and confusion. CT scan of the brain was normal and again family members decided to seek traditional treatment. The condition worsened and she was brought back to the hospital. Clinically, she was confused and disorientated. There was generalized oedema. Examination of the breast revealed a fungating right breast lesion. There was no specific bony tenderness except from generalized body ache. Laboratory Investigation done showed she was anaemic with severe hypoalbuminaemia and hypercalcaemia ranging from 2.5-3.1 mmol/L. Among the radiological investigations a repeat CT scan confirmed that it was a locally advanced breast carcinoma with right axillary lymph node metastases. In addition, there were multiple hypoechoic lesions at segments V and VII of the liver and a small lung nodule which did not suggest malignant infiltration. The serum i-PTH was elevated (13.53 pmol/L) with normal serum phosphorus and Vitamin D. A 99mTc-Methyl diphosphonate (Tc99m MDP) whole body bone scan with single photon emission computed tomography (SPECT) was done but did not show any evidence of skeletal metastases. The patient was diagnosed with Humoral hypercalcaemia of malignancy and treated with saline infusion and intravenous Zolendronic acid. The calcium returned to normal and she became orientated and not drowsy anymore.

In view of persistent bleeding and massive loss of proteinaceous fluid from the tumour, the patient was counseled for right breast mastectomy which was agreeable. A debulking mastectomy with primary skin closure was performed as the axillary nodes were encasing the axillary vessels. The final histology confirmed a metaplastic carcinoma (squamous cell carcinoma), Bloom and Richardson grade III. On immunohistochemical study; the malignant cells were positive to p63, CKMNF, CK5 and CK6. The serum calcium post-op dropped to (1.8- 1.9 mmol/L) and her hypoalbuminaemia improved dramatically. Unfortunately, she refused further treatment and represented a month later presented with chest wall recurrence and currently undergoing chemotherapy.

Discussion

Though paraneoplastic syndrome has been identified during the middle of the last century, it hasn't been fully discovered and understood until nowadays (7). Nevertheless, it is undeniable that the number of the cancer patients has increased over the past few decades. In return, it is expected to come across more cases that resemble or might add to our knowledge of PNS pathogenesis, methods of therapy and early diagnosis, all of which will contribute to a better prognosis and improve the life expectancy for the patients.

Most of PNS cases are associated with neurological disorders that present in either known cancer cases or those with occult tumours (8). Those disorders have been related to the tumour producing antibodies that target the nervous system as for an example Anti-Ro, Anti-Ma, Anti-Hu and Anti-Yo. Some other cases have been suggested to be caused by an autoimmune response of T-cells which attack the nervous system due to the resemblance between it and the tumour's antibody (9).

Humoral hypercalcaemia of malignancy (HHM) is a paraneoplastic syndrome that is most commonly associated with breast cancer and presents with hypercalcemia. Though there are few possible reasons

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to which elevated serum calcium level can be attributed to, the most common cause remains the secretion of parathyroid hormone related protein (PTHrP). This osteolytic effect resulted from metastasis or due to the effect of 1 a-hydroxylase produced by certain types of tumours. Ectopic secretion of PTH is a rare condition that has been reported in few cases up to date (3,10).

Though breast cancers have been associated with hyperparathyroidism and hypercalcaemia, the reason behind this correlation is yet to be understood (11). Some studies suggested the possibility of breast cancer associated hypercalcaemia to lead to hyperparathyroidism due to parathyroid adenoma and vice versa (12).

In this paper, we present a middle-aged lady with metaplastic breast cancer with an ectopic PTH-like hormone secretion by the tumour. This is supported by the evidence of hypercalcaemia and elevated parathyroid hormone level and normal bone scan. Unfortunately, we could not proceed with immunohistochemistry evaluation for anti-PTH and PTHrP of our tissue samples due to unavailability these tests neither in our center nor in other pronounced medical centers. In our search for literature and case reports discussing ectopic parathyroid hormone producing tumours, there were a few case reports describing parathyroid hormone secreting lung carcinoma, thyroid carcinoma, pancreatic and other GI related malignancies and ovarian carcinomas (13). There was only a single case report published suggesting the association between ectopic parathyroid hormone secretion and breast carcinoma (14) making our case as the second. Following mastectomy of and axillary dissection of the affected side the patient serum calcium level dropped to 1.8-1.9 mmol/l along with normal PTH level, which concluded the ectopic source of PTH.

Conclusion

Secondary bone metastases contribute to the majority of causes for hypercalcaemia in breast cancer. Although being infrequent, humoral hypercalcaemia of malignancy is a rare event, which should be thoroughly investigated in patients with breast cancer. Parathyroid adenoma may co-exist with breast cancer and need to be excluded. Having an elevated serum calcium level can be attributed to few etiologies and HHM not to be overlooked despite its rarity.

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