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Case report

A rare case of medullary carcinoma thyroid metastasizing to bilateral breast parenchyma

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Abstract

Medullary carcinoma of the thyroid (MTC) commonly spreads through the lymphatics to distant sites such as lung, liver and bone. Spread to the breast is rare. We report a case of metastatic MTC which progressed to develop nodal metastases to cervical and mediastinal regions, visceral metastases to the liver, lung and ultimately to bilateral breasts. Clinically it is important to distinguish metastatic breast lesions from primary breast cancer as each is managed differently. Both cytological and radiological investigations were done followed by excision biopsy. Histopathological examination of post excision breast specimen revealed metastatic medullary carcinoma, with positive immunohistochemical staining for calcitonin. A brief review of literature and differential diagnosis is also presented.

KEY words: medullary carcinoma, metastasis, breast nodules, HYNEC octreotide scan

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Introduction

Medullary carcinoma of the thyroid (MTC) originates from the parafollicular C-cells and accounts for 3–4% of all malignant thyroid neoplasms. It occurs sporadically (75% of cases) or as part of the inherited syndrome known as multiple endocrine neoplasia type 2 (MEN II syndrome) [1]. Currently, there is no effective treatment for patients with locally advanced or metastatic disease as this tumor is usually unresponsive to conventional chemotherapy or radiotherapy. Typically MTC metastasizes through lymphatics to mediastinal lymph nodes, lung, liver and bone.

Case report

A 20-year-old female presented to our cancer center with history of left lobectomy and neck nodal dissection in April 2006. Referred sections were reviewed by histopathology department and revealed a thyroid tumor consistent with medullary carcinoma thyroid (Figure 1). She was diagnosed as T2N1bM0 stage II medullary carcinoma of thyroid. Baseline work up for MEN II syndrome was unremarkable. Her baseline I-131 MIBG scan at a serum Calcitonin level of 1829 pg/ml was unremarkable (not shown). Completion thyroidectomy was done. Her postoperative serum calcitonin level dropped to 393 pg/ml in March 2007 followed by 676 pg/ml in June 2007. In January 2008, HYNIC octreotide scan (Figure 2) performed at 4 and 24 hours demonstrated an avid lesion in proximal shaft of right humerus and upper part of the chest. Bone scan (Figure 3) performed in January 2008 also showed a linear increased tracer uptake in proximal part of the right humeral shaft correlating with the increased uptake seen on HYNIC-Octreotide scan. In addition increased uptake was seen in mid thoracic spine, right acetabulum and iliac wing. Patient received radiation therapy for right upper humeral head lesion in February 2008.

On follow up, post radiotherapy calcitonin levels once again began to rise – 1500 pg/ml in September 2008. Anterior/posterior

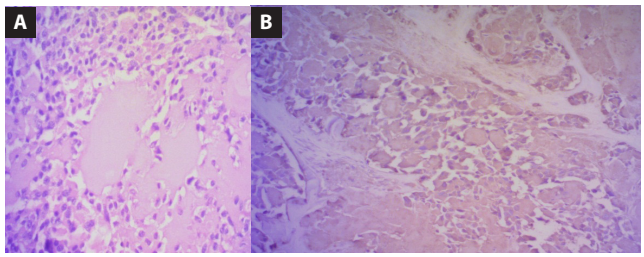

Figure 1A. High power view of thyroid show a cellular neoplasm. Monomorphic plasmacytoid cells with salt and pepper chromatin and eosinophilic material (amyloid) in tumor cells; **B** Calcitonin immunohistochemistry: positive cytoplasmic staining in thyroid tumor cells

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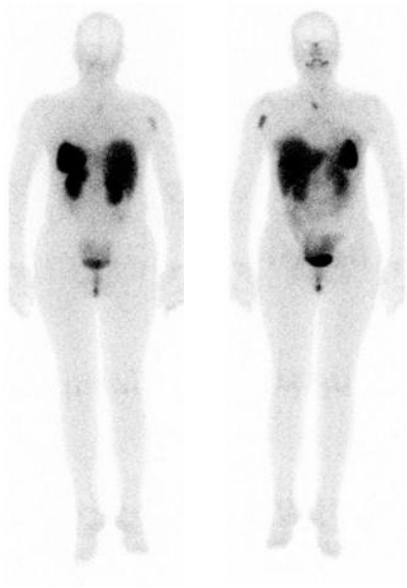

Figure 2. HYNIC octreotide scan demonstrated an avid lesion in proximal shaft of right humerus and upper part of the chest

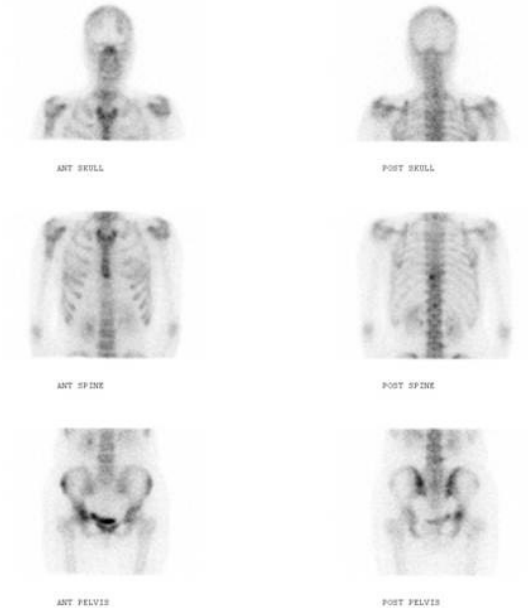

Figure 3. Bone scan showed linear increase in tracer uptake in proximal part of the right humeral shaft, mid thoracic spine, right acetabulum and iliac wing

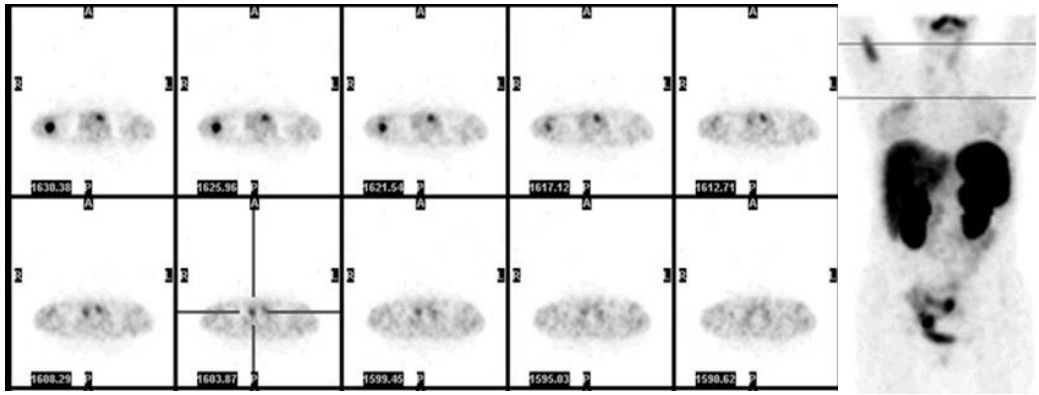

Figure 4. HYNIC Octreotide scan showed a new focus of uptake in the mediastinum as well as mild focal uptake in bilateral breasts. Uptake in the humerus was less intense compared with the previous scan

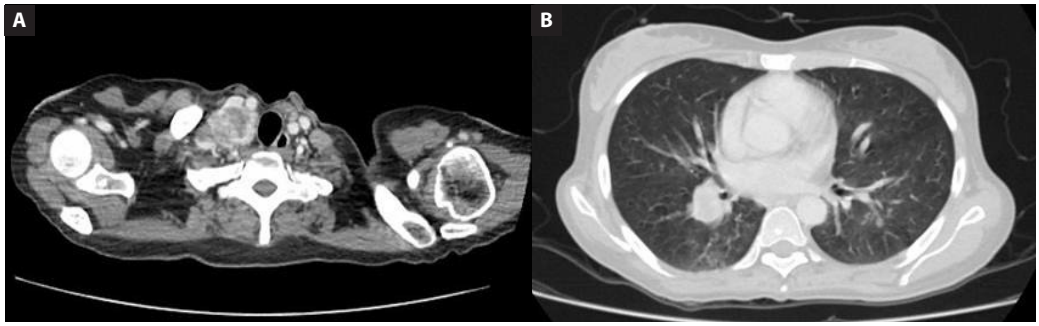

Figure 5A, B. Axial CT images showing (**A**) right supraclavicular necrotic lymph node (**B**) right hilar nodule

spot view and SPECT images of the thorax using HYNIC Octreotide (Figure 4) showed a new focus of uptake in the mediastinum as well as mild focal uptake in bilateral breasts. Uptake in the humerus was less intense as compared with the previous scan.

Contrast enhanced CT (CeCT) images (Figure 5) in September 2008 also showed disease progression with calcified cervical and mediastinal nodes. However, patient was asymptomatic at that time. She remained asymptomatic and serum calcitonin progressively

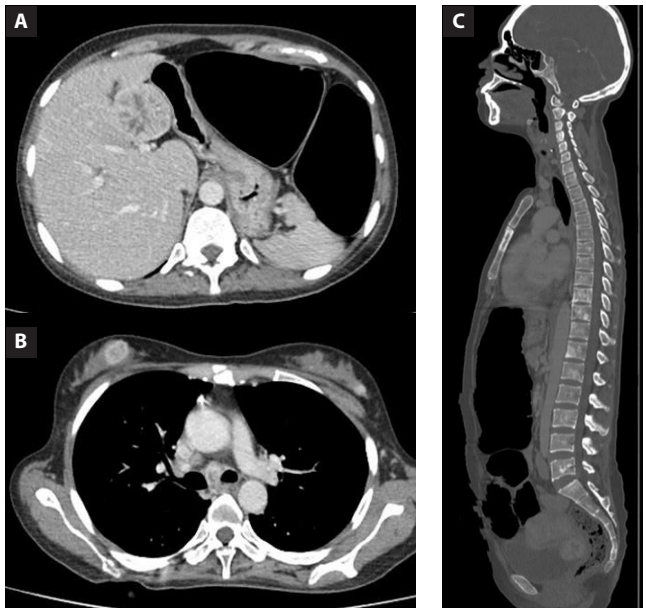

Figure 6A. Axial CT image show a representative metastatic liver lesion; **B.** Axial CT image show enhancing bilateral breast nodules and interval progression in mediastinal nodes (previous CT not shown); **C.** Sagittal CT image show sclerotic osseous metastases

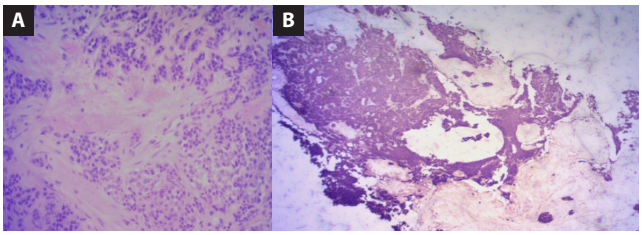

Figure 7A. H&E of breast tru-cut biopsy show an infiltrative and cellular tumor of plasmacytoid cells with round nuclei, salt and pepper chromatin and eosinophilic material in tumor cells; **B.** Calcitonin immunohistochemistry: positive staining in tumor cells

increased to 16521 pg/ml in September 2012. She developed palpable nodules in bilateral breasts.CeCT (Figure 6) performed at the same time showed progressive disease with hepatic, osseous and mediastinal nodal metastasis.

Tru-cut biopsy of breast nodules was performed. Microscopic features (Figure 7) revealed infiltrative and cellular tumor composed of plasmacytoid cells with round nuclei, salt and pepper chromatin and eosinophilic material were present within the tumor clusters. Desmoplastic stroma was also present.

Discussion

Carcinoma of thyroid metastatic to breast is extremely rare. Metastatic tumors to breast account for 0.8 to 6.6% of all breast malignancies [2]. Very few cases have been reported in literature and to our knowledge only 6 cases were classified as secondary metastasis from medullary Carcinoma thyroid [3–8]. Medullary carcinoma of thyroid commonly metastasizes to cervical lymph nodes, liver, lung and bones. Calcifications are frequently seen in cervical lymph nodes and liver [3]. Metastatic carcinoma to the breast arises, in most cases, secondary to primary breast malignancy on the other side particularly in females as opposed to hematopoietic malignancies (leukemia, lymphoma) and prostate carcinoma in males, which are common metastatic tumors to male breast [2, 4]. Accurate diagnosis of secondaries to breast is important to avoid unnecessary radical surgical procedures and to institute appropriate therapy. There are no reliable clinical criteria to distinguish primary breast tumors from secondary metastasis. However, on literature review, a superficial sharply circumscribed lesion in upper outer quadrant of breast with skin tethering or multiple superficial hard nodular masses should raise the concern of secondary tumor, especially if the patient is suffering from known malignancy [4, 9, 10]. Ultimate diagnosis is based on histologic features. Histological features suggestive of metastatic disease include a periductal or perilobular distribution in the absence of *in situ* ductal or lobular component. There is minimal elastosis and desmoplasia associated with these lesions. Final confirmation usually requires immune-histochemical staining to establish the diagnosis [4, 6, 11].

Most of the metastatic tumors in breast have predilection for younger or middle aged women, likely due to better blood supply in this age group that leads to blood-borne metastasis [11, 12]. Overall prognosis of such cases is usually grave with approximately 90% of the patients dying within a year of diagnosis [13].

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