An Unusual Presentation of Medullary Thyroid Carcinoma

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Abstract Medullary thyroid carcinoma (MTC) is extremely uncommon having varied presentations & their prognosis is not exactly known; but as MTC is an aggressive tumor hence it needs to be documented in literature to help to know the behaviour of this variant. We report a rare presentation of medullary carcinoma of thyroid in a 48 years old man who presented with huge swelling at left side of neck extending from parotid to supraclavicular region with normal-sized thyroid gland of long duration. FNAC & incision HPE of this swelling was inconclusive so we had operated this swelling. Immunohistochemistry reported it as metastatic Medullary

carcinoma of thyroid; tumor cells express Cytokeratin, Calcitonin, EMA, Synaptophysin, Chromogranin-A. The stroma shows deposits of Amyloid, which have been confirmed by Congo red staining. Post-operatively FNAC from thyroid gland supported the diagnosis of Medullary carcinoma. Post-operatively the residual mass was regressed with chemotherapy & radiotherapy. The calcitonin level also decreased following this treatment. There was no recurrence at 11 months but ultimately patient died with metastasis.

Keywords Medullary thyroid carcinoma · Neck mass · Unknown primary

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Introduction

Hazard et al. [1] segregated medullary thyroid carcinoma (MTC) as a distinct entity in 1959. MTC is an uncommon carcinoma accounting for about 10 % of all malignant thyroid tumors. These tumors are usually firm painless nodules, usually in the lateral two-thirds of the gland. They are aggressive and 50 % of these tumors may present with lymph node metastases at the time of initial diagnosis. Distant metastases to the liver, lung, or bone may occur in 15–25 % of cases. Calcitonin production by tumor cells is distinct and proves its origin from C-cells [2]. The stage of the tumor is the most important prognostic factor. Under the microscope, these tumors have a varied appearance with round to oval to spindle cells arranged in vague nests, often with an infiltrative appearance. Melanocytic differentiation in MTC is very rare [3]. Huge swelling at left side of neck extending from parotid to supraclavicular region with normal-sized thyroid gland is very rare presentation of MTC, thus needs to be documented in order to

know the exact behaviour of this variant. This is the first reported case from Indian sub-continent from available English literature!

Case Report

A 48 years male, an agricultural worker, presented to the Otorhinolaryngology out-patient department of SSKM hospital, Kolkata with a huge swelling at left lateral aspect of neck. It was noticed as a small 3 cm (approx.) firm swelling 15 years back at left upper jugulodigastric region. He did not pay attention because it was asymptomatic. Since last 2 years it started to increase fast & extended above up to left parotid region to downward including supraclavicular region. It was firm to hard, non-tender, surface irregular, mobility restricted & skin was free (Fig. 1). Facial nerve function was normal. General survey & other systemic examination did not revealed any significant abnormality. Clinically thyroid gland was normal at that time. Our clinical diagnosis was between malignant parotid tumor & metastatic neck node from unknown primary.

FNAC from left parotid region gives a suspicion of benign adnexal lesion (Syringocystadenoma). A repeat FNAC from other laboratory gives a suspicion of metastatic carcinomatous deposit in left cervical lymph nodes. We had gone for an incision biopsy during which mass bled profusely. Histopathological examination was inconclusive, but raised a suspicion of parotid tumor.

Fig. 1 Huge swelling at left side of neck extending from parotid to supraclavicular region (pre and post op)

Fig. 2 Contrast enhanced CT scan of neck revealed large heterogeneously enhancing mass

Contrast enhanced CT scan of neck revealed large heterogeneously enhancing lobulated outlined mass lesion arising from left parotid region displacing prestyloid parapharyngeal space anteromedially & carotid space medially with invasion of platysma & loss of subcutaneous fat, loss of fat plane & masseter muscle is seen at places (Fig. 2). A conglomerated lymph nodal mass with necrotic areas & amorphous calcific foci along left internal jugular chain & posterior triangle (level II, III, IV and V nodes) with loss of fat plane with perivertebral muscles, extending up to left supraclavicular fossa. Left sided internal jugular vein is compressed & displaced anteriorly. Left axillary, supraclavicular & paraesophageal lymphadenopathy is present. There is a hypodense non-enhancing area at left lobe of thyroid gland.

With this bewildering investigation report, we planned for the excision of mass. A collar with lazy 'S' incision was given & mass was exposed which bled significantly. It was a firm to hard mass from parotid to supraclavicular region & deeply adhered with neck structures. With great difficulty we had excised up to supraclavicular region; but due to blood loss & deteriorating condition of the patient, we had planned to keep this supraclavicular part for second stage operation. Histopathological examination report came in favour of malignant tumor but they could not specify it. Immunohistochemistry reported it as metastatic MTC. The tumor cells express Cytokeratin, Calcitonin, EMA, Synaptophysin, Chromogranin-A; and are immunonegative for TTF-1 (Fig. 3). The stroma shows deposits of Amyloid, which have been confirmed by Congo red staining (Fig. 4). Post-operatively we had done FNAC from thyroid gland which supported the diagnosis of Medullary carcinoma. The calcitonin level was 250 pg/ml at this time.

For the residual mass at supraclavicular region, we had done MRI (Fig. 5). It revealed a heterogeneously enhancing soft tissue mass with areas of necrosis in the posterior triangle of neck with supraclavicular extension & loss of fat plane with supraspinatus muscle. There are secondaries in the head of humerus. Other muscles of the rotator cuff, neurovascular structures, and articular surfaces of shoulder joint with joint spaces appear normal.

Fig. 3 Immunohistochemistry reported it as metastatic Medullary carcino

Fig. 4 The stroma shows deposits of Amyloid, which have been confirmed

As the residual mass was unresectable, it was decided to treat with adjuvant chemotherapy & radiotherapy; and mass was regressed with it. The calcitonin levels were 80 and 90 pg/ml at respectively 4 and 8 months post-radiotherapy. Patient was doing well after treatment except left sided facial palsy post-operatively & there was no local recurrence in 11 months follow-up. Then after 1 month, patient developed sudden hemiparesis for which neurologist advised him Methylcobalamin tablets along with bone scan to exclude bone metastasis. But before getting bone scan done, patient developed urinary retention and succumbed to it.

Discussion

Medullary carcinoma of thyroid is a tumor of thyroid parafollicular C-cells, which are derived from neural crest. MTC can mimic any tumor structurally and functionally and has also been described as solid carcinoma, hyaline carcinoma and C-cell carcinoma [1]. Classically tumor cells are round to polygonal with amphophilic granular cytoplasm and have medium sized nucleus. Tumor cells are spread in solid sheets separated by highly vascular stroma, hyalinised collagen and amyloid [4].

Our patient was a 48-years old man with small swelling in the neck for 15 years which grew hugely to involve whole of the left side of neck extending from parotid to supraclavicular region within 2 years. Histopathological examination showed features of malignant tumor. Tumor cells were positive for Calcitonin which is the most specific marker for parafollicular cells [1]. Positive immunostaining for Cytokeratin, Chromogranin-A, Synaptophysin and Carcinoembryonic antigen confirmed the diagnosis of MTC. MTCs are generally negative for Thyroglobulin as has been seen in the present case. The demonstration of immunoreactive calcitonin within the neoplastic cells and the lack of thyroglobulin reactivity further support the diagnosis of a pure medullary carcinoma.

Medullary thyroid carcinoma can have an aggressive behavior, and little is known about the molecular basis for clinical outcome. Defining risk of recurrence or metastasis is difficult, and it has been limited to clinical and pathologic features, such as advanced age, cervical lymph node metastases, and stage at presentation. Frequency of allelic loss in tumor suppressor genes may provide a useful adjunctive prognostic test in MTC [5]. Distant metastases and the local extra-thyroidal extent of the primary tumor have a significant effect on the prognosis of MTC, lymph node metastases and other clinical factors being less important, as in our case, we treated local thyroid and lymph nodes disease by surgery and radiotherapy along with chemotherapy but ultimately patient succumbed to distant metastasis. The biological virulence of sporadic MTC may be clinically significantly higher than that of MTC in MEN2A [6]. MTC has a much lower cure rate than does the “well differentiated” thyroid cancers (papillary

Fig. 5 MRI showing heterogeneously enhancing soft tissue mass with areas of necrosis

and follicular), but cure rates are higher than anaplastic thyroid cancer. Overall 10 year survival rates are 90 % when all the disease is confined to the thyroid gland, 70 % with spread to cervical lymph nodes, and 20 % when spread to distant sites is present. The best prognosis occurs in young patients undergoing total thyroidectomy and neck dissection. External beam RT significantly reduces local relapse in patients with limited nodal disease [7] but in our case even the disease was extensive, it was suppressed with radiotherapy.

Calcitonin is a very specific marker of MTC that allows preoperative diagnosis. Serum calcitonin assay is particularly useful to define the postoperative state of patients (cured, apparently cured, not cured) and, because of its great sensitivity, it has a major place in the postoperative follow-up. There is always a need for a regular biochemical follow-up (Calcitonin should be measured every 4 months for the first few years and then every 6 months for ever) because recurrence may appear many years after the initial surgery [8]. As in our case, there was no local recurrence at 11 months post-radiotherapy but there was slight increase in calcitonin levels at 8 months in comparison to at 4 months which probably was the only indication of distant metastasis.

Conclusion

Swelling involving whole of the left side of neck extending from parotid to supraclavicular region with normal-sized thyroid gland is a very rare presentation of medullary carcinoma. There is a need to report more cases of varied presentations in the literature for exact categorization and prognostication of this subtype of thyroid carcinoma.

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Conflict of Interest None.

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