Case report: A challenging clinical problem of calcitonin negative medullary thyroid cancer (MTC) diagnosis and surveillance

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BACKGROUND:

Medullary thyroid carcinoma is a neuroendocrine tumor that originates from malignant proliferation of thyroid para follicular C–cells, it represents 1 to 10% of all thyroid cancers. (1) Para follicular C-cells are derived from neural crest ectoderm and ultimo branchial body and account for 1% of all thyroid cells.(2)Para follicular cells synthesize and secrete calcitonin which regulates calcium homeostasis. Mean survival rate of patients with MTC is 8.6 years with 10 years survival rate ranging from 69% to 89%. (3) In 75% of the cases, MTC occurs sporadically, however in 25% of the cases occurrence is hereditary associated with germline mutation of RET proto-oncogene on chromosome 10.(4). The familial form is generally termed as multiple endocrine neoplasia (MEN). MEN 2A includes MTC, hyperparathyroidism and pheochromocytoma and MEN 2B includes pheochromocytoma, mucosal neuromas and gastrointestinal neurogangliomas. Sporadic form of MTC grows slowly, it is well differentiated and locally aggressive. However, familial form can invade adjacent organs, metastasize to lymph nodes, central compartment (level IV to VI) are frequently involved followed by level II to V. It can also disseminate hematogenously to liver, lungs and bones and has worse prognosis. (3) In almost 100% of the cases, MTC is associated with high levels of calcitonin and carcinoembryonic (CEA). Both CEA and calcitonin are used for diagnosis and surveillance of MTC. MTC with normal serum levels of calcitonin is a very rare entity and only a few cases reported in the literature. In this case report, we will present a rare case of MTC with normal range serum calcitonin levels, how it was diagnosed and how follow up done post operatively.

CASE PRESENTATION:

55 years lady presented with a few-month history of neck swelling associated with compressive symptoms i.e shortness of breath (SOB). CT neck showed a large right thyroid nodule with central necrosis of 53 mm with retrosternal extension up to superior mediastinum. There was a 360-degree encasement of the right common carotid artery. Multiple enlarged lymph nodes at bilateral cervical stations II and III. She underwent fine-needle aspiration cytology (FNAC) of the right thyroid lobe nodule and bilateral lymph nodes, histopathology of thyroid nodule showed typical MTC features but lymph nodes turned out to be reactive. Immunohistochemical staining for calcitonin and CEA was negative but positive for other neuroendocrine markers i.e synaptophysin and chromogranin A. Serum calcitonin and CEA levels were also in normal range. So, a rare diagnosis of calcitonin negative MTC was made. As the disease was inoperable because of vascular encasement, a plan for ERBT external beam radiation therapy to the neck was made.

PRACTICAL IMPLICATIONS:

1. Normal level of calcitonin and CEA does not rule MTC and the possibility of calcitonin negative MTC should be considered in suitable patients.
2. Surveillance of CTNMTC should be done with imaging techniques for the localization of disease recurrence like ultrasound neck, CT-scan, MRI and FDG-PET.