Melanin-producing Medullary Thyroid Carcinoma – A Case Report.

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ABSTRACT

Outcome Objective
Report a case of an extremely uncommon subtype of medullary thyroid carcinoma (MTC) in a complex patient. At the conclusion, the participants should be knowledgeable about melanin-producing MTC and the need for better categorization and prognostic information.

Methods
A case presentation of a patient with a complex medical history including malignant melanoma and chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) with melanin-producing MTC.

Results
We present a case of melanin production within MTC in a 64-year-old female with a history of malignant melanoma and CLL/SLL. While undergoing chemotherapeutic treatment for CLL/SLL, routine PET imaging showed an FDG avid right solid thyroid nodule. Thyroid ultrasound, nuclear imaging and fine needle aspiration resulted in the patient’s presentation to otorhinolaryngology and right thyroid lobectomy followed by completion thyroidectomy. Microscopic examination revealed typical architecture of MTC with amyloid deposition and unique focal areas of melanin pigmentation. Immunohistochemical staining showed tumor cells positive for CEA, calcitonin, synaptophysin, chromogranin, Cam5.3, AE1-3, TTF-1, Melan-A, S100, HMB45 and MITF.2 Given this patient’s history of melanoma, final diagnosis was delayed until genetic testing was completed.

Conclusion
There are a variety of subtypes of MTC including but not limited to follicular, squamous and melanotic carcinoma. This case report serves to increase awareness of this extremely uncommon tumor subtype that may be difficult to differentiate from melanoma. Future reports and studies should elucidate prognosis and exact categorization of this uncommon subtype of thyroid cancer – both of which are not well studied to date.

INTRODUCTION

There are a variety of subtypes of medullary thyroid carcinoma (MTC) including but not limited to follicular, squamous and melanotic carcinoma. This case report serves to increase awareness of this extremely uncommon tumor subtype that may be difficult to differentiate from melanoma. Future reports and studies should elucidate prognosis and exact categorization of this uncommon subtype of thyroid cancer – both of which are not well studied to date.

CASE REPORT

A 64-year-old female with a complex medical history presented to our clinic with an FDG avid right thyroid nodule. Her past medical history was significant for rheumatoid arthritis, hypertension, malignant melanoma, stroke and CLL/SLL for which she was actively undergoing chemotherapy. As part of her treatment protocol she underwent routine PET imaging which revealed an FDG avid nodule in the right thyroid lobe (Figure 1A). This nodule was then evaluated with ultrasound showing a solid nodule with microcalcification in the inferior aspect of the right lobe measuring 2.0 x 1.1 x 1.7cm. Additionally, nuclear imaging revealed a “cold” nodule (Figure 1B).

Fine needle aspiration showed a malignant neoplasm with atypical plasmacytoid mononucleated and few binucleated cells (Figure 2). In view of her history of melanoma, S100 and HMB45 immunocytochemical stains were performed and these were positive. Concern for metastatic melanoma or MTC arose. Patient denied any history of flushing, headaches, diarrhea or palpitations, radiation exposure and family history of thyroid cancer. Thyroid function tests were within normal limits. Carcinomembryonic antigen (CEA) and Calcitonin levels were elevated to 3.6ng/mL and <2.0pg/mL, both within normal limits.

The patient returned to the operating room for a completion thyroidectomy which revealed an incidental 0.2mm papillary microcarcinoma. Further post-operative testing was negative for pheochromocytoma and mutations in the RET gene.

The patient expired 5 months after thyroidectomy from complications related to metastatic pulmonary disease.

DISCUSSION

Medullary thyroid malignancies arise from parafollicular C cells and may secrete calcitonin, carcinoembryonic antigen (CEA), histaminidases, prostaglandins, and serotonin.1,2 Blood levels of calcitonin and CEA are used as markers for MTC. Generally, calcitonin is >100 pg/mL in cases of MTC. Histologically, there are many variants of MTC including follicular, squamous, true papillary form, clear cell, small cell and melanotic carcinoma.3

The patient presented here had a melanin producing MTC, which was histologically challenging to diagnose due to her history of malignant melanoma as both melanin-producing MTC and melanoma would demonstrate positivity for HMB45 and other melanomaspecific features/immunostaining. The patient’s elevated calcitonin and CEA which normalized after surgical resection helped to confirm the diagnosis of melanin-producing MTC.

REFERENCES


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Figure 1: Imaging A: PET CT Scan with a right FDG avid Thyroid nodule. B: Nuclear Imaging. Right inferior pole “cold” nodule.

Patient underwent a right thyroidectomy without complication. The tumor was a well-circumscribed, non-capsulated nodule measuring 1.6 x 1.0 x 1.5cm confined within the right inferior thyroid lobe, consistent with melanin producing MTC. The neoplasm showed lobular growth of round, polygonal cells with abundant eosinophilic cytoplasm and the presence of multi-nucleated tumor giant cells (Figure 3). Focal areas of tumor cells had melanin pigment and stroma within the tumor showed pink, homogenous areas positive for congo red (amyloid) (Figure 4). Immunostains revealed tumor cells positive for CEA, Calcitonin, Synaptophysin, Chromogranin, Cam5.3, AE1-3, TTF-1, Melan-A, S100, HMB45 and MITF.2 BRAF was negative for the V600E mutation.

Figure 2: Cytology (papanicolaou stain) x400, Cellular smear showing a dispersed population of mononucleated atypical plasmacytoid cells with eccentric nuclei

Post-operatively her CEA was 3.6ng/mL and calcitonin was <2.0pg/mL, both within normal limits.

The patient returned to the operating room for a completion thyroidectomy which revealed an incidental 0.2mm papillary microcarcinoma. Further post-operative testing was negative for pheochromocytoma and mutations in the RET gene.

Figure 3: Round and polygonal tumor cells with eosinophilic cytoplasm and prominent nucleoli, arranged in a lobular growth pattern, within focal melanin production.

Figure 4: Congo red staining showing depositions of extracellular, pink, homogenous material with characterizing apple-green birefringence under polarized light.

Figure 5: Microscopy showing melanin pigmentation.