urgent, end-of-life planning must be given high priority in order to optimize the quality of the patient's remaining life.

Thyroid

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What Lies Beneath? - Medullary Thyroid Cancer in Nodular Graves' Disease

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Background: Medullary thyroid carcinoma (MTC) accounts for 1%-2% of thyroid cancers in the United States (US). MTC originates from thyroid parafollicular C-cells, occurring either sporadically or hereditarily as part of type 2 multiple endocrine neoplasia (MEN) or familial MTC (FMTC). Hyperthyroidism is prevalent in approximately 1.2%, and Graves' Disease (GD) is the most common cause of hyperthyroidism in the US. GD is an autoimmune disorder that results in increased thyroid hormone production due to the stimulation of TSH receptor by thyrotropin receptor antibodies (TRAb). Thyroid carcinoma in general is uncommon in GD patients, while MTC is extraordinarily rare. We report a case of sporadic MTC in GD, which is extremely rare. A recent publication stated that there were only 15 reported cases of MTC coexisting in GD until 2019. **Clinical Case:** A 62-year-old male with hypertension, diabetes and obesity presented to the endocrine surgery clinic with symptoms of diaphoresis, chest pain and fullness, shortness of breath, and palpitations. The patient had a brother with a pancreatic mass of unknown pathology and multiple family members with thyroid disease. On physical exam, there was a palpable non-tender left-sided nodule with no lymphadenopathy. His FT4 was 8.5 (0.76-1.46 ng/dL), TSH was <0.006 (0.36-3.74 μIU/dL) and thyroid-stimulating antibody was 1.25 (<0.10 IU/L). Ultrasound showed a multinodular goitre with a dominant nodule in the left lower pole measuring 2.3x1.9x1.5 cm. He was diagnosed with GD, treated with methimazole, and his symptoms improved. Subsequent nuclear medicine uptake scan showed diffusely increased uptake and a cold nodule in the left thyroid lobe. Repeat labs showed low TSH (<0.01μIU/dL) and elevated FT4, CEA, calcitonin, PTH, metanephrine, and normetanephrine (1.04 ng/dl, 5.2 (3-5 ng/ml), 796 (<18 pg/ml), 58.10 (18.40-88.00 pg/mL), 90 (< OR = 57 pg/ml) and 222 (< OR = 148 pg/ml), respectively). A thyroid fine-needle aspiration (FNA) was suggestive of MTC (Bethesda Category VI). Total thyroidectomy with left central lymph node dissection revealed a 2.5cm MTC confined in the left lobe with focal lymphovascular invasion. His postoperative course was uneventful, and CEA and calcitonin levels trended down (1.1 ng/ml and <2 pg/mL, respectively). **Conclusion:** The coexistence of medullary thyroid carcinoma and Graves' Disease is rare, incidental, with five-year survival rates lower than other thyroid cancers. A delayed diagnosis of MTC would be detrimental. Patients with thyroid nodules and GD are five times more likely to be diagnosed with thyroid carcinoma. Radiation, chemotherapy and thyroidectomy are standard treatment options for MTC, with total thyroidectomy being the preferred option. It is necessary to evaluate patients with GD for possible thyroid cancers, especially in the presence of nodules.

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Will Real Time Visualization of Needle in Target Thyroid Nodules Minimize False Negative FNA Results?

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Introduction: Prevalence of thyroid nodules in the adult population based on detection by ultrasonography is about 20-76% of which only 5% account for thyroid cancer. All patients with a suspected thyroid nodule either on physical examination or noted incidentally on other imaging should be evaluated with thyroid ultrasound. Any thyroid nodule >= 1 cm on ultrasound should be investigated with FNAC. Ultrasound guided FNAC techniques are used to reduce false negative results. We present a patient with suspicious finding on initial thyroid ultrasound and subsequent negative FNAC presenting a few years later with papillary thyroid cancer. **Case Presentation:** A 32 y.o. female with history of thyroid nodule and thyroiditis presented to the endocrine clinic for follow-up of her thyroid nodule. 5 years ago, she was diagnosed with thyroid nodule, which was found on an ultrasound scan for workup of her dysphagia. The thyroid ultrasound then showed diffusely heterogeneous thyroid gland with an ill-defined area of decreased echogenicity in the right lobe and left superior lobe and possible nodule in the lower pole left thyroid. Blood work showed TSH of 1.71 (n 0.34-3.00 uIU/ml) and thyroid peroxidase antibody levels was 27.8 (n < 9.0 IU/ml). A CT scan of neck with contrast was done and no concerning mass was seen. The patient had a follow-up ultrasound after 8 months which showed small bilateral thyroid lesions, somewhat ill-defined. The patient had an FNA biopsy of the right thyroid nodule: the results were consistent with a benign follicular nodule. A follow-up thyroid ultrasound was done in a year, and the findings were unchanged. The patient came back 3 years later for follow-up with complaints of a new palpable nodule in the neck. Ultrasound showed unchanged right thyroid nodule and some new cervical adenopathy. The ultrasound showed a 2.2 cm heterogeneous lymph node with punctate echogenic foci along the right lateral margin of the right internal jugular vein at the level of the thyroid gland, Subsequently FNA biopsy of the right cervical node and right thyroid node were done. The cells from lymph nodes were positive for malignancy and cells from the right thyroid nodule were atypical. Overall the appearance was consistent with papillary thyroid carcinoma. Subsequently the patient underwent total thyroidectomy and right modified lymph node dissection and the pathology results came back as multifocal papillary thyroid cancer right side 1.2 cm and left side 0.4 cm,

with metastasis to 2 lymph nodes. **Conclusion:** The reported false negative rate of ultrasound-guided FNAC is variable. Success of US-FNA depends on experience of operator and cyto-pathologist and the intrinsic nature of the nodule. Malignancy rates of only 1-2% are reported with repeat FNA in prior benign nodules. Good FNA techniques and real-time visualization of needle in target nodules can further decrease false negatives.

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Xeroderma Pigmentosum: An Uncommon Risk Factor for Aggressive Follicular Thyroid Carcinoma

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Introduction: Follicular thyroid carcinoma (FTC) is the second most common thyroid cancer, which typically presents in an older populations, and carries a near 100% 5-year relative survival rate if diagnosed prior to cancer spreading outside of the thyroid. **Clinical Case:** A 26-year old female presented to emergency room with persistent jaw pain, despite course of antibiotics prescribed by dentist. She has a past medical history of xeroderma pigmentosum (XP) with over 130 surgeries for malignant skin lesions, as well as benign multinodular goiter for which she underwent total thyroidectomy at the age of 18, with pathology reporting benign tissue and follicular adenoma. Emergency room imaging of maxillofacial/sinus incompletely captured a mass in the left paratracheal region, extending into the lumen of the trachea. Patient was then transferred to University Hospital for further evaluation. Dedicated neck imaging confirmed 4.6cm mass in expected area of thyroid gland, invading into left tracheal wall, cervical esophagus, and hypopharynx. Additional imaging revealed numerous pulmonary nodules, and a 4mm enhancing focus of left superior temporal gyrus. Nuclear positron emission tomography imaging revealed regions of hypermetabolic activity in the left maxillary sinus, the facial nodules, cervical lymph nodes, and mass like region of hypermetabolic activity in the thyroid bed. Biopsy confirmed follicular thyroid parenchyma, concerning for follicular carcinoma. Patient then underwent mass resection and tracheostomy. Some thyroid tissue was left on contralateral side to malignancy due to adjacency to only functional recurrent laryngeal nerve. Pathology following surgery confirmed follicular thyroid carcinoma, with evidence of angioinvasion. Thyroglobulin mass spectrometry prior to surgery was 302 ng/mL. **Conclusion:** While it is well known that patients with XP suffer from early development of mucocutaneous and ocular cancers in sun-exposed areas, these patients also have increased risk for multinodular goiter as well as internal malignancies. Furthermore, treatment of any internal malignancy is limited due to inability for patients with XP to be treated with radiation. Providers for patients with XP should have very low thresholds to investigate all new symptoms aggressively, maximizing chances of diagnosing malignancies in early stages.

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Zebra Case of Papillary Thyroid Cancer in MEN-2 Syndrome

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Introduction: The occurrence of papillary thyroid cancer in patients with familial medullary thyroid cancer (FMTC) is extremely rare and underreported. **Case Presentation:** A 51-year-old caucasian female with no past medical history who presented to primary care physician for her annual visit. She denied any complaints. Vital signs were unremarkable. Physical examination was remarkable for large left thyroid nodule without cervical lymph nodes enlargements. Family history was significant for metastatic MTC of her two sisters (at the age of 55, 60) and her niece at age of 21. She previously declined genetic testing. Labs were unremarkable including serum calcium of 8.3 mg/dL. Thyroid function panel revealed a TSH of 2.1 μU/mL, Free T4 of 1.4 ng/dL, Thyroid peroxidase (TPO) antibody of <6 IU/mL. Neck ultrasonography revealed a mid-left thyroid hypoechoic nodule of 1.8 ×1.5 cm, without cervical lymph nodes enlargements. Fine needle biopsy revealed a papillary thyroid cancer, follicular variant. The diagnosis confirmed by two university pathologists, without any evidence of MTC. Genetic testing revealed a germline mutation in RET oncogene exons 13. Further labs revealed normal metanephrines of 12 pg/mL and normal normetanephrine of 31 pg/mL, normal serum calcitonin was less than 2 pg/mL (0-5), normal serum CEA was 2.5 ng/mL (0-5), elevated anti- thyroglobulin (anti-TG) antibodies of 1234 iu/mL (0-0.9), and elevated thyroglobulin of 50 ng/mL (1.5-38.5). The patient was referred to ENT for total thyroidectomy. Further, she was treated with radioactive iodine ablation by 155 mCi of iodine 131. Follow up whole body thyroid scan revealed no evidence of residual or recurrence. The patient was treated with 112 mcg levothyroxine with a target of TSH less than 0.1. On six months follow up, repeated neck ultrasonography revealed no remnant of thyroid tissue. Follow up Thyroglobulin (TG) was less than 0.1 ng/mL, TSH 0.05 μU/mL, FT4 of 1.98 ng/dL, and calcitonin was still less than 2 pg/ml. Genetic testing of her daughters (24, 31) revealed germline mutations in RET-oncogene exons 13 and was referred for prophylactic thyroidectomy. **Discussion:** FMTC is an inherited syndrome characterized by the presence of only MTC without hyperparathyroidism or pheochromocytoma and is considered a variant of MEN2A. Most cases of MEN2A have been attributed to mutations in the intracellular portion of RET, and somatic mutations in RET have been identified in 50% of cases of sporadic FMTC. We recommend in patients with germline RET mutations and a family history of MTC, the diagnosis of papillary thyroid cancer should be confirmed by two pathologists, and patients should be tested for serum calcitonin, serum calcium, and metanephrines/normetanephrine levels. Genetic testing of first-degree relatives of FMTC at an early age is essential in guiding major management decisions such as the timing of prophylactic thyroidectomy.