

counterpart. Among other factors this could be explained by changing diagnostic criteria and by FTC potential for remote distant and often unpredictable metastases sites. **Clinical Cases:** In our high volume major academic referral center we have encountered three intriguing cases of metastatic FTC with negative surgical thyroid pathology. The first patient is a 61-year-old woman, who at age 50 was diagnosed with 5.4x3.5x4.2 cm left thyroid nodule (TN). FNAB reported hyperplastic nodule versus follicular neoplasm, subsequent surgical pathology report after lobectomy showed hyperplastic nodule. At age 58 she developed a pathological fracture of the 5th thoracic vertebra and pathology report indicated follicular carcinoma of thyroid origin. TG level at this time was 577 ng/ml. Pathology report from completion thyroidectomy again showed nodular hyperplasia, but reexamination of previously resected lobe demonstrated minimally invasive FTC. The second patient is an 83-year-old woman who at age 68 underwent lobectomy for left sided-goiter, pathology report showed benign follicular adenoma. At age 77 she was found to have right-sided skull mass which was determined to be a follicular carcinoma of thyroid origin. Pathology report from completion thyroidectomy was consistent with nodular hyperplasia. At age 82 the patient was noticed to have increased RAI uptake in thyroid bed, sternum, kidneys, and gastroesophageal junction. TG level at this time was 2214 ng/ml. The third patient is a 56-year-old woman initially diagnosed with a 3.5x2.8x2.2cm right TN at age 53. Lobectomy, performed for diagnostic and therapeutic purposes, showed benign follicular adenoma. At age 56 she developed a pathological fracture of the 3rd thoracic vertebra, follicular carcinoma of thyroid origin was shown on pathology report. TG level at this time was 1694 ng/ml. The patient underwent completion thyroidectomy demonstrating multinodular hyperplasia. **Conclusion:** This case series emphasizes on the pitfalls of follicular neoplasms diagnosis and management. We suggest prolonged clinical and biochemical surveillance of the patients with what appears to be follicular adenoma after lobectomy. Following serum thyroglobulin perhaps represents the most cost-effective surveillance approach of those patients.

Thyroid

THYROID CANCER CASE REPORTS

A Unique Presentation of Metastatic Follicular Thyroid Cancer Associated with Hyperthyroidism and an Active Graves' Orbitopathy

Mohammad Al-Jundi, Fellowship¹, Sriram Gubbi, MD², Maziar Rahmani, MD, PhD³, Padmasree Veeraraghavan, RN², Craig Cochran, RN², Robert Beckmann, MD⁴, Peter Mathen, MD⁴, Anam Akmal, MD⁵, Jaydira Del Rivero, MD⁶, Joanna Klubo-Gwiezdzinska, MD, PhD MHS².

¹Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD, USA, ²National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, USA, ³Division of Developmental Biology, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD, USA, ⁴Radiation Oncology Branch, National Cancer Institute, Bethesda, MD, USA, ⁵Providence Medical Group Olympia

Endocrinology, Auburn, WA, USA, ⁶National Cancer Institute, Bethesda, MD, USA.

Background: Graves orbitopathy (GO) developing in a thyroidectomized patient with hormonally active metastatic follicular thyroid cancer (FTC) is an extremely rare event. We report a unique patient with GO and hyperthyroidism developing 13 years after FTC diagnosis. **Case:** A 79-year-old Caucasian female diagnosed with FTC T3N0M1 with lung metastases in 2005, was treated with total thyroidectomy and cumulative radioiodine (RAI) activity of 700 mCi between 2005 and 2010, with post-treatment scans revealing RAI-avid disease. Despite RAI treatment-associated stable disease in the lungs, the patient developed bone metastases and required external beam radiation (EBRT; 30 Gy in 10 fractions) to the left acetabular lesion in 2011. In 2015, she presented with clinically symptomatic tumor growth in the lungs and bones and biochemical disease progression with thyroglobulin levels rising from 255 ng/ml in 2014 to 273141 ng/mL in 2019. The patient completed repeat EBRT to the left iliac bone in December 2019 (30 Gy in 10 fractions). She was on weight-based suppressive levothyroxine treatment between 2005 and 2019 until she developed atrial fibrillation with a rapid ventricular response and was diagnosed with thyrotoxicosis with TSH < 0.01 mIU/mL (normal 0.36 - 5.60) and free T4 5.93 ng/dL (normal 0.9 - 1.7). An iatrogenic cause of thyrotoxicosis was ruled out on the basis of persistent clinical and biochemical hyperthyroidism after reduction, and subsequently, cessation of levothyroxine treatment. Further workup was significant for elevated thyroid stimulated immunoglobulin (TSI) of 23.9 IU/l (normal: < 1.3) and thyrotropin receptor antibodies (TRAb) of 10.39 IU/L (< or =1.75), consistent with Graves' disease. The patient achieved and maintained euthyroidism on methimazole treatment. In April 2019, she was diagnosed with active GO and was treated with intravenous methylprednisolone, which was discontinued four weeks later due to steroids-induced severe myopathy. Given a high clinical activity score of 6 and magnetic resonance imaging of the orbits revealing a significant bilateral symmetric extraocular muscle enlargement and increased retro-orbital fat with no evidence of optic nerve compromise, she underwent radiation therapy to the orbits (20 Gy in 10 fractions), which was completed in December 2019. Subsequently, in 2020, the patient underwent 8 cycles of treatment with a monoclonal antibody against insulin-like growth factor I receptor - teprotumumab. Subjectively, she reported improved eye swelling and no vision changes, but developed drug-induced partial hearing loss, which is thought to be reversible. **Conclusion:** Metastatic, progressive FTC can be associated with an autoimmune response, leading to stimulation of well-differentiated cancer tissue to overproduce thyroid hormones resulting in overt hyperthyroidism, as well as retroorbital fibroblasts activation leading to GO.

Thyroid

THYROID CANCER CASE REPORTS

An Unusual Case of Coexistence: De-Differentiation of a Papillary Thyroid Carcinoma into Squamous Cell Carcinoma