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Introduction: Papillary thyroid carcinoma is the most common endocrine malignancy. Distant metastasis from differentiated thyroid carcinoma is infrequent, usually seen in lungs and bone. The incidence of bone metastasis is 1%-7% in papillary thyroid carcinoma. Hurtlhe cell carcinoma is a rare malignancy of the thyroid gland that can present with local or distant metastases. Main treatment for metastatic well-differentiated thyroid carcinoma includes radioactive iodine (^{131}I) and surgical resection.
Clinical case 1: In 2019, a 57 year-old woman, without significant prior medical history, with diffuse upper back and thoracic (10th -12th rib location) pain complaints, for over a year, is submitted to full body bone scintigraphy which reveals a lytic lesion located in the 10th left rib: histology is compatible with metastatic disease, from thyroid follicular carcinoma. Thoracic-abdominal-pelvic computed tomography (CT) has no sign of disease, but thyroid ultrasound shows a left located 24 mm nodule. The patient is submitted to total thyroidectomy and after histology revealed a papillary thyroid carcinoma (follicular variant), ^{131}I treatment takes place (5550 MBq /150 mCi). Post–treatment^{131}I scintigraphy presents with neck foci, in relation with thyroid residual tissue along with intense uptake in a massive lesion around the 10th left rib. Excision of this lesion is decided. The patient remains under clinical and imaging surveillance, being treated with levothyroxine 125 µg and without further complications, until today.
Clinical case 2: In 2018, a 78 year-old woman, with prior medical history of hypertension and dyslipidemia, is sent to Neurology practice in the set of diplopia of recent onset. During the evaluation, a thoracic CT reveals a single 4 mm pulmonary lesion and a calcified infracentimetric thyroid nodule. The patient is submitted to bronchofibroscopy and immunohistochemistry of the collected tissue was compatible with metastasis of oncocytic thyroid carcinoma. Thyroid nodule citology is suggestive of Hurthle cell thyroid carcinoma. Total thyroidectomy with central neck lymphadenectomy takes place and histology confirms the diagnosis. After 131I treatment (5550 MBq/150 mCi), 131I scintigraphy reveals 131I uptake foci on the neck, in relation with thyroid residual tissue and a pulmonary uptake focus (known lesion). A second 131I treatment is performed and posterior scintigraphy shows improvement of metastatic disease. The patient remains under clinical and imaging surveillance, being treated with levothyroxine 100 µg and without further complications, until today.
Conclusion: These cases reflect the importance of patient complaints in the differential diagnosis, especially osteoarticular complaints, showing that thyroid cancer can present itself already in the metastatic phase and the need to better treat our patients.

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Glioblastoma Multiforme and Papillary Thyroid Carcinoma: Rare Combination of Primary Malignancies

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Introduction: Studies have reported thyroid cancer patients are potentially at 30% increased risk of getting second primary cancer when compared to the general population. We are describing a young Caucasian male patient who was diagnosed with two synchronous cancers, papillary thyroid cancer (PTC) and glioblastoma multiforme (GBM). **Case Report:** A 52 year old Caucasian male with past medical history of hypertension, partial right thyroidectomy in 1999 for thyroid nodular disease, and postsurgical hypothyroidism on levothyroxine. He underwent FNA of left thyroid nodule found on routine monitoring of thyroid nodules showed to be suspicious for malignancy. He underwent left hemi-thyroidectomy in July 2019, revealing PTC, follicular variant, encapsulated, noninvasive type measuring 0.9 x 0.9 x 0.5 cm, completely excised with negative margins; reminder of the right hemi-thyroidectomy performed in February 2020, revealing cystic adenomatoid nodule and no evidence of malignancy. Postoperative thyroglobulin and thyroglobulin antibodies levels were undetectable. A diagnostic whole body iodine scan didn't show metastasis hence Iodine-131 treatment was not warranted. A week following the right hemi-thyroidectomy he presents to the ER with apraxia, difficulty with concentration, visual difficulty, headaches. CT scan of the brain revealed left occipital region revealed a 3.7 x 2.3 cm lesion concerning for malignancy. A follow up contrast-enhanced MRI brain showing multiple ring-enhancing lesions identified within the left posterior occipital lobe measuring 1.7 x 1.8 cm, additional occipital lobe lesion measuring 2.7 cm, mid and posterior parietal lobe measuring 3.0 cm extending to collateral sulcus measuring 2 x 3 x 1.9 cm compressing the posterior horn of left lateral ventricle. Patient underwent suboccipital craniotomy, pathology revealing glioblastoma NOS, WHO grade IV; further biomarker analysis was not available. CT of the chest, abdomen, pelvis showed no evidence of metastatic disease. Postoperative MRI of the brain revealed postoperative changes with resection of the left occipital portion of the lesion with additional enhancing regions in the left parietal and temporal lobes and splenium unchanged. Patient underwent concurrent, definitive chemo-radiation with temozolomide, now on maintenance temozolomide and levothyroxine. **Conclusion:** PTC is the most common thyroid malignancy, affecting young patients less than 45 years old. GBM can occur in people of any age, but they are more frequent in older adults. Physicians should maintain high surveillance for second primary cancers at a variety of sites in patients who have been found or treated for primary cancers, especially at a young age. Further evaluation of genetic and environmental factors between papillary thyroid cancer and glioblastoma multiforme will improve our understanding of the etiology of these malignancies.

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Hurthle Cells Adenoma With Distant Metastases Refractory to Radioiodine

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Introduction: Adenoma of the thyroid is defined as an encapsulated follicular tumor that is well delimited in relation to the adjacent parenchyma and whose cells do not exhibit the nuclear alterations of papillary thyroid carcinoma (PTC), and in the absence of capsular and vascular invasion. Adenoma, including the of Hurthle cells, is considered a benign tumor. No additional treatment is recommended after resection of the tumor. **Case:** A 64-year-old man was submitted to total thyroidectomy because of a nodule measuring 3.5 cm with indeterminate cytology (predominance of Hurthle cells). Histology revealed an Hurthle cells adenoma of 3.2 cm. The tumor did not exhibit vascular or capsular invasion, the cells did not contain nuclei of PTC, and no necrosis or mitoses were observed. Five years after surgery, serum thyroglobulin (Tg) was elevated (25 ng/ml) during euthyroidism (TSH 0.6 mUI/l) and in the absence of anti-Tg antibodies. Serum calcitonin was undetectable. The patient developed a progressive increase in Tg and neck ultrasonography (US), chest computed tomography (CT), and FDG-PET/CT were performed. US revealed atypical lymph nodes (the largest with 12 mm) and cytology showed abundance of Hurthle cells. Chest CT detected multiple nodules, the largest measuring 15 mm, and FDG-PET/CT revealed areas of cervical and pulmonary uptake corresponding to the lesions seen on US and CT. The patient received 100 mCi radioactive iodine and post-therapy whole-body scanning showed mild uptake only in the thyroid bed. The patient continues to show progressive increase in Tg (last measurement > 1,000 ng/ml), as well as progression of metastases. He remains under follow-up and on therapy with tyrosine kinase inhibitor. The histology result was revised by two pathologists with broad experience in thyroid pathology who confirmed the initial findings compatible with adenoma. **Conclusion:** The present case shows that, although rare, Huthle cells tumors can develop metastases even when the tumor is < 4 cm and unequivocally without nuclei of PTC or capsular and vascular invasion, thus considered benign (adenoma). As observed in this case, these metastases can be macrometastases, distant, and refractory to radioiodine. **Reference:** Lloyd RV, Osamura RY, Klöppel G, Rosai J, ed. WHO Classification of Tumours of Endocrine Organs. 4th edition Lyon: IARC; 2017

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Identification of a Novel DICER1 Germline Mutation in Thyroid Follicular Adenoma Using Whole Exome Sequencing

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Backgrounds: DICER1 protein is a member of the ribonuclease III family of proteins that cleaves non-coding small RNA precursors to generate mature miRNAs, which in turn regulate gene expression post-transcriptionally. Thyroid abnormalities are frequently observed in DICER1 syndrome with multinodular goiter present in families in which a germline *DICER1* mutation is segregating. Recently, we identified a germline *DICER1* mutation in a family with multiple tumors using whole exome sequencing (WES). **Methods and Materials:** Following informed consent, WES of peripheral blood DNA was carried out on affected individual. Sanger sequencing was performed to confirm the *DICER1* variant detected by WES and to assess her family for mutation in the same *DICER1* exon (exon 20). **Results:** An 8 year-old girl presented with abdominal mass. Laparoscopic radical nephrectomy was done due to Wilms tumor. At age 12, palpable mass on the right thyroid lobe was found, and right hemithyroidectomy was performed. She was diagnosed with follicular adenoma, and she started to take levothyroxine. At age 13, palpable thyroid mass on the left thyroid lobe was identified, and total thyroidectomy was performed due to progressively enlarged remnant thyroid gland with multiple nodules. The pathological result was adenomatous goiter with a cystic change. During the evaluation, a 1.5cm follicular cyst in the left ovary, 0.7cm cystic lesion in the right middle lobe of the lung, and air-trappings in both lungs were observed. We performed WES which revealed a novel heterozygous missense mutation, c.3506C>G(p.S1169*) in exon 20 of the *DICER1* gene. During the follow-up, she showed a severely enlarged right kidney with multiple septated cysts. Right total nephrectomy was done due to hemorrhage progression in cysts and biopsy revealed cystic nephroma. Continuous renal replacement therapy was applied after right nephrectomy, and maintenance hemodialysis was applied. **Conclusions:** We identified a novel *DICER1* germline mutation in a family with thyroid follicular adenoma, Wilms tumor, and contralateral progressive cystic nephroma which is the first report in Korea.

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Incidental Diffuse Sclerosing Variant Papillary Thyroid Cancer in Grave's Disease

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The diffuse sclerosing variant papillary thyroid carcinoma (DSPTC) is an uncommon form of this neoplasm. Some studies describe its high propensity for tumor invasion, metastasis, and mortality compared with classic papillary thyroid carcinoma. Histologic features of DSPTC may resemble