CASE STUDY #5

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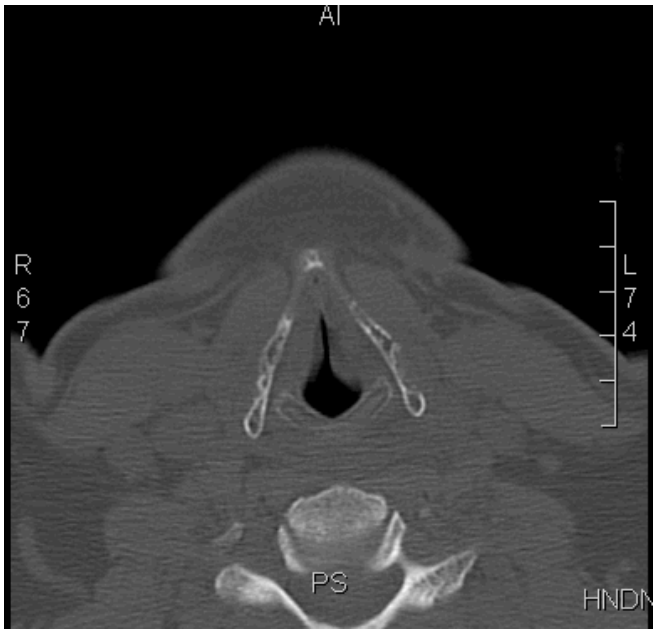
CANADA

Mr B. is a 59 year old male with no known medical illness except for dyslipidemia and a yearly followed abdominal aorta aneurysm. He presented to his family doctor with new onset cough, hoarsness and odynophagia. He was a heavy smoker for years but stopped 25 years ago; his alcool intake is estimated to 2-3 beers per day. Considering the clinical presentation, he was diagnosed with a laryngitis. However, given a persistant symptomatology despite appropriate treatment, he was referred to our tertiary care center with a neck CT and MRI, a chest CT and a thyroid ultrasound.

Thyroid U/S : 2.0 x 2.1 x 2.2 cm left dominant thyroid nodule with irregular borders in intimate contact with the tracheoesophageal groove. Multiple bilateral subcentimetric non-specific thryoid nodules are also visualized. No suspicious lymph nodes in central compartment. In right level III, there is a 12 x 12 x 17 mm suspicious lymph node. A cluster of lymph nodes is seen in the left level IIB with one dominant measuring 7 x 4 mm. Cytoponction of this lymph node was negative.

FNA: (Left dominant thyroid nodule) Suspicious for Papillary Carcinoma

Neck CT : Heterogeneous left superior 22 mm-nodule with a core calcification. Posterior extension of this mass with thining of the posterolateral aspect of the cricoid cartilage and invasion suspicion.



Chest CT : Multiple subcentimeric unspecific hilar adenopathies.

Neck MRI : Left superior pole thyroid lesion of 2.7 x 1.7 cm with cricoid invasion and suspected esophagal extension.

At his visit in July, he had no more symptoms of odynophagia but chronic cough and hoarsness were still an important complaint. The patient denied hypo/hyperthyroidism symptoms, weight loss and asthenia. Flexible laryngoscopy proved left vocal cord paralysis. A pulmonary endoscoscopy performed by an experimented thoracic surgeon showed no tumoral extension in the trachea. Esophageal endosonography, however, revealed tumoral invasion of the muscularis propria distally to the superior esophageal sphincter.

We performed a total thyroidectomy with bilateral central and lateral neck dissection. During the surgery, the right thyroid lobe was easily dissected. The difficulty resided mostly in dissecting the left lobe which seemed completely adherent to the laryngotracheal structure. We started by resecting the inferior pharyngeal constrictor muscles as well as esophageal muscles at its left cervical portion. The bougie proved to be a useful tool in performing the latter without penetrating the mucosa. Once this was done, the left lobe was easier to mobilize and was further dissected from the larynx and cricoid cartilage. The inferior horn of the left thyroid cartilage as well as ½ cm of the left cricoid showed signs of gross invasion. Thus, we performed a left thyroid cartilage horn resection and a shaving of the left cricoid cartilage at its external portion. The excised specimen was sent to pathology (details of pathology not yet available but should be for further discussion during the meeting).

Questions :

1- What would have been the optimal preoperative investigations for this patient? Esophagoscopy? Esophagoscopy and esophageal endosonography ?
2- What would be the most appropriate treatment modality of the cricoid cartilage lesion? Shaving vs laryngectomy ?
3- Is adjuvent radiotherapy indicated in this case?

CASE STUDY #6

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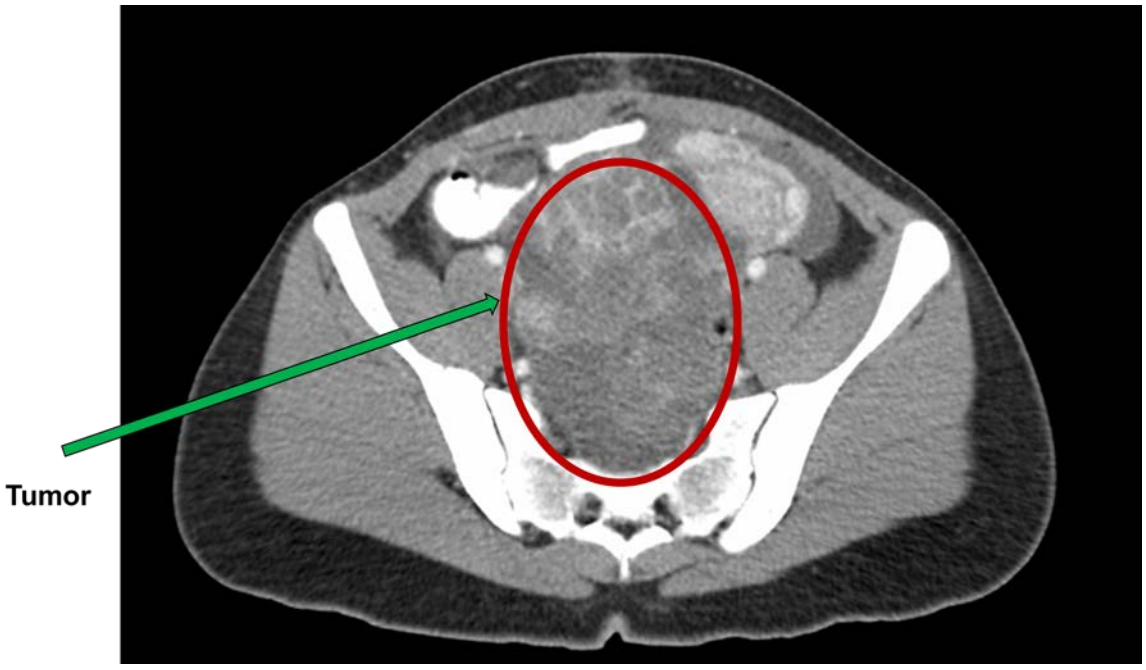
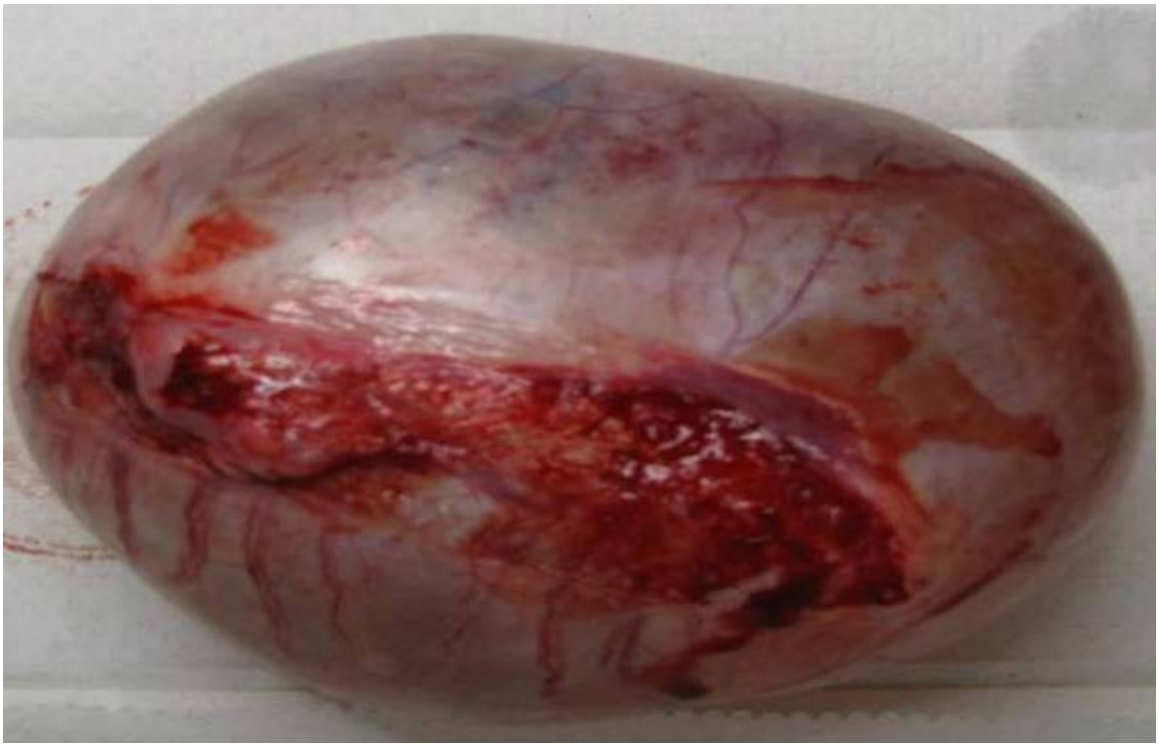
Ms. AB is a 19 year old African American female. At the age of 14, in 2008, she had a benign left ovarian cystic teratoma resected. In 2010, a benign cystic teratoma with predominant thyroid tissue was resected from the right ovary. In September 2012 she presented to the ER with worsening abdominal pain and was admitted to the GYN service. Sonogram revealed a mixed solid and cystic pelvic mass measuring 10.6X7.9X7.6 cm. She underwent exploratory laporatomy in September 2012 and was found to have a large right adnexal mass with widespread nodules involving the peritoneum, omentum, spleen, bladder, uterus and rectal and abdominal walls. The intra-operative surgical impression was of widespread metastatic ovarian carcinoma and consequently the procedure was terminated by the GYN surgeon. However, Pathology reported follicular tissue with colloid in the widespread nodules and their impression was Peritoneal Strumosis. The Endocrinology service was consulted and the working diagnosis became Metastatic Struma Ovarii. In December 2012, CT revealed a large complex mass measuring 12.0 X 8.1 X 11 cm arising from the right adnexal area. Multiple enhancing soft tissue peritoneal nodules were noted including a lesion anterior to the spleen measuring 2.3 X 2.9 cm. She then underwent total hysterectomy, bilateral oophorectomy, omentectomy and splenectomy. Surgical pathology revealed well differentiated follicular thyroid carcinoma of ovarian origin. The tissue was positive for thyroglobulin and TTF-1. The diagnosis of metastatic Malignant Struma Ovarii was thus confirmed. Molecular marker testing was negative for BRAF, RAS, RET/PTC and TP53 mutations.

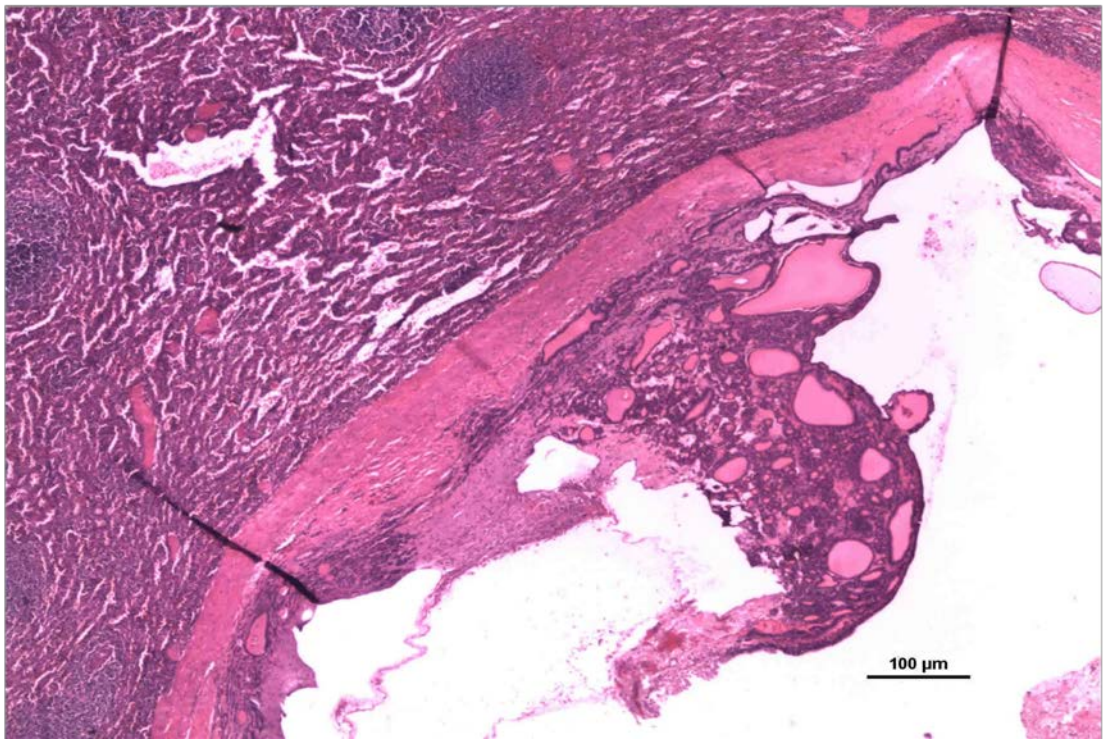
Prior to surgery in December 2012, the patient was clinically and biochemically euthyroid (TSH 0.998 uIU/ml, T4 9.2 ug/dl, free T4 ng/dl 1.11, T3 122 ng/dl) and had a serum thyroglobulin of 229 ng/ml in the absence of antiTG antibodies. In April 2013, prior to total thyroidectomy, TSH and free T4 remained normal at 0.928 and 1.28 respectively while serum TG was 49.1 ng/ml with antiTGab undetectable. No lesions were found in the thyroidectomy specimen. Post-thyroidectomy ^{131}I ablation treatment was given. Dosimetry evaluation revealed whole body isotope retention of 32.27% at 6 days. Photodense areas in the thyroid bed, abdomen and pelvis were seen on scan. The calculated maximum safe treatment dose of ^{131}I was 200 mCi. An initial dose of 62.8 mCi was administered. Three months post-thyroidectomy, without thyroxine supplementation, TSH and T4 remained normal at 1.16 uIU/ml and 8.8 ug/dl respectively. Four months post-thyroidectomy, TSH rose to 4.82 uIU/ml while T4, free T4 and T3 were each normal at 7.3 ug/dl, 1.2 ng/dl and 99 ng/dl respectively. Serum thyroglobulin was 69.7 ng/ml in the continued absence of antiTGab. L-thyroxine was begun. It is planned to perform a followup whole body isotope scan with dosimetry and a second ^{131}I ablation in October (six months post thyroidectomy).

1. Does the entity of Benign Peritoneal Strumosis exist or is this always metastatic well differentiated thyroid cancer?
2. If we see significant uptake in the second nuclear scan what are our options?


Tumor



Spleen: Capsular involvement



Case Study #7

Sarah Catherine Oltmann, MD
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Madison, WI

HA is an 88 y.o. male who initially presented with complaints of voice hoarseness. During the work up of these complaints, he was found to have a left sided vocal cord paresis, along with vocal fold leukoplakia. This led to a CT scan of his neck to evaluate for any masses causing compression or disruption of his recurrent laryngeal nerve, and bilateral thyroid nodules were discovered. The largest was on the left, measuring 2.5 cm. A fine needle aspiration of this nodule was suspicious for papillary thyroid cancer. Further ultrasound examination of his neck demonstrated a suspicious lymph node in the left lateral chain. Given its location behind the carotid artery, it was not amenable to preoperative FNA biopsy. Based on this constellation of findings, he underwent a total thyroidectomy with central and lateral neck dissection. Incidentally, at time of surgery, nerve monitoring was used, and a strong signal was noted in bilateral recurrent laryngeal nerves. His voice hoarseness resolved immediately post-op.

His final pathology revealed a diagnosis of multi-focal medullary thyroid cancer, without lymphovascular invasion, and with 0 out of 9 lymph nodes involved. Tumor markers were sent off in the immediate post-operative period, with a calcitonin of 20.3, and a CEA of 37. Since that time they have normalized and remained stable.

This prompted referral for genetic testing, which returned positive for a RET mutation at Exon 16 (Arg912Pro). Testing of his adult children revealed that 2 out of the 4 were also positive. None of the grandchildren were noted to be positive.

With over a year of follow up, he is disease free and doing well.

Case Study #8

Chhaya D. Makhija, MD
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69 y.o. male seen followup of his **papillary thyroid carcinoma T4 N1b M1**, **stage IVc** with known pulmonary metastasis and newly diagnosed right choroidal mets, while on Pazopanib systemic therapy. Of note, he has history of melanoma in past.

Papillary thyroid cancer: initially diagnosed in **2006, s/p** total thyroidectomy and central neck dissection. Pathology showed **multifocal tumor with extrathyroidal extension**. Largest nodule focus was **1.7 cm**. He received his first dose of **radioactive iodine with 340 millicuries** at that time.

He had **recurrence in his left neck and underwent left lateral neck dissection**. He received a **second dose of radioactive iodine of 313** millicuries at that time and then he had **external beam radiation therapy** because of extension of the tumor.

He had a **third dose of radioactive iodine with 192.7 millicuries of I-131 in 2009 because of rising thyroglobulin** and no resectable disease. A post treatment scan showed foci of increased activity in the left lower lobe of the lung, superior mediastinum, and right clavicular region, and he has known pulmonary metastasis, however, not all of the pulmonary lesions were RAI avid.

Pulmonary lesions were continuing to slowly increase in size along with his thyroglobulin. We started **pazopanib, tyrosine kinase inhibitor, in August 2011.** radiographically his disease had been relatively stable, however, his thyroglobulin continued to rise with the highest being 139 with negative ab. In Feb 2013 CT of his neck and chest showed essentially stable disease in his lungs without clear progression.

At his last visit in April 2013, a new right retinal mass was identified. He was seen at University of Iowa for biopsy of the mass since the etiology was unclear (met thyroid cancer versus melanoma). The biopsy was consistent with metastatic papillary thyroid cancer. Unfortunately, he developed panendophthalmitis and required surgical removal of his right eye in May 2013. The choroidal mass was also completely excised and measures 3.5 x 9.5 mm. PAS positive, the tumor demonstrated staining for pancytokeratin, ck7, thyroglobulin, and TTF. CK20 negative. Near the apex of the tumor, tumor can be seen extending from the choroid into the subretinal space where there is a breach in Bruch's membrane likely from the previous FNA.

In addition, repeat CT of the chest prior to his choroid biopsy identified a left infrahilar node that had dramatically increased in size from Feb, 2013. It measured 3.8 x 3.2 cm (previously 2.4 x 2.3 cm). There was also mass effect along the left paraspinal region and post obstructive atelectasis and infiltrate in the left lower lobe and left pleural effusion. He received 3000 cGy in 10 fraction to the gross disease in lower mediastinum, left hilum and left lower lobe. This was completed in June 2013.

In regards to his **post-surgical hypothyroidism**, he is taking Synthroid 250mcg daily, with 2 additional 125 mcg pills during the week.

After resection of choroidal metastasis and failure to respond to pazopanib, what would be the next treatment option?

Patient was started on vandetanib (off label use).