A Recurrent Paraganglioma with RET and SDHC Mutations

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Introduction
Paragangliomas are rare neuroendocrine tumors arising from sympathetic or parasympathetic extra-adrenal paraganglia. These tumors are closely related to pheochromocytomas and are derived from neural crest cells. A paraganglioma that arises from a sympathetic chain can secrete catecholamines, while those arising from a parasympathetic chain tend to be nonfunctional. The majority of paragangliomas diagnosed are sporadic, however, 1/3 were associated with an inherited syndrome. In particular, hereditary paragangliomas in the head and neck region are associated with SDH enzyme complex mutations. These tumors have also occurred with NF1 and VHL tumor syndromes. Paragangliomas are rarely seen in the MEN2 syndrome secondary to a RET gene mutation. We present a rare occurrence of recurrent paraganglioma with simultaneous RET and SDHC mutations.

Case Presentation
A 50-year-old female presents with right ear pain and tinnitus for multiple weeks. She was treated with several antibiotic courses for presumed otitis media. However, her symptoms persisted and she was referred to an ENT specialist who obtained a CT scan of her sinuses and temporal bone. This revealed a large glomus tumor of the middle ear with extension into the hypotympanic air cells and jugular bulb. She underwent a transcervical excision of the tumor and a tympanoplasty. Pathology confirmed a jugulotympanic paraganglioma. She was symptom-free until she presented with pre-auricular swelling and tinnitus a few months later. She underwent a head MRI that revealed a 2.3 cm lobulated enhancing tissue within the right jugular foramen, concerning for residual tumor (Figure 1). She underwent excision and pathology was positive for enhancing tissue within the right jugular foramen, concerning for residual tumor secondary to a RET gene mutation. We present a rare occurrence of recurrent paraganglioma with simultaneous RET and SDHC mutations.

Discussion
Our literature review did not yield any cases of simultaneous RET and SDHC mutations in patients diagnosed with a paraganglioma. The SDHC gene mutation is in itself rare – found to occur in 4% of patients with parasympathetic paragangliomas. The SDHC mutation rarely leads to hereditary paraganglioma syndromes compared to the SDHB and SDHD gene mutations. The SDHC protein is one of four subunits that constitute succinate dehydrogenase, which functions as complex II of the mitochondrial electron transport chain. The RET gene variant is a proto-oncogene which encodes a transmembrane receptor tyrosine kinase expressed in neural crest precursor cells. A gain-of-function mutation in this gene leads to the autosomal dominant tumor syndromes known as MEN2A and MEN2B. Bilateral adrenal pheochromocytomas are common in these syndromes, but paragangliomas are rarely seen. Of note, the patient did not have any symptoms or signs concerning for catecholamine excess. This is not unusual for paragangliomas especially in the head and neck region, as the tumor arises from parasympathetic paraganglia. A recent case series found that 31% of patients with paragangliomas had catecholamine hypersecretion.

Conclusion
Our case demonstrates the unusual presentation of simultaneous RET and SDHC mutations in an individual with a recurrent paraganglioma. It highlights the importance of genetic testing and screening for tumor syndromes in patients diagnosed with a paraganglioma.

References