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SDHD Mutation: Nonfunctional paragangliomas presenting as bilateral carotid body tumors with syncope

Background:

A mutation of the SDHD gene is associated with hereditary paraganglioma-pheochromocytoma (PGL/PCC) syndromes which most commonly originate in the head and neck region, and usually form in the carotid body. Paragangliomas (PGL) can be secretory or non-secretory with about 95% of head and neck PGL being non-secretory. They can rarely present with symptoms due to compression, however, as in this case of a 29 year-old female presenting with syncope.

Clinical Case:

A 29 year-old female presented for evaluation after syncope. She had a syncopal event and fell down while walking in her home. Syncope was preceded by about 15 minutes of flushing, nausea and palpitations. She reported similar episodes once weekly in the preceding months, which generally lasted an hour. Initial workup included normal vital signs at presentation, normal ECG and echocardiogram, normal TFT, CBC, complete metabolic panel. Subsequent head/neck CT revealed bilateral masses in the carotid bifurcations consistent with carotid body tumors. Further history revealed a family history of bilateral carotid body tumors in her father which had never been evaluated. Plasma and urine metanephrines were normal. She underwent carotid body tumor excision. The left carotid body tumor was successfully excised and pathology revealed a paraganglioma with positive synaptophysin and chromogranin stains. Genetic testing revealed an SDHD (succinate dehydrogenase complex subunit D) gene mutation. Repeat biochemical assessment 4 months later was again negative and patient remained asymptomatic postoperatively.

Conclusion:

Paragangliomas can be secretory or non-secretory with about 95% of head and neck paragangliomas being non-secretory, as in this case. Symptoms can arise from catecholamine hypersecretion, which generally presents as hypertension, headaches, diaphoresis, flushing, anxiety or palpitations, and can be episodic or sustained, or mass effect. Syncope as a presenting symptom is rare, however, and has not been quantified but only reported in case reports. The exact etiology of syncope in our patient is not clear. Hereditary PGL/PCC syndromes should be suspected in any individual with multiple, recurrent, early-onset (age less than 45 years) or family history of PGL/PCC, as these syndromes are inherited in an autosomal dominant manner.

Adrenal

ADRENAL - HYPERTENSION

Prevalence and Incidence of Fractures in Patients with Adrenal Adenomas: A Population-Based Study of 1003 Patients

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Background: Adrenal adenoma is reported in around 5% of adults undergoing cross-sectional imaging. Although most adenomas are considered non-functioning (NFAT), up to 48% present with mild autonomous cortisol secretion (MACS). Several studies reported increased prevalence and incidence of vertebral fractures in MACS; however conclusions are limited by small sample size, selection bias, inadequate reference population and length of follow up.

Objective: To determine the prevalence and incidence of site-specific fragility fractures in a population-based cohort of patients with adrenal adenomas.

Methods: Residents of local community with a radiographic diagnosis of adrenal adenoma between 1995 and 2017 were identified using a centralized epidemiologic database and matched with reference subjects for sex and age. All subjects were followed through 2017, until death or migration from the community. MACS was diagnosed based on cortisol level ≥1.8 mcg/dl after overnight 1mg dexamethasone suppression, NFAT based on cortisol level <1.8 mcg/dl, and patients not tested with dexamethasone were considered as adenoma with unknown cortisol secretion (AUCS).

Results: Of 1003 patients with adrenal adenomas (581 women (58%), median age of diagnosis 63 years (20–96)), 136 (14%) were diagnosed with NFAT, 86 (9%) with MACS, and 781(78%) with AUCS. At the time of diagnosis, patients had higher BMI (median 30 vs 28 kg/m^2, p<0.001), and higher prevalence of tobacco use (70% vs 54%, p<0.001) than reference subjects. Of 154 patients and 113 reference subjects with BMD available at baseline, patients had a higher median BMD at the total hips (0.93 vs 0.89, p=0.02) but similar median BMD at lumbar spine (1.05 vs 1.03, p=0.49) when compared to reference subjects. However, patients had a higher prevalence of fractures than reference subjects (any fracture: 50% vs 42%, p<0.001, vertebral fracture: 6.5% vs 3.7%, P=0.004). When adjusted for age, sex, and prior history of fracture, patients with adenoma had HR of 1.24 (CI 95% 1.04–1.48) for developing a new fracture and HR of 1.18 (CI 95% 0.97–1.44) when also adjusted for BMI and smoking. Subgroup analysis demonstrated that the prevalence of fractures at the time of diagnosis was higher in all 3 subgroups at any fragility fracture site when compared to reference subjects (NFAT: 44% vs 37%, MACS: 48% vs 43%, AUCS: 51% vs 43%); patients with MACS had the highest incidence of new fracture after 5 years of follow up when compared to AUCS and NFAT (cumulative incidence: MACS 25% vs NFAT 19% vs AUCS 16%), though the differences were not significant.

Conclusions: Patients with adrenal adenomas have higher prevalence of fractures at the time of diagnosis. During follow up, patients with adenoma have a higher incidence of fractures even when adjusted for sex, age, and prior history of fracture, possibly due to underlying undiagnosed abnormal cortisol secretion.