Bilateral Pheochromocytomas in an Adolescent Patient with Biallelic Mutations in the Von Hippel-Lindau Gene

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Introduction

- Pheochromocytomas and paragangliomas are catecholamine-secreting neuroendocrine tumors that can arise in association with known genetic syndromes or sporadically.
- Pheochromocytomas, which originate from the adrenal medulla, are treated with surgical resection. It is the resection that introduces the endocrine consequence of post-operative adrenal insufficiency.
- We report a case of bilateral pheochromocytomas in an 11-year-old patient with biallelic Von Hippel-Lindau (VHL) gene mutations thus far described as being variants of uncertain significance (VUS).

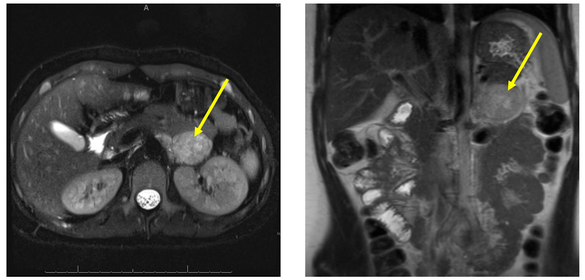
Case Presentation

- Work-up for congenital polycythemia featured gene sequencing at age 2, which detected two mutated alleles in the VHL gene: c.227T>A (p.Phe76Tyr) and c.416C>G (p.Ser139Cys).
- Baseline plasma normetanephrines and metanephrines were collected at age 2 and repeated annually from age 8 onward.
- By age 11, she began to experience headaches, diaphoresis, tachycardia, dyspnea with activity, and elevated blood pressures.

Results

Age (years)	**Normetanephrines** (ref 0 – 0.89 nmol/L)	**Metanephrines** (ref 0 – 0.49 nmol/L)
2	0.68 nmol/L	0.25 nmol/L
8	**0.92**	0.21
9	0.81	0.18
10	**1.65**	0.19
11	**13.10**	0.15
11, *repeated one month later*	**15**	0.15

Table 1: screening of plasma normetanephrines and metanephrines. Baseline labs obtained at age 2; annual screening since age 8.



Images 1, 2: MRI abdomen with contrast depicting bilateral solid adrenal mass lesions corresponding to pheochromocytomas, larger on left than right. Left: 3 x 3.7 x 3.4 cm. Right: 1.4 x 1.7 x 1.8 cm.

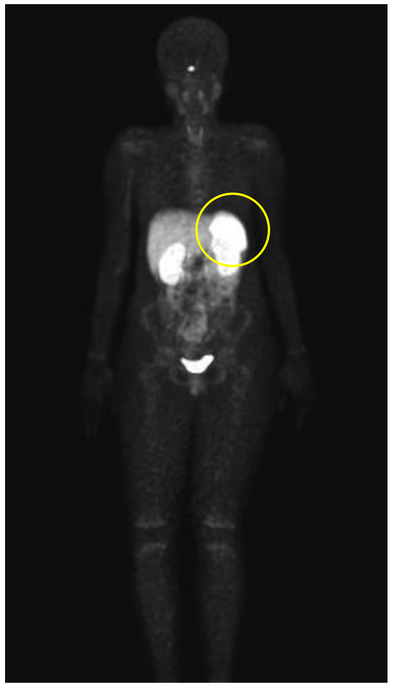


Image 3: 68Ga DOTATATE PET scan, demonstrating isolated activity in left adrenal mass. No additional foci to suggest metastatic disease.

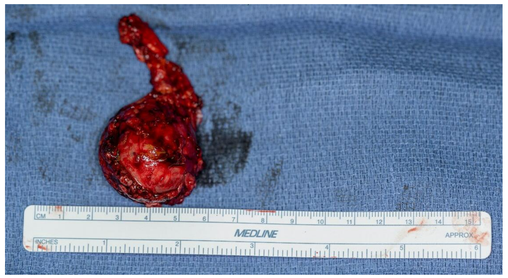


Image 4: Final pathology specimen: pheochromocytoma, 3.2 cm, confined to the adrenal gland.

Discussion

- Surgical intervention was guided by a DOTATATE PET scan that revealed activity in only the left adrenal mass, so a unilateral adrenalectomy was performed to avoid permanent adrenal insufficiency.
- She tolerated surgery well with resolution of symptoms and will continue to receive surveillance of the residual right adrenal mass.
- To date, her mutations are described as VUS, but the combination of her history and future course may show these mutations to be clinically significant.