Family (Hyper)Tensions

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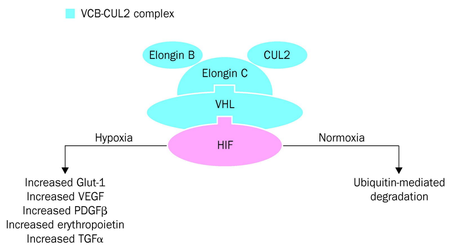
Introduction

Von Hippel-Lindau (VHL) disease is an autosomal dominant hereditary syndrome caused by germline loss-of-function mutation in the VHL tumor suppressor gene and characterized by the development of various benign and malignant tumors associated with unregulated Hypoxia-Inducible Factor (HIF) complex activity.



Case Presentation

HPI: An 18-year-old male with VHL who had been lost to follow-up presented to an ophthalmology office with acute left sided vision loss and floaters for three days. Ophthalmologic exam revealed bilateral retinal capillary hemangioblastomas, retinal edema, and left intraretinal hemorrhage. He received intravitreal bevacizumab and was transferred to the ED.

Physical Exam:
BP 183/148 HR 108 T 36.7 ° C R 20 SpO2 100 % on RA

Young, thin male in no acute distress without any significant physical exam findings on admission.

Further history: Episodes of panic, diaphoresis, and palpitations which are not situational, for the past few years. At times associated with headaches and pre-syncopal symptoms. All other ROS negative.

Social history: Patient previously had follow-up and regular medical care while living with mother (who also has VHL) but moved to another state about 5 years prior and was lost to all follow-up.

Lab Test	Value	Ref Range & Units
Renin, supine	2.1 H	0.2-1.6 ng/mL/hr
Aldosterone, supine	5.0	≤ 16.0 ng/dL
Epinephrine	50	10 - 200 pg/mL
Norepinephrine	8208 H	80 - 520 pg/mL
Dopamine	54 H	0 - 20 pg/mL
Metanephrines	0.19	0.00 - 0.49 nmol/L
Normetanephrines	27.50 H	0.00 - 0.89 nmol/L

Hospital Course

DAY 1
- Admitted to ICU on nicardipine infusion
- Endocrinology consulted

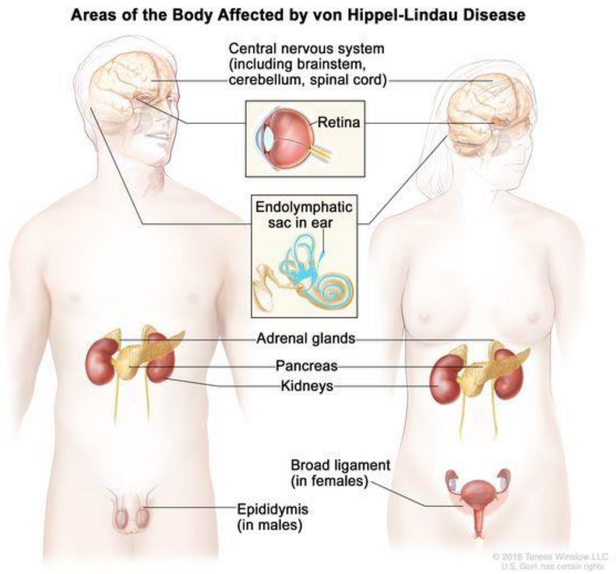
DAY 2
- Started on doxazosin
- Lisinopril later added and nicardipine off

DAY 3
- Transfer to floor
- CT scan completed
- Doxazosin uptitrated

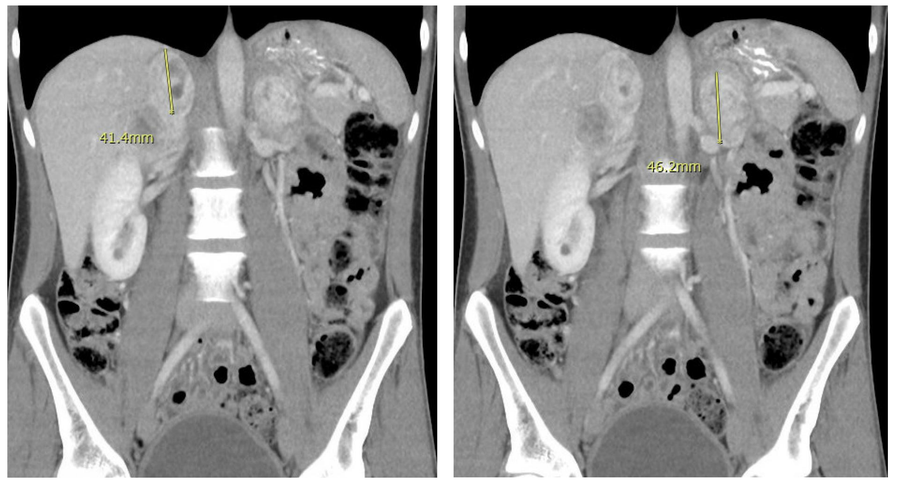
DAY 4
- Surgery consulted, await confirmatory labs
- Improving BP control

DAY 5
- Discharged home with stable BP, but persistent left sided visual deficit
- Plan for outpatient bilateral adrenalectomy

Organs Affected by VHL



CT Abdomen & Pelvis: Multiple bilateral large heterogeneously enhancing adrenal lesions with cystic and necrotic changes, favored to represent pheochromocytoma in the appropriate clinical context.



VHL Screening Recommendations

Surveillance Modality (Tumors being screened)	AGE[1]					
	<5 years	Beginning at age 5y	Beginning at age 11y	Beginning at age 15y	Beginning at age 30y	Beginning at age 65y[1]
History and Physical Examination[2]	Yearly from age 1 year	Yearly	Yearly	Yearly	Yearly	Yearly
Blood Pressure and Pulse (Pheochromocytomas/paragangliomas)	Yearly from age 2 years	Yearly	Yearly	Yearly	Yearly	Yearly
Dilated Eye Examination[3] (Retinal Hemangioblastomas)	Every 6-12 months, beginning before age 1 year	Every 6-12 months	Every 6-12 months	Every 6-12 months	Yearly	Yearly
Metanephrines[4] (Pheochromocytomas/paragangliomas)	——	Yearly	Yearly	Yearly	Yearly	Stop routine[1]
MRI Brain and Spine w/wo Contrast[5,6,7] (CNS Hemangioblastomas)	——	——	Every 2 years[8]	Every 2 years[8]	Every 2 years[8]	Stop routine[1]
Audiogram (Endolymphatic sac tumors)	——	——	Every 2 years	Every 2 years	Every 2 years	Stop routine[1]
MRI Abdomen w/wo Contrast[5,6,7] (Renal cell carcinomas, Pheochromocytomas/paragangliomas, Pancreatic neuroendocrine tumors/cysts)	——	——	——	Every 2 years[9]	Every 2 years[9]	Stop routine[1]
MRI Internal Auditory Canal[10] (Endolymphatic sac tumors)	——	——	——	Once	——	——

Discussion

- VHL disease affects approximately 1 in 36,000 people worldwide (10,000 cases in the U.S and 200,000 cases worldwide), with most cases occurring in families. VHL disease affects males and females and all ethnic groups equally.
- Our patient had a strong maternal family history of this disease and received confirmatory genetic testing at age three.
- People who have VHL disease may experience tumors and/or cysts in up to ten parts of the body, including the brain, spine, eyes, kidneys, pancreas, adrenal glands, inner ears, reproductive tract, liver and lung.
- Within families, both penetrance and age at disease presentation can vary. Further, appearance and severity of VHL lesions differs widely between individuals, highlighting the importance of regular surveillance and screening.
- Our patient suffered from symptoms of his pheochromocytomas for years and had progressed to hypertensive emergency with vision loss before presenting to care. Fortunately, he has received definitive management and his young age may prove protective.

Take Home Points

- Von Hippel-Lindau disease is a heritable multisystem cancer syndrome with up to 10 body systems affected.
- VHL disease is different for every person affected, even with the same family, and it is impossible to predict exactly how and when it will present.
- Multidisciplinary management and careful surveillance are crucial to prevent increased morbidity and mortality.

References

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