Von Hippel-Lindau Syndrome: Implications for Nursing Care

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Von Hippel-Lindau syndrome (VHL) is an autosomal dominant inherited disorder characterized by the formation of both benign and malignant tumors and cysts in various parts of the body. Identification of individuals and families affected with this disorder is imperative to implement appropriate screening measures so as to detect complications early and to reduce the morbidity and mortality associated with the diagnosis.

Case Study 1

A 39-year-old man named S.E. had complete resection of two hemangioblastomas. The patient had other comorbidities including diabetes, obesity, and recurrent gastric ulcers. Subsequent testing demonstrated a 5 cm renal mass on the left kidney. S.E. underwent a left partial nephrectomy, which demonstrated clear cell renal cancer. After his surgery, S.E. was referred for genetic counseling and consideration of genetic testing.

The genetics professional constructed a pedigree for the patient. S.E.'s father had died at age 59 from high blood pressure and a stroke, and a fraternal twin brother had been successfully treated for a cerebellar hemangioblastoma two years prior. S.E. also had two younger sisters and three children, all of whom were in good health. S.E.'s mother died from obstetric complications and little is known about her family history. Genetic testing was offered and S.E. tested positive for a deleterious VHL mutation. Subsequently, his twin brother, one sister, and two of his children tested positive for the deleterious VHL mutation.

Case Study 2

A 29-year-old man named P.L. presented to his primary care provider with a history of palpitations, headaches, and an eight-month history of uncontrolled hypertension. Urine studies revealed elevated catecholamines. Magnetic resonance imaging showed large bilateral adrenal masses. At surgery, bilateral pheochromocytomas (catecholamine-secreting tumors of the adrenal glands) were resected. Family history was obtained as the presence of bilateral pheochromocytomas is suggestive of a hereditary cancer syndrome. P.L.'s mother was 62 years old, had diabetes, and was obese. She was adopted at birth and had no information about her biologic family. P.L.'s father was 63 years old with no major health problems and no family history of malignancy. P.L. had two healthy siblings and no offspring. During his visit with the genetics professional, P.L. was questioned about any personal or family history of vision problems. He stated that he had been experiencing some blurry vision in his right eye. He was then referred to an ophthalmologist and was found to have a unilateral retinal angioma. Genetic testing of the VHL gene was performed and a deleterious mutation was detected, confirming the clinical diagnosis of VHL. Imaging was negative for renal cell carcinoma or additional hemangioblastomas. P.L.'s mother and father underwent genetic testing for the same mutation and both were found to be negative, as were his two siblings.

Pathophysiology

VHL is an inherited disorder characterized by the formation of both benign and malignant tumors and cysts in various parts of the body. Tumors may occur during young adulthood; however, the signs and symptoms of VHL can develop throughout life. VHL is an autosomal dominant hereditary cancer syndrome caused by mutations in the VHL tumor suppressor gene located on chromosome 3. VHL is estimated to occur in 1 of every 30,000–40,000 individuals (Lindor, McMaster, Lindor, & Greene, 2008).

VHL follows Knudson's (1996) "two-hit" model for carcinogenesis. In inherited cases, the first hit is a VHL germline (inherited) mutation. The second hit is a somatic (acquired) mutation. Tumor formation requires mutations in both VHL alleles in the somatic tissue. Individuals with VHL have a predisposition for developing renal cell carcinomas, pheochromocytomas, central nervous system hemangioblastomas, retinal hemangioblastomas, endolymphatic sac tumors, and renal and pancreatic cysts (see Table 1). Genetic (DNA) testing for germline VHL mutations costs less than $1,000, often is covered by insurance, and is capable of detecting about 100% of all described VHL mutations (Frantzen, Links, & Giles, 2009; Kaelin, 2007). When the clinical diagnosis of VHL is confirmed by germline genetic testing, implementation of appropriate screening can significantly decrease a patient's morbidity and mortality.

Table 1. Clinical Features of von Hippel-Lindau Syndrome: Occurrence and Age of Onset

Tumor Type	Average Age at Diagnosis (Years)	Frequency (%)
Renal cell cancer (clear cell)	40 (16–69)	35–75
CNS hemangioblastomas	30	50–79
Retinal hemangioblastoma	21–28	70
Pheochromocytoma	25–34	3.5–17
Pancreatic islet cell carcinomas	24–35	7.5–25
Endolymphatic sac tumors	16–28	11–16
Epididymal cystadenoma	14–40	7–27

CNS—central nervous system

Note. Based on information from Frantzen et al., 2009; Lindor et al., 2008.