Clinical Presentation

VHL disease is variably associated with retinal angiomas, brain and spinal cord hemangioblastomas, renal cell carcinomas, pheochromocytomas, angiomas of the liver and kidney, and cysts of the pancreas, kidney, liver, and epididymis. Symptoms typically begin during the third or fourth decade. Retinal inflammation with exudates, hemorrhage, and retinal detachment may antedate cerebellar symptoms (headache, vertigo, and vomiting) or signs (incoordination, dysmetria, and ataxia).

Diagnosis/Differential

The diagnosis of VHL disease is suspected in individuals with characteristic lesions such as hemangioblastomas, multiple renal cysts and renal cell carcinoma, pheochromocytoma, and endolymphatic sac tumors. Clinical diagnostic criteria have been established. Molecular genetic testing of *VHL* detects mutations in 90% to 100% of those meeting clinical criteria.

Treatment

Early evaluation and repeated imaging studies are indicated once the diagnosis has been made, and genetically at-risk relatives should also be evaluated. Retinal detachments and tumors are treated by laser therapy. Surveillance for brain tumors, renal cell carcinomas, pheochromocytomas, and epididymal tumors is instituted and appropriated medical and surgical interventions are provided.

Prognosis

Survival depends on management of tumors. Aggressive surveillance has increased survival (where the median had been less than 50 years).

For a deeper discussion on this topic, please see Chapter 417, "Congenital, Developmental, and Neurocutaneous Disorders," in Goldman-Cecil Medicine, *25th Edition.*

SUGGESTED READINGS

Adzick NS, Thom EA, Spong CY, et al: A randomized trial of prenatal versus postnatal repair of myelomeningocele, N Engl J Med 364:993–1004, 2011.

Barkovich AJ, Guerrini R, Kuzniecky RI, et al: A developmental and genetic classification for malformations of cortical development: update 2012, Brain 135:1348–1369, 2012.

Cuddapah VA, Pillai RB, Shekar KV, et al: Methyl-CpG-binding protein 2 (MECP2) mutation type is associated with disease severity in Rett syndrome, J Med Genet 51:152–158, 2014.

Grzadzinski R, Huerta M, Lord C: DSM-5 and autism spectrum disorders (ASDs): an opportunity for identifying ASD subtypes, Mol Autism 4:12–17, 2013.

Gutmann DH, Parada LF, Silva AJ, et al: Neurofibromatosis type 1: modeling CNS dysfunction, J Neurosci 32:14087–14093, 2012.

Hagerman RJ, Berry-Kravis E, Kaufmann WE, et al: Advances in the treatment of Fragile X syndrome, Pediatrics 123:378–390, 2009.

Kanekar S, Kaneda H, Shively A: Malformations of dorsal induction, Semin Ultrasound CT MR 32:189–199, 2011.

Kanekar S, Shively A, Kaneda H: Malformations of ventral induction, Semin Ultrasound CT MR 32:200–210, 2011.

Lo W, Marchuk DA, Ball KL, et al: Updates and future horizons on the understanding, diagnosis, and treatment of Sturge-Weber syndrome brain involvement, Dev Med Child Neurol 54:214–223, 2012.

Nigg JT: Attention-deficit/hyperactivity disorder and adverse health outcomes, Clin Psychol Rev 33:215–228, 2013.

Richard S, Gardie B, Couvé S, et al: Von Hippel-Lindau: how a rare disease illuminates cancer biology, Semin Cancer Biol 23:26–37, 2013.

Vaz SS, Chodirker B, Prasad C, et al: Risk factors for nonsyndromic holoprosencephaly: a Manitoba case-control study, Am J Med Genet A 158A:751–758, 2012.

Volpe P, Campobasso G, De Robertis V, et al: Disorders of prosencephalic development, Prenat Diagn 29:340–354, 2009.

Volkow ND, Swanson JM: Adult attention deficit – hyperactivity disorder, NEJM 369:1935–1944, 2013.

Wallingford JB, Niswander LA, Shaw GM, et al: The continuing challenge of understanding, preventing, and treating neural tube defects, Science 339:1047–1054, 2013.