Von Hippel-Lindau disease diagnosis

Diagnostic criteria

Formal criteria for the diagnosis of Von Hippel-Lindau disease have not been published.

Suspected VHL

VHL should be suspected in an individual (with or without a family history of VHL) who has:

1. retinal angioma, especially at a young age

2. spinal or cerebellar hemangioblastoma

3. adrenal or extra-adrenal pheochromocytoma

4. renal cell carcinoma (RCC), if the individual is < 47 years old, or has a personal or family history of other tumors typical of VHL

5. multiple renal and pancreatic cysts

6. neuroendocrine tumors of the pancreas

7. endolymphatic sac tumors

8. less common: multiple papillary cystadenomas of the epididymis or broad ligament.

Establishing the diagnosis of VHL

The diagnosis of VHL is established in a proband with clinical features listed below and/or by identification of a heterozygous germline pathogenic variant in the VHL gene by molecular genetic testing.

If the clinical features are absent, a patient with this variant is diagnosed with VHL and should be surveilled as such, even if clinical or radiographic findings are inconclusive.

Clinical diagnostic criteria

● an individual with no known family history of VHL with ≥ 2 charateristic lesions:

○ ≥ 2 HGB of the retina, spine or brain, or a single HGB in association with a visceral manifestation (e.g. multiple renal or pancreatic cysts)

○ renal cell carcinoma

○ adrenal or extra-adrenal pheochromocytoma

○ less common: endolymphatic sac tumors, papillary cystadenomas of the epididymis or broad ligament, or neuroendocrine tumors of the pancreas

an individual with a family history of VHL with ≥ 1 of the following:

○ retinal angioma

○ spinal or cerebellar hemangioblastoma

○ adrenal or extra-adrenal pheochromocytoma retinal angioma

○ renal cell carcinoma

○ multiple renal and pancreatic cysts

The detection of tumours specific to Von Hippel-Lindau disease is important in the disease's diagnosis. In individuals with a family history of VHL disease, one hemangioblastoma, pheochromocytoma or renal cell carcinoma may be sufficient to make a diagnosis. As all the tumours associated with VHL disease can be found sporadically, at least two tumours must be identified to diagnose VHL disease in a person without a family history.

Genetic diagnosis is also useful in VHL disease diagnosis. In hereditary VHL, disease techniques such as Southern blotting and gene sequencing can be used to analyse DNA and identify mutations. These tests can be used to screen family members of those afflicted with VHL disease; de novo cases that produce genetic mosaicism are more difficult to detect because mutations are not found in the white blood cells that are used for genetic analysis.