Neurological Manifestations of Von Hippel Lindau Syndrome

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Objectives

• Understand how VHL hemangioblastoma tumors affect the function of the brain and spinal cord.
• Understand how VHL lesions in the brain and spinal cord are diagnosed.
• Understand how VHL lesions in the brain and spinal cord are treated and the associated treatment outcomes.

Overview

• VHL Hemangioblastoma Tumors
• Clinical Symptoms
• Treatment
• Outcomes

Disclosures

• None
• No conflicts of interest
Neurological Manifestations of VHL

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VHL Epidemiology

<table>
<thead>
<tr>
<th>VHL degree of incidence</th>
<th>1 in 36,000</th>
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<tr>
<td>VHL point prevalence</td>
<td>1 in 38,000</td>
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<tr>
<td>Age range of diagnosis (years)</td>
<td>Infancy to 70</td>
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<tr>
<td>Average age of diagnosis (years)</td>
<td>26-29</td>
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<tr>
<td>Average age for full penetrance of VHL</td>
<td>70</td>
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<tr>
<td>Male-female penetrance</td>
<td>1:1</td>
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<tr>
<td>De novo VHL mutations</td>
<td>20%</td>
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<tr>
<td>Familial VHL mutations</td>
<td>80%</td>
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Hemangioblastoma

- WHO Grade 1 Tumor (benign).
- Very common in patients with VHL.
- Commonly seen in Brain and Spinal Cord.
Benign Hemangioblastoma?

- The most common cause of demise in VHL patients appears to be from posterior fossa hemorrhages associated with hemangioblastoma and also renal cell carcinoma.


Hemangioblastoma Diagnosis/Screening

- MRI – excellent view of tumor and surrounding brain and spinal cord – study of choice.
- Screen brain and spinal cord
- Tumors are often nodular (solid) but they can also have a cyst.

Hemangioblastoma

- MRI showing hemangioblastoma tumors (bright) in the cerebellum, brainstem and spinal cord.

Hemangioblastoma Brain

- Most commonly seen in the cerebellum and brainstem but can also be seen in the other lobes of the brain.

- Symptoms will depend on location, tumor size, tumor bleeding, and swelling.
Neurological Manifestations of VHL

Brain Anatomy

- Most common in the cerebellum and brainstem but can be seen in the other lobes of the brain.

Brain Function

- Symptoms will depend on location, tumor size and hemorrhage

Hemangioblastoma Clinical Symptoms

- Cerebellar tumors can bleed and obstruct flow of spinal fluid – nausea, loss of coordination, vomiting, lethargy.
- Brainstem lesions can cause swallowing, breathing, visual and lethargy symptoms.
**Hemangioblastoma**

- MRI showing hemangioblastoma tumors (bright) in the cerebellum, brainstem and spinal cord.

**Hemangioblastoma Clinical Symptoms**

- Spinal lesions can cause weakness (paralysis), balanced issues with walking, sensory symptoms, bowel and bladder dysfunction.

**Hemangioblastoma Natural History**

- The vast majority of VHL hemangioblastomas will remain asymptomatic and will never require treatment.
- Close surveillance with MRI Brain and Spine is advised.


**Hemangioblastoma Treatment**

- Surgery (First Option especially with onset of symptoms)
- Radiation Therapy
Hemangioblastoma
Surgical Treatment

- Symptomatic lesions

- Asymptomatic lesions (controversial)
Radiotherapy

- 186 Pts with 517 lesion.
- Overall survival rates of 94% at 3 years, 90% at 5 years, and 74% at 10 years.
- Associated tumor control rates were 92% at 3 years, 89% at 5 years, and 79% at 10 years.

Kano et al J Neurosurg 2015

Radiotherapy Differential Response

- Sporadic versus VHL HB (57 Pts).
- 5- and 10-year tumor control rates of 67 and 44%, respectively, for sporadic HB
- Compared to 97 and 83%, respectively, for VHL-related HB (67).
- Besides VHL pathology, SRS was much effective for small and solid tumors compared to large and cystic tumors.

Hanakita et al Neuro Oncol 2014

Radiotherapy Spinal lesions

- Radiographic and clinical outcomes in 34 spinal tumors.
- Following SRS treatment, 94% of the tumors were either stable or regressed with local control rates at 1, 3, and 5 years being 96, 92, and 92%, respectively.
- Symptom improvement was associated with 81% of treated lesions.

Pan et al Neurosurg Focus 2017

Hemangioblastoma Outcomes

- Overall favorable with surgery and/or Radiation Therapy.
- Radiation is favorable for spinal cord tumors that are small and solid.
- Tumors with cysts are more favorable than tumors without cyst (solid tumors).

Final Thoughts

• Lesions that are symptomatic or demonstrate worrisome radiographic features warrant surgery resection if safely feasible.
• Radiosurgery remains an acceptable alternative to surgical resection.
• Excellent long-term outcomes can be expected with surgery and radiation.

References


THANK YOU VERY MUCH