Introduction

Von Hippel-Lindau Disease (VHLD) is an autosomal dominant neoplastic syndrome that results from a germline mutation in the tumoral suppressor VHL gene (Chromosome 3p25-26). VHLD incidence is about one in 36,000 live births.

Disease spectrum is characterized by the development of multiple cancers and cysts (Figure 1). A clear genotype-phenotype relation is present, allowing for a subtypes classification:

- Type 1: Retinal haemangioblastomas, CNS haemangioblastomas, renal cell carcinoma and pancreatic neoplasms and cysts.
- Type 2A: Pheochromocytomas, retinal haemangioblastomas and CNS haemangioblastomas.
- Type 2B: Pheochromocytomas, retinal haemangioblastomas, CNS haemangioblastomas, renal cell carcinoma and pancreatic neoplasms and cysts.
- Type 2C: Pheochromocytoma only

Screening is mandatory for close relatives. (Figure 1).

Case Report

A Portuguese caucasian male aged 23 years old (identified as “A”) police officer was referred to the Endocrine Inpatient Department because of recent genetic diagnosis of VHLD during family screening. His mother, the index case (“B”), and his aunt (mother’s monozigotic twin sister) identified as “C” were also diagnosed VHLD and shared the same mutation in VHL gene.

c.482QX-A (p.Arg161Gln) in the exon 3 of VHL gene in heterozygosity

Patient A

Completely asymptomatic:
- Normal arterial pressure
- No anxiety or vegetative paroxysms
- No visual disturbance
- No cardiovascular complaints
- No neurologic complaints

Unremarkable physical examination

Patient B

Previously diagnosed and treated of:
- Bilateral pheochromocytoma (Bilateral suprarenalctalyctoma)
- Retinal angiomas (Phococtogulation)
- Renal angiomas (Phococtogulation)
- Pancreatic cancer (Pacrectomy)
- Medullar angiomas under surveillance

Patient C

Previously diagnosed and treated of:
- Bilateral pheochromocytoma (Bilateral suprarenalctalyctoma)
- Retinal angiomas (Phococtogulation)
- Breast cancer (Mamctectomy)
- Medullar angiomas under surveillance

Patient D, E and F

Asymptomatic
Negative for VHL gene mutation

Complementary diagnostic tests

Adrenal CT-scan

Nodular solid lesion centered inside the right adrenal, with 25mm of height diameter, with well defined borders. This lesion hyperfixates at 60 seconds (137HHU attenuation) and has 51% calculated washout. The mass probably corresponds to a pheochromocytoma.

Solid lesion on the Li right paravertebral aspect, with 3x1.5cm. This lesion strongly but heterogeneous hyperfixates the contrast, probably corresponding to a paraganglioma.

Two millimetric nodular hypodense lesions in the left kidney’s inferior pole, probably corresponding to cortical cysts.

Creanencephalic and spinal MRI

Morphologic and sinal anomaly lateral and anterior to the spine, at the level of L3 and intersomatic adjacent spaces. This lesion is T1 hypointense and T2 hyperintense, and has cystic-necrotic areas. Sinal intensification (of solid type) after contrast bolus.

Ophthalmologic Examination

Uneventful

MBIG scintigraphy

Right adrenal hyperfixation suggestive of pheochromocytoma

Discussion and Conclusion

Ten to 20% of pheochromocytomas are familial. VHLD is one of such hereditary syndromes. The VHLD-associated pheochromocytomas present in younger patients and are often multiple or bilateral.

We describe the clinical case of a young male diagnosed VHLD during genetic screening. Although completely asymptomatic and without clinical evidence of autonomous catecholamine production, a pheochromocytoma and a paraganglioma were diagnosed on morphologic and functional images. Despite the apparent normal secretory nature of the lesions, presurgical preparation with α-blockers, exo normal saline and β-blockers was performed. The patient was submitted to right Aparenotectomy, as well as excision of the paraganglioid lesion, and anamnopathologic examination confirmed the initial suspicion of RIGHT ADRENAL Pheochromocytoma and RIGHT LUMBAR PARAGANGLIOMA. No other components of the VHL were found, namely brain, retinal, pancreatic or renal lesions.

Genetic testing allows, for the early identification of VHLD patients, after one index case. As reported, these subjects may be asymptomatic although it is more uncommon that lesions would reach such dimensions and still remain non secretory and clinically silent. Also despite the same genetic abnormality, the phenotype was different from other affected relatives, and gender may be a relevant factor. Close follow up is justified given the complex and variable presentation that may become life threatening.

Bibliography:


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