

A RARE CASE OF VON HIPPEL-LINDAU DISEASE IN A STUDENT

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Abstract

The Von Hippel-Lindau syndrome belongs to a rare diseases category and it is autosomal dominant inherited. It is caused by an alteration of the VHL gene on the short arm of chromosome 3. The incidence of this syndrome is of 1/36000 newborns. The Von Hippel-Lindau syndrome is characterized by benign or malign tumors at the level of several organs, tissues and systems in patients with a suggestive family medical history.

The presence of a retinal or cerebral hemangioblastoma can suggest a Van Hippel-Lindau syndrome

and imposes supplementary investigation for detecting the presence of tumors also in other organs. This syndrome can be detected from early childhood to young adult age.

Secondary prevention significantly increases the life expectancy for this category of patients. The present article presents the case study of a female student, 20 years old, with a positive family background for the Von Hippel-Lindau syndrome (father and brother both with a positive diagnosis), which manifested the first symptoms of the syndrome when she was 18 years old.

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INTRODUCTION

The Von Hippel-Lindau syndrome is an autosomal dominant genetic disease, caused by an alteration of the VHL gene on the short arm of chromosome 3. (3q25-26). (Image number. 1) [1].

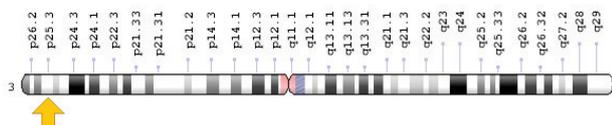


Image number 1. Mutation of the VHL gene, the short arm of chromosome 3 (3q25-26) [1]

The VHL gene (Von Hippel Lindau gene) is a tumor suppressing gene that is responsible for the controlled cellular growth and division [1].

The mutation of this gene on the short arm of chromosome 3 determines a rapid and uncontrolled cellular growth and division, leading to the appearance of tumors and cysts distinctive to the Von Hippel Lindau syndrome.

This syndrome is defined by the presence of several tumors in several tissues and organs, the most frequent ones being found in kidneys, adrenal glands, central nervous system, inner ear, eye, epididymis, pancreas, causing the appearance of renal carcinoma, pheochromocytoma, central nervous system hemangioblastoma, retinal angioma, endolymphatic sac tumors, pancreatic cysts and carcinoma.

In the specialty literature two types of VHL syndrome are described:

– type 1: renal carcinoma associated with hemangioblastoma

– type 2 with three subtypes: 2A (pheochromocytoma associated with hemangioblastoma), 2B (pheochromocytoma associated with renal carcinoma) and subtype 2C (isolated pheochromocytoma) [2].

VHL syndrome is a very rare genetic disorder, it affects men and women equally. In Great Britain it's incidence is of 1 in 36.000 newborns [3].

Hemangioblastomas are characteristic to Von Hippel-Lindau syndrome [4]. They are mainly located in the central nervous system (80% at cerebral level and 20% at spinal cord level). (Image number 3) [5,6].

Approximately 60% of cerebral hemangiomas are located at cerebellar level. (Image number 2) [7]



Image number 2. Computer tomography image in a patient with left cerebellar hemangioblastoma – transverse section [7]

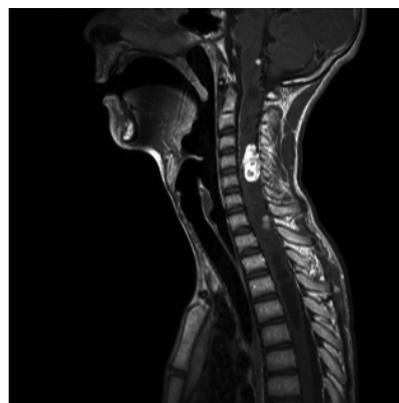


Image number 3. Computer tomography image in a patient with spinal cord hemangioma – sagittal section [7]

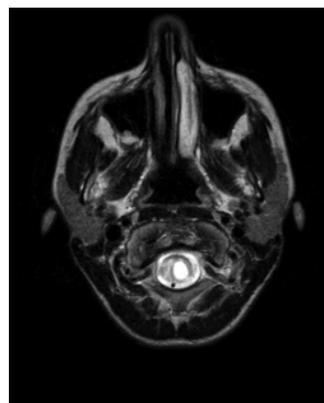


Image number 4. Computer tomography image in a patient with spinal cord hemangioma – transverse section [7]

The diagnosis of this disease can be established even early, in the asymptomatic stage, for the patients with a positive family history, using both imagistic methods (CT, MRI, abdominal ultrasonography) and

biological methods (dosage of urinary metanephrines and performing scintigraphy with metaiodobenzylguanidine if a pheochromocytoma is suspected) [8].

An ophthalmologic consult is necessary (retinal examination or fundus examination, and eventually an angiography) in order to identify retinal hemangioblastomas, seeing that 50% of patients with a mutation in the VHL gene also have retinal hemangiomas. These lesions can be observed during a simple fundus examination.

The onset is frequently during early childhood and puberty, but sometimes the first symptoms can appear even at 60-65 years.

The average age of disease onset is 26 years. Approximately 20% of children with Von Hippel-Lindau disease have the first ocular or renal symptoms before turning 10 [8].

Symptoms may vary depending on where tumors are located. Many patients are asymptomatic, but in those with a positive family history the genetic testing for the mutation of the VHL gene is mandatory.

The diagnosis criteria include the association of several major and minor lesions: retinal hemangioblastoma, cerebral hemangioblastoma (located especially at cerebellar and spinal cord level), renal carcinoma or polycystic kidney, neuroendocrine tumors of the pancreas, tumors of the endolymphatic sac [9].

If not all six lesions are present, then, for a clear diagnosis, the presence of one major lesion and a positive family history of the disease are enough.

If there is no family history of the disease, then two major lesions are needed for the diagnosis, from which one has to be the neuroblastoma [10].

For the differential diagnosis one must take into account neurofibromatosis, pheochromocytoma, tuberous sclerosis, polycystic kidney disease, retinal aneurism, cerebral tumors, pancreatic tumors, etc.

Von Hippel –Lindau disease in a student. Case presentation

In the following we will present the case of a 20-year-old student who addressed the students' medical office with the above-mentioned diagnosis in order to obtain the medical scholarship according to the scale.

From the family history we note that the father was diagnosed with von Hippel-Lindau disease at the age of 26 and died at a young age (the patient cannot remember her father's age at the time of death). The patient has a brother, aged 18, who was diagnosed with von Hippel-Lindau disease.

Personal medical history

The current illness started in adolescence with visual disturbances, dizziness, equilibrium disturbances, ocular pulsations, right supraorbital pain, parieto-occipital headache, which is why she addressed a pediatrician who, after conducting clinical and paraclinical investigations, directed the patient to a neurological and ophthalmologic consult.

Imaging investigations were recommended after the neurological specialist consultation.

Tomography examination and nuclear magnetic resonance describe two occipital localized brain tumors with imaging characteristics of hemangioblastomas. At thoraco-abdominal level, the presence of other tumors is not described.

The ophthalmologic consult measured a visual acuity of 1 (in decimal scale, without correction).

The fundus examination for the right eye is normal, but in the left eye it identifies the afferent and efferent vessel of a superotemporal angioma, with a diameter of 2DP and without bleeding or exudative elements. The ophthalmologist's recommendation is laser therapy for the retinal angioma.

Following the specialty examinations and considering the positive family history the final diagnosis was that of the von Hippel-Lindau disease. (criteria used: positive family history of the disease and the presence of at least one major lesion).

Approximately one year ago, the patient's condition worsened, exhibiting intracranial hypertension (vomiting not preceded by nausea, major headache); the patient was admitted in the neurosurgical unit where the right occipital tumor was extirpated; the postoperative progression was favorable, the student re-adapting quickly to the university environment, successfully passing all exams. The patient did not request physical education exemption, wishing to participate in sports classes.

The particularity of the case

The presence of a very rare disease in a student who addressed the students' medical office with the above-mentioned diagnosis in order to obtain the medical scholarship contributes to the particularity of the case by being the only pathology of this kind in the special records of our office and the only case encountered so far in my professional experience.

The von Hippel-Lindau disease was quickly diagnosed with regards to the important family history (diagnosed and deceased father, a diagnosed brother), leading to successful, on time therapeutic intervention and periodic monitoring of the patient for secondary prevention.

The social and educational reintegration has been successful, with the student having good results at the exams and wanting to participate in the physical education classes.

The prognosis of the disease in this case is favorable given the early diagnosis, the early intervention and the secondary prevention.

The life expectancy of patients diagnosed with the von Hippel-Lindau disease increased, the primary and secondary prevention and the genetic testing increasing the survival chances of these patients, approaching those of the general population. (10).

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