

CASE REPORT

Isolate vertigo crisis revealing an endolymphatic sac tumor

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Abstract

Endolymphatic sac tumors are rare entities that have a destructive potential on the temporal bone. They are aggressive tumors presenting as low-grade papillary adenocarcinoma, but there are no reports of metastasis in the literature. The Von Hippel–Lindau disease is a hereditary condition caused by germinal mutations of the tumor-suppressor VHL-gene. We present the case of an endolymphatic sac tumor associated with the Von Hippel–Lindau disease at a 46-year-old patient revealed by an isolate vertigo crisis, discussing the management of the tumor and the clinical, imaging, genetic and histopathologic features of it. Conclusions: Endolymphatic sac tumors have recently been described as part of the Von Hippel–Lindau disease, a genetic disorder involving the development of hypervascular tumors. The treatment depends on the size of the tumor, however surgical approach is the most successful choice and can be associated or not with radiotherapy.

Keywords: endolymphatic sac, tumor, Von Hippel–Lindau.

□ Introduction

Endolymphatic sac tumors (ELSTs) are very rare non-metastasizing neuroectodermal tumors arising from the proximal, intrapetrosus portion of the endolymphatic sac, invading the dura mater and the petrous bone.

The first report concerning the ELSTs was in 1984, when Hassard AD *et al.* [1] described it as an “aggressive middle ear tumor”, but it is in 1989 that Heffner DK [2] characterized ELSTs as a tumor deriving from the endolymphatic sac epithelium of the internal ear, referring to it as a “low-grade adenocarcinoma of the endolymphatic sac”.

The Von Hippel–Lindau (VHL) disease is an autosomal dominant genetic condition due to a mutation in the VHL-tumor suppressor gene, generally revealed between 18 and 30-year-old, with an incidence of about 1 to 36 000 newborns [3]. This condition’s manifestations include the development of highly vascularized benign and malignant tumors such as central nervous system and retinal hemangioblastomas, renal cysts and renal carcinoma, pheochromocytoma, pancreatic cysts, pancreatic endocrine tumors and the ELSTs (in about 11% of cases [4]).

We present a patient diagnosed with VHL disease whom we discovered an ELST, describing clinical, imaging, genetic, histopathologic and treatment features.

□ Patient, Methods and Results

We present the case of a 46-year-old woman known to have the VHL-disease for 16 years. Her medical history revealed that she had undergone in the past five surgical procedures for cerebellar hemangioblastomas

and renal cystic tumors, as well as numerous photocoagulation sessions for retinal hemangioblastomas. Genetic testing revealed a missense germline mutation in exon 3 of the VHL gene, but the genetic testing performed in the patient’s son did not find the familial mutation.

The patient presented in August 2008 at the Emergency Department of Lariboisière Hospital with acute vertigo crisis lasting for a few hours, with no tinnitus or hearing loss. The neurological examination was normal.

The CT-scan performed showed a small lytic lesion at the level of the posterior face of the right petrous bone (Figure 1) that appeared hyperintense on MRI (Figure 2).



Figure 1 – Axial CT-scan showing a small lytic lesion (arrow) at the level of the posterior face of the right petrous bone regarding the endolymphatic sac.

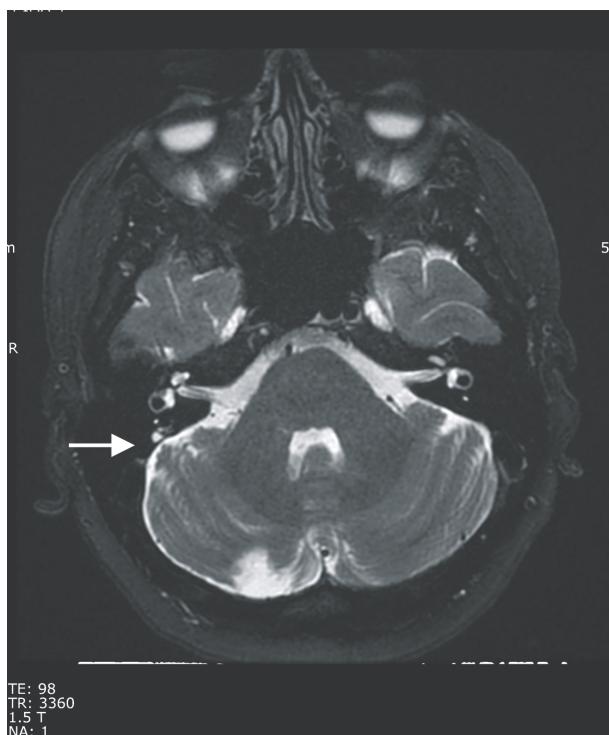


Figure 2 – Axial T1-weighted MRI showing a small heterogeneous, hyperintense lesion (flash) of the right petrous bone.

Surgical intervention consisted in complete removal of the tumor along with the adjacent dura using a retro-labyrinthine approach. The tumor had a hypervascular pattern and a piece of temporalis fascia was used to close the posterior fossa.

Histopathological examination showed a papillary pattern with vacuolated cells, these structures resembling to thyroid follicles (Figure 3), so the diagnosis of low-grade papillary adenocarcinoma of the endolymphatic sac was problematic. Immunohistochemistry examination of the surgical specimen showed strong reactivity for cytokeratin.

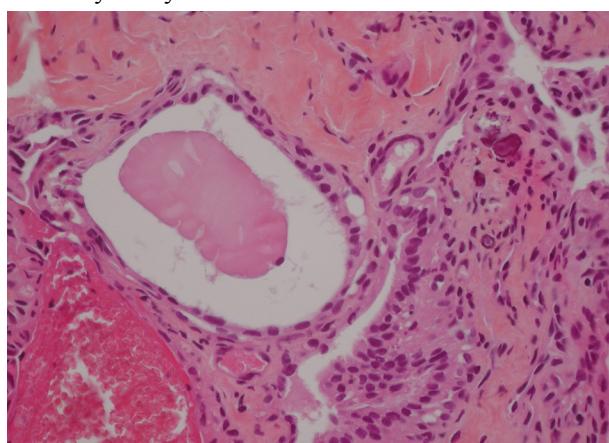


Figure 3 – Histopathology showing a papillary pattern with clear, vacuolated cells forming a structure resembling a thyroid follicle containing PAS-positive colloid.

Audiologic examination six months later was normal.

The patient is currently followed-up for the VHL-disease using regular imaging and physical examination, including ophthalmologic exam.

Discussion

The endolymphatic sac is situated between the petrous periosteum and the dura mater of the posterior cranial fossa, posterior to the internal auditory canal. That is why there are several extension possibilities: lateral, medial or both ways. The lateral extension is in fact through the mastoid into the middle or external ear, while the medial extension is towards the cerebellopontine angle and the jugular foramen.

Bambakidis NC *et al.* [5] suggested a grading system based on the extension of the tumor: grade 1 – tumor limited to the petrous bone, external auditory canal and/or middle ear; grade 2 – extension to the posterior cranial fossa; grade 3 – extension to the posterior cranial fossa and the middle cranial fossa; grade 4 – extension to the clivus and/or sphenoid wings. According to this classification, our case was classified as a grade 1 tumor.

The symptoms in case of ELSTs depend on the tumoral volume and the direction of growth.

The most common symptom is progressive sensorineural hearing loss resulting from the tumor invasion of the endolymphatic sac and the subsequent endolymphatic hydrops. The interesting fact about our presented case was the discovery of the tumor after an acute vertigo crisis mimicking a Ménière's crisis, at a patient with diagnosed VHL-disease, without any hearing loss or other otological signs.

The other symptoms that can be encountered at a patient presenting with an ELST are: otalgia, otorrhea, facial palsy, tinnitus and rarely jugular foramen syndrome [2, 6].

CT-scan usually shows bony erosion of the posterior face of the petrous bone, and the lesion appears heterogeneous or hyperintense on MRI, which was the case of our patient.

Thus, the differential diagnosis of these rare tumors includes tympano-jugular paraganglioma, the pseudotumors of the petrous bone, meningioma, thyroid and renal cancer metastasis.

Histopathology examination typically reveals a papillary architecture and a highly vascularized stroma containing many cystic spaces with PAS-positive colloid. The papillary epithelium is often lined by cuboidal cells with minimal pleomorphism. In our case, the diagnosis of low-grade adenocarcinoma of the endolymphatic sac was difficult because of the histological aspect of the specimen that resembled a thyroid metastasis, but the clinical context of the VHL-disease pleaded in favor of an ELST.

The VHL-disease is a genetic disorder in which the mutation of the VHL-tumor suppressor gene leads to the main manifestations of the disease represented by highly vascularized tumors. Two forms of VHL-disease are described, according to the presence (type 2) or the absence (type 1) of pheochromocytoma.

During the last years, the genetic progress allowed the characterization of the VHL-gene that plays an important role in angiogenesis. This gene has been mapped to the short arm of the chromosome 3 (3p25–26) and is

made up of three exons coding a protein of 213 amino acids (pVHL) found in all tissues. In fact, the pVHL is part of a protein complex taking part in the process of protein degradation. This complex induces the expression of HIF (Hypoxia Inducing Factor) that activates more than 40 genes implicated in the process of angiogenesis.

In case of hypoxia or mutation of the VHL-gene, the HIF accelerates the induction of the VEGF (Vascular Endothelial Growth Factor) and subsequently the angiogenesis, explaining the hypervasculature pattern of the tumors associated with the VHL-disease (the ELST included).

Kawahara N *et al.* [7] recently demonstrated that the inactivation of the VHL-gene is implicated in the development of ELSTs.

Under these circumstances, genetic testing the patient and his/her relatives proves to be very important in the diagnosis of the VHL-disease in the case of patients presenting an ELST or reassuring the members of the family in case of sporadic tumors and thus the necessity of performing or not a regular follow-up.

Regarding the management of the tumor, complete surgical removal represents the main and the most successful treatment option. In our case, the complete removal of the tumor was possible because of the small size of the mass that did not need preoperative embolization. Other treatment options such as gamma- or cyber-knife need to be evaluated on larger series.

Conclusions

Endolymphatic sac tumors are recently described entities that are why their management and the role of

genetic testing are not standardized. These tumors must be taken into consideration for differential diagnosis of cerebellopontine angle tumors. Their frequent association with the VHL disease makes the genetic testing and the regular follow-up crucial for the early discovery of any recurrence or new manifestation of the disease.

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