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Case Report

A Bilateral Vestibular Schwannoma is Not Always Related to Neurofibromatosis Type 2

Andi Abeshi, Gian Gaetano Ferri

[1]Department of Medical and Surgical Sciences (DIMEC), Otolaryngology and Audiology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy

ORCID iDs of the authors: A.A. 0000-0001-7110-9503, G.G.F. 0000-0001-5421-2410.

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Bilateral vestibular schwannomas are commonly diagnosed in patients affected by neurofibromatosis type 2, a genetic disease caused by a heterozygous mutation in the gene region encoding neurofibromin-2. Sporadic bilateral vestibular schwannomas are very rare entities affecting almost exclusively elderly people.

We present the case of a senior woman who was followed up with the "wait-and-scan" strategy for a unilateral vestibular schwannoma that later developed as a contralateral tumor, compatible with vestibular schwannoma, raising questions about its nature and risk of having been transmitted in offspring. Genetic testing excluded mutations of the neurofibromatosis type 2 gene.

The presence of bilateral vestibular schwannomas is often considered pathognomonic of neurofibromatosis type 2, but the estimated probability of sporadic bilateral tumors in the absence of other neurofibromatosis type 2 features is 50% over 70 years of age. Therefore, the NF2 gene assessment is in any case recommended in these patients not only for an evaluation of the risk of being transmitted. The treatment strategy should be carefully personalized for each patient, considering the size of the tumors, symptoms, and hearing function together with the patient's age.

KEYWORDS: Vestibular schwannoma, magnetic resonance imaging, neurofibromatosis 2.

INTRODUCTION

Vestibular schwannomas (VS) are benign nerve sheath tumors of the eighth cranial nerve affecting 1/500 people annually.[1] Bilateral VS (BVS) mainly occurs in patients affected by neurofibromatosis type 2 (NF2), caused by heterozygous mutation in the gene region encoding neurofibromin-2, with an estimated incidence of 1 in 25-33 000 live births.[2] Whereas in sporadic cases, the genetic mechanism of tumorigenesis is explained by the occurrence of 2 events of biallelic loss within chromosome 22 of the same nerve sheath cell. The probability of these events to take place bilaterally, as in a sporadic BVS scenario, is extremely rare (estimated at about 1 in 2 million).[2] Sporadic BVS have been reported in literature as entities affecting almost exclusively elderly people.[3,4]

We present the case of a senior woman who was followed up with the "wait-and-scan" strategy for a unilateral VS in the only ear with serviceable hearing, which later developed as a contralateral tumor, compatible with VS at magnetic resonance imaging (MRI), raising questions about its nature and risk of having been transmitted in offspring. Our institution does not require Institutional Review Board approval for single case reports, and despite this, the authors received consent and permission from the patient to report the description and figure presentation of her case.

CASE PRESENTATION

A 76-year-old woman presented at our tertiary center for an episode of vertigo associated with a left moderate sensorineural hearing loss. Magnetic resonance imaging revealed a 4.7 × 3 mm intracanalicular VS of the left superior branch of the vestibular nerve (Figure 1). Due to the size of the tumor, the age of the patient, and the presence of a dated right profound hearing loss caused by an episode of sudden sensorineural hearing loss, the "wait-and-scan" strategy was adopted.

No substantial growth of the tumor was observed in the following 3 years of follow-up. After 4 years, the MRI also revealed a contralateral 2.6 × 2.3 mm intracanalicular tumor, compatible with an inferior branch VS (Figure 2).

Corresponding author: Gian Gaetano Ferri, e-mail: giangaetano.ferri@unibo.it

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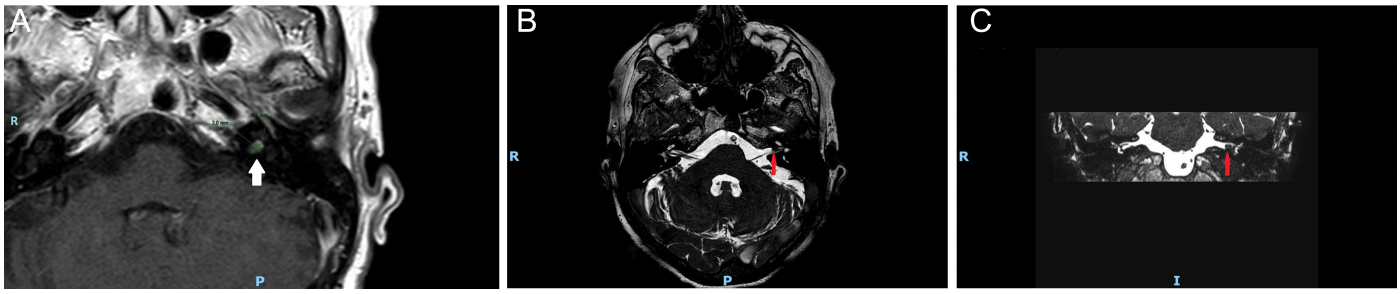

Figure 1. T1- and T2-weighted MRI showing (red yellow in T2 images) a left intracanalicular VS. (A) axial T1; (B) axial T2; (C) coronal T2. MRI, magnetic resonance imaging; VS, vestibular schwannomas.

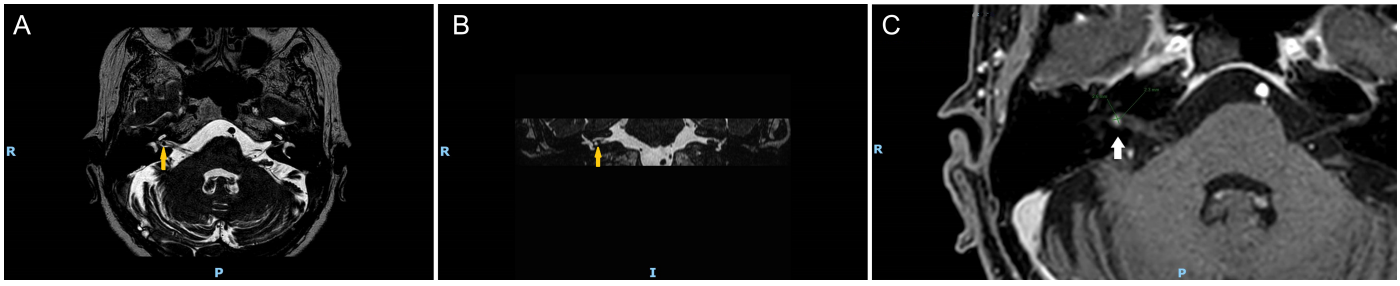

Figure 2. T1- and T2-weighted MRI with the yellow arrow (T2 images) pointing to the recently appeared right intracanalicular VS. (A) axial T2; (B) coronal T2; (C) axial T1. MRI, magnetic resonance imaging; VS, vestibular schwannomas.

The origin of the tumor was established by neuroimaging and Vestibular Evoked Myogenic Potentials (VEMPs) integration. The absence of oVEMPs and indicative MRI images suggested a left superior branch VS. For the right lesion, the radiologic images were not as suggestive as for the left side. The absence of cVEMPs in the ipsilateral ear suggested a right inferior branch VS. Video Head Impulse Test (V-HIT) and caloric tests were not performed in this case.

Genetic counseling was performed and the examination of NF2 gene *locus* for mutations or polymorphisms was required. The extracted DNA from peripheral blood was analyzed by next-generation sequencing on an Illumina MiSeq sequencer (Illumina, San Diego, Calif, USA).

The *locus* of the *SMARCB1* gene 22q11.23 was also investigated, the mutations of which are associated with Schwannomatosis *SMARCB1* related, also known as type 3 neurofibromatosis.

The results were negative for known mutation or polymorphisms. The patient had no other features of NF2 with no evidence of ocular, cutaneous, or other central nervous system involvement and no history of radiation exposure.

At the last, fifth-year follow-up, the right VS slightly grew (from 2.6 × 2.3 to 3.6 × 4 mm) while the left one showed no significant variations (Figure 3). Hearing function did not change in the only hearing ear.

DISCUSSION

The increased availability and technologic improvement of MRI explain the increasing incidence of VS in the last decade.[1] Traditionally the presence of BVS was considered pathognomonic of NF2 until the revision of the Manchester criteria for the diagnosis of NF2, also considering the age at presentation.[3]

NF2 gene is located on *locus* 22q12.2. Both single nucleotide mutations (70%) and gene rearrangements (30%) have been described. More than 50% of patients have de novo mutations, a third of which are mosaicisms. Nonsense or frameshift mutations which transcripts truncated protein structures generally have a more severe clinical presentation (earlier presentation and more aggressive tumors).[5]

Although rare, atypical forms of NF2 with low growth potential of tumors and negative germline mutation can be diagnosed in the elderly. These atypical forms might be explained by the occurrence of somatic mosaicism in the tumor tissue.[6] In this case, due to

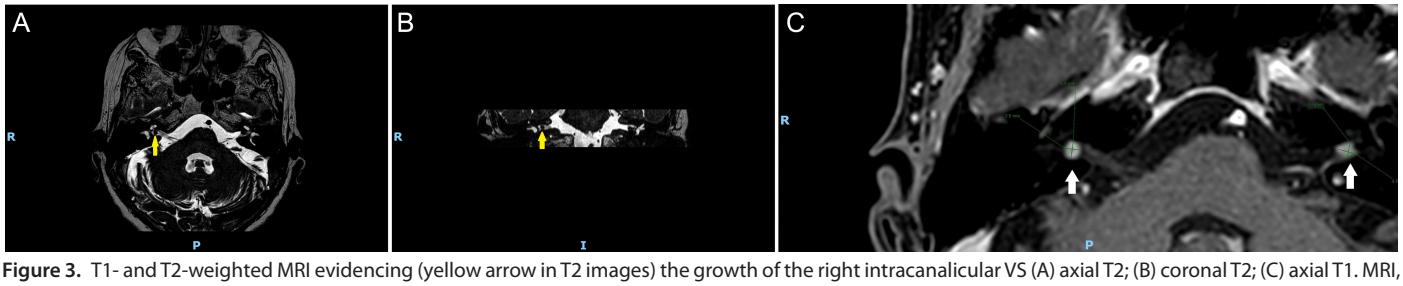

Figure 3. T1- and T2-weighted MRI evidencing (yellow arrow in T2 images) the growth of the right intracanalicular VS (A) axial T2; (B) coronal T2; (C) axial T1. MRI, magnetic resonance imaging; VS, vestibular schwannomas.

the "wait-and-scan" strategy applied, tumor material was not available to confirm this hypothesis.

Our patient, largely over 70 years old, would not meet the current NF2 criteria as neither of the tumors was diagnosed prior to 70 years of age.[3] The estimated probability of sporadic BVS in absence of other NF2 features is nearly 25% of BVS cases over 50 years and 50% over 70 years of age.[3]

The NF2 gene assessment is recommended in these patients not only for an evaluation of the risk of being transmitted but also for preventing medico-legal issues.

The management of BVS might be very challenging. If the tumor extends into the cerebellopontine angle, surgery might be a valid option for the non-hearing ear. Chemotherapy (bevacizumab) or gamma knife radiotherapy will be considered in case of tumor growth in the only hearing ear. Surgery with concomitant cochlear implantation might be a solution if the conservative treatment fails.

CONCLUSION

In elderly people, the presence of a BVS is not always related to NF2. Even in case of a unilateral vestibular schwannoma, there is a possibility that a metachronous contralateral tumor will eventually develop. If it happens, a genetic testing is strongly recommended and the treatment strategy should be carefully personalized for each patient.

Informed Consent: Informed consent was obtained from the from the patient to report the description and figure presentation of her case.

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