Bilateral spontaneous regression of vestibular schwannoma in neurofibromatosis type 2: a case report

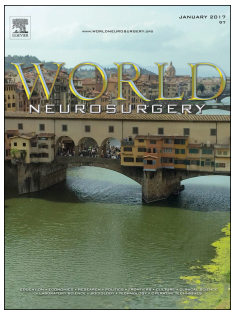
Sebök, M; van Niftrik, C H B; Bozinov, O

Abstract: BACKGROUND Patients with neurofibromatosis type 2 and bilateral vestibular schwannoma (VS) are frequently treated surgically for any tumor progression, and often repeated surgery or radiation treatment is even considered. Some VS progression occurs without the development of new clinical symptoms, or it does not progress in size over many years, even in the absence of any specific treatment. CASE DESCRIPTION We report now a 61-year-old male patient with neurofibromatosis type 2 presenting with bilateral VS. In a long-term follow-up, both had increased in size but also showed bilateral spontaneous regression during an 11-year follow-up period with a "watch and wait" strategy. CONCLUSIONS We emphasize conservative treatment ("watch and wait") in older patients even with long-term tumor progression without significant compression related clinical symptoms.

DOI: https://doi.org/10.1016/j.wneu.2018.02.075

Originally published at:
Sebök, M; van Niftrik, C H B; Bozinov, O (2018). Bilateral spontaneous regression of vestibular schwannoma in neurofibromatosis type 2: a case report. World Neurosurgery, 113:195-197.
DOI: https://doi.org/10.1016/j.wneu.2018.02.075

Accepted Manuscript



Bilateral spontaneous regression of vestibular schwannoma in neurofibromatosis type 2: a case report

M. Sebök, MD, C.H.B. van Niftrik, MD, O. Bozinov, MD

PII: S1878-8750(18)30346-2

DOI: 10.1016/j.wneu.2018.02.075

Reference: WNEU 7490

To appear in: *World Neurosurgery*

Received Date: 7 December 2017

Revised Date: 10 February 2018

Accepted Date: 12 February 2018

Please cite this article as: Sebök M, van Niftrik CHB, Bozinov O, Bilateral spontaneous regression of vestibular schwannoma in neurofibromatosis type 2: a case report, *World Neurosurgery* (2018), doi: 10.1016/j.wneu.2018.02.075.

Bilateral spontaneous regression of vestibular schwannoma in neurofibromatosis type 2: a case report

M. Sebök MD[1,2], C.H.B. van Niftrik MD[1,2], O. Bozinov MD[1,2]

Affiliations:

[1] Department of Neurosurgery, University Hospital Zurich, University of Zurich, Switzerland

[2] Clinical Neuroscience Center, University Hospital Zurich, Zurich, Switzerland

Corresponding author

Martina Sebök, MD

Department of Neurosurgery, University Hospital Zurich

Frauenklinikstrasse 10, 8091 Zurich, Switzerland

Phone: +41-44-2551111, Fax: +41-44-2554505

E-mail: martina.seboek@usz.ch

Abstract

Background:

Patients with neurofibromatosis type 2 and bilateral vestibular schwannoma (VS) are frequently treated surgically for any tumor progression, and often repeated surgery or radiation treatment is even considered. Some VS progression occurs without the development of new clinical symptoms, or it does not progress in size over many years, even in the absence of any specific treatment.

Case Description:

We report now a 61-year-old male patient with neurofibromatosis type 2 presenting with bilateral VS. In a long-term follow-up, both had increased in size but also showed bilateral spontaneous regression during an 11-year follow-up period with a "watch and wait" strategy.

Conclusions:

We emphasize conservative treatment (“watch and wait”) in older patients even with long-term tumor progression without significant compression related clinical symptoms.

Key words: conservative management, magnetic resonance imaging, neurofibromatosis type 2, spontaneous regression, tumor volume, vestibular schwannoma, “watch and wait”

Introduction

Neurofibromatosis type 2 (NF2) often occurs with unilateral or bilateral vestibular schwannomas (VS). [1] Natural history studies of VS have shown disease progression over time, although the rate of progression varies, and symptoms are not necessarily directly correlated with tumor growth. [2, 3] For instance, Mautner et al. [4] in their longitudinal study concluded that VS growth rates in NF2 tend to decrease with increasing age. Moreover, some VS progress without coinciding progressive clinical symptoms, whereas others are stable over many years, even in the absence of treatment. [3, 5-7] Particularly, approximately only 20-35 per cent of sporadic VS grow after diagnosis, although this percentage is higher in NF2. [8, 9] Therefore, the question how to manage VS is of crucial importance in the treatment of the disease. Management options include the conservative ''watch and wait'' strategy, surgery, radiation, and chemotherapy. [10] Although progressively growing tumors are frequently treated immediately, irrespective of progressive symptomology, [11] it has been questioned if every progression should be treated.[9] Especially in the older population, one can opt for a "watch and wait" strategy.

In this case report, we report on an elderly patient with the bilateral spontaneous regression of initially growing VS in NF2 during an 11-year period of a “watch and wait” strategy.

Case report

Presentation, history, and examination findings.

A 61-year-old patient with NF2 and bilateral VS, an intraventricular meningioma on the right side, three falx meningiomas, and thoracal and lumbal neurinomas (Th2, Th5 and L3) consulted our neurosurgical department for the first time in 2006. Already in the 1980s, the patient suffered from deafness on the left side. NF2 was confirmed with genetic tests without prior family history. The first presentation at our hospital was in the 1990s at the department of otorhinolaryngology with acute partial hearing loss on the right side. In 2009, an audiogram showed moderate sensorineural hearing loss on the right side. A magnetic resonance imaging (MRI) study of the brain revealed stationary bilateral VS (Figure 1). The other tumors showed no mass effect, and therefore, a surgical intervention was not foreseen. The patient was also reticent regarding any treatment. Therefore, we went for a conservative “watch and wait” strategy and planned new clinical and radiological follow-ups. In the following years, frequent cerebral imaging showed a discrete progression of right-sided VS; the radiographic result correlated with progressive hearing loss. An audiogram showed a remaining 5% speech discrimination on the right side. In the long term, the right-sided VS showed a clear progression, and the left-sided VS showed no clear growth (Figure 1). At this point, a possible intervention (surgery or radiotherapy) was discussed with the patient. The intent was to perform any kind of hearing-preserving treatment. The case was discussed in an interdisciplinary skull base conference, where the consensus was not to operate but rather to save the remaining hearing in the short term. The patient was also opposed to any kind of treatment. The follow-up MRI in 2015, two years later, showed that both VS were stable in size. At the most recent follow-up in May of 2017, however, the MRI images showed that the VS on both sides presented with spontaneous regression (on the right side: 5.8 x 8.5 mm, before: 6.4 x 11 mm; on the left side: 1.2 x 1.4 mm, before: 1.4 x 1.5 mm) (Table 1). No treatment was initiated or administered and the medication history for supplement intake of patient (pharmaceutical or herbal), in particular BIO 100, was negative.

With regard to his other intracranial mass lesions, the intraventricular meningioma and one of the falx meningioma were discretely progressive in size. The rest of the tumors was stable over the whole period. None showed signs of growth regression in any of the MR imaging.

Discussion

Many studies on the natural history of VS in past decades mostly excluded patients with NF2. [12-14]. For instance, Stangerup et al. [8] studied the natural history of non-NF2-related VS; however, no reports of tumor regression were seen over a mean observation period of 3.6 years. Selesnick and Johnson [15] included 571 cases, of which 16 involved patients who had NF2. A total of 46% of the observed tumors showed no growth during a mean observation period of three years. There was no report of tumor regression.

The mechanisms of spontaneous regression of VS are still unknown. Luetje [14] in his study hypothesized that the shrinkage of VS was due to spontaneous intratumoral vascular thrombosis and subsequent ischemic necrosis following fibrosis. A patient characteristic supporting the hypothesis is that the largest degree of tumor regression occurred in the patient presenting with the largest tumor.

According to our experience, we discuss another hypothesis, which might explain spontaneous tumor regression. A lack of quality blood vessels for sustaining the blood supply in large tumors could be the possible genesis of the shrinkage of the right-sided VS in our case, which lost approximately one-third of its volume in the past year and was previously slowly progressive, especially in a long-term follow-up.

Another important fact in the treatment decision-making is age. Mautner et al. [4] published the trend of decreasing VS growth rate with increasing age. Maniakas et al. [16] reviewed 19 articles to assess the long-term outcome of the available treatment for VS in NF2 and reported that microsurgery seems to show the worse overall results, with half of the cases losing their useful hearing as well as half showing tumor recurrence. Stereotactic radiation showed very good tumor control with poor hearing preservation. They concluded, in agreement with our case, that conservative management continues to be the most benign treatment option with satisfactory results as long as tumor stability is ensured. Similarly, the results of a hypofractionated stereotactic radiosurgery outcome study by Teo et al. [17] for large VS speak for a “watch and wait” strategy. Among 587 patients, just six had NF2, but they appeared to have higher rates of tumor progression and less favorable functional outcomes compared with sporadic VS.

This leads to an important question about the treatment of VS in patients with NF2. At which volume cut-off and by which clinical symptoms should treatment be initiated? Our patient initially showed long-

term tumor progression without new neurological deficits in past years, after which spontaneous regression set in at some point.

Especially in the older population, watch and wait strategy should be primarily considered, and we recommend surgery only in enlarging VS with compressive symptoms.

Conclusion

We report on a patient with bilateral spontaneous regression of VS in NF2 and emphasize conservative treatment ("watch and wait") in older patients even with long-term tumor progression without significant clinical symptoms.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

1. Ardern-Holmes, S., G. Fisher, and K. North, *Neurofibromatosis Type 2.* J Child Neurol, 2017. **32**(1): p. 9-22.
2. Fisher, L.M., et al., *Concordance of bilateral vestibular schwannoma growth and hearing changes in neurofibromatosis 2: neurofibromatosis 2 natural history consortium.* Otol Neurotol, 2009. **30**(6): p. 835-41.
3. O'Reilly, B., C.D. Murray, and D.M. Hadley, *The conservative management of acoustic neuroma: a review of forty-four patients with magnetic resonance imaging.* Clin Otolaryngol Allied Sci, 2000. **25**(2): p. 93-7.
4. Mautner, V.F., et al., *Vestibular schwannoma growth in patients with neurofibromatosis Type 2: a longitudinal study.* J Neurosurg, 2002. **96**(2): p. 223-8.
5. Plotkin, S.R., et al., *Hearing improvement after bevacizumab in patients with neurofibromatosis type 2.* N Engl J Med, 2009. **361**(4): p. 358-67.
6. Phi, J.H., et al., *Radiosurgical treatment of vestibular schwannomas in patients with neurofibromatosis type 2: tumor control and hearing preservation.* Cancer, 2009. **115**(2): p. 390-8.
7. Blakeley, J.O., et al., *Consensus recommendations for current treatments and accelerating clinical trials for patients with neurofibromatosis type 2.* Am J Med Genet A, 2012. **158a**(1): p. 24-41.
8. Stangerup, S.E., et al., *The natural history of vestibular schwannoma.* Otol Neurotol, 2006. **27**(4): p. 547-52.
9. Smouha, E.E., et al., *Conservative management of acoustic neuroma: a meta-analysis and proposed treatment algorithm.* Laryngoscope, 2005. **115**(3): p. 450-4.
10. Baser, M.E., et al., *Methodological issues in longitudinal studies: vestibular schwannoma growth rates in neurofibromatosis 2.* J Med Genet, 2005. **42**(12): p. 903-6.
11. Tos, M., S. Charabi, and J. Thomsen, *Clinical experience with vestibular schwannomas: epidemiology, symptomatology, diagnosis, and surgical results.* Eur Arch Otorhinolaryngol, 1998. **255**(1): p. 1-6.
12. Yoshimoto, Y., *Systematic review of the natural history of vestibular schwannoma.* J Neurosurg, 2005. **103**(1): p. 59-63.
13. Rosenberg, S.I., *Natural history of acoustic neuromas.* Laryngoscope, 2000. **110**(4): p. 497-508.
14. Luetje, C.M., *Spontaneous involution of acoustic tumors.* Am J Otol, 2000. **21**(3): p. 393-8.
15. Selesnick, S.H. and G. Johnson, *Radiologic surveillance of acoustic neuromas.* Am J Otol, 1998. **19**(6): p. 846-9.
16. Maniakas, A. and I. Saliba, *Neurofibromatosis type 2 vestibular schwannoma treatment: a review of the literature, trends, and outcomes.* Otol Neurotol, 2014. **35**(5): p. 889-94.
17. Teo, M., et al., *The Outcome of Hypofractionated Stereotactic Radiosurgery for Large Vestibular Schwannomas.* World Neurosurg, 2016. **93**: p. 398-409.

Figure Captions

Caption figure 1:

Chronologic presentation of gadolinium-enhanced MRI with a two-year interval showing initial bilateral growth of both vestibular schwannomas and interestingly, bilateral spontaneous regression in 2017 without any initiated treatment regimen. For illustrative purposes, we applied a voxel-to-voxel affine transformation to align all the acquired gadolinium-enhanced MRI using SPM 12 (Statistical Parameter Mapping Software, Wellcome Department of Imaging Neuroscience, University College of London, London, UK)

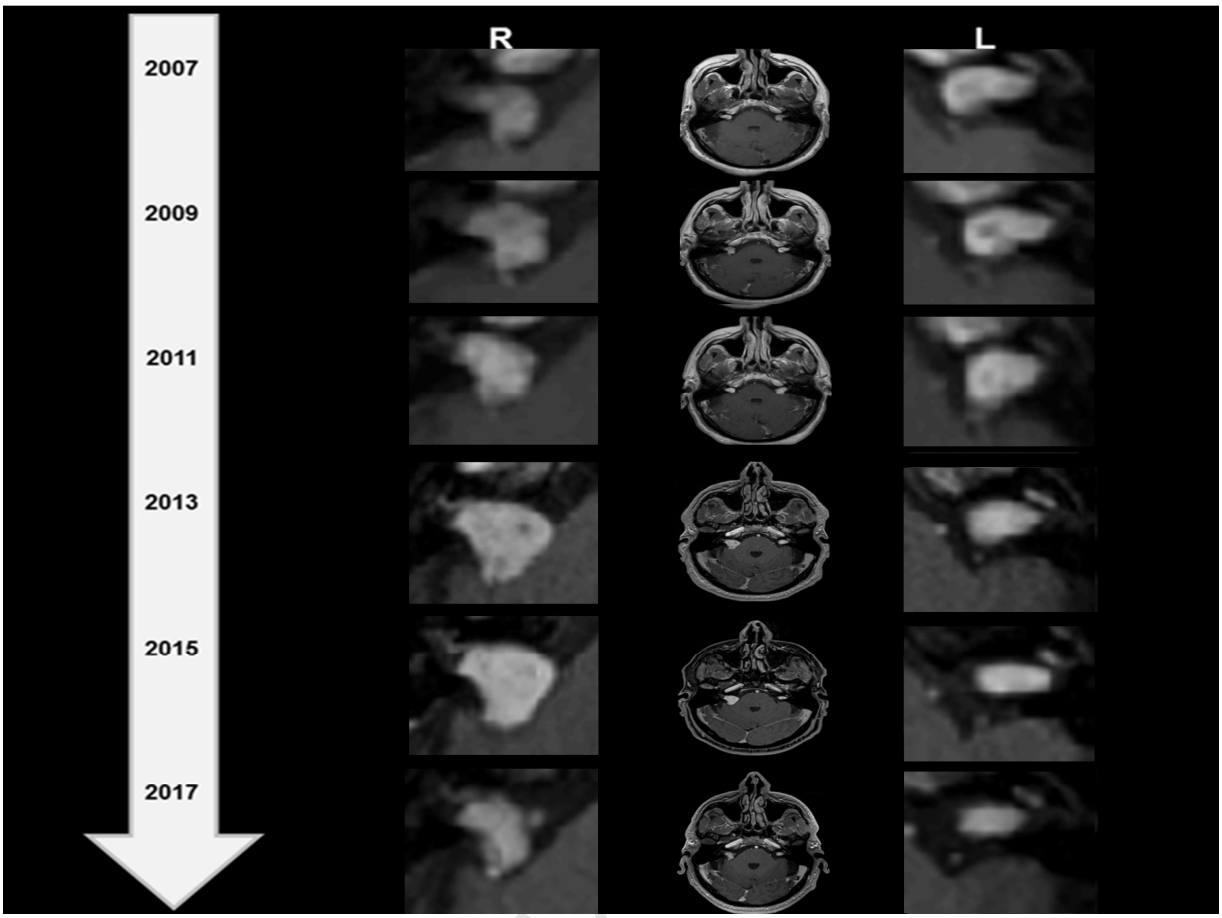
Caption figure 2:

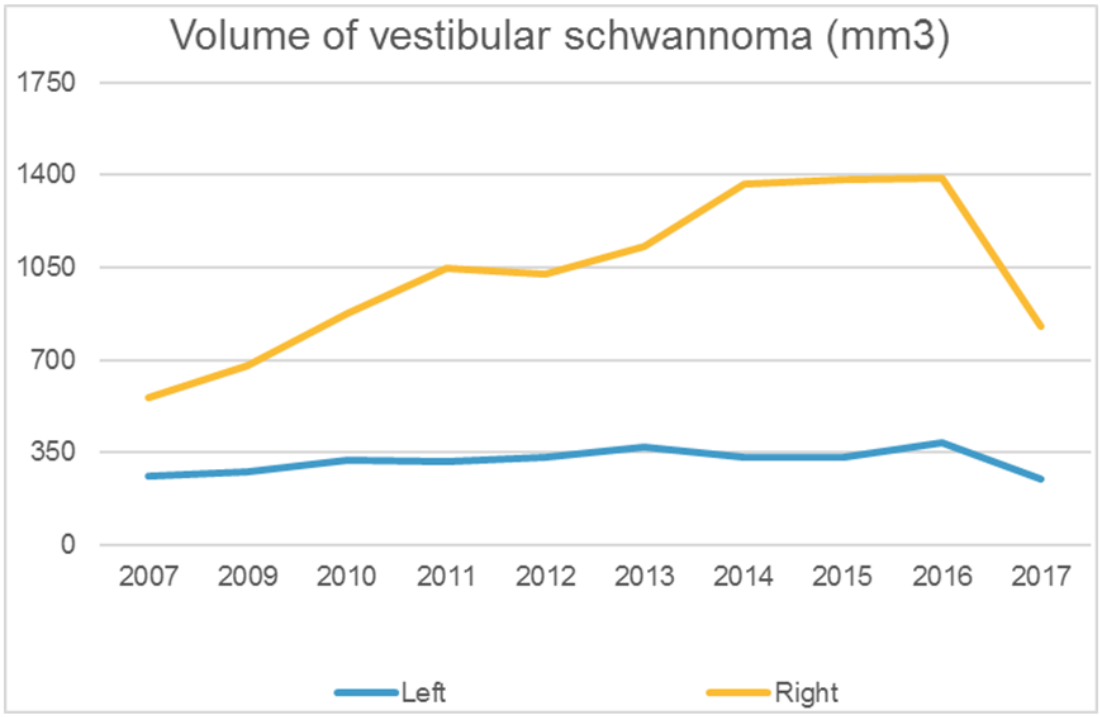
Graph showing changes in volume (mm^3) of left- and right-sided VS over the years.

Table 1. Volume (mm^3) of left and right sided vestibular schwannoma over the years

Year	Left	Right
2007	260	557
2009	278	676
2010	323	878
2011	315	1049
2012	330	1023
2013	370	1127
2014	331	1363
2015	330	1383
2016	386	1387
2017	249	827

*The volume analysis of vestibular schwannoma in gadolinium-enhanced MR images was done with iPlan 3.0 ENT from Brainlab.




Volume of vestibular schwannoma (mm3)
1750
1400
1050
700
350
0
2007
2009
2010
2011
2012
2013
2014
2015
2016
2017
Left
Right

Highlights

- Bilateral spontaneous regression of vestibular schwannoma in neurofibromatosis type 2 without any treatment and any medication history.

- In the older population, spontaneous regression should be taken into account.

- Surgery only in progressive lesions with compression-related clinical symptoms that should resolve after treatment.

Abbreviation list:

MRI – magnetic resonance imaging

NF2 – neurofibromatosis type 2

VS – vestibular schwannoma