Case Report: Contralateral Progression of a Vestibular Schwannoma After Resection in a Patient with Neurofibromatosis Type 2

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BACKGROUND AND IMPORTANCE: Bilateral vestibular schwannomas (VS) are a distinctive feature of neurofibromatosis type 2 (NF2) that result in a serious reduction in the quality of life for patients. The growth rates of these schwannomas are variable, and the early detection of increased growth is fundamental for improving outcomes.

CLINICAL PRESENTATION: A 17-year-old man with NF2 and bilateral VS presented with complete right facial paralysis and sudden right hearing loss less than 1 month after resection of a left VS. Imaging revealed rapid growth of the right VS with intratumoral hemorrhage, and the patient underwent urgent surgical resection with some improvement in symptoms.

DISCUSSION: Existing literature indicates a similar phenomenon after a longer post-operative period; however, none have shown such rapid symptomatology. Multiple etiologies were explored for this presentation, including the sudden decompression from the primary resection, paracrine factors, and hypervascularity from prior radiation.

CONCLUSION: VS resection in a patient with NF2 may be followed by rapid growth in the contralateral VS, leading to severe symptom presentation. Patients should be counseled regarding this risk to enable early detection and intervention.

KEY WORDS: Growth, Resection, Neurofibromatosis 2, Vestibular schwannoma, Case report

Neurofibromatosis type 2 (NF2) is an inherited autosomal dominant syndrome resulting from mutations in the *NF2* gene, a tumor suppressor responsible for the production of the cytoskeletal protein Merlin. Bilateral vestibular schwannomas (VS) are a distinctive feature of NF2 that develop in 90%–95% of diagnosed patients and manifest clinically as unequal hearing loss.[1] Surgical resection of these tumors is the mainstay of treatment.[2-5] However, observation is a viable option for slow-growing tumors.[2] Rarely, the contralateral tumor can undergo rapid growth over several months postoperatively.[6] We report the case of a patient with NF2 and a previously stable right VS that underwent rapid growth over several weeks after resection of the contralateral left VS.

ABBREVIATIONS: LD, longest diameter; **NF2,** neurofibromatosis type 2; **VS,** vestibular schwannomas.

CLINICAL PRESENTATION

A 17-year-old man with a history of NF2, bilateral VS with previous radiosurgery, and shunted hydrocephalus underwent surgery for a left-sided VS resection due to progressive growth and worsening brainstem compression. He had baseline bilateral facial weakness (House-Brackmann III). Postoperatively, the patient had baseline hearing preservation on the contralateral (right) side and stable facial function. On postoperative day 32, the patient presented to the emergency room with sudden-onset complete right-sided hearing loss and facial paralysis. On imaging before the left-sided VS resection, the right mass had a growth rate of 0.1 mm/year with the longest diameter (LD) 19.8 mm (0.5% increase in 11 months; Figure 1). On repeat imaging, the right mass had grown from 5.1 to 24.8 mm along the LD (25.8% increase over 1 month; Figure 2). This growth was accompanied

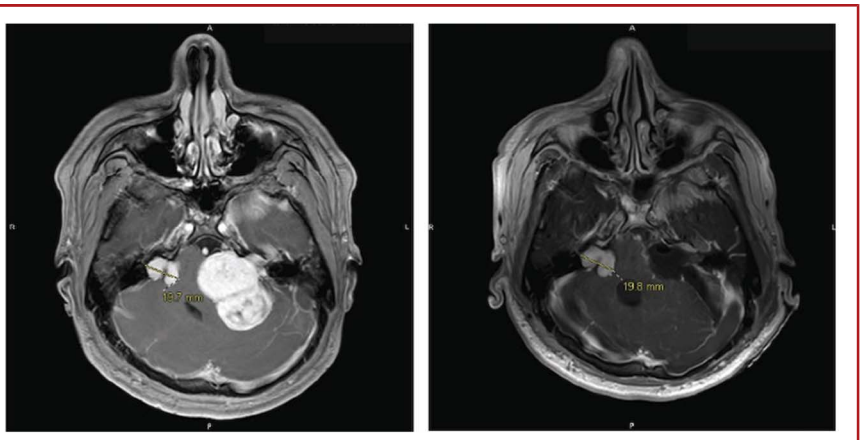

FIGURE 1. *(Left) Imaging of bilateral VS approximately 1 year before presentation, the left VS measures 19.7 mm along the LD. (Right) Postoperative imaging of right VS approximately 1 month before presentation, the right VS measures 19.8 mm along the LD. LD, longest diameter; VS, vestibular schwannomas.*

by a right-sided intratumoral hemorrhage (Figure 2). No imaging was available between postoperative day 1 and postoperative day 32. On volumetric analysis using BrainLab (BrainLab AG), the right-sided VS growth rate increased from 0.70 cm^3/year preoperatively to 11.36 cm^3/year 1 month postoperatively (2.50-3.43 cm^3; 37.2% increase; Figure 3).

After the patient provided consent for the procedure, he underwent a right retrosigmoid craniotomy for urgent resection of the tumor due to the sudden development of symptoms. During the procedure, CNVII was thin and unresponsive to stimulation. Brainstem auditory evoked potentials were absent. A gross total resection was achieved. Postoperatively, the patient continued to have complete right-sided hearing loss and House-Brackmann VI facial nerve palsy. The postoperative course was uncomplicated, and he was discharged on postoperative day 3. The pathology was consistent with schwannoma. At the 4-year follow-up, the patient continued to have complete bilateral hearing loss and right House-Brackmann VI facial nerve palsy. To date, imaging has not shown any evidence of recurrence with his other tumors staying stable.

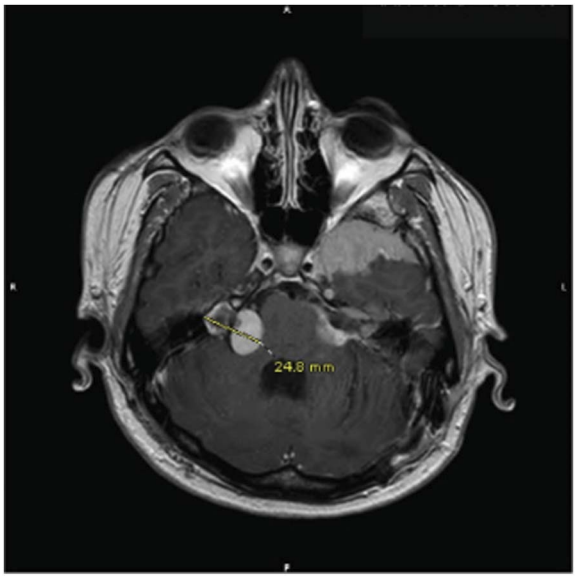

FIGURE 2. *Imaging of right vestibular schwannoma on presentation with new onset of right facial weakness and sudden right hearing loss. The right vestibular schwannomas measures 24.8 mm along the longest diameter.*

DISCUSSION

Algorithms for the management of VS in NF2 are heavily dependent on tumor size, growth rate, and patients' hearing.[7,8] Unfortunately, there is no reliable way of preserving hearing in NF2 patients; however, it is best achieved with surgery.[9] Gamma knife radiosurgery is another viable option for VS treatment because of greater control of tumor progression. However, because of the significant mass effect and prior radiosurgery, it was not pursued for this procedure.[10] This case highlights the need for further consideration of secondary factors in patients with bilateral VS, assisting in patient education about surgical complications and treatment plans.

We present a patient with acute contralateral hearing loss due to accelerated VS growth after the resection of a VS only 32 days prior. Currently, limited studies have shown that resection of a VS is associated with increased growth of the contralateral tumor.[11] Peyre et al[6] retrospectively reviewed 11 patients with NF2 and bilateral VS and found that 6/11 patients experienced increased contralateral VS growth after resection; 5/6 patients underwent resection. These patients were younger, matching the current

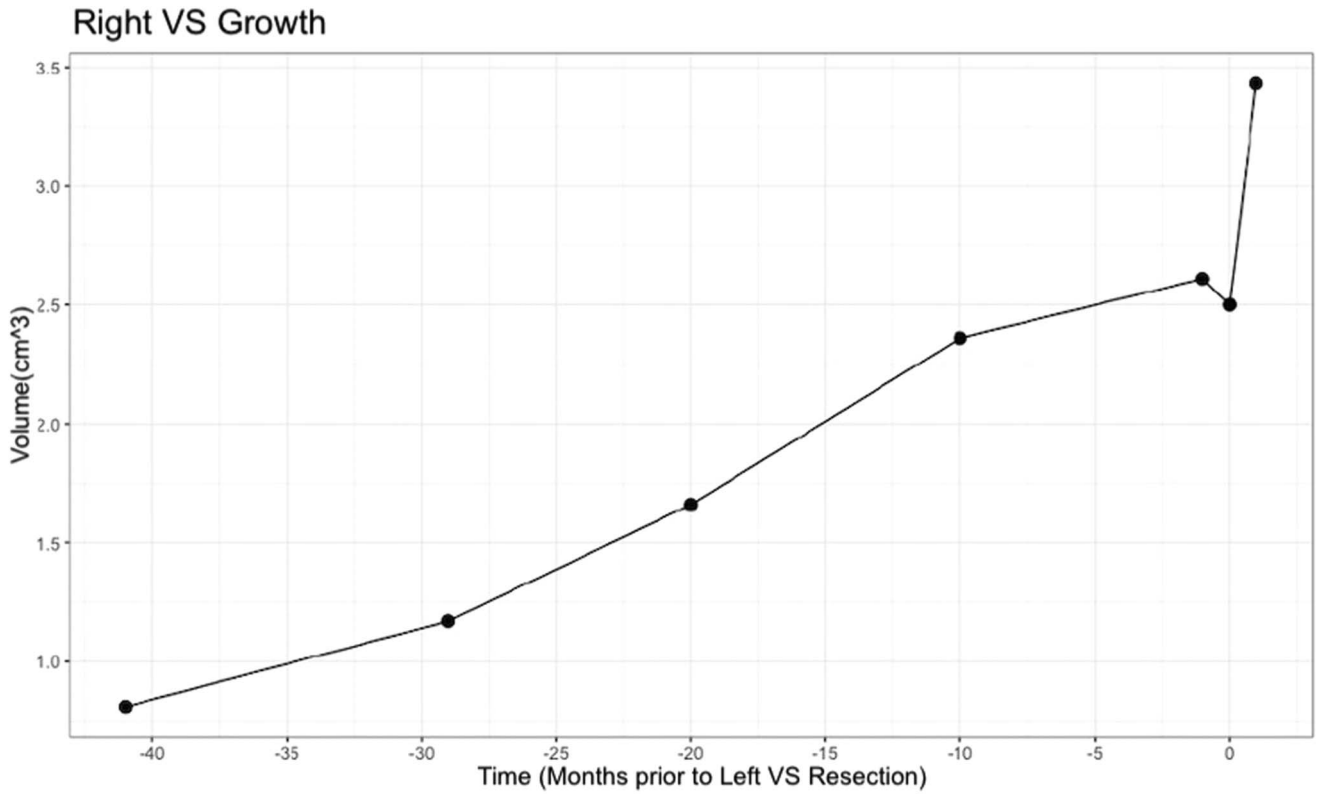

FIGURE 3. *Plot showing volumetrics of right VS, measured using BrainLab. Time is measured in months before left VS resection. VS, vestibular schwannomas.*

paradigm that VS growth rates are inversely correlated with age and associated with tumors that had significant brainstem compression preoperatively.[12] Notably, patients in the study had operations, on average, 3 years after the resection of their first VS, contrasting with this case as symptoms developed within 1 month of the surgery.

Conversely, there have been reports of a decrease in VS growth rate and regression after contralateral resection. Peyre et al[6] included 2 patients in their series who experienced a notable decrease in VS growth rate and 1 patient who experienced minimal tumor regression. Furthermore, von Eckardstein et al[13] reported 2 NF2 patients with a similar postoperative course. Both tumors demonstrated a slight increase immediately but later regressed to 23% and 15% of the original maximum volume postoperatively.

The pathophysiology of accelerated VS growth rates after contralateral resection remains unclear. One hypothesis states that—after the resection of a large tumor—a decompressive effect increases the potential space for contralateral VS growth.[6,14,15] In this case, the lack of equal pressure in the posterior fossa and the normalization of the brainstem after resection could have contributed to the right-sided VS exponential growth rate. Another hypothesized mechanism is the paracrine signaling cascade from the resected VS.[15] Pallini et al[16] presented a case study that demonstrated the involvement of growth factors, from the epidermal growth factor family, that are released from a proximal meningioma in an NF2 patient, causing an acceleration in bilateral VS growth. Unrelated to the excision of another tumor, rare cases of VS intratumoral hemorrhage have been implicated in rapid tumor growth.[17,18] The hypervascularity due to radiation from the first operation might have contributed to the hemorrhage.[18] Cassis et al[19] discuss the expression of endothelial growth factor receptor around VS postoperatively, inducing tumorigenesis. In the index case, given the small area of intratumoral hemorrhage, it is likely that a combination of intratumoral hemorrhage and paracrine and decompressive effects are behind the symptomatic exponential growth seen. In either case, further research is needed to elucidate a clear mechanism.

Limitations

Current postsurgical management algorithms for VS in NF2 recommend annual brain imaging.[20] Surgery for the contralateral tumor is not indicated based on Congress of Neurological Surgeons consensus guidelines unless it is required for hearing preservation if the VS is <1.5 cm along the LD.[21] To preserve CNVII and CNVIII function, short-interval imaging in the immediate postoperative period is needed to detect the sudden

onset of growth. Nonetheless, NF2 patients should be counseled on the potential for rapid growth of a contralateral VS in the early postoperative period. Previous work, in combination with this case, indicates that growth rates can range from weeks to months with early detection needed to maximize patient outcomes. These complications should not serve as a deterrent to surgical intervention, but rather as a caution for monitoring NF2 patients during the postoperative period. Ultimately, further clinical and biomolecular research is needed to establish which patients are most at risk of this phenomenon to optimize surveillance and the timing of surgical intervention.

As the patient is deaf and has not been seen for a recent follow-up, we are unable to elicit the patient's perspective at this time.

CONCLUSION

Bilateral VS is a defining feature of NF2 that requires regular monitoring and prompt intervention to preserve the functions of both CNVII and CNVIII. As in this case, contralateral progression of VS in NF2 after resection can occur as soon as 1 month after contralateral resection. Patients should be counseled about this rare, but morbid, phenomenon.

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