Original Article

Pediatric vestibular schwannomas: Evaluation of clinical features, treatment strategies and long-term results of 10 cases

İbrahim Başar[1], Şahin Hanalioğlu[2], Fırat Narin[3], Burçak Bilginer[4]

[1]Department of Neurosurgery, Siirt State Hospital, Siirt, Turkey
[2]Department of Neurosurgery, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Ankara, Turkey
[3]Department of Neurosurgery, Van Regional Training and Research Hospital, Van, Turkey
[4]Department of Neurosurgery, Hacettepe University School of Medicine, Ankara, Turkey

ABSTRACT

Objectives: This study aims to analyze and discuss the epidemiology, clinical-radiological features, differential diagnosis, histopathological characteristics, treatment strategies and long-term follow-up results of pediatric vestibular schwannomas (VSs) treated at a single institution.

Patients and Methods: Medical records of 10 pediatric patients (3 males, 7 females; mean age 14.9±2.3 years; range 11 to 18 years) who were operated for VSs in our department between January 2000 and December 2017 were retrospectively reviewed. The prognostic variables were age, gender, neurological examination at the time of application, radiologic findings, localization, associated factors, amount of resection (total [100%], near total [90-100%] or subtotal [<90%] resection), histopathological grading and adjuvant treatment.

Results: Two patients had neurofibromatosis type 2 (NF2), while others were sporadic cases. Mean age at diagnosis was 14.9±2.3 years. Major presenting symptoms and signs were hearing loss, tinnitus, headache, imbalance, hemiparesis and facial numbness. Patients had an average of 2.5±1.0 years of symptom duration. In eight of 10 patients, total or near-total tumor resection was achieved. Although the facial nerve was anatomically preserved in all patients, early facial dysfunction occurred in 60%. At the end of an average follow-up of 9.4±5.0 years, 80% of patients had normal or acceptable facial nerve function (House-Brackmann grade I or II), whereas two patients had permanent facial paralysis (House-Brackmann grade V or VI). Tumor progression and recurrence were observed in two patients.

Conclusion: Pediatric VSs are rare tumors commonly associated with NF2. Expected long-term survival necessitates effective treatment. Microsurgery is a powerful strategy with possibility of total tumor removal and minimal morbidity rates. Radiosurgery can be used particularly in residual or recurrent tumors or those not exceeding 2-3 cm, although long-term results are not well known in children.

Keywords: Cerebellopontine angle; microsurgery; pediatric; schwannoma; tumor; vestibular.

Vestibular schwannomas (VSs) originate from the neuroglia-Schwann cell junction in the vestibular branch of the eighth cranial nerve (CN) or from the distal sheath Schwann cells at a point close to this junction.[1-5] Schwannomas in the neuroaxis are rare.[6,7] Incidence of this tumors is fairly rare (13 cases in one million persons per year) and increases between fourth and sixth

Received: April 28, 2018 **Accepted:** July 13, 2018

Correspondence: Şahin Hanalioğlu, MD, PhD. SBÜ, Dışkapı Yıldırım Beyazıt Eğitim ve Araştırma Hastanesi, Beyin ve Sinir Cerrahisi Kliniği, 06110 Altındağ, Ankara, Turkey. **e-mail:** sahinhanalioglu@gmail.com

Doi: http://dx.doi.org/10.5606/Tr-ENT.2018.57966

Citation:
Başar İ, Hanalioğlu Ş, Narin F, Bilginer B. Pediatric vestibular schwannomas: Evaluation of clinical features, treatment strategies and long-term results of 10 cases. Tr-ENT 2018;28(3):116-125.

decades.[1,2] Vestibular schwannomas constitute 8% of all primary intracranial tumors, 30% of posterior fossa tumors and the most common cause (85%) of pontocerebellar angle tumors.[8,9] The incidence in childhood is considerably lower than in adult population.[1,2] For this reason, the differential diagnosis is not well characterized in children. Neurofibromatosis type 2 (NF2) association is common in schwannomas, which account for approximately 2% of posterior fossa tumors in the pediatric population.[10] Treatment planning criteria pertinent to adults may not always be adequate for the pediatric group. Features such as tumor localization, size, presentation and relationship with risk factor should be evaluated individually for each patient to select the most appropriate treatment strategy.

Schwannomas are well-restricted, encapsulated mass lesions with soft or firm consistency, histologically benign characteristics without malignant degeneration and have a low growth rate (1-10 mm/year). These tumors often present with problems related to hearing. Diagnosis of patients who are admitted with a slowly progressing clinical picture might be delayed for as long as 3.5-4 years after the onset of complaints.[11] Female sex is more commonly affected and gestation has been shown to induce tumor growth which is thought to be associated with estrogen receptors 2.[12]

Therefore, in this study, we aimed to analyze and discuss the epidemiology, clinical-radiological features, differential diagnosis, histopathological characteristics, treatment strategies and long-term follow-up results of pediatric VSs treated at a single institution.

PATIENTS AND METHODS

Patient charts and electronic health records of 10 VS patients (3 males, 7 females; mean age 14.9±2.3 years; range 11 to 18 years) who were surgically treated at Hacettepe University Department of Neurosurgery between January 2000 and December 2017 were reviewed retrospectively. Patients without surgical management were excluded regardless of tumor size. The latest clinical information of some patients was accessed via outpatient clinic visits or telephone interview. The study protocol was approved by the Hacettepe University Ethics Committee. A written informed consent was obtained from patients, their parents or legal guardians. The study was conducted in accordance with the principles of the Declaration of Helsinki.

The prognostic variables were age, gender, neurological examination at the time of application, radiologic findings, localization, associated factors (NF2), amount of resection (total (100%), near total (90-100%) or subtotal (<90%) resection), histopathological grading and adjuvant treatment. Tumor regrowth after total or near-total resection was regarded as "recurrence" and enlargement of the tumor volume after partial or subtotal excision was described as "residual progression". Histopathological subtypes were classified according to World Health Organization (WHO) Central Nervous System Tumor Classification criteria valid at the time of diagnosis. Facial functions were assessed using the House-Brackmann scale. All patients who underwent pre- and postoperative magnetic resonance imaging (MRI) were followed for as long as 10 years.

Statistical analysis

Parametric data with normal distribution were presented as mean ± standard deviation, non-normal distribution parametric data and nonparametric data as median (range) or percentage. IBM SPSS version 22.0 (IBM Corp., Armonk, NY, USA) program was used for statistical analysis. A p value <0.05 was considered to be statistically significant.

RESULTS

Demographic, clinical, radiological characteristics, surgical and follow-up results of patients were presented in Table 1. Ratio of females to males was 2.3. In our clinic, nearly 600 children underwent surgery for posterior fossa tumors during the same period and only 10 of them (1.7%) were VS. The proportion of VSs within pontocerebellar angle tumors was found to be 40%. Presence of NF2 was genetically established in two patients with bilateral VSs.

Symptom durations before diagnosis ranged between six months and 3.5 years (mean 2.5±1.0 years). The most common presenting symptoms, in decreasing frequency, were hearing loss,

Table 1. Demographic, clinical, radiological characteristics, surgical and follow-up results of pediatric patients with vestibular schwannomas

No	Age/Gender	Symptoms and signs	NF2	Side	Tumor size (largest diameter) (cm)	Extent of resection	Postoperative /follow-up examination	Follow-up duration (year)	Follow–up information
1	15/F	Hearing loss, tinnitus, facial paralysis, facial hemihypoesthesia, imbalance, contralateral mild hemiparesis	No	Right	6.3	Subtotal	Permanent facial paralysis, trigeminal hypoesthesia	15.7	residual tumor progression →radiosurgery
2	12/F	Hearing loss, tinnitus, headache	No	Left	4.8	Near total	Temporary facial paralysis	11.8	No progression or recurrence
3	17/F	Facial numbness, hearing loss	No	Right	3.5	Total	Temporary facial paralysis, CSF fistula	18	No progression or recurrence
4	13/M	Headache, tinnitus, imbalance	Yes	Bilateral (right)	3.3	Near total	Ataxia	9.5	No recurrence on the same side, minimal progression on the contralateral side
5	16/M	Hearing loss, tinnitus, mild facial paralysis, imbalance	No	Right	4.2	Total	Persistent facial paralysis	6.8	Recurrence →radiosurgery
6	14/M	Headache, nausea, imbalance, hearing loss	No	Left	3.8	Total	Temporary facial paralysis	5.2	No progression or recurrence
7	17/F	Hearing loss, tinnitus, facial hemihypoesthesia	Yes	Bilateral (left)	4.1	Near total	Normal except hearing loss	3.9	No progression or recurrence
8	11/F	Hearing loss, tinnitus, headache	No	Left	2.5	Total	Normal except hearing loss	13.3	No progression or recurrence
9	18/F	Hearing loss, tinnitus, facial hemihypoesthesia, contralateral hemiparesis	No	Right	5.0	Near total	Temporary facial paralysis	5.5	No progression or recurrence
10	16/F	Hearing loss, swallowing difficulty, dysphonia, earache	No	Left	3.7	Subtotal	Unilateral lower cranial nerve findings	4.7	No progression or recurrence

NF2: Neurofibromatosis type 2; CSF: Cerebrospinal fluid.

tinnitus, headache, imbalance, and motor weakness (contralateral hemiparesis due to brainstem compression), facial numbness and weakness (subjective or objective). Two patients had mild facial weakness at presentation. None except one of the patients had serviceable hearing on lesion side preoperatively (serviceable hearing was defined as pure tone average less than 50 dB and speech discrimination greater than 50%). Five patients (50%) had gait disturbance or imbalance. Hypoesthesia and paresthesia were recorded in four patients (40%) at the distribution of the trigeminal nerve. Nausea and vomiting were detected in only one patient, and one patient had swallowing difficulty and dysphonia indicating lower CN involvement. When examined in terms of other neurological findings, papilledema, nystagmus, abducens (lateral gaze) palsy and cerebellar ataxia were detected in three patients. Mean (maximal) diameter of the excised tumors

was 4.1±1.1 cm, and the largest tumor was measured as 6.3x4.2x3.9 cm. Six of the eight sporadic tumors were greater than 4 cm. The patient with the largest tumor size was referred to our center with signs of hydrocephalus. NF2-associated two schwannoma cases were smaller in size than the sporadic cases.

A team of pediatric neurosurgeons, a neurootologist, pediatric neurologists, neuroanesthetists, neuro-oncologists and radiation oncologists decided on the treatment plan for patients with pediatric VSs with a multidisciplinary approach. Magnetic resonance images of patients were carefully evaluated in order to plan the surgical approach preoperatively. Total or near-total excision of tumor could be achieved in eight patients (80%) with microsurgical techniques via a suboccipital retrosigmoid approach in the sitting position (Figure 1). The facial nerve could be anatomically preserved in all cases. Operative duration varied between four-seven hours (mean 5.4±2.0 hours).

Histopathological evaluation was performed according to the WHO criteria at the time of diagnosis and the pathology results of all patients

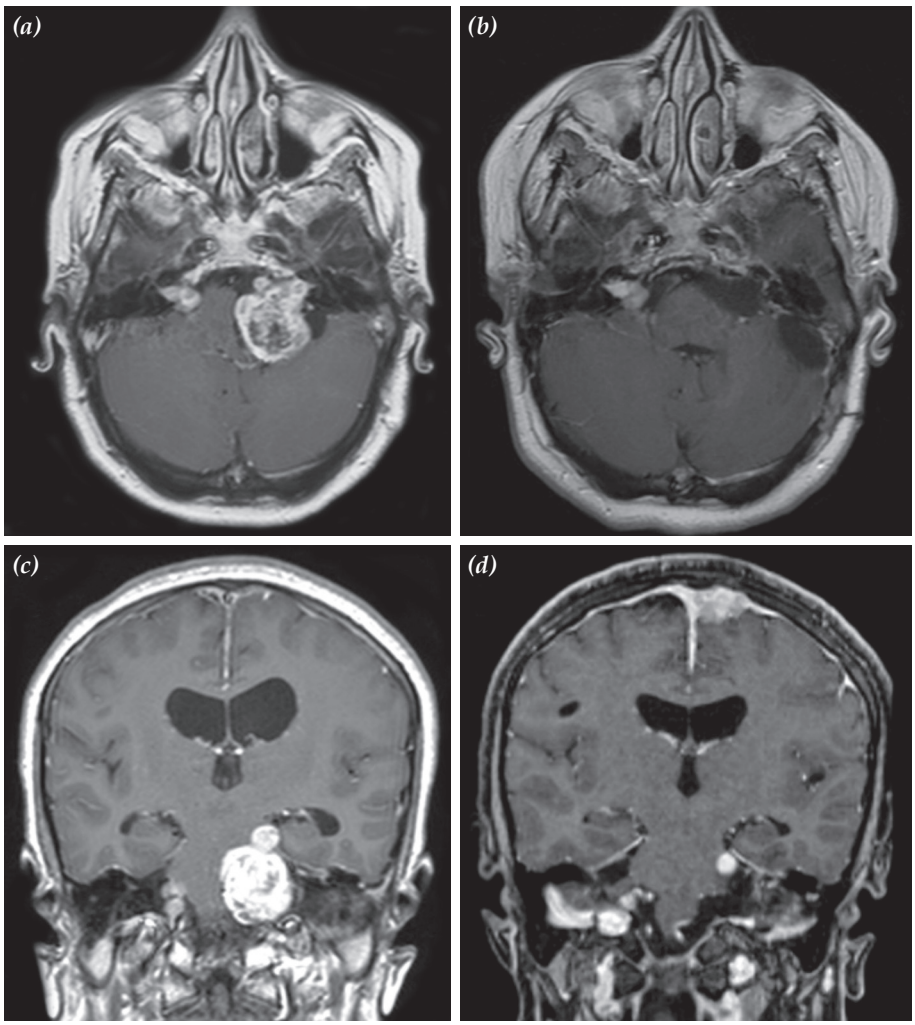

Figure 1. *Near-total excision of a giant vestibular schwannoma in left posterior cerebellopontine angle in a 17-year-old female patient with neurofibromatosis type 2.* ***(a, c)*** *Preoperative;* ***(b, d)*** *Postoperative contrast-enhanced magnetic resonance imaging. Note that patient had a small right-sided vestibular schwannoma and a left-sided parasagittal meningioma.*

were reported as WHO grade I schwannoma. None of the patients had atypical histological findings.

Cerebrospinal fluid fistula developed in one of the operated patients. In the early postoperative period, although the majority of patients (60%) had House-Brackmann grade IV and V facial paralysis, after two years of follow-up, facial nerve functions returned to normal or acceptable levels (House-Brackmann grade I or II) in four of these patients. At the last follow-up visit, only two patients had permanent facial paralysis (House-Brackmann grade V or VI). No patients had serviceable hearing on the ipsilateral ear postoperatively. Mean follow-up period of the patients was 9.4±5.0 years. Four patients had mild to moderate neurological deficits (facial paralysis, lower cranial paralysis, ataxia, etc.), whereas 60% of patients did not have any neurological deficits (except hearing loss) at the end of this duration. Residual progression developed in one patient in whom the tumor tissue could be removed subtotally for the protection of the vestibulocochlear and facial nerves and the patient was referred to radiotherapy. Recurrence was observed in one of the patients who underwent near-total resection. This patient did not undergo second surgery and was referred to radiosurgery.

DISCUSSION

Cerebellopontine angle (CPA) tumors, and thus VSs, are rarely seen in children. They have been poorly characterized because the literature mainly consists of case reports and small case series. While constituting a very small portion (2%) of all posterior fossa tumors seen in childhood, VSs constitute 8% of primary intracranial tumors in the general population. Vestibular schwannomas account for the majority of the CPA tumors seen in adults. In one large series[10] of pediatric CPA tumors, VSs also comprised the largest portion (60%), followed by meningioma (6%) and epidermoid cysts (5%), similar to adult population.[10,13,14] Likewise, Cunningham et al.[15] reported that rate of VS is 86% on the basis of data obtained from a study with 115 pediatric lateral skull base lesions. However, in a study of Zúccaro and Sosa's[16] which consisted of 33 cases of pediatric CPA tumors, this rate was only 24%. In our series, when all CPA tumors were considered, the schwannoma rate was found to be 40% in the pediatric population.

Vestibular schwannomas are the second most frequent extra-axial tumors in the adult population. They are mostly sporadic; however, may also be observed as a component of NF2 familial syndrome, particularly during adolescence or young adulthood. Non-NF2 cases are rarely encountered in the pediatric population.[8] On the other hand, significant proportion of unilateral pediatric VSs, assessed as sporadic at the time of diagnosis, has been reported to be diagnosed with NF2 at a later stage in life.[10] The rate of VSs is 96% in patients with genetically detected NF2, taking into consideration both unilateral and bilateral tumors.[17] In their study that analyzed pediatric CPA tumors, Holman et al.[10] reported that 6% of children with schwannoma showed NF2 trait. In our study, the rate of patients who were operated due to non-sporadic (NF2-related) schwannoma was only 20%. This may be due to the fact that a significant proportion of patients with NF2 become symptomatic in young adulthood, not in childhood. The risk of unilateral tumor emerging as the first presentation of NF2 is related to the age of the patients. The age group with the highest risk of developing contralateral tumor is <30 years.[18] Even if the first genetic analysis of the patients who are thought to be NF2 is negative, it does not provide a definite rule-out because a causative mutation still cannot be identified in a considerable portion of affected NF2 children.[18]

According to the literature, when NF2 patients with unilateral schwannoma or NF2-associated tumors are considered, 45% of the patients developed bilateral VSs after a five-year period following the initial presentation.[19] In a younger patient group with NF2 character, spinal tumors and meningiomas were reported before bilateral schwannomas were detected.[20,21] These data reveal the importance of close follow-up and surveillance in the NF2 population.

The clinical presentation of schwannomas can be very diverse.[4,5,11,22-25] For example, while

tumors reaching 2 cm in size can cause headache and trigeminal nerve compression findings, increased intracranial pressure syndrome may occur in lesions large enough to cause compression on the fourth ventricle.[4,5,8,11] This diversity of symptoms can be due to different tumor growth patterns, size and individual anatomical variations.[5] Hearing loss and tinnitus are among the most common reasons for referral. In approximately one fourth of the patients, hearing loss develops slowly, thus early diagnosis and timely surgery are important. Similar to Evans et al.'s[20] study, Holman et al.[10] found hearing loss at 25% frequency in patients with NF2. Holman et al.[10] reported that the size of VS in sporadic cases and rate of admission with hearing loss were higher than in children with NF2. This positive result is associated with the early screening of patients with NF2, even if they are asymptomatic. The frequency of auditory dysfunctions in VS patients is similar to the results obtained from studies on all CPA tumors and was found to be about 20%.[26] Middle or lateral location of the mass occurs as a poor prognostic indicator in terms of the protection of hearing compared with schwannomas showing medial placement.[2,22]

The importance of evaluating some clinical variables such as audiometric, radiological and neurophysiologic findings is emphasized in order to obtain a preliminary information about the possible loss of postoperative hearing ability in the literature.[10] In addition, a number of studies have been conducted to determine the pre-surgical factors to predict facial nerve results in schwannoma surgery. Wong et al.[27] reported that factors such as advanced patient age, large dimensions of tumor and position according to surrounding anatomical structures (adhesion, compression, wrapping of normal structures by tumor tissue, etc.), cystic or solid tumor character, surgical access route and increasing extent of surgical resection are factors affecting the prognosis negatively.

In their study on pediatric patients, Walcott et al.[28] demonstrated that the preoperative symptom duration was 31 months similar to adult cases. Likewise, this period was 30 months in our study. Prolonged duration of symptoms and delayed diagnosis can be attributed to the fact that the symptoms cannot be adequately expressed or are neglected by children.

When evaluated in terms of tumor size, a meta-analysis including 1,345 adult patients with VS reported a mean tumor size of 11.8 mm, whereas this value was 4.57 cm in pediatric VS series consisting seven cases.[28,29] This rate was 1.5 cm, similar to that of adults in the study of Holman et al.[10] When the tumor sizes of patients included in our series were examined, we detected a mean tumor size of 4.4 cm in the values close to the study of Walcott et al.[28] These values reported for the pediatric population have been observed to be significantly larger than the sizes reported for adults in the literature.

While mortality and morbidity rates were considerably high in these patients in the middle of last century, this ratio has been reduced considerably by the development of microsurgical techniques and functional monitoring methods.[30-32] Surgical approach, timing of the surgery, appropriate options of treatment, tumor size and serviceable hearing ability are all important factors to be taken into account during the decision-making stage.[33-35]

Although translabyrinthine, middle fossa, and retrosigmoid approaches can be selected by neurosurgeons in VS surgery at the present time, the most important factor in this regard is that the surgical team prefers the approach that they are most experienced in.[36] We used retrosigmoid approach in all of our cases that we included in our study. It may be possible to easily access the surgical boundaries and to protect the CNs with this approach, where the entire angle anatomy is readily visible. At the same time, this approach may provide anatomical relief that may allow nerve repair in case of possible CN damage. Samii and Matthies.[36,37] used suboccipital retrosigmoid transmeatal approach in their series of 1,000 cases published in 1997 with very low surgical mortality (1.1%) and morbidity rates. The cystic nature of the tumor and preoperative neurologic deficits were reported as risk factors, similar to the results of our study.

In VS treatment, one of the most valuable adjunct factors in determining the treatment strategy is the preoperative MRI. Images should be well examined before surgery in order to

reveal the facial nerve-tumor relationship, the stiffness of the tumor, and selection of optimal surgical approach.[27] The success of surgery depends on the complete removal of the tumor without additional neurological deficits. Samii and Matthies's[37,38] study of 1,000 cases achieved a total resection rate of 97.9%. This rate was 90% in our study. In the same study, rate of mortality was 1.1%, hemiparesis was 1%, quadriparesis was 0.1% and lower CN damage was 5.5%.[38] Anatomic protection rate of the facial nerve was 93% and functional protection rate was 51% according to the same study results. In our series, facial nerve anatomic protection rate was 100% and long-term functional protection rate was 80%.

Wong et al.[27] assumed that surgical resection of tumors with larger extension to the front of the internal acoustic canal may result in worse results in the facial nerve and gross total resection can be possible less frequently in these tumors. If a patient undergoes gross total resection, the risk of recurrence is very low.[28] Recurrences can be explained with microscopic spread during surgery and tumor growth when the suitable nutritional conditions are found.[39]

As stated, schwannoma surgery is open to complications as in all other tumor surgeries. However, the most striking complication here is facial nerve dysfunction. The preservation of facial nerve function, which is accepted as the single most important determinant of quality of life in postoperative period, is of great importance particularly in children.[40] Facial nerve injuries become dramatic in the pediatric age and can have deep psychosocial traces. When determining the treatment modality, all these possible complications should be handled cautiously and various strategies should be applied to reduce or postpone the morbidity.[28,41]

A good assessment of preoperative function of the CNs such as hearing and facial nerves in schwannoma treatment is of high importance when considering the possibility of damage during tumor resection. Successful surgical management should provide total tumor resection on one hand and should not cause neurological deficit on the other hand. This may only be possible with proper identification of a patient who should undergo surgical procedure, determination of the optimal surgical approach and successful intraoperative monitoring. For this purpose, it may be said that the most basic principle in schwannoma treatment is patient-specific planning. Zolotova et al.[42] evaluated the selection criteria of patients for surgery and determined the contribution of the auxiliary modern equipment for surgery to the extent of tumor resection by setting an algorithm. Cerebellopontine angle schwannomas may cause compression and traction on the brainstem and surrounding anatomic structures, including the CNs V through XII depending on delayed diagnosis due to slowly evolving clinical symptomatology.[43] Yin et al.[44] suggests that children presenting with concomitant hearing loss and cognitive disturbances should be suspected for VS. Considering the seventh CN injury, which is regarded as an important morbidity due to the psychosocial aspects of facial dysmetria created in children, the preservation of the facial nerve has critical value in the surgical treatment of VS, although it is even more difficult in pediatric VS than adult counterparts.[44,45] In addition, early diagnosis is important in VS surgery in terms of both suitability for surgery and reducing associated mortality and morbidity, most importantly facial paralysis, in patients suitable for surgery.

Treatment options in VS patients include clinical-radiological observation, surgery, and radiosurgery. For the elderly, the non-symptomatic patients and those in poor general condition, clinical follow-up is an appropriate treatment option, and surgical procedure is not planned as the first option in these patients. If surgical procedure is planned in a patient with VS and NF2, this thinking should be converted into practice rapidly. Considering the possible loss in hearing functions, observation may be suitable in patients who are genetically identified as NF2, who do not accept surgery, those who are unsuitable for surgery or with schwannoma on the side while their hearing ability is good.[46,47] However, it is emphasized in the literature that early surgical intervention should be considered if the follow-up of the tumor is an important risk source for the protection of hearing.[48,49]

In patients with NF2 in whom bilateral schwannomas are common, the purpose is to

protect hearing. However, this approach does not imply that radical surgery should always be planned in such patients to protect the hearing. In some cases, only subtotal resection is performed for decompression and operation is terminated.[41,51]

Age, clinical condition, size of the tumor, NF2 association and some features such as tumor relationship with surrounding anatomic structures are the defining characteristics that determine which of the treatment options should be performed such as follow-up, surgery, or radiosurgery. Different therapeutic options are adopted based on the aforementioned factors, not a standard method of treatment exists. Treatment modalities by neurosurgeons in VS cases vary considerably when the tumor location and size, radiological features, neurological and clinical characteristics of the patient are considered. For example, if the hearing function is also intact in cases with asymptomatic-NF2, follow-up can be performed regardless of tumor size. Surgery or radiosurgery may be planned when clinical deterioration is present or important anatomical or functional structures as fourth ventricle-brainstem are exposed to compression and in tumors smaller than 1.5 cm but showing rapid growth or tumors larger than 1.5 cm.

Radiosurgery is a viable management option for adult VS with good tumor control and functional preservation rates. The role of radiosurgery after microsurgery with incomplete resection has also been investigated and has been shown to be an effective method both in preventing tumor regrowth and preserving facial function.[50] The literature is scarce regarding radiosurgical management of pediatric VSs due to risks such as secondary tumors to radiation and lack of long-term follow-up results. One study investigating 25 pediatric NF2-associated VS found that treatment outcome of radiosurgery for VS in children with NF2 was not favorable compared with previous reports of affected adults.[51] Therefore, current standard of care for pediatric VS remains microsurgery to achieve total removal of the tumor while preserving function. However, stereotactic radiosurgery can be applied as part of bimodal therapy in pediatric patients with large-size tumors and when subtotal removal is anticipated to preserve facial nerve function.

This study has some limitations. First, the sample size is relatively small to draw conclusions regarding epidemiology and treatment strategies. Second, it combines both NF and non-NF associated VS, which are known to behave differently. Third, this is a retrospective case series, therefore the study suffers inherent biases of this type of investigation, such as heterogeneity in diagnostic, treatment and follow-up strategies, data collection and data completeness. However, the current study provides insights into pediatric VS as the literature is scarce regarding this rare pathology. Clinical results presented here also underlines the crucial role of multidisciplinary management of this entity.

In conclusion, VSs are rare in childhood and an association with NF2 is often observed. Vestibular schwannomas may cause hydrocephalus, various CN and brain stem findings by reaching quite large sizes. Because of the long life expectancy, effective treatment is necessary. VS surgery with suboccipital retrosigmoid craniotomy is an effective approach in that both the tumor can be totally removed and the possible morbidity can be minimized. Careful preoperative clinical-radiologic planning and intraoperative neuromonitoring are of critical importance for determining the surgical strategy and producing successful clinical results.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Tos M, Stangerup SE, Cayé-Thomasen P, Tos T, Thomsen J. What is the real incidence of vestibular schwannoma? Arch Otolaryngol Head Neck Surg 2004;130:216-20.
2. Babu R, Sharma R, Bagley JH, Hatef J, Friedman AH, Adamson C. Vestibular schwannomas in the modern era: epidemiology, treatment trends, and disparities in management. J Neurosurg 2013;119:121-30.
3. Lin EP, Crane BT. The Management and Imaging of Vestibular Schwannomas. AJNR Am J Neuroradiol 2017;38:2034-2043.

4. Samii M, Matthies C. Management of 1000 vestibular schwannomas (acoustic neuromas): the facial nerve--preservation and restitution of function. Neurosurgery 1997;40:684-94.
5. Mautner VF, Lindenau M, Baser ME, Hazim W, Tatagiba M, Haase W, et al. The neuroimaging and clinical spectrum of neurofibromatosis 2. Neurosurgery 1996;38:880-5.
6. Rusell DS, Rubinstein LJ. Pathology of Tumors of the Nervous System. 4th ed. London: Edward Amold; 1977.
7. Rout D, Pillai SM, Radhakrishnan VV. Cervical intramedullary schwannoma. Case report. J Neurosurg 1983;58:962-4.
8. Grossman RG, Hamilton WJ. Acoustic neuromas. In: Grossman RG, editor. Principles of Neurosurgery. New York: Raven Press Ltd; 1991. p.149-52.
9. Harner SG, Laws ER Jr. Clinical findings in patients with acoustic neurinoma. Mayo Clin Proc 1983;58:721-8.
10. Holman MA, Schmitt WR, Carlson ML, Driscoll CL, Beatty CW, Link MJ. Pediatric cerebellopontine angle and internal auditory canal tumors: clinical article. J Neurosurg Pediatr 2013;12:317-24.
11. Matthies C, Samii M. Management of 1000 vestibular schwannomas (acoustic neuromas): clinical presentation. Neurosurgery 1997;40:1-9.
12. Kasantikul V, Brown WJ. Estrogen receptors in acoustic neurilemmomas. Surg Neurol 1981;15:105-9.
13. Brackmann DE, Bartels LJ. Rare tumors of the cerebellopontine angle. Otolaryngol Head Neck Surg (1979) 1980;88:555-9.
14. Hitselberger WE, Gardner G Jr. Other tumors of the cerebellopontine angle. Arch Otolaryngol 1968;88:712-4.
15. Cunningham CD 3rd, Friedman RA, Brackmann DE, Hitselberger WE, Lin HW. Neurotologic skull base surgery in pediatric patients. Otol Neurotol 2005;26:231-6.
16. Zúccaro G, Sosa F. Cerebellopontine angle lesions in children. Childs Nerv Syst 2007;23:177-83.
17. Matthies C, Thomas S, Moshrefi M, Lesinski-Schiedat A, Frohne C, Battmer RD, et al. Auditory brainstem implants: current neurosurgical experiences and perspective. J Laryngol Otol Suppl 2000;27:32-6.
18. Evans DG, Ramsden RT, Gokhale C, Bowers N, Huson SM, Wallace A. Should NF2 mutation screening be undertaken in patients with an apparently isolated vestibular schwannoma? Clin Genet 2007;71:354-8.
19. Baser ME, Friedman JM, Wallace AJ, Ramsden RT, Joe H, Evans DG. Evaluation of clinical diagnostic criteria for neurofibromatosis 2. Neurology 2002;59:1759-65.
20. Evans DG, Birch JM, Ramsden RT. Paediatric presentation of type 2 neurofibromatosis. Arch Dis Child 1999;81:496-9.
21. Evans DG, Huson SM, Donnai D, Neary W, Blair V, Newton V, et al. A genetic study of type 2 neurofibromatosis in the United Kingdom. II. Guidelines for genetic counselling. J Med Genet 1992;29:847-52.
22. Badie B, Pyle GM, Nguyen PH, Hadar EJ. Elevation of internal auditory canal pressure by vestibular schwannomas. Otol Neurotol 2001;22:696-700.
23. Chandrasekhar SS, Brackmann DE, Devgan KK. Utility of auditory brainstem response audiometry in diagnosis of acoustic neuromas. Am J Otol 1995;16:63-7.
24. Luse SA. Electron microscopic studies of brain tumors. Neurology 1960;10:881-905.
25. Neu M, Strauss C, Romstöck J, Bischoff B, Fahlbusch R. The prognostic value of intraoperative BAEP patterns in acoustic neurinoma surgery. Clin Neurophysiol 1999;110:1935-41.
26. Moffat DA, Ballagh RH. Rare tumours of the cerebellopontine angle. Clin Oncol (R Coll Radiol) 1995;7:28-41.
27. Wong RH, Copeland WR, Jacob JT, Sivakanthan S, Van Gompel JJ, van Loveren H, et al. Anterior Extension of Tumor is as Important as Tumor Size to Facial Nerve Outcome and Extent of Resection for Vestibular Schwannomas. J Neurol Surg B Skull Base 2017;78:473-480.
28. Walcott BP, Sivarajan G, Bashinskaya B, Anderson DE, Leonetti JP, Origitano TC. Sporadic unilateral vestibular schwannoma in the pediatric population. Clinical article. J Neurosurg Pediatr 2009;4:125-9.
29. Stuart FA, Segal TY, Keady S. Adverse psychological effects of corticosteroids in children and adolescents. Arch Dis Child 2005;90:500-6.
30. Kluwe L, Mautner V, Heinrich B, Dezube R, Jacoby LB, Friedrich RE, et al. Molecular study of frequency of mosaicism in neurofibromatosis 2 patients with bilateral vestibular schwannomas. J Med Genet 2003;40:109-14.
31. Matthies C, Samii M, Krebs S. Management of vestibular schwannomas (acoustic neuromas): radiological features in 202 cases--their value for diagnosis and their predictive importance. Neurosurgery 1997;40:469-81.
32. Otto SR, Brackmann DE, Hitselberger WE, Shannon RV, Kuchta J. Multichannel auditory brainstem implant: update on performance in 61 patients. J Neurosurg 2002;96:1063-71.
33. Bennett M, Haynes DS. Surgical approaches and complications in the removal of vestibular schwannomas. 2007. Neurosurg Clin N Am 2008;19:331-43.
34. Briggs RJ, Luxford WM, Atkins JS Jr, Hitselberger WE. Translabyrinthine removal of large acoustic neuromas. Neurosurgery 1994;34:785-90.
35. Jung S, Kang SS, Kim TS, Kim HJ, Jeong SK, Kim SC, et al. Current surgical results of retrosigmoid approach in extralarge vestibular schwannomas. Surg Neurol 2000;53:370-7.
36. Samii M, Matthies C. Management of 1000 vestibular schwannomas (acoustic neuromas): surgical management and results with an emphasis on complications and how to avoid them. Neurosurgery 1997;40:11-21.
37. Samii M, Matthies C. Management of 1000 vestibular schwannomas (acoustic neuromas): hearing function in 1000 tumor resections. Neurosurgery 1997;40:248-60.
38. Samii M, Matthies C. Acoustic neurinomas associated with vascular compression syndromes. Acta Neurochir (Wien) 1995;134:148-54.
39. Schmerber S, Palombi O, Boubagra K, Charachon R, Chirossel JP, Gay E. Long-term control of vestibular

schwannoma after a translabyrinthine complete removal. Neurosurgery 2005;57:693-8.
40. Prasad D, Steiner M, Steiner L. Vestibular schwannoma. Crit Rev Neurosurg 1999;9:340-8.
41. Samii M, Matthies C, Tatagiba M. Management of vestibular schwannomas (acoustic neuromas): auditory and facial nerve function after resection of 120 vestibular schwannomas in patients with neurofibromatosis 2. Neurosurgery 1997;40:696-705.
42. Zolotova SV, Golanov AV, Kotel'nikova TM, Soboleva OI, Gorlachev GE, Fil'chenkova NA, et al. Stereotactic radiotherapy and radiosurgery in treatment of patients with intracranial schwannomas. Zh Vopr Neirokhir Im N N Burdenko 2010;1:18-23. [Abstract]
43. Puanhvuan D, Chumnanvej S, Wongsawat Y. Peripheral nerve function estimation by linear model of multi-CMAP responses for surgical intervention in acoustic neuroma surgery. Physiol Rep 2017:23.
44. Yin L, Ma Z, Li C, Luo S. Unilateral Vestibular Schwannomas in Childhood without Evidence of Neurofibromatosis: Experience of 10 Patients at a Single Institute. Turk Neurosurg 2017;27:333-338.
45. Kartush JM, Graham MD, LaRouere MJ. Meatal decompression following acoustic neuroma resection: minimizing delayed facial palsy. Laryngoscope 1991;101(6 Pt 1):674-5.
46. Bozorg Grayeli A, Kalamarides M, Ferrary E, Bouccara D, El Gharem H, Rey A, et al. Conservative management versus surgery for small vestibular schwannomas. Acta Otolaryngol 2005;125:1063-8.
47. Hoistad DL, Melnik G, Mamikoglu B, Battista R, O'Connor CA, Wiet RJ. Update on conservative management of acoustic neuroma. Otol Neurotol 2001;22:682-5.
48. Rosahl SK, Tatagiba M, Gharabaghi A, Matthies C, Samii M. Acoustic evoked response following transection of the eighth nerve in the rat. Acta Neurochir (Wien) 2000;142:1037-45.
49. Selesnick SH, Jackler RK. Clinical manifestations and audiologic diagnosis of acoustic neuromas. Otolaryngol Clin North Am 1992;25:521-51.
50. Brokinkel B, Sauerland C, Holling M, Ewelt C, Horstmann G, van Eck AT, et al. Gamma Knife radiosurgery following subtotal resection of vestibular schwannoma. J Clin Neurosci 2014;21:2077-82.
51. Choi JW, Lee JY, Phi JH, Wang KC, Chung HT, Paek SH, et al. Clinical course of vestibular schwannoma in pediatric neurofibromatosis Type 2. J Neurosurg Pediatr 2014;13:650-7.

