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Gross-total *versus* near-total resection of large vestibular schwannomas. An institutional experience

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Abstract

Objective: We will report our experience of the surgical treatment of large vestibular schwannomas (VSs). *Patients, Materials and Methods*: We conducted a retrospective study of patients operated on for Koos grade IV VS between 2007 and 2015 at the Department of Neurosurgery, Emergency County Hospital, Târgu Mureş, Romania. We studied the general preoperatory clinical data, the preoperative and postoperative facial nerve status, preoperative hearing on the affected side, and any postoperative complications, including death. *Results*: Sixty-six cases were included in our study. The mean age was 52.95 years and 66.7% (*n*=44) of the sample were female. All patients had suffered from tinnitus and this had been followed by loss of serviceable hearing on the affected side in 89.4% (*n*=59) of cases. Preoperative facial palsy was found in 53% (*n*=35) of patients. The mean tumor size was 40.35 mm. Gross-total resection (GTR) was achieved in 24 (36.36%) cases, while near-total resection (NTR) was obtained in 42 (63.64%) cases. New-onset facial palsy or degradation of the preoperative facial deficit occurred in 12 (18.18%) cases, most of whom were patients with a GTR (*n*=9, 37.5%). This was statistically significant. There were no significant postoperative differences between the GTR and NTR groups. There was one death in the GTR group. *Conclusions*: We conclude that near-total tumor removal provides good surgical results and better postsurgical quality of life for patients when compared to gross-total tumor resection. Therefore, this should be the end goal of the resection of large VSs.

Keywords: vestibular schwannoma, near-total resection, gross-total resection, facial nerve.

Introduction

Vestibular schwannomas (VSs) represent 8% of all intracranial tumors and over 80% of cerebellopontine angle lesions, with a variable incidence of one to 20 cases per million people. VSs are unilateral or sporadic in 95% of cases [1–8].

Histopathologically, schwannomas are common peripheral nerve sheath neoplasms, represented by the proliferation of a clonal population of Schwann cells. They are benign, well-circumscribed, usually solitary, and localized in the head and neck regions, or extremities. A common intracranial location is the vestibular branch of cranial nerve (CN) VIII, within the internal auditory meatus, from where they spread expansively into the cerebellopontine angle [9, 10].

Large VSs require a different approach to smaller tumors as patients present with intracranial hypertension, multiple CN deficits, and/or signs of brainstem/cerebellum compression; all of which make surgery very challenging and increase the postoperative complication rate [11–17].

The surgical management of large VSs is controversial. Treatment options include gross-total resection (GTR), in one or multiple stages; near-total resection (NTR), followed by radiosurgical treatment; or NTR followed by observation with regular imaging follow-up [11, 18–25].

Aim and scope

In this study, we aimed to (*i*) determine the prevalence of Koos grade IV VSs in our surgical group, (*ii*) analyze GTR and NTR rates in our Koos IV surgical patients, and (*iii*) compare the outcomes of GTR and NTR resections, in our surgically treated Koos grade IV VS patients, specifically regarding postoperative facial function and surgical outcomes. To these ends, we conducted a retrospective comparative study of Koos grade IV VS patients whose surgery comprised GTR and those whose surgical treatment was NTR.

Patients, Materials and Methods

Patients

The patients in our study were a retrospective sample who underwent operations on Koos grade IV VSs between January 2007 and December 2015 in the Department of Neurosurgery, Emergency County Hospital, Târgu Mureş, Romania. To quantify risk and predict the surgical outcome, we chose the Koos grading system, as previous research has proven its validity [4, 26–28].

Inclusion criteria

- Patients undergoing surgery for Koos grade IV VSs;

▪ Patients without neurofibromatosis (NF) type 2;
▪ Patients with complete documentation and follow-up data for at least 60 months.

Figure 1 summarizes these inclusion criteria and describes the final patient sample.

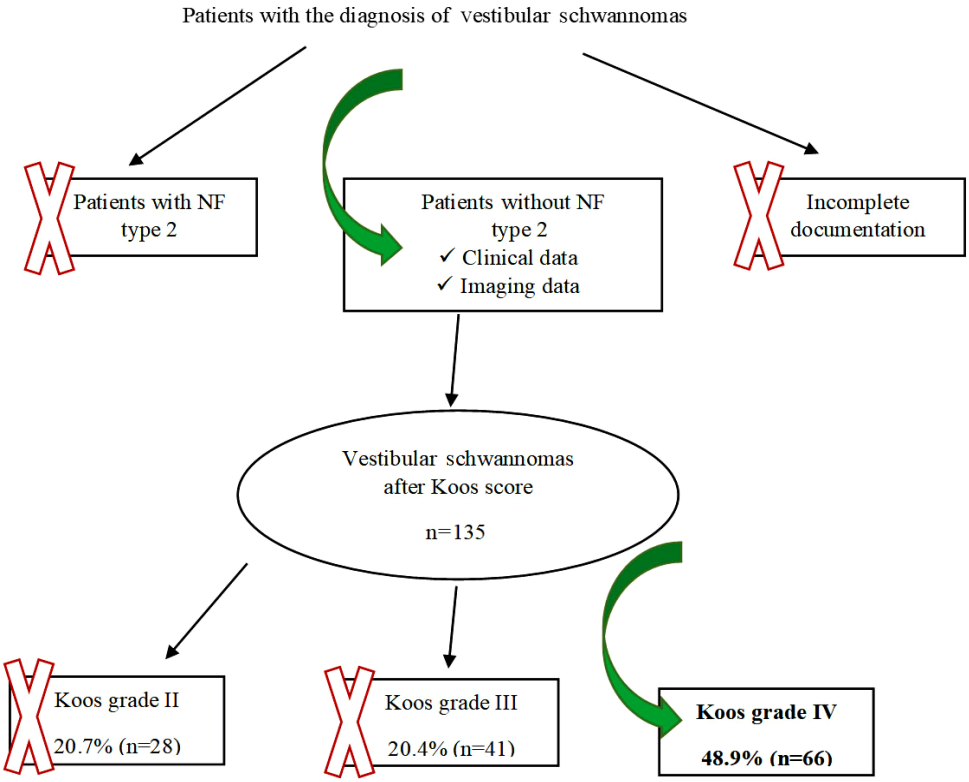

Figure 1 – ***Inclusion criteria and final study groups. NF: Neurofibromatosis.***

Evaluation of facial nerve function

Facial nerve function was determined before surgery, 24 hours after surgery, and 60 months after surgery. This was ascertained using House–Brackmann (HB) grading scores [29].

Facial nerve impairment was categorized as:

• Minimal-to-mild dysfunction (MMD) of the facial nerve for HB grades I–III;
• Moderate-to-severe dysfunction (MSD) of the facial nerve for HB grades IV–V.

Evaluation of hearing

Patients' hearing was evaluated before and after surgery. We used the new Hannover classification system as our measure of auditory acuity [30, 31].

Neuroimaging evaluation

Preoperative evaluative imaging included magnetic resonance imaging (MRI) and computed tomography (CT) scans (with 3 mm slices). MRI scans were repeated the day after the operation and contrast-enhanced images taken. The degree of tumor resection was classified through analysis of these images.

When the postoperative MRI revealed areas of contrast enhancement (90–95% tumoral resection), the tumor resection was classed as an NTR. When the images showed no tumoral enhancing residue (>95% tumoral resection), the resection was classed as a GTR. The quality of the resection was judged by the Senior Neurosurgeon (among the authors of this study) and an independent radiologist.

Control MRIs were performed on all patients in our sample three months after surgery. The NTR cases also underwent yearly MRIs for at least five years (Figure 2, a and b; Figure 3, a–c).

Surgical technique

All procedures were performed under general anesthesia, with the patient in a prone or "park bench" position. A standard retrosigmoid suboccipital craniectomy was performed. Patients who presented with significant obstructive hydrocephalus required external ventricular drainage. The drainage outlet was opened before dural incision in these patients. After incising the dura in an inverted "T" shape, the dural flaps were reflected towards the transverse and sigmoid sinuses. The arachnoid membranes caudal to the tumor were initially opened to release cerebrospinal fluid (CSF). Then, by gently retracting the cerebellum, the tumor was exposed and the *cisterna magna* could be easily approached caudally. This was opened to allow additional CSF release. Using this technique, a cerebellar retractor is rarely needed. The tumor capsule was coagulated using bipolar cautery and incised. An ultrasonic aspirator was then applied to aggressively debulk the tumor. After sufficient internal debulking, microdissection of the tumor capsule was initiated at the inferior pole of the tumor, gently releasing the posterior inferior cerebellar artery (PICA) and the lower CNs. Subsequently, the superior pole of the tumoral capsule was dissected, beginning at the tentorium towards CN V.

Great care had to be taken because the facial nerve often adheres to the superior pole of the tumor. The superior petrosal vein is easily injured during this stage

of the procedure. The tumoral capsule was then mobilized from the brainstem towards the *porus acusticus internus*. After the dura was dissected from the petrous bone, the inferior wall of the internal acoustic canal was drilled using a diamond drill. Irrigation was especially important at this point to avoid the thermal injury of CN VII. After tumoral resection, meticulous hemostasis was effectuated using bipolar and contact hemostatic agents. The dura was closed so watertight, and the incision closed in the standard fashion (Figure 4).

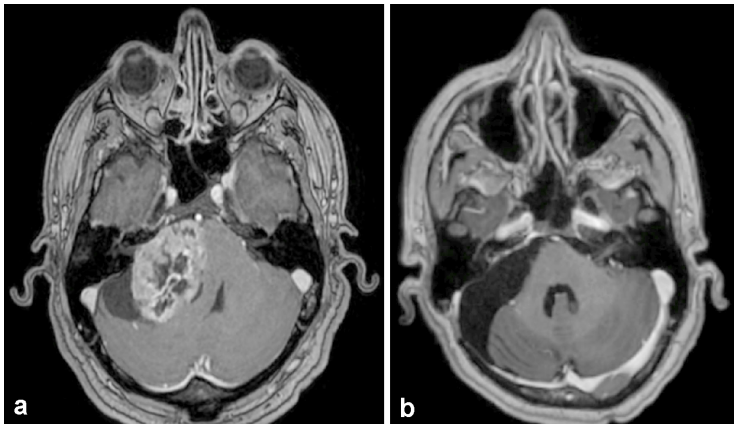

Figure 2 – ***Patient with GTR: preoperatory MRI (a) and at 5-year follow-up (b). GTR: Gross-total resection; MRI: Magnetic resonance imaging.***

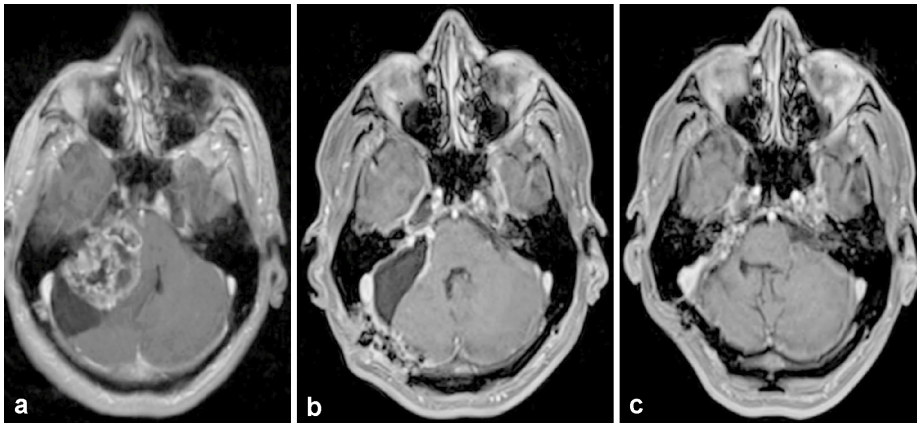

Figure 3 – ***Patient with NTR: preoperatory MRI (a), post-operatory MRI (b), and at 5-year follow-up (c). NTR: Near-total resection; MRI: Magnetic resonance imaging.***

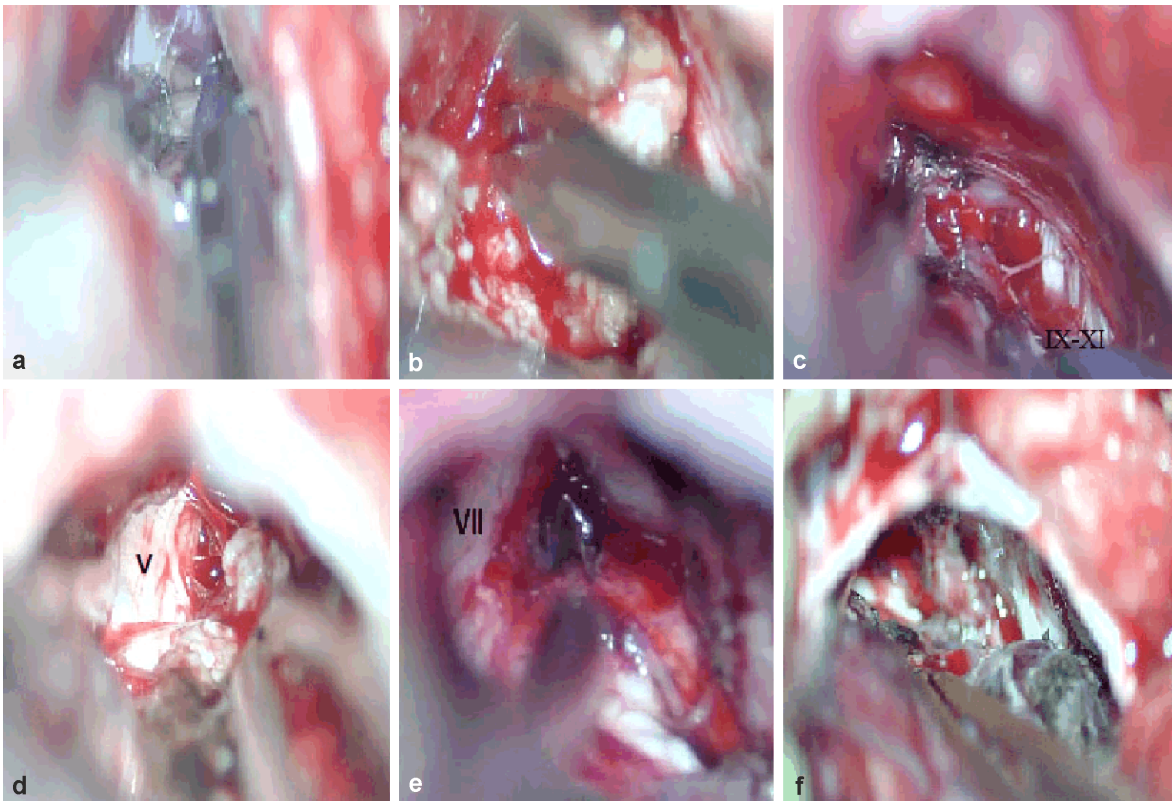

Figure 4 – ***(a–f) Aspects of the surgical procedure. V: Trigeminal nerve; VII: Facial nerve; IX–XI: Lower cranial nerves.***

It is important to note that GTR was never considered the primary end goal of surgery, and was pursued only in cases without strong adhesions, or with an acceptable dissection plane.

Statistical methods

The two patient groups were compared using the Fisher exact test to establish any differences in postoperative deficits of the facial nerve or surgical complications. $P<0.05$ was considered statistically significant. Statistical analyses were performed using GraphPad Prism 8 (GraphPad Software Inc., California, USA).

Results

Prevalence of large VS (Koos grade IV)

Of the 135 cases of VSs that were surgically treated in our Department between January 2007 and December 2015, 66 (48.9%) met the inclusion criteria for our study. Over these eight years, the frequency with which Koos grade IV VSs were seen in our Department remained constant. We saw an average of seven cases a year, with a range of four to 11 cases a year (Figure 1).

Preoperative clinical characteristics

The mean age of our patients was 52.92 years (with a range of 21 to 75 years), 66.67% (*n*=44) of whom were females.

Tinnitus was experienced by all patients, followed by complete hearing loss (H5) in 89.4% (*n*=59) of cases. The remaining patients had substantial deficits to audition (H4). There were signs of cerebellar and brainstem compression in 78.8% (*n*=52) of patients, headaches were reported by 69.7% (*n*=46) of patients, and 53% (*n*=35) presented with hydrocephalus.

Table 1 presents the general data and the clinical symptomatology of the patients included in our sample, at presentation.

Table 1 – ***General data and clinical symptomatology at presentation***

General data (*n*, %)	
Koos grade IV patients	66 (48.9%)
Gender	
Males	Females
22 (33.3%)	44 (66.7%)
Mean age [years]	Range [years]
52.95	21–75
Clinical symptomatology at presentation (n, %)	
Tinnitus	66 (100%)
Hearing loss	59 (89.4%)
Signs of cerebellar or brainstem compression	52 (78.8%)
Headache	46 (69.7%)
Facial nerve dysfunction*	35 (53%)
Intracranial hypertension signs	35 (53%)
Trigeminal sensory dysfunction	25 (37.9%)
Other nerves affected (IV, VI, IX–XI)	12 (18.2%)

*All cases of facial nerve dysfunction were classified as MMD of the facial nerve (grades I–III according to HB score). *n*: No. of patients; MMD: Minimal-to-mild dysfunction; HB: House–Brackmann.

Preoperative facial palsy

Preoperatively, minimal-to-mild facial nerve palsy (MMD) was present in 53.03% (*n*=35) of our patients. The remaining patients presented with no facial nerve palsy.

Tumor characteristics and type of resection

The mean tumor size was 40.35 mm (with a range of 32 to 63 mm). Of the 66 Koos IV surgically treated cases in our sample, GTR was achieved in 24 (36.36%) cases, while NTR was achieved in 42 (63.64%) cases. The mean tumor size was 39.28 mm in the GTR group and 40.78 mm in the NTR group.

Anatomical preservation of the facial nerve was achieved in all cases.

Comparison between 24-hour postoperative facial nerve function and the type of resection

New-onset facial palsy or degradation of preoperative facial deficits occurred in 12 (18.18%) cases. Nine (37.5%) of these were from the GTR group of 24 patients, three (7.2%) were from the 42 patients in the NTR group. This was a statistically significant difference [p=0.0057, odds ratio (OR)=0.1282]. Three (7.2%) patients in the NTR group who had presented with preoperative MMD of the facial nerve showed increased postoperative dysfunction, advancing to MSD. In the GTR group, four (16.7%) cases escalated from preoperative MMD to postoperative MSD of the facial nerve, and five (20.8%) patients showed MSD of the facial nerve postoperatively, despite no preoperative deficit (Table 2).

No patients presented with HB grade VI paralysis following surgery.

Table 2 – ***Facial nerve function after HB scores and degree of resection***

GTR	**Preoperatory status**	**Post-surgery stable**	**Post-surgery worsened (MSD)**
No facial deficit	8 (33.3%)	3 (12.5%)	5 (20.8%)
Present preoperative deficit (MMD)	16 (66.7%)	12 (50%)	4 (16.7%)
NTR	**Preoperatory status**	**Post-surgery stable**	**Post-surgery worsened (MSD)**
No facial deficit	23 (54.8%)	23 (54.8%)	–
Present preoperative deficit	19 (45.2%)	16 (38.1%)	3 (7.2%)
Follow-up (60 months)	**Stable deficit**	**Improvement**	
GTR	18 (75%)	3 (14.3%)	
NTR	17 (40.5%)	2 (10.5%)	

HB: House–Brackmann; GTR: Gross-total resection; NTR: Near-total resection; MMD: Minimal-to-mild dysfunction; MSD: Moderate-to-severe dysfunction.

Histopathological characteristics

Microscopically, the aspects were typical. Schwann cells were spindle-shaped, with elongated, tapered nuclei. Conventional schwannomas have two main architectural patterns, usually admixed. The Antoni A pattern consists of fascicles of spindle-shaped neoplastic Schwann cells,

with indistinct cytoplasmic borders and elongated nuclei. The Antoni B pattern incorporates more stellate cells with variable lipidization, in a loosely textured area with microcystic changes. Verocay bodies consist of areas of nuclear palisading (parallel nuclear arrays). Degenerative changes are extensive in larger tumors, including hyalinized, ectatic, thrombosed blood vessels, areas of intratumoral hemorrhage, calcification, cystic change, and, occasionally, foci of necrosis.

Immunohistochemically, the neoplastic Schwann cells showed typical nuclear and cytoplasmic S100 protein positivity, SRY-box transcription factor 10 (SOX10) expression, and a low mindbomb E3 ubiquitin protein ligase-1 (MIB-1) labeling index (Figure 5, a–c).

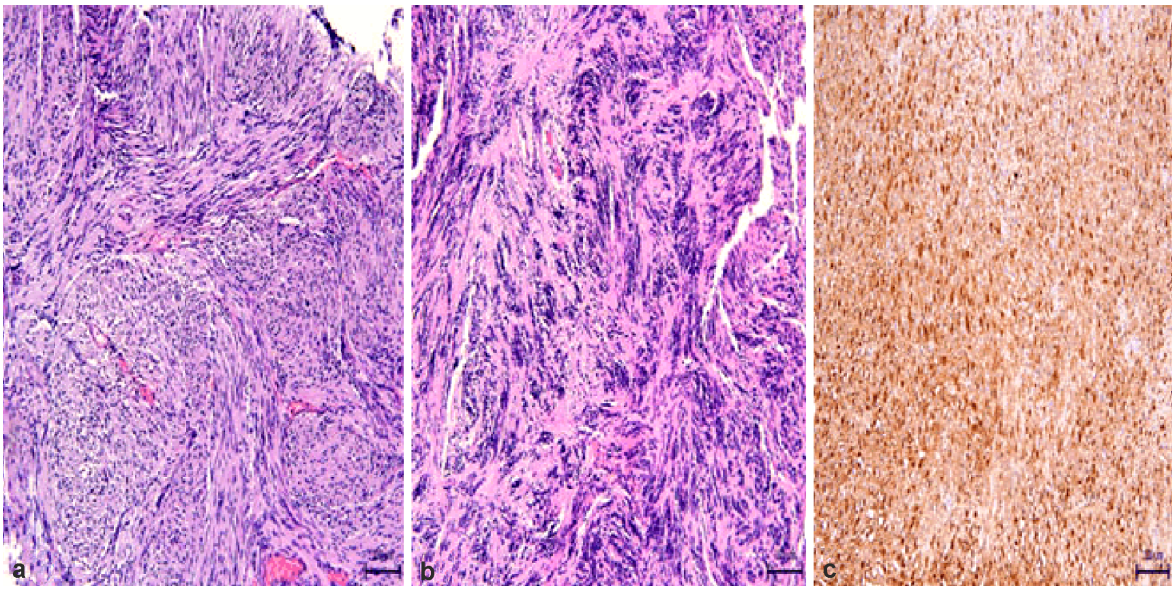

Figure 5 – ***Characteristic histological features (×100) include Antoni A and Antoni B areas (a), and parallel arrays of nuclei forming Verocay bodies (b). Schwannomas show nuclear and cytoplasmic S100 immunoreactivity (c).***

Postoperative deaths and complications

Overall mortality was 1.52% (n=1), a total of one death; this was in the GTR group. Other significant postoperative complications consisted of eight (12.1%) cases of postoperative hydrocephalus requiring a ventriculoperitoneal shunt, four (6%) cases of CSF leakage, four (6%) cases of postoperatory lower CN deficits, one case (1.52%) of posterior fossa hemorrhage, and one case (1.52%) of significant postoperative brainstem deficit. There were no statistical differences between complications in the GTR and the NTR groups (Table 3).

Table 3 – ***Postoperative complications***

Degree of removal	GTR	NTR	*p*-value
CSF leakage	3 (12.5%)	1 (2.4%)	0.13
Hydrocephalus requiring shunt*	4 (16.7%)	4 (9.5%)	0.44
Severe damage to the brainstem	1 (4.2%)	–	–
Posterior fossa hemorrhage	–	1 (2.4%)	–
Lower CN deficits	3 (12.5%)	1 (2.4%)	0.13
Death	1 (4.2%)	–	–

GTR: Gross-total resection; NTR: Near-total resection; CSF: Cerebrospinal fluid; CN: Cranial nerves. *This is a complication of the tumor size not a consequence of the surgical intervention.

Long-term follow-up and improvement of facial function

Facial function was followed for 60 months, and no cases were lost to follow-up. At 24 months following surgery in the NTR group, out of the 19 cases that had exhibited preoperative facial nerve dysfunction, improvements were observed in two (10.52%) cases. The GTR group included 21 patients with preoperative facial deficits, three (14.3%) of whom showed improvement at the follow-up (Table 2). No further improvement of facial function was seen in any of the patients at subsequent follow-ups.

At a 60-month follow-up, imaging found a small increase in the size (up to 1.5 mm) of the tumor residue in two cases from the NTR group (Figure 3). Control imaging at 60-month follow-ups found no tumor regrowth in any patients from the GTR group (Figure 2).

Discussions

In this retrospective study, we endeavored to determine the prevalence of postoperative complications associated with giant VSs and the risk of tumor regrowth depending on tumoral resection quality.

In recent years, numerous studies have reported a significant decrease in the number of large VSs (Koos grade IV). The recent reported incidence is between 2% and 12.5% [10, 16, 28]. This is most likely due to an increase in early diagnoses [2, 4, 19, 32–35].

The patients in our study were selected from cases seen in the neurosurgery department of a tertiary care center over eight years. During this period, there were 48% of cases with Koos grade IV VSs. Nevertheless, the mean age of the patients in our study was approximately five years younger than the averages seen in equivalent European studies [32]. This implies that we may have seen earlier occurrences in our population. In addition to this, educational and cultural factors appear to engender

ignorance regarding VS-induced hearing loss, a symptom amply demonstrated by the loss of serviceable hearing in all of our giant VSs patients. These factors are, in our opinion, the leading causes of delayed diagnosis and increased prevalence of Koos grade IV VS.

The therapeutic goal in the treatment of VSs is the complete removal of the tumor with preservation of the anatomical and functional integrity of facial nerves [24]. However, with giant VSs, this goal often cannot be achieved. Performing a total resection in these cases can significantly reduce the patient's postoperative quality of life since there seem to be significant correlations between the size of VSs, the possibility of total resection, the degree of impaired facial nerve function, and the rate of postoperative complications. As such, the literature is replete with debates over whether or not surgeons should primarily seek GTR or NTR in these cases [13, 15, 18, 20, 36–39].

We chose to perform all surgeries using the suboccipital "retractorless" retrosigmoid approach, due to the familiarity of our team with this approach and a proven likelihood of positive outcomes [40]. We did not aggressively strive for total tumor resection in any of our giant VS surgeries. Nevertheless, GTR was achieved in 36% of cases.

Upon admission, the patients in our study commonly presented with mild facial nerve dysfunction of HB grade 1–3 (53%), most often due to an extremely delayed diagnosis. Under these circumstances, preservation of facial function is difficult, and, despite no precise data in the existing literature, we believe that the best the surgeon can do in this respect is aim for postsurgical status that maintains the preoperative level of nerve dysfunction.

Seol *et al.* were able to preserve good facial nerve function in 44.4% of their NTR cases and 15.4% of their GTR cases in the immediate postoperative period [41]. Supporting this finding, we observed that GTR leads to a significantly greater incidence of immediate postoperatory facial nerve palsy than does NTR (37.5% *vs.* 7.14%), and, in patients without preoperatory facial deficits, significant postoperatory facial nerve dysfunction only occurred among patients who had undergone a GTR. We believe that this is because the tumor has already injured the facial nerve, either by compression, stretching, or discrete tumoral infiltration [42]. Therefore, the supplemental manipulation generally required for GTR increases the risk of aggravated postoperative palsy. To avoid this, we feel that leaving a tiny piece of tumor capsule adherent to the facial nerve can be beneficial.

At the 24-month follow-up, similar, but relatively modest (10–15%), improvements in facial function were seen in both the NTR and GTR groups, demonstrating what we believe is the importance of postoperative facial nerve status in giant VSs.

As demonstrated by other authors [43], our results indicate that surgery leads to an improvement in hydrocephalus. Of the cases in our sample who presented with preoperatory hydrocephalus, 87.9% did not require the subsequent placement of a ventriculoperitoneal shunt.

CSF leakage was present in 6% of our patients. While GTR seemed to be associated with a higher risk of CSF fistulas (12% *vs.* 2.4% in the NTR group), the sample in this study was too small for this to be a statistically valid difference. Nevertheless, in all cases, lumbar drainage resolved all of the leaks within a maximum of 72 hours.

In our experience, albeit with a limited number of cases seen over a relatively short 60-month timeframe, when considering the growth speed of VSs [44], NTR cases do not show significant local recurrence. This affirms previous research indicating that NTR allows the preservation of facial nerve function without significantly increasing the risk of recurrence. In many cases, it also assures a better post-surgical quality of life for the patient [25]. Furthermore, some authors have suggested that gamma knife radiosurgery is an efficient and safe adjuvant treatment, with a high tumor growth prevention rate, that can be used after total or partial tumor removal [45–47].

Conclusions

Large VSs remain a medical challenge. Their management requires alternative surgical strategies because most patients present with severe preoperative symptomatology and there are significant additional surgical risks. We conclude that near-total removal should be the end goal of the resection of these difficult-to-treat tumors.

Conflict of interests

The authors have no conflict of interests to disclose.

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