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Microsurgery for patients diagnosed with neurofibromatosis type 2 complicated by vestibular schwannomas

Clinical experience and strategy for treatments

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Abstract

Most patients diagnosed with neurofibromatosis type 2 (NF2) have bilateral vestibular schwannomas (VS). Through reviewing surgical method and clinical outcomes, we tried to find out a strategy for treatments in NF2 patients with VS.

We retrospectively reviewed patients diagnosed pathological NF2 and have had microsurgery (MS) for VS in the PLA Army General Hospital. Seventeen patients were included from January 2000 to December 2016. Fifteen patients had progressive hearing impairment, and 7 ears were totally deaf. Computed tomography and magnetic resonance imaging were used for preoperative and postoperative evaluation. House–Brackmann (H-B) classification was used to evaluate facial function, and the hearing outcome was classified according to American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) hearing classification system. The outcomes included functional hearing, facial function, and complications.

In the 17 patients, 9 were men, and the mean age was 27.2 years old. The mean duration of disease was 38.4 months. Twenty-six VS were excised. Nine patients with bilateral VS and unilateral surgery had repeated surgery for the contralateral tumor after 3 to 12 months. The hearing preservation rate was 41.6%. In the 26 excisions for VS, 24 had intact facial nerve. In the other 2 tumor excision, damaged facial nerves had head-to-head adhesion using biological fibrin glue. The rate of facial nerve function preservation was 60%. No mortality or major complication was reported. The follow-up time ranged from 11 to 78 months with a mean value of 39 months.

MS is an effective treatment for NF2 patients with VS. The operation for bilateral VS should be staged according to tumor size and bilateral hearing function. However, methods on how to preserve functional hearing and facial function remain the issue. Further randomized controlled studies are needed to find out a better treatment for NF2 patients with VS according to the overall condition.

Abbreviations: AAO-HNS = American Academy of Otolaryngology-Head and Neck Surgery, ABR = auditory brainstem evoked response, BAEP = brainstem auditory evoked potentials, CM = conservative management, CT = computed tomography, H-B = House–Brackmann, MRI = magnetic resonance imaging, MS = microsurgery, NF1 = neurofibromatosis type 1, NF2 = neurofibromatosis type 2, SCH = schwannomatosis, SDS = sound discrimination score, SR = stereotactic radiation, VS = vestibular schwannomas.

Keywords: facial nerve, hearing impairment, microsurgery, neurofibromatosis type 2, stereotactic radiation, vestibular schwannoma

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1. Introduction

Neurofibromatosis is a group of 3 distinct diseases: neurofibromatosis type 1 (NF1), neurofibromatosis type 2 (NF2), and schwannomatosis (SCH). NF2 is an autosomal dominant disease. The NF2 tumor suppressor gene is on chromosome 22q 12–2;[1] and the birth incidence is approximately 1 in 33,000, with prevalence of 1 in 56,161.[2] According to the National Neurofibromatosis Foundation (NNFF) criteria,[3] patients would be confirmed with NF2 diagnosis if there were bilateral vestibular schwannomas (VS). The first symptoms of NF2 include neural or skin tumor, vision loss, tinnitus, weakness, vertigo; but, NF2 may sometimes be asymptomatic.[4]

Approximately, 95% of patients diagnosed NF2 have bilateral vestibular schwannomas (VS), which is the most classic feature of NF2. Although NF2 majorly involves the auditory nerve, it may invade cranial or spinal nerve. In the cranial nerve, it often invades the vestibular nerve and trigeminal verve; and in spinal tumors, it often presents as schwannoma, spinal meningioma, astrocytoma, or ependymoma. Other clinical symptoms include hearing impairment, claudication or unsteady gait, and subcutaneous

skin tumors. The most common age of disease onset ranged from 20 to 40 year old, with mean age of 25 year old.[5]

Although VS is a kind of benign tumor, it often presents in multiplicity and grows rapidly, which would result in hearing loss. The initial symptoms of NF2 are tinnitus, unilateral or bilateral hearing impairment, and vestibular dysfunction.[6,7] Treatments for VS include microsurgery (MS), stereotactic radiation (SR), and conservative management (CM). However, ways to treat VS remain uncertain due to the consideration on the anatomic site and functional outcomes.[8] The key points of treatment for VS are to preserve at least one side of functional hearing and to avoid facial palsy. MS is the main treatment for NF2 patients with VS. The goal of treatment is total tumor excision with preservation of vestibulocochlear nerve and hearing function. However, there are still controversies in treatments. NF2 patients with VS are at high risk of complications with other neurological tumors, such as meningioma, glioma, and ependymoma; hence, the treatment should be individualized according to clinical symptoms and the overall condition.

In this study, we retrospectively reviewed all the patients diagnosed NF2 with pathological evidence that underwent microsurgery for removal of VS in the PLA Army General Hospital from January 2000 to December 2016. Through reviewing the surgical method and clinical outcomes, we tried to conclude a strategy for treatments in NF2 patients with VS.

2. Materials and methods

2.1. Patient population

We reviewed all the patients diagnosed NF2 with pathological evidence for microsurgery on VS removal in the PLA Army General Hospital from January 2000 to December 2016. After retrospective review, 17 patients were included with the diagnosis of NF2 according to NNFF criteria;[3] of which, 11 patients had bilateral VS. The medical records were reviewed, and the summary of basic data is presented in Table 1. In the 17 patients, 9 were men, and 8 were women. The mean age was 27.2 year old, with the range of 14 to 47. Three patients were below 20 year old, and 2 patients were above 40 year old. The mean disease duration was 38.4 months, ranging from 7 to 108 months. Two patients had family history of NF2 with bilateral VS, and 1 patient had family history of NF2 with unilateral VS and multiple meningioma. In addition, 3 of the 17 patients had gamma-knife surgery as treatment for VS before the microsurgical treatment.

Table 1

Basic data.

Patient number (n)	
All	17
Male	9
Female	8
Age, years	
mean	27.2
range	14–47
Disease duration, months	
mean	38.4
range	7–108
Family history	
NF2	3
Clinical symptoms	
Tinnitus	17
Impaired hearing	15
Seizure attack	1
Facial numbness	3
Atypical trigeminal neuralgia	1
Unsteady gait	3
Headache or dizziness	13
Hoarse and choking	1
Blurred vision	1
Bilateral lower limbs weakness	1

2.2. Clinical expression

The initial symptom was high pitched tinnitus, unilateral, or bilateral. Fifteen patients had progressive hearing impairment, and 7 ears were totally deaf. Other clinical symptoms were seizure attack, facial numbness, atypical facial pain, headache, dizziness, hoarseness, choking, bilateral lower limb weakness, and abnormal gait.

In the physical examination, 3 patients had diffused subcutaneous neurofibromas, and 6 patients had pigmentations over the neck, chest, and 4 limbs. Seven patients had positive Romberg's sign accompanied with walking instability and abnormal tandem gait. According to preoperative House–Brackmann (H-B) classification[9] for facial nerve function, 23 sides were grade I (normal), 2 sides were grade II (mild dysfunction), and 1 side was grade III (moderate dysfunction).

2.3. Preoperative audiometric evaluation

All patients had audiometry preoperatively, including pure tone audiometry, sound discrimination score (SDS), tympanometry, auditory brainstem evoked response (ABR), and brainstem auditory evoked potentials (BAEP). The hearing outcome was classified according to the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) hearing classification system, and was reported in Table 2. H-B classification and audiometry were performed after discharge and 3 months postoperation.

2.4. Preoperative imaging valuation

All patients had computed tomography (CT) and magnetic resonance imaging (MRI) as part of their diagnosis. The tumors of NF2 could be multiple and polymorphic, and there might be various kinds of tumors at the same time. The most common tumor in NF2 patients is bilateral vestibular schwannoma, and the second is meningioma. Brain and spinal MRI is necessary in management because some NF2 patients could be complicated with other cranial nerve schwannoma or intraspinal multiple neurofibroma.

In the 17 patients, 11 patients had bilateral VS, and other 6 were unilateral VS accompanied with intracranial meningioma, cerebral schwannoma, and intraspinal tumor, which belonged to segmental NF2. Twenty-eight schwannomas were found.

Table 2

Hearing classification according to AAOHNS.

Class	Pure tone, dB	SDS (%)	Preoperation (n = 26)	Postoperation (n = 26)
A	<30	≧70	2	0
B	30–50	≧50	10	5
C	>50	>50	7	8
D		<50	7	13

Twenty-two schwannomas were noted with funnel-shaped enlargement in the internal auditory meatus, and 3 were showed with bone destruction. MRI showed 12 large tumors (≧40 mm), 9 median tumors (21–39 mm), and 5 small tumors (≦20 mm). Most of the bilateral VS were anisometric, with tumors size of 17 to 61 mm, and the mean diameter was 41.6 mm. All patients had repeat MRI 3 days and 3 months after the operation.

2.5. Microsurgery

The aim of microsurgery in NF2 patients with bilateral VS are decompression and hearing preservation. For those with unilateral VS, the aim of surgery is to release mass effect from intracranial schwannoma and intraspinal tumors.

For those patients with brain compression, neural function damage, seizure, obstructive hydrocephalus, convex meningioma or parafalcine meningioma, we would excise the bigger or symptomatic tumor. In the 11 patients with bilateral VS, 9 patients had bilateral tumors sized $>$ 3 cm and had tumor excision in sequence. The remaining 2 patients had 1 tumor sized $<$ 3 cm with residual hearing and 1 tumor sized $>$ 3 cm with poor hearing, the larger tumor would be the operative site. One patient had combined meningioma and 3 patients had multiple intraspinal neurofibromas. All of the patients had microsurgery for tumor excision.

The microsurgery was performed using the suboccipito-retrosigmoidal approach and micro bone flap craniotomy was used for tumor excision. Neural navigation was used for preoperative positioning and route of design. Three patients had half-sitting position, and all others had lateral position. C-shaped incision was made behind ear with bone flap over occipital scales and positioning under neural navigation, then a hole was drilled over the intersection of transverse sinus and sigmoid sinus. The bone flap was about 2.5×3.5 cm. Lower edge of the transverse sinus and posterior edge of the sigmoid sinus were exposed. Dura was cut, and the cerebellar medulla oblongata was exposed. With the cerebellum pulled to posterior lateral side, the tumor was exposed.

During tumor excision, protection of facial and auditory nerve is important. Electrophysiological monitoring may be applied for positioning of the nerve, including trigeminal nerve and facial nerve evoked potentials, somatosensory evoked potentials, and BAEP. During the intraoperative monitoring, the cochlear nerve wave was affected while grinding posterior wall of internal acoustic meatus, dissecting or electrocoagulating structures near the internal acoustic meatus, maneuvering the tumors in internal acoustic meatus, and clamping the tumor blood vessels. Intraoperative continuous electrophysiological monitoring would be helpful for nerve positioning and potentially prevent nerve damage.

3. Results

Twenty-six VS were removed. Nine patients with bilateral VS and unilateral surgery had repeated surgery for the contralateral tumor after 3 to 12 months. Among the 26VS, 22VS were total excised, and 4 VS with subtotal excision for protection of hearing were treated with gamma-knife 3 months postoperatively. The follow-up time ranged from 11 to 78 months, with a mean value of 39 months. No tumor recurrence was observed during follow-up.

3.1. Postoperation hearing function

The hearing function was evaluated 6 months postoperatively. The postoperative evaluation was reported in Table 2: 5 ears were in Class B, 8 ears were in Class C, and 13 ears were in Class D. Class A and Class B were defined as serviceable hearing. Preoperatively, 46% of ears had Class A or B hearing, and postoperatively, 19.2% of ears were in Class A and B. Among 12 ears with functional hearing preoperatively, the hearing preservation rate was 41.6% postoperatively. Those ears that lost hearing prior to surgery remained deaf postoperatively.

3.2. Postoperation function of facial nerve

In the 26 tumor excisions, 24 (92.3%) had intact facial nerve. In other 2 tumor excisions, damaged facial nerves had head-to-head adhesion using biological fibrin glue. After 6 months, the function of facial nerve was evaluated by H-B classification, and the results were presented in Table 3. Grade I and Grade II were defined as excellent facial nerve function. Postoperatively, 100% of the cases with small VS were in H-B Grade I or II function. In the 9 cases with medium-sized tumors, 66.7% had Grade II function, and in the 12 cases with large-sized tumors, 33.3% had Grade II function after surgery. Among the 25 cases with Grade I or II function preoperatively, 15 cases (60%) had excellent facial nerve function postoperatively. Overall, the rate of excellent facial nerve function was 57.7% postoperatively.

3.3. Complications

There is no mortality, hemiplegia, cerebrospinal fluid leakage, intracranial infection, or hematoma reported. One patient had cerebellum contusion complicated with edema. Three patients had intracranial gas accumulation, and 2 patients had subcutaneous fluid effusion that subsided after drainage. One patient had brain damage and needed nasopharyngeal tube feeding and improved after 3 months.

4. Discussion

About 90 to 95% patients with NF2 have bilateral VS, and it is difficult to establish total tumor excision with preservation of hearing function.[1] Treating bilateral VS is more difficult than unilateral VS due to the risk of bilateral hearing loss and facial palsy. Along with improvements in surgical technique, preserving the hearing function and intact facial nerve becomes an important

Table 3

Tumor size and facial function.

	Preoperative facial function (H-B)			Postoperative facial function (H-B)			
Tumor size, cm	I	II	III	I	II	III	IV
Small (≦2)	5			1	4		
Medium (2.1–3.9)	9				6	3	
Large (≧4)	9	2	1		4	6	2
Total	23	2	1	1	14	9	2

H-B = House–Brackmann.

issue. In this retrospective study, it showed that preservation of facial nerve function was good for small-sized VS, and for the cases with Grade I or II function preoperatively, 60% of cases were in these 2 grades postoperatively. The rate of hearing preservation was 41.6%, which still need further improvement.

In treating NF2 patients with VS, the main goal is to preserve functional hearing and facial nerve function. Chen et al[10] had reported 103 cases of VS, including 2 cases of NF2; in 18 cases with tumor size ≦2 cm, rate of facial nerve function preservation (H-B: Grade I-II) was 100%. In 46 cases with tumor size 2.1 to 3.9 cm, the preservation rate was 89.1%, and in 39 cases with tumor size ≧4 cm, the preservation rate was 69.2%. It was concluded that the rate of facial nerve function preservation will decrease with the increase in size of VS. The observation was consistent with the current study. However, in our study, the rate of facial nerve function preservation was much lower in patients with medium-sized and large-sized VS tumor than those in Chen et al.[10] The reason may be associated with the difference of patient selection between the 2 studies. Brackmann et al[11] had reported 28 cases of NF2 with 40 VS. The mean tumor size was 1.1 cm (range: 0.5–3.2 cm), and most of the tumors were below 1.5 cm. After 1 year postoperation, the rate of facial nerve function at H-B: Grade I to II was 92.2%. The result was similar to the current study, which indicated that patients with small-sized tumor (≦2 cm) would benefit from microsurgery and have a higher rate of facial nerve function preservation. Nowak et al[8] reported that there were unsatisfactory results for facial nerve function (H-B: Grade IV–V) in 8 out of 37 larger tumors (≧2 cm). Taken together with the present study, it showed that management of large-sized tumors remain a clinical challenge and is associated with a worse outcome of facial nerve function compared to small-sized tumor. To preserve facial nerve function, excision of tumor around facial nerve should be conservative. In the present study, the rate of facial nerve preservation was high (92.3%). However, it did not reflect the rate of facial nerve function preservation (57.7%). It was reported that use of supramaximal stimulation intraoperatively is safe and useful in predicting good facial function.[12] However, it is not reliable for identifying patients that may develop long-term facial weakness in the future.

Microsurgery is an effective treatment for VS in NF2. However, control of tumor progression and preservation of hearing function remain an issue. In our study, rate of hearing preservation was 41.6% and there is still room for improvement. The low preservation rate may be associated with the hardness of tumor, incomplete membrane, blurred margin between tumor and auditory nerve, and nerve damage related to the surgery. Brackmann et al[11] reported that among the cases in Class A or B hearing preoperatively, 65% of cases maintained the hearing class postoperatively. In this study, 92.5% of the VS were small sized, not exceeding 2 cm. However, Nowak et al[8] reported that only 3 ears preserved their preoperative good hearing, and hearing was preserved in cases of small VS (≦2 cm). Therefore, early surgical intervention with small size (≦2 cm) VS for patients with NF2 may prevent the hearing loss. In Samii et al,[13] it was concluded that the goal of surgery in NF2 patients with VS should be complete removal and avoidance of functional impairment. Thus, to choose treatments according to individual's condition, such as tumor size, and patient demand is the most important.

Radiation might be the alternative choice for residual tumor. In the Maniakas and Saliba[14] study in 2014, SR have better tumor control than microsurgery; however, microsurgery had better hearing preservation than radiation. Mathieu et al[15] reported that gamma knife had a high local tumor control rate of 81% in 15 years,[16] but the hearing preservation at 5 years was 48%. In this study, there is no tumor recurrence under MS+SR. It might be a choice to remove tumor by microsurgery and treat residual tumor by SR. Kim et al[17] reported 17 NF2 patients with VS treated with MS, fractionated gamma knife radiosurgery, single session gamma knife radiosurgery, and CM. A relatively lower local control rates were reported in the MS and CM groups; however, hearing preservation in all groups could not be accomplished effectively. For only 17 patients included, it is never easy to jump into conclusions.

However, there were some limitations in the study. The number of included cases was relatively small, and both children and adults are included. The disease duration ranged from 7 to 108 months, which might be a potential bias, and the baseline hearing function varied too. This is a small retrospective cohort and no statistical analyses have been used to determine if any of the observations deviate from the norm or any previously published information on VS patients. It needs further studies to prove the results in the future.

5. Conclusion

Most NF2 patients have bilateral VS. MS is a safe and effective treatment for NF2 patients with symptomatic VS. Early treatment of small-sized VS may offer the best chance in preservation of hearing and facial nerve function. The treatment for bilateral VS should be individualized according to clinical symptoms and overall condition. However, how to preserve functional hearing and facial nerve remains an issue. Further studies are needed in order to find out the best treatment for NF2 patients with VS.

Author contributions

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