

Available online at www.sciencedirect.com



American Journal of OTOLARYNGOLOGY

American Journal of Otolaryngology-Head and Neck Medicine and Surgery xx (2012) xxx-xxx

www.elsevier.com/locate/amjoto

Salvage surgery of vestibular schwannoma after failed radiotherapy: The Gruppo Otologico experience and review of the literature

Sami Tanbouzi Husseini, MD, FEBORL-HNS^{a,*}, Enrico Piccirillo, MD^a, Abdelkader Taibah, MD^a, Tamama Almutair, MD^b, Giulio Sequino, MD^a, Mario Sanna, MD^c

^aDepartment of Otology and Skull Base Surgery, Gruppo Otologico, Piacenza-Italy ^bLeiden University Medical Center (LUMC), Leiden-The Netherlands ^cDepartment of Otology and Skull Base Surgery, Gruppo Otologico, Piacenza-Italy, University of Chieti, Chieti-Italy Received 12 August 2012

Abstract

Objectives: The use of radiation therapy has largely widespread and becomes in many centers the preference modality of treatment for symptomatic patients who are old, medically unfit for surgical therapy, those who refuse surgery and in some recurrent or residual growing tumors.

The risk of radiotherapy failure in the treatment of vestibular schwannoma might be underestimated in the literature. The purpose of this study is to show the Gruppo Otologico experience with salvage surgery to better understand the surgical outcomes and difficulties in treating vestibular schwannoma after failed radiotherapy.

Study design: Retrospective chart review of patients who required salvage surgery of vestibular schwannoma after failed radiotherapy.

Settings: Quaternary referral otology and skull base center.

Results: Between 1987 and 2010, 2500 cases of VS underwent surgical treatment at the Gruppo Otologico. Nineteen patients had received stereotactic radiation therapy before the surgical treatment. The interval time between radiotherapy and surgical salvage ranged from 1 to 10 years.

In all the cases decision of surgery was taken following an increase in tumor size with or without new onset of symptoms. Complete tumor removal was achieved in 86.6% of the cases through a transotic, transcochlear or enlarged translabyrinthine approach with trans-apical extension.

Difficult dissection of the tumor was encountered in 93.3% the cases. The facial nerve was anatomically preserved in 93.3% but its function was worsened in 73.3% of patients after at least 6 months of follow up. Malignant transformation of the vestibular schwannoma was encountered in one patient.

Conclusion: Complete surgical resection of VS is more difficult after radiotherapy with relatively poor facial nerve outcomes and nearly impossible hearing preservation.

Patients who receive radiation therapy for the treatment of vestibular schwannoma should be made aware of its potential complications and risk of failure, especially in young patients and NF2 cases. © 2012 Elsevier Inc. All rights reserved.

1. Introduction

Vestibular schwannoma (VS) is a tumor that arises from schwann cells of the vestibular nerve. The incidence ranges from 10 to 20 per million/year and it accounts for 75% of cerebellopontine angle tumors, 10% of intracranial tumors,

E-mail address: drsam_t@yahoo.com (S.T. Husseini).

and 5% of such tumors occur in patients with neurofibromatosis type 2 (NF2) [1].

The cornerstone treatment is complete surgical resection that requires an experienced surgical team. With the advances in microsurgical techniques and intraoperative monitoring tools, excellent outcomes have been achieved in terms of preservation of the facial nerve (FN) and whenever possible serviceable hearing.

In 1969 Leksell introduced the use of stereotactic radiation therapy for VS treatment [2]. Since then the use of radiation therapy became largely widespread because it

^{*} Corresponding author. Department of Otology and Skull Base Surgery, Gruppo Otologico, Piacenza-Italy, Via Emmanueli, 42, 29100 Piacenza, Italy. Tel.: +39 3277686838; fax: +39 0523453708.

^{0196-0709/\$ –} see front matter @ 2012 Elsevier Inc. All rights reserved. http://dx.doi.org/10.1016/j.amjoto.2012.09.012

seems less invasive than surgery. In many centers it becomes the modality of treatment for symptomatic elderly patients, medically unfit for surgical therapy, patients who refuse surgery, tumors occurring in the only hearing ear and in some recurrent or residual growing tumors.

The main disadvantage of radiation therapy is the nonremoval of the tumor that retains the risk of growth and thus requiring long term follow up.

In this paper we present the Gruppo Otologico experience with VS salvage surgery in patients who failed radiation therapy. A literature review and an analysis of the previous reported series were also performed.

2. Materials and methods

Between April 1983 and December 2010, two thousand three hundred eighty vestibular schwannoma were resected by the senior author (M.S.). After departmental and institutional review board approval, a retrospective chart review was conducted on all cases of VS surgically treated after having received radiation therapy at other centers.

Surgical resection following radiotherapy was performed in nineteen patients. Four patients were excluded from this study because they had previous surgery before radiation therapy. Fifteen patients were included; 6 males and 9 females.

The mean age at surgery was 52 ± 14.8 years [20-77 years]. Two patients had NF 2.

The most common symptoms before surgery were dizziness (60%), worsening of hearing loss (53.3%), facial nerve paralysis (26.6%) and facial numbness (13.3%). One patient presented with intracranial hypertension 1 year following radiotherapy; a VP shunt was inserted and the resection of the tumor was performed 3 weeks later (Table 1).

The average size of the tumor preoperatively was 3.16 ± 0.57 cm. In all the cases decision of surgery was taken after an increase in tumor size of at least 5 mm with new onset of symptoms.

The methods of radiation therapy were single stage; Gamma Knife was performed in 14 cases and Cyberknife was performed in one case. The interval time between radiotherapy and surgical salvage ranged from 1 to 10 years with a mean of 2.9 years.

The approaches were chosen according to the tumor extension. Extended translabyrinthine approach with or without transapical extension was most commonly used followed by transcochlear type A and transotic approach [3]. Two patients with NF2 underwent brainstem implantation after tumor removal.

The intraoperative findings, postoperative facial nerve outcomes and complications were reviewed. These data were compared with those from a control group who consisted of fifteen patients having vestibular schwannoma treated primarily by surgery during the same period at our institution. These patients were chosen randomly from our computer database in a way that they matched the same range of age, tumor size and surgical approaches of the first group.

To avoid a selection bias 2 patients from the control group having NF2 were selected. All the tumors were resected by the same surgeon (M.S).

The statistical comparisons between the two groups were achieved using the Pearson chi-square test for categorical variables and the Student t-test for continuous variables. Statistical significance was present if P < 0.05, two-tailed.

We performed also a detailed search in PubMed and Medline database with a complete review of all the English literature published until December 2010 regarding surgical salvage of vestibular schwannoma. Papers containing series of five or more patients who underwent surgical salvage of their tumor after failed radiation therapy (including our series) were selected for analysis.

Eight publications complied with our inclusion criteria [4–11].

3. Results

3.1. Patients

Difficult dissection of the tumor was encountered in 14 patients from the group who received radiotherapy. Difficult dissection has been defined according to the following parameters:

- Absence of the peritumoral arachnoidal plane.
- Abundant intraoperative bleeding.
- Excessive adherence to the brainstem, cerebellum, facial nerve or trigeminal nerve.

The tumor was adherent to these structures in the following percentage: FN (86.6%), brainstem (60%), cerebellum (46.6%), and trigeminal nerve (26.6%). Complete tumor removal was achieved in 13 cases (86.6%).

In one patient the tumor was highly adherent to the surrounding structures and especially to the facial nerve. The dissection of the tumor reached a point where it was impossible to differentiate between the tumor and the nerve leaving a doubt about a complete tumor removal.

One patient underwent near total resection of his tumor because of the cystic component. Left in place was only part of the cyst wall that remained stable with no sign of growth after 6 years.

The facial nerve was anatomically preserved in 14 cases (93.3%). In one case the nerve was sacrificed and reconstructed using a sural nerve graft that failed; one year later a hypoglossal to facial nerve anastomosis was performed.

In 11 patients (73.3%), the facial nerve function after one year of the surgery was worse than the preoperative status. One patient developed transient postoperative vocal cord paralysis.

Malignant transformation of vestibular schwannoma was encountered in one patient who received radiation therapy

Table 1
Demography, symptoms, intraoperative findings and surgical outcomes in 19 patients who underwent surgical resection of VS after failed radiotherapy.

Patient	Age∖ Sex	Side	Size	Hearing Pre	New symptoms	FNG pre\post	Interval time between Rx and surgery	Approach	Total Resection	Plane of cleavage	Excessive Tumor adherence to			Complications and notes	
											FN	BS	Ce	Vth	
Solitary VS	59\F	R	3.4 cm	Dead ear	FP, ICH	2\4	1y	ТО	Y	Ν	Y	Y	Ν	Y	-
olitary VS	45\F	L	3 cm	Dead ear	FP, FNumb	3\3	2y	ETLA+TA	Y	Υ	Y	Ν	Ν	Y	-
olitary VS	62\F	L	3.2	Dead ear	Dizziness FNumb	1\3	1.5y	ETLA+TA	Y	Ν	Y	Ν	Υ	Y	VCP
Solitary VS	49\F	L	3 cm	30 DB	HL	1\3	1.5y	ETLA	Υ	Ν	Υ	Ν	Ν	Ν	-
olitary VS	59\M	R	3.5	15DB	Dizziness HL	1\3	2y	ETLA+TA	Y	Ν	Y	Y	Ν	Ν	-
olitary VS	28\F	R	4 cm	20DB	Dizziness HL	$1 \setminus 1$	4y	ETLA+TA	Υ	Υ	Ν	Ν	Ν	Ν	-
olitary VS	52\F	R	2 cm	60DB	Dizziness HL	1\3	8y	ETLA	Υ	Ν	Υ	Y	Y	Ν	-
olitary VS	68\F	L	4 cm	Dead ear	DizzinessFP	2\3	2y	ETLA+TA	Υ	Υ	Υ	Υ	Ν	Ν	-
olitary VS	77\M	R	3.5 cm	30DB	HL	$1 \setminus 1$	1.5y	ETLA	Ν	Υ	Y	Ν	Ν	Ν	-
Solitary VS	47\M	L	3 cm	Dead ear	Dizziness	1\3	4y	ETLA	Υ	Ν	Y	Y	Y	Ν	-
olitary VS	64\M	R	2.5 cm	Dead ear	Dizziness HL	1\1	1.5y	ETLA	Υ	Υ	Ν	Ν	Ν	Ν	-
Solitary VS	59\F	R	3.2 cm	Dead ear	Dizziness HL	1\6	10y	ETLA+TA	Y	Ν	Y	Y	Y	Ν	FN was cut and reconstructed with sural nerve graft that failed
Solitary VS	51\M	L	3.8 cm	Dead ear	Dizziness	1\6	1.5 y	ETLA+TA	?	Ν	Y	Y	Y	Ν	-
VF2	40\F	R	2.4 cm	Dead ear	HL	1\2	1.5y	ETLA+TAABI	Y	Ν	Y	Y	Y	Ν	-
NF2	20\M	L	3 cm	55 DB	FP	4\6	5y	TC A+ABI	Y	Ν	Υ	Y	Y	Y	Malignant VS

Table 2

S.T. Husseini et al. / American Journal of Otolaryngology-Head and Neck Medicine and Surgery xx (2012) xxx-xxx

Patients	Mean of age (y)	Average of tumor size (cm)	Mean of preoperative FN grading (HB)	Difficult dissection of the tumor (%)	Mean of postoperative FN grading (HB)	Complete resection of the tumor (%)				
Irradiated (15)	52	3.16	1.46	93.3	3.2	86.6				
Non irradiated (15)	53.6	3.22	1.52	20	2.1	93.3				
P value	0.83	0.82	0.33	0.02*	0.011*	0.9				

Summary of the comparison between the two groups of patients irradiated vs non irradiated.

Abbreviations: FN, facial nerve; y, year; HB, House-Brackmann grading,

* P value is significant if<0.05.

5 years prior to surgery; he passed away three months postoperatively secondary to a respiratory failure [12].

None of the patients had any recurrence of the disease after a follow up that ranged from 1 to 7 years.

In comparison with the control group, the patients who received radiation therapy prior to surgical intervention had a worse postoperative FN function (P=0.011) with more difficult tumor dissection (P=0.02).

On the other hand, difficult dissection of the tumor was encountered in three patients from the control group. One patient had cystic VS, one patient had a tumor size of 4 cm that was completely removed but after accidental FN interruption that was reconstructed using a sural nerve graft. The third patient was a case of NF2 having a tumor size of 3.5 cm.

No statistical significance was detected when comparing age, tumor size, preoperative FN grading or adequacy of tumor removal between the two groups (Table 2).

3.2. Literature review

The data from these articles compiled with our series resulted into 135 patients who didn't respond to radiation therapy and underwent surgical removal of the VS.

One paper reported by Slattery et al. was abandoned because it consisted of the same group of patients included in a larger study published by Friedman et al. 10 years later.

Also excluded from the analysis were the publications/ reports that only mentioned the number of cases that failed

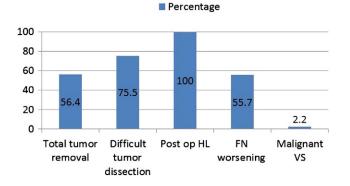


Fig. 1. Summary of surgical outcomes and pathology results of the data pooled from all the series in the literature (135 patients) describing surgical salvage of VS after radiotherapy failure. Abbreviation: FN, facial nerve; HL, hearing loss; op, operative; VS, vestibular schwannoma.

the radiation therapy without giving any details and outcomes about the surgical intervention [13,14].

Surgical outcomes and intraoperative findings are summarized in Fig. 1 and Table 3.

The most common approach for tumor removal was the translabyrinthine followed by retrosigmoid, transcochlear type A, trans-otic and middle cranial fossa approach.

Total tumor removal was achieved from 0 to 89% and in one study the aim of the surgery was only decompression for symptoms relief [11].

Difficult dissection of the tumor ranged from 43 to 100%. None of these patients had postoperatively any serviceable hearing in the operated ear and 25–83% had worsening of their FN function. Malignant vestibular schwannoma was reported in three cases (2.2%) (Table 3).

4. Discussion

Decision making in the management of vestibular schwannoma remains a controversial issue in neuro-otology and skull base surgery.

The percentage of tumor growth during conservative management is variable in the literature depending on the length of the follow up period and the number of published cases.

Rosenberg et al. indicated that out of 80 patients 57.7% continued to grow whereas 34.6% remained stable and 7.7% regressed after a mean follow up of 52.8 months [15].

On the other hand Alsanosi et al. found in a study over a 197 patients followed for up to 40.8 months that 28% of VS progressed, 69% remained stable and 3% involuted [16].

The largest study by Stangerup et al. included 322 patients demonstrated that only 29% of the tumors have grown within a mean period of 42 months [1].

A monitoring period with MRI (Wait and Scan policy) of at least 12 months is recommended before taking the decision of treating small non-cystic VS.

Our experience with conservative management of VS showed that 163 out of 318 patients (57.5%) had no growth of their tumor after a mean follow up of 24 months, 102 (32.1%) had slow growth of the VS (1–5 mm/year) and in 53 patients (16.7%) the tumor grew fast (>5 mm/year). Only 94 patients (29.6%) were treated surgically after a mean period of 18 months (unpublished data).

Although the surgical choice is the mainstay of treatment for total tumor removal, the use of radiation therapy is more and more elected specially during the last decade.

Table 3

Surgical outcomes and tumor characteristics of patients who underwent salvage surgery after radiotherapy failure(series published in the English literature containing \geq 5 cases).

Author	Nb	NF 2	Revision surgery	Interval time between Rx and surgery	Total removal	Approach	Difficult dissection of the tumor	HP	FN worsening	Malignant VS
Pollock 1998	13	0	6	7 m-6y	7 (53%)	RS: 11 TLA:1 Comb: 1	8 (61.5%)	0	10 (77%)	1
Battista 2000	12	5	4	3 m-6y	NA	RS:2 TLA:10	9 (79%)	0	10 (83%)	0
Limb 2005	9	NA	0	NA	3 (33.3%)	RS: 8 TLA: 1	9 (100%)	?	5 (56%)	0
Friedman 2005	38	10	0	5.2 m-15.8y	30 (78.9%)	RS:1 TLA:34 MCF:2 TC A:1	34 (89%)	0	16 (42%)	0
Iwai 2007	6	1	2	4m-12y	0	RS:6 IAC was not opened	6 (100%)	NA	2 (33%)	0
Shuto 2008	12	NA	4	6m-10y	0	RS: 12	7 (58.3%)	0	3 (25%)	0
Roche 2008	23	0		10m-8y	15 (65.2%)	RS:5 TLA:18	10 (43%)	0	15 (65.2%)	0
Lee 2010	7	NA	4	3 m-6y	0	Only decompression	N\A	0	NA	1
Our study	15	0	0	1y-10y	13 (86.6%)	ETLA:5 ETLA+TA: 7 TO:1 TC A: 2	14 (93.3%)	0	14 (73.3%)	1

Abbreviations: m, month; y, year; Com, combined; ETLA, extended translabyrinthine approach; FN, Facial nerve; HP, hearing preservation; IAC, internal auditory canal; NA, not available; Nb, number; NF2, Neurofibromatosis type 2; RS, retrosigmoid; Rx, radiotherapy; TCA, transcochlear type A; TO, transotic; TA, transapical; VS, vestibular schwannoma.

This could be attributed to the fact that radiation therapy is less invasive than surgical treatment with a short hospital staying (≤ 1 day), a rapid recovery, better quality of life post treatment, and a control rate of the tumor that ranges from 87 to 98.4% [11,17].

There are two main different modalities of radiation therapy in the treatment of vestibular schwannoma:

- The single session protocol or *Stereotactic Radiosurgery* that consists of delivering to the tumor a single high-dose of radiation. The skull should be rigidly immobilized to a frame. The radiation beams can be delivered by a modified linear accelerator machine or a Leksell Gamma Knife machine which is more commonly used in the treatment of vestibular schwannoma.
- The fractionated type or *Stereotactic Radiotherapy* consists of giving the required radiation dose over several sessions. This technique is performed through a linear accelerator machine with a relocatable frame (Novalis, Radionics) or with a frameless image-guided, robotic system (Cyberknife).

Regardless the source of radiation in stereotactic radiotherapy (proton, photon, neutron, or ion beams), the tumor center receives the maximal radiation dose (isodose) that gradually decreases in the periphery and surrounding structures. The effect of radiation therapy doesn't show until 4–6 weeks post treatment when the acute inflammatory

reaction starts to appear with a progressive focal edema and an increase in the volume of the tumor that might become 26-280% larger than the initial size [18].

Pollock et al. noted three types of VS enlargement after radiation surgery: type 1 showed tumor regression to the initial size or even less. In type 2 the tumor remained stable after the initial enlargement and the patient remained asymptomatic with no need of any treatment.

Type 3 was devoted for the tumor that continued to enlarge with subsequent risk of compressive symptoms and need for further intervention [18].

On magnetic resonance imaging (MRI), a loss of central enhancement is found in 93% of the tumor. Multi-septated cyst formation is also common after radiation therapy secondary to tumor necrosis and protein leak from the intratumoral vessels (Fig. 2). This reaction remains active till 12–18 months after radiotherapy when the chronic inflammation starts to resolve and be replaced by glial formation to the surrounding structures.

The excessive scarring of the tumor to the adjacent nerves in addition to the direct toxic effect of the radiation with the surrounding vasculitis elucidates the delayed occurrence of radiation induced neuropathies and even demyelination of the nerves [19].

The complication of radiation therapy is underestimated and has not been properly addressed in the literature. The most common complications are hearing loss, trigeminal hypoesthesia and facial nerve paralysis with an incidence

S.T. Husseini et al. / American Journal of Otolaryngology-Head and Neck Medicine and Surgery xx (2012) xxx-xxx

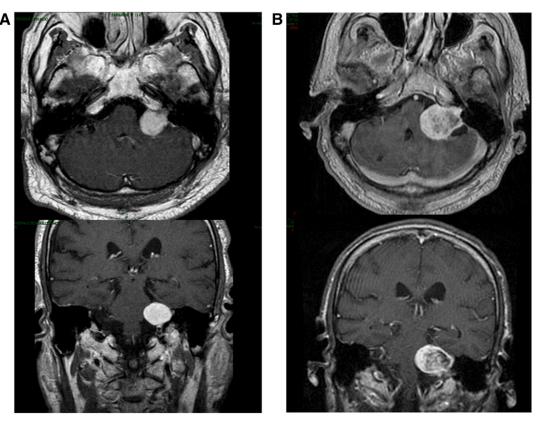


Fig. 2. A, Axial and coronal MR images (T1 weighted with contrast) obtained from a 52-year-old woman with left vestibular schwannoma who received radiotherapy for a 2.3 cm diameter tumor. B, Enlargement of the vestibular schwannoma with loss of central enhancement and cystic formation 1 year after radiotherapy.

that ranges from (25% to 89%), (19% to 34%) and (8% to 32%) respectively [19–21].

These complications can occur up to 28 months post radiotherapy even without tumor growth [21].

The pathophysiology of hearing loss following radiotherapy could be explained by several mechanisms:

- Damage to the auditory pathways even from direct effect of the radiation or secondary to a decrease in blood flow due to vasculitis and hyalinization of vessel walls.
- Compression of the cochlear nerve in the internal auditory canal secondary to the tumor enlargement.
- Acute intracochlear hemorrhage.

Less common complications are ataxia, cerebral edema, hemifacial spasm, quadriplegia, hydrocephalus and malignant transformation of the VS [5].

The incidence of hydrocephalus secondary to radiotherapy ranges from 4% to 14%. It can occur even without evidence of increase in the tumor size or compression by the tumor.

The pathophysiology of communicating hydrocephalus following radiotherapy is explained by tumor necrosis that results into elevation of CSF protein that obstructs the arachnoid granulations with subsequent CSF malabsorption [22].

A publication by Jeon et al. showed that nine of 90 patients who received radiotherapy as primary treatment of VS developed communicating hydrocephalus whereas only one of 146 patients (0.68%) who underwent primary surgical resection of the tumor developed this complication. Up to this date, our experience with VS surgery revealed 2 out of 2380 patients (0.0008%) who underwent surgical resection of their tumor developed postoperative communicating hydrocephalus.

Malignant brain tumor following stereotactic radiotherapy of VS has been reported in several studies. It occurred from 6 months to 19 years after radiation therapy [12,23,24].

Ron and Sadetzki reported that brain tissue exposure to radiation doses as low as 1 Gy was sufficient for the development of a secondary tumor. Radiation induced malignant brain tumor has been reported in solitary schwannoma as well as in NF2 [12]. Warren et al. demonstrated that VS removed from NF2 patients previously irradiated had more chromosomal anomalies than non irradiated tumors. Besides, Baser et al. mentioned that NF2 patients who have received radiotherapy had a 14-fold increased risk of developing malignant brain tumors [24].

Despite its low incidence, the risk of radiation induced malignant brain tumor and de novo benign cerebral tumors should be considered in the counseling and the decisionmaking process of VS treatment.

S.T. Husseini et al. / American Journal of Otolaryngology-Head and Neck Medicine and Surgery xx (2012) xxx-xxx

Since 1993, in order to decrease the incidence of radiosurgery complications, the doses of radiation have been reduced to 15-25 Gy of isodose and 10-15 Gy of marginal dose [25].

Radiation therapy is abused in some centers who recommend such treatment for all VS regardless the age of the patient, the size of the tumor, the presence of cystic component and without clear evidence of tumor growth [26,27].

It is generally accepted that radiation therapy should not be given for tumors greater than 3 cm due to two reasons:

- To avoid compressive symptoms following normal expected growth that occurred within the first year
- To prevent the morbidity related to radiation therapy, due to the fact that such large tumors need a higher therapeutic dose.

Our experience in VS surgery with a tumor size less than 3 cm (1710 cases) shows excellent outcomes regarding functional preservation of the facial nerve (93.5% grade 1–3) as well as preservation of serviceable hearing in cases of small tumors (<1.5 cm) with non enlarged internal auditory canal (36.4%). Complete resection of the tumor was achieved in 96.2% of these patients with minimal morbidity and no recurrent tumor was encountered after at least 3 years of follow up.

Excellent results are also reported by other specialized referral skull base and neuro-otology centers that showed no major benefits of radiotherapy on surgery [7].

The rate of tumor control with radiotherapy might be overestimated in the literature.

It should be considered that the percentage of vestibular schwannoma that grew following a "wait and scan" period ranged from 28 to 73% [15,16]. In many centers stereotactic radiotherapy is performed before the proof of any tumor growth, the good result following radiotherapy might be attributed to the natural course of the disease and not to the efficacy of the radiation [28].

In addition, in many articles the rate of failure didn't include the group of asymptomatic patients who showed progressive tumor enlargement for more than 2 years post radiation and didn't require further therapy up to the time of the studies [11].

In almost all the publications that reported good control of the tumor growth following radiation therapy, the mean follow up period ranged from 2 to 5 years, which is considered as an inadequate period in comparison to the follow up needed to define the success of radiation therapy in the treatment of benign brain tumors (pituitary tumor, meningioma).

Breen et al. reported that tumor control rate following radiotherapy for nonfunctional pituitary adenoma decrease with time even after 20 years of follow up [29].

Maire et al. has reported a patient who required surgical salvage of VS 19 years after radiotherapy.

Besides, most of these papers showed the experience with the high dose of radiation.

By no means, the use of reduced dosage of radiation since 1993 might decrease the tumor control rate with a subsequent increase in the number of cases requiring surgical intervention.

Therefore long term follow up studies (up to 2 decades) using the small radiation dose are necessary to prove the efficacy of such modality of treatment.

As mentioned previously a tumor enlargement within 1 year after radiotherapy is a normal finding and should not be considered as an indication of surgery unless the patient has compressive symptoms or severe complications secondary to tumor growth (brainstem compression, hydrocephalus). The cranial nerves during this period are very vulnerable to be injured during surgical manipulation.

Most authors agreed that removal of VS is more difficult in a patient who received radiation therapy than in a patient who didn't [5-8].

Difficulties in tumor dissection ranged from 43% to 100% of the cases. Most commonly they found a loss of the peritumoral arachnoidal plane with thickening of the arachnoid, adjacent scarring to the facial nerve, trigeminal nerve and brainstem. Other intraoperative difficulties were adherence of the tumor to the cerebellum, lower cranial nerve, anterior inferior cerebellar artery and excessive intraoperative bleeding [5,9].

The postoperative facial nerve function outcomes varied from a report to another depending on the completeness of tumor removal, but in all the cases the results were much worse than the patients who didn't receive radiation therapy.

Iwaie et al. found that 33% of their patients had worsening of the facial nerve function after at least 11 months of follow up even though in all cases the internal auditory canal was not opened and residual tumors were left on the facial nerves [8].

Friedman et al. recommended subtotal resection of irradiated tumor when it is adherent to the facial nerve. Despite this protocol, these patients had poorer facial nerve function outcomes than the nonirradiated group.

Regardless of the approach and whether the tumor was totally or subtotally removed, no single case was encountered with preserved postoperative serviceable hearing.

We prefer to perform the enlarged translabyrinthine, transotic or transcochlear approaches to ensure total removal of the tumor because in most of our cohort, the tumor size was greater than 1.5 cm or the patients had a poor hearing status.

In our series complete tumor removal was achieved in 84.2% of the cases. Residual cystic walls of the tumor were left in two VS with no sign of growth after a follow-up period of 3 y and 6 y respectively.

Around 73.3% of our patients had worsening of FN function postoperatively, and 63.6% of those who complained from this deterioration had HB facial nerve grade 2-3.

These relatively poor facial nerve outcomes are attributed not only to the loss of plane between the tumor and the nerve but also to the reduction of the neural regeneration secondary 8

to radiation therapy. This deficit in neural regeneration and the capacity of spontaneous recovery from surgical trauma could be attributed to the decrease in blood supply of the nerve following radiation therapy [7].

According to our experience we believe that complete tumor resection is the gold standard therapy to prevent a second salvage surgery that will be much more difficult with a high morbidity rate and to avoid the risk of malignant tumor transformation.

We recommend subtotal or near total resection only in cases of elderly patients or with cystic tumor when the cyst wall could be left on vital and neurovascular structures [30].

5. Conclusion

Radiation therapy should not be considered as an optional treatment of vestibular schwannoma without a clear and documented evidence of tumor growth. The patients should be made aware of its complications and risk of failure, especially in young patients and NF2 cases.

Surgical resection of VS after failed radiotherapy is very challenging with relatively poor facial nerve outcomes and very difficult hearing preservation.

We recommend the neuro-otology and skull base centers to publish their experiences with surgical salvage of VS to carry out an optimal protocol for the treatment of VS after failed radiation therapy.

References

- Stangerup SE, Caye-Thomasen P, Tos M, et al. The natural history of vestibular schwannoma. Otol Neurotol 2006;27:547-52.
- [2] Leksell L. A note on the treatment of acoustic tumors. Acta Chir Scand 1971;137:763-5.
- [3] Sanna M, Mancini F, Russo A, et al. Atlas of Acoustic Neurinoma Microsurgery. 2nd ed. Piacenza: Thieme; 2010. p. 60-80.
- [4] Pollock BE, Lunsford LD, Kondziolka D, et al. Vestibular schwannoma management. Part II. Failed radiosurgery and role of delayed microsurgery. J Neurosurg 1998;89:949-55.
- [5] Battista RA, Wiet RJ. Stereotactic radiosurgery for acoustic neuromas: survey of the American Neurotology Society. Am J Otol 2000;21:371-81.
- [6] Limb CJ, Long DM, Niparko JK. Acoustic neuromas after failed radiation therapy: challenges of surgical salvage. Laryngoscope 2005; 115:93-8.
- [7] Friedman RA, Brackmann DE, Hitselberger WE, et al. Surgical salvage after failed irradiation for vestibular schwannoma. Laryngoscope 2005;115:1827-32.
- [8] Iwai Y, Yamanaka K, Yamagata K, et al. Surgery after radiosurgery for acoustic neuromas: surgical strategy and histological findings. Neurosurgery 2007;60:75-82.
- [9] Shuto T, Inomori S, Matsunaga S, et al. Microsurgery for vestibular schwannoma after gamma knife radiosurgery. Acta Neurochir (Wien) 2008;150:229-34.

- [10] Roche PH, Khalil M, Thomassin JM, et al. Surgical removal of vestibular schwannoma after failed gamma knife radiosurgery. Prog Neurol Surg 2008;21:152-7.
- [11] Lee CC, Yen YS, Pan DH, et al. Delayed microsurgery for vestibular schwannoma after gamma knife radiosurgery. J Neurooncol 2010;98: 203-12.
- [12] Husseini ST, Piccirillo E, Taibah A, et al. Malignancy in vestibular schwannoma after stereotactic radiotherapy: a case report and review of the literature. Laryngoscope 2011;121:923-8.
- [13] Kapoor S, Batra S, Carson K, et al. Long-term outcomes of vestibular schwannomas treated with fractionated stereotactic radiotherapy: an institutional experience. Int J Radiat Oncol Biol Phys 2011;81:647-53.
- [14] Phi JH, Kim DG, Chung HT, et al. Radiosurgical treatment of vestibular schwannomas in patients with neurofibromatosis type 2: tumor control and hearing preservation. Cancer 2009;115:390-8.
- [15] Rosenberg SI. Natural history of acoustic neuromas. Laryngoscope 2000;110:497-508.
- [16] Al Sanosi A, Fagan PA, Biggs NDW. Conservative management of acoustic neuroma. Skull Base 2006;16:95-100.
- [17] Yang I, Aranda D, Han SJ, et al. Hearing preservation after stereotactic radiosurgery for vestibular schwannoma: a systematic review. J Clin Neurosci 2009;16:742-7.
- [18] Pollock BE. Management of vestibular schwannomas that enlarge after stereotactic radiosurgery: treatment recommendations based on a 15year experience. Neurosurgery 2006;58:241-8.
- [19] Schulder M, Sreepada GS, Kwartler JA, et al. Microsurgical removal of a vestibular schwannoma after stereotactic radiosurgery: surgical and pathologic findings. Am J Otol 1999;20:364-7.
- [20] Flickinger JC, Lunsford LD, Coffey RJ, et al. Radiosurgery of acoustic neurinomas. Cancer 1991;67:345-53.
- [21] Lunsford LD, Linskey ME. Stereotactic radiosurgery in the treatment of patients with acoustic tumors. Otolaryngol Clin North Am 1992;25: 471-91.
- [22] Jeon CJ, Kong DS, Nam DH, et al. Communicating hydrocephalus associated with surgery or radiosurgery for vestibular schwannoma. J Clin Neurosci 2010;17:862-4.
- [23] Rowe J, Grainger A, Walton L, et al. Risk of malignancy after gamma knife stereotactic radiosurgery. Neurosurgery 2007;60:60-5.
- [24] Baser ME, evans DG, Jackler RK, et al. Neurofbromatosis 2, radiosurgery and malignant nervous system tumors. Br J Cancer 2000;82:998.
- [25] Pollock BE, Lunsford LD, Norén G. Vestibular schwannoma management in the next century: a radiosurgical perspective. Neurosurgery 1998;43:475-81.
- [26] Noren GD, Hirsch A, Lax I. Gamma knife surgery in acoustic tumors. Acta Neurochir Suppl (Wein) 1993;58:104-7.
- [27] Ogunrinde OK, Lunsford LD, Flickinger JC, et al. Cranial nerve preservation after stereotactic radiosurgery for small acoustic tumors. Arch Neurol 1995;52:73-9.
- [28] Yamamoto M, Jimbo M, Ide M, et al. Is unchanged tumor volume after radiosurgery a measure of outcome? Stereotact Funct Neurosurg 1996; 66(Suppl 1):231-9.
- [29] Breen P, Flickinger JC, Kondziolka D, et al. Radiotherapy for nonfunctional pituitary adenoma: analysis of long-term tumor control. J Neurosurg 1998;89:933-8.
- [30] Piccirillo E, Wiet MR, Flanagan S, et al. Cystic vestibular schwannoma: classification, management, and facial nerve outcomes. Otol Neurotol 2009;30:826-34.