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Research Article

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Prospective Study of Glomus Jugulare and Tympanicum Tumors: Clinical Findings, Surgical Approach and Outcomes, Short-Term Follow-Up: A Clinical Perspective

Golmehr Sistani[1], Masoud Motasaddi Zarandi[1*], Nasrin Yazdani[1], Mohammad Taghi Khorsandi Ashtiani[1] and Zahra Mokhtari[1]

Abstract

A glomus tumor is the most common primary tumor of the middle ear, typically presenting with pulsatile tinnitus and unilateral hearing loss. This study provides a clinical perspective of glomus tumors.

Methods: A prospective study was performed on 26 patients (10 with glomus tympanicum and 16 with glomus jugulare) from January 2009 to January 2011 in Amir Alam Hospital (tertiary referral center). All patients underwent neurological examination, audiometry, and radiological survey before and after surgery. A questionnaire was completed by patients to evaluate their postoperative quality of life. The Fisch classification was used in this study.

Results: The mean age of the patients was 45.4 years. Hearing loss was the most common symptom and pulsatile tinnitus the most common symptom prompting the patients to seek medical care. Ten glomus tympanicum patients underwent surgery using the transcanal or transmastoid approaches and 16 glomus jugulare patients underwent pre-op embolization and surgery via the infratemporal approach. One patient underwent adjuvant radiotherapy due to incomplete resection. Small tumors were removed without rerouting of the facial nerve. For large tumors (classes C, D, and sometimes B), our approach was anterior rerouting of the nerve. When the nerve was involved, we transected the involved part and grafted it to the greater auricular nerve. Post-operatively, vertigo and tinnitus significantly decreased, while the air-bone gap increased in jugulare patients and reduced slightly in tympanicum. Of all the patients, 42.3 had pre-operative lower cranial nerve deficits and 26.7% found new deficits after surgery. Eight patients with glomus jugulare developed facial nerve paralysis post-operatively that eventually resolved to grade I-II House-Brackmann in follow-up. There was also one recurrence. The most common cause of depressive mood and anxiety in patients after surgery was facial nerve dysfunction.

Conclusions: Surgical removal is an acceptable approach for achieving total tumor removal. Although immediate post-op morbidities (especially facial nerve palsy) in the infratemporal approach were considerable, follow-up showed improvement of nerve dysfunctions. The high percentage of pre-operative cranial deficits (42.3%) suggests that the majority of the deficits were related to the late diagnosis of the tumor, not to the treatment modality or surgical approach. This fact highlights the importance of physicians paying attention to the red flags of this disease.

Keywords

Glomus tympanicum; Glomus jugulare; Surgical approach; Preoperative; Postoperative

Introduction

In 1941, Guild described the paraganglion tissue that was close to the jugular bulb and Jacobson`s nerve in the middle ear to glomus bodies [1]. In subsequent research, Rossenwasser and Otani found a vascular histologic similarity to carotid body-like tumor [2]. Glomus tumors are classified by their origin of tumor involvement [3], so that tumors confined to the middle ear and mastoid with intact jugular bulb are called glomus tympanicum. These originate from vascular structures along the tympanic branch of IX (Jacobson`s nerve) and the auricular branch of X (Arnold`s nerve). Glomus jugulare tumors arise from the paraganglia in the adventitia of the dome of the jugulare bulb or over the promontory [4], while those from the perineurinum of the vagus nerve are glomus vagale tumors [5].

Glomus tumors are the most common primary neoplasms of the middle ear. Females are four to six times more likely to develop them than males. However, in familial tumors, males are more affected [6]. Secretory functions and multi-centricity are rare and often occur in familial forms [6].

Glomus tumors grow slowly but relentlessly and most often present as an asymptomatic, space-occupying mass lesion [6,7]. As the tumor progresses, it produces symptoms which are varied by involvement patterns, compression and dysfunction of adjacent neurovascular structures, especially cranial nerves. The aim of treatment is hearing conservation and the reduction of neurological deficits [8,9]. Surgery, not unlike the tumor's growth, is associated with morbidities which have led to controversies in management of glomus tumors [10], especially glomus jugulare with intracranial extension. This study describes pre-operative and post-operative symptoms and signs, and then discusses treatment modalities and surgical strategies and outcomes.

Materials and Methods

A prospective study was performed on 30 patients with glomus tumors from January 2009 to January 2012 in Amir-Alam Hospital, which is the largest referral center of otolaryngology in Iran. All patients underwent a complete neurological examination, audiometry, and radiological survey before surgery and during follow-up. As follow-up, a radiologic work up (CT scan or MRI) was performed 6 and 18 months after surgery. Additionally, audiometry tests were performed, including pure-tone audiometry (PTA) and speech reception threshold (SRT). Urinary catecholamine screening was conducted in cases where functional tumors were suspected. Patients' quality of life was also assessed in the follow-up phase.

***Corresponding author:** Masoud Motasaddi Zarandi, Tehran University of Medical Sciences, Otorhinolaryngology Department and Research Centre, Amir-Alam Hospital, Taghavi Street, North Sadi Street, Tehran- 1145765111, Iran, E-mail: mmotesadizarandy@yahoo.com

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All 26 patients returned for follow-up investigations, which lasted on average 18.2 months. Ten patients presented with glomus tympanicum and 16 with glomus jugulare. Of these, 20 (76.9%) were female and six were male. The female-to-male ratio was 3.33. The mean age at diagnosis was 45.4 years, with a range from 23 to 74. The first peak was between 55-50 years and the second peak between 45-40 years, respectively.

All patients underwent surgery, and only one patient (due to incomplete resection) required post-surgical radiotherapy. The incomplete resection was due to bleeding during surgery. Pre-operative embolization was performed in glomus jugulare tumors. Three of the cases had undergone surgery for glomus jugulare tumors prior to our study. Two of these had been operated on once before at other hospitals and underwent surgery for the second time at our center, while the third of the three cases had already undergone surgery twice before at our center (18 and 10 years ago) and underwent surgery for the third time. These cases were included in the study in order to assess clinical findings at the recurrence time.

To assess the effect of surgery on the patients' quality of life, a questionnaire was completed by patients during follow-up visits. We deployed the questionnaire, which was used by Briner et al. [10]. This questionnaire was provided in patients' primary language (Farsi). It contained items like resumption of work, housekeeping abilities, mood assessment, and whether or not the patient would recommend the operation to other patients.

The Fisch classification of glomus tumors was used in this study [11] and data was analyzed by a statistical software package (PSPP). Nevertheless, statistical analysis in such a small sample may not be useful.

Results

Sixteen patients had right-sided tumors and 10 had left-sided ones. Family history of glomus tumors was negative in all cases. The most common symptom was hearing loss (88.5%) but pulsatile tinnitus was the most frequent initial complaint (73.1%) that led the patients to seek out medical assistance. Table 1 contains a list of the initial complaints. Symptoms and signs are reported in Table 2 and 3 according to tumor types and classifications. Vertigo prevalence in Class D patients was 71.4%, in contrast to a prevalence of 10% in Class A patients ($p \leq 0.028$). Half of the patients who presented with headache had Class C tumors, and none of the Class A patients had headache ($p \leq 0.030$).

Small glomus tympanicum tumors (Class A) were removed using the transcanal approach and larger tumors extending to the mastoid (Class B) were removed by the transmastoid approach. At first, all patients with glomus jugulare tumors (classes C and D) underwent preoperative embolization to reduce bleeding during surgery, after which surgery via the infratemporal approach Fisch type A was performed. One of patients underwent adjuvant radiotherapy due to incomplete re-sectioning.

Dealing with facial nerves during surgery was categorized as follows: In cases with normal function of the facial nerve pre-operatively, we tried to preserve function and continuity of the nerve by removing the tumor with the retrofacial approach without rerouting of the nerve, especially in small tumors. External auditory canal and hearing could also be preserved by this approach [12]. In large tumor cases (classes C, D and sometimes B), the approach was anterior rerouting of the nerve. When the facial nerve was involved, the involved part was resected and grafted with the greater auricular nerve. Finally, when we faced an infiltrated nerve with normal function or acceptable contraction of facial muscles, the nerve was left intact with a small part of the tumor around it.

In the post-operative follow-up, pulsatile tinnitus resolved in 14 patients and decreased in the rest ($p \leq 0.001$). Two glomus tympanicum patients with CHL (conductive hearing loss) got normal hearing and two patients became deaf. Hearing changes are shown in Figure 1. Headache was resolved in two patients and vertigo was completely eradicated in six patients and decreased in the others with Class D glomus jugulare ($p \leq 0.030$). After surgery, pain was relieved in three of five patients with otalgia.

The facial nerve was affected in four cases before surgery. Three of these cases, including one man and two women, had House-Brackmann grade II-III and the fourth patient was a woman with grade V.

In the immediate post-operative period, facial nerve dysfunctions were observed in eight of the remaining 22 patients with normal pre-operative facial nerve function. Seven of them had grade II-III and one of them had grade IV facial nerve paralysis.

All patients with pre-operative or post-operative facial nerve dysfunction (except the one with preoperative grade V) showed progressive improvements at their follow-up examinations. The facial nerve was not affected in any of the patients with glomus

Initial Complaint	Tumor Type		Total
	Tympanic n(% of initial complaint)	Jugulare n(% of initial complaint)	n(% of initial complaint)
Tinnitus	8(80)	11(68.8)	19(73.1)
HL	1(10)	3(18.8)	4(15.4)
Dysphonia	0	2(12.5)	2(7.7)
Headache	1(10)	0	1(3.8)

HL: hearing loss; n: number

Table 1: Initial complaint that led to search for Health Centers by tumor types.

Symptoms/ Signs(S&S)	Tumor Types		
	Tympanic n(% of S&S)	Jugulare n(% of S&S)	Total n(% of S&S)
Number	10	16	26
Pulsatile Tinnitus	8(80)	14(87.5)	22(84.6)
Otalgia	2(20)	3(18.8)	5(19.2)
Hearing Loss	9(90.0)	14(87.5)	23(88.5)
CHL	5(50)	4(25)	9(34.6)
SNHL	1(10)	1(6.3)	2(7.7)
MHL	2(20)	2(12.5)	4(15.4)
Deaf	1(10)	7(43.8)	8(30.8)
Vertigo	2(20)	7(43.8)	9(34.6)
Headache	2(20)	4(25)	6(23.1)
Dysphonia	0	6(37.5)	6(23.1)
Dysphagia	0	5(31.3)	5(19.2)
Aspiration	0	4(25)	4(15.4)
Blurred Vision	0	1(6.3)	1(3.8)
HTN Crisis	0	1(6.3)	1(3.8)
Length of History (average in months)	24.8	33.1	-

CHL: conductive hearing loss; SNHL: sensorineural hearing loss; MHL: mixed hearing loss; n: number

Table 2: Presenting symptoms and signs by tumor types at diagnosis.

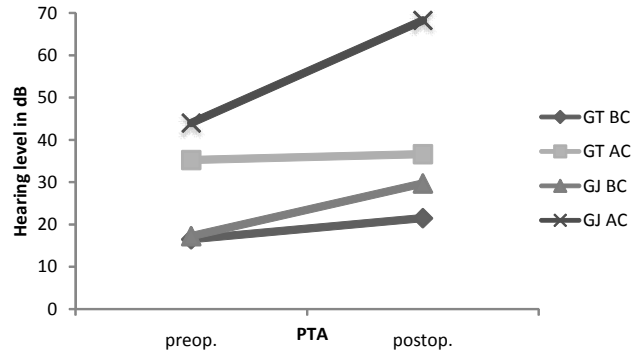

Figure 1: Preoperative and postoperative hearing loss changes by tumor type (GT: Glomus Tympanicum; GJ: Glomus Jugulare; BC: bone conduction; AC: air conduction).

Symptoms/Signs	Tumor Class				
	A n(% of S&S)	B n(% of S&S)	C n(% of S&S)	D n(% of S&S)	Total n(% of S&S)
Number	10	3	6	7	26
Pulsatile Tinnitus	9(90)	2(66.7)	6(100)	5(71.4)	22(84.6)
Otalgia	1(10)	1(33.3)	2(33.3)	1(14.3)	5(19.2)
Hearing Loss	9(90)	3(100)	5(83.3)	6(85.7)	23(88.5)
CHL	6(60)	1(33.3)	1(16.7)	1(14.3)	9(34.6)
SNHL	1(10)	0	1(16.7)	0	2(7.7)
MHL	2(20)	1(33.3)	0	1(14.3)	4(15.4)
Deaf	0	1(33.3)	3(50)	4(57.1)	8(30.8)
Vertigo	*1(10)*	2(66.7)	1(16.7)	5(71.4)	9(34.6)
Headache	*0*	2(66.7)	3(50)	1(14.3)	6(23.1)
Dysphonia	0	0	2(33.3)	4(57.1)	6(23.1)
Dysphagia	0	0	2(33.3)	3(42.9)	5(19.2)
Aspiration	0	0	1(16.7)	3(42.9)	4(15.4)
Blurred Vision	0	0	0	1(14.3)	1(3.8)
HTN Crisis	0	0	0	1(14.3)	1(3.8)
Length of History (average in months)	26.6	18	32	37	-

CHL: conductive hearing loss; SNHL: sensorineural hearing loss; MHL: mixed hearing loss; n: number

Table 3: Presenting symptoms and signs by tumor class at diagnosis.

tympanicum. However, 42.3% of patients had pre-operative cranial nerve deficits (VII, IX, X, XI, XII) and 38.5% developed new deficits after surgery (Table 4); 26.7% out of this 38.5% had lower cranial nerve deficits (IX, X, XI, XII). Pre-operative and post-operative facial nerve dysfunctions and lower cranial nerve deficits are summarized in Table 4. In patients with shoulder dysfunction, physical therapy caused improvement and pain reduction.

The follow-up revealed that one male patient developed recurrence 18 months after surgery. His initial complaint at diagnosis was pulsatile tinnitus, whereas at the recurrence, he had no symptoms (the tumor recurrence was found in imaging). His treatment consisted of observation with serial imaging at regular intervals. At the first consideration, three cases were operated on due to recurrences. Two patients had undergone surgery in other hospitals (one five years and the other two years prior to the time of the study). These two cases had pulsatile tinnitus both at the initial diagnosis and at the recurrence. One woman had been operated on twice previously (18 and 10 years ago) at our center. Her principal symptom in both recurrences was headache. She became deaf after the second surgery but no facial or cranial nerve dysfunctions were reported after all three surgeries.

One patient had hypertensive crisis with stress, but her urinary level of catecholamine metabolisms was normal. None of the remaining cases had symptoms suggestive of secretory tumor. Seven patients (26.9%) had hypertension, whereas the mean prevalence of hypertension in Iran is 12.54% [13].

Two patients did not return to work for one year after surgery, one because of dysphonia (she was a teacher) and the other who was suffering from left ear hearing loss, developed right ear hearing loss, post-operatively. Other than for these two patients, the others returned to their former occupations after three weeks on average. Seven patients were housewives or retired before surgery and none of them reported problems with housekeeping. Facial nerve dysfunction was the most common complaint led to a depressive mood within six months after surgery. All patients with glomus tympanicum recommended the same treatment to other patients and 75% of patients with glomus jugulare recommended it.

Discussion

The gender distribution of patients corresponded with most of the studies and there is a predilection of right-side involvement. Even though the prevalence of hearing loss was more than tinnitus, the most common initial complaint was pulsatile tinnitus. This finding suggests that pulsatile tinnitus more than unilateral hearing loss leads a patient to seek medical care. Ignoring unilateral hearing loss may be due to the slow growth of the tumor and the delay between the first symptoms and the diagnosis [14]. Before surgery, vertigo was significantly more common in Class D tumors, and after surgery vertigo remained in three patients with Class D tumors. From this finding, it is possible that vertigo may represent tumor advancement. Headache is a non-specific common symptom in tumors located at the base of the skull, but no Class A patients reported headache. Pulsatile tinnitus and vertigo decreased significantly after surgery. The mean hearing level of patients with glomus tympanicum remained almost the same post-operatively but became worse in glomus jugular patients (Figure 1). Additionally, the air-bone gap increased in glomus jugulare patients after surgery, whereas it slightly decreased in glomus tympanicum patients.

Overall, facial nerve dysfunctions significantly increased after surgery. The main causes of nerve dysfunction were manipulation and transposition of facial nerves during surgery as well as grafting of the involved parts. Furthermore, when the epineurium was involved, the risk of nerve impairment due to surgery increased. In these cases, the infiltrated epineurium was removed under continuous neuromonitoring. Although post-operative facial nerve dysfunction considerably increased, the occurrence was temporary and improved at follow-up examinations.

Tumors of the posterior cranial base usually produce otologic

Cranial nerve	Preoperative CNDs	New postoperative CNDs
VII	4	8
IX	6	1
X	6	1
XI	6	2
XII	8	2

CNDs: cranial nerve deficits

Table 4: Preoperative and postoperative cranial nerve deficits.

symptoms along with facial and lower cranial nerve dysfunction. Lustig and Jackler reported that the prevalence of lower cranial nerve dysfunction was almost 20% for pre-operative patients and 35% for new post-operative ones [15] (Fayad, Keles and Brackmann reported 27 % and 19%, respectively [4]). In our study, 42.3% of patients had lower cranial nerve deficits (IX, X, XI, XII) pre-operatively and 26.7% developed new deficits after surgery (Table 4). All of the patients with post-operative lower cranial nerve deficits had incomplete paralysis, and neurological examination of the lower cranial nerve was almost normal one year after surgery. A high percentage of pre-operative lower cranial nerve deficits may imply late diagnosis of tumors but could also be due to the fact that patients with cranial nerve morbidities are often candidates for surgery. Monitoring nerve function during surgery can help to preserve nerve function. It is worth noting here that Amir-Alam Hospital is the largest center of otolaryngology in Iran, and therefore the more complicated cases (i.e., recurrent cases and patients with morbidities or large tumors) are typically referred to us.

Treatment of glomus tumors, especially glomus jugulare, is controversial. Treatment modalities include surgery, radiotherapy, observation, or a combination of these approaches. Age, tumor size and location, health status such as co-morbidities, patient preference, and pre-operative status of the lower cranial nerves all play roles in the decision-making regarding treatment modality [3,8]. The main treatment for glomus tympanicum is surgery [16,17] due to the high percentage of total tumor removal, low recurrence rate, and minimum post-operative complications [18]. Our study confirmed the efficacy of this treatment. All tympanicum tumors were removed totally and no recurrence was observed in follow- up. Also noteworthy is that, after surgery, average hearing levels improved.

Treatment of glomus jugulare is more challenging. Surgery is preferred when the patient is young or has prior lower cranial nerves dysfunction, aggressive or malignant growth, or a secretory tumor. In any case, the patient's health should be appropriate for surgery [3,19,20]. Pre-operative embolization is suggested for all large glomus jugulare to reduce bleeding and operative time [3]. Subtotal resection is suggested for large tumors, where a total resection leads to significant neurological deficits or vascular structural injury, and also for tumors with intracranial extension or in elderly patients with normal facial or lower cranial nerve function [21-23]. In subtotal resection, the possibility of re-growth should be considered, and so radiotherapy can be used as an adjuvant therapy or patients observed with serial imaging.

Given the controversy surrounding glomus jugulare surgery, it is advisable to carefully determine the best approach according to tumor class [20]. The infratemporal approach (Fisch type A) provides an excellent means for complete removal of tumors [8,10,24,25]. Post-operative, temporary facial nerve dysfunction is common with this procedure. Cosetti et al. point out significant complications with this approach, such as long operative time, increased bleeding, higher risk of cranial nerve deficits, higher possibility of tracheotomy, and longer hospitalization [22]. These potential risks and morbidities should especially be considered in older patients with co-morbidities, as older patients are less able to fully rehabilitate compared to younger patients and thus the procedure can have a significant impact on their quality of life [22]. Briner et al. described infratemporal approach type A as the best approach for total tumor removal, short operative time, limited bleeding and a minor wound infection [10]. However, with this procedure, a greater risk of facial and lower cranial nerve impairment is unavoidable (as evidenced by the 26.7% post-operative lower cranial nerve deficits in this study). Nevertheless, all cranial nerve paralyses were incomplete and all resolved in follow-up.

In the infratemporal approach, when additional space is needed, the limited facial nerve rerouting can help [8]. Otologic techniques, including endaural or postauricular approaches, are appropriate with a high possibility for total tumor removal and minimum morbidities [3,19]. Nevertheless, the posterolateral approach better preserves facial nerves, although it is not recommended for larger tumors [26]. Techniques for decreasing complications of the infratemporal approach include the fallopian bridge technique by Pensak and Jacker and the Brackmann technique restrict transposition of facial nerves [27,28]. As brainstem lesions can cause IX-X paralysis and dysphonia [10], an extradural approach prevents brainstem damage and decreases tracheostomy [10].

Another modality of treatment is radiotherapy, which is preferable in cases with poor surgical prognosis, recurrence, advanced age, patient's choice, or as a post-operative adjuvant. Complications of radiotherapy include external auditory canal's stenosis, osteoradionecrosis, radiation-induced neoplasm, and xerostomia [18,29]. Pollock also reported vocal cord paralysis due to repeated kamma knife surgery [30]. Persistent trigeminal neuropathy and temporary impairment of VII, IX, X, XII and XIII cranial nerves were observed in a study using CyberKnife stereotactic radiotherapy for glomus jugulare tumor treatment [31]. Nowadays, stereotactic radiosurgery and radiotherapy are advisable in large tumor cases where morbidity due to surgery is high [14]. Two studies show high tumor control rates by radiosurgery and radiotherapy with function-preserving intent [23,32].

One recurrence (3.8%) was found 18 months after surgery which, according to a median growth rate of 1.0 mm per year and a doubling time of 4 years, was likely due to incomplete resection [33]. The asymptomatic radiologic finding of the recurrence highlights the importance of imaging follow-up of tumors. As mentioned earlier, three patients experienced recurrence and received further surgery. The mean age of the patients at recurrence time was 37.9 years, which was less than the average of all patients (45.4 years). This may indicate that the growth of glomus tumors is more aggressive in young patients [22]. All cases with recurrence had glomus jugulare, and half were male, suggesting that glomus tumors tend to have more aggressive patterns in males.

In other findings in our study, surgical removal had little effect on the patients' ability to return to work, facial nerve deficit due to surgery was the main reason for depressive moods shortly after surgery, and providing enough information regarding prolonged recovery time can be helpful in reducing patients' concerns [10]. All patients with glomus tympanicum recommend the same surgery to other patients. This fact highlights minimum post-operative complications and improvement of symptoms by surgery in patients. 75% of patients with glomus jugulare recommend the same treatment, which implies more post-operative complications in these patients.

Conclusion

As mentioned, the main treatment of glomus tympanicum is surgery due to the high percentage of total tumor removal, low recurrence rate, and minimum post-operative complications. Likewise, surgery is also an acceptable procedure for glomus jugulare tumors to achieve total tumor removal. Although immediate post-op

morbidities (especially facial nerve dysfunction) were considerable, short-term follow-up showed improvement of dysfunctions and minimal morbidity due to surgery. On the other hand, recent studies show radiotherapy and function-preserving surgery with adjuvant radiotherapy provide a high tumor control rate with little morbidity [23,32,34]. This approach should especially be considered in older patients with comorbidities where complications of surgery could significantly influence their quality of life. Although a long-term study by Pollak shows 75% progression-free survival at 10 years, long-term data is limited regarding patients with jugular tumors who undergo radiation therapy [12,30]. It is worth mentioning that patients with cranial nerve morbidities are often candidates for surgery. As a matter of fact, in our study, 11 of the 16 patients (68.7%) with glomus jugulare had cranial nerve deficits at the time of diagnosis, surgery was considered.

A general overview of the study shows that most cases with cranial nerve morbidities were due to late diagnoses (a high rate of pre-op lower cranial nerve deficits). This fact highlights the importance of physicians paying close attention to the red flags of this disease, which will hopefully lead to earlier diagnosis of glomus tumors. As well, selecting the most suitable treatment modality and approach, having an expert surgical team, using adjuvant radiotherapy in cases with incomplete resection, and following up with regular serial imaging can be helpful in reducing morbidity and recurrence.

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Author Affiliations

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[1]*Otorhinolaryngology Research Centre, Tehran University of Medical Sciences, Tehran, Iran*