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The endolymphatic sac tumor: challenges in the eradication of a localized disease

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Abstract

Objective Identify the critical points that lead to recurrences and lack of radicality in endolymphatic sac tumors (ELSTs).
Study design Retrospective case study and review of the literature.
Setting Tertiary referral center.
Patients Thirteen cases of ELST were included in the study and their preoperative, intraoperative and postoperative data were analyzed and compared to a review of the literature.
Intervention(s) Therapeutical.
Main Outcome Measure(s) Prevalence of recurrent and residual tumors, comparison to the literature and analysis of ELST characteristics.
Results Diagnosis was made 26 ± 17 months after the onset of symptomatology, and an ELST was preoperatively suspected in only six cases. At the time of surgery, 10 patients suffered from hearing loss. Preoperative symptoms or audiometry could not predict labyrinth infiltration, although speech discrimination scores were significantly associated with labyrinth infiltration ($p = 0.0413$). The labyrinth was infiltrated in 8 cases (57.1%), and in 7 cases (46.7%) the tumor eroded the carotid canal, whereas 6 cases (40%) presented an intradural extension. A gross total resection was achieved in 11 cases. There were two residual tumors, one of which because of profuse bleeding, and one recurrence (23.1%). A mean of 22.8% of recurrent or residual tumors are described in the literature based on 242 published cases, in more than half of the cases as a consequence of subtotal tumor resection (STR).
Conclusions Recurrence derives mostly from the difficulty to identify the extension of the tumor due to the extensive bone infiltration. Accurate diagnosis and correct preoperative planning, with embolization when possible, will facilitate surgery and avoid STR due to intraoperative bleeding. Long follow-ups are important in order to avoid insidious recurrences.

Keywords Endolymphatic sac tumor · Von hippel-lindau disease · Low-grade adenocarcinoma · Temporal bone tumor

Introduction

The anatomy, physiology and pathophysiology of the endolymphatic sac (ELS) have fascinated scientists for centuries, its complete purpose still remains vague, and particular functions are being unveiled only as a result of the diseases that affect it [1].

Similarly, the ELS tumor (ELST) has been largely neglected as a distinct entity, up until 1989, when Heffner described a series of 20 cases of a "low-grade papillary adenocarcinoma of the temporal bone of probable ELS origin" [2]. Finally, in 2005, the World Health Organization Head and Neck tumor classification acknowledged and incorporated the term ELST [3]. Since then nearly 250 cases have been reported in the literature, granting the rarity to this tumor [2, 4–26]. It represents nearly 2% of all temporal bone lesions [24].

ELSTs develop either sporadically or as part of the autosomal dominant von Hippel-Lindau (VHL) disease, which is caused by a mutation of the synonymous tumor suppressor transcribing gene. A VHL gene mutation has also been

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found in sporadic ELSTs; therefore, it is not a prerogative of the VHL disease, suggesting a common tumorigenesis [27]. The VHL protein plays a pivotal role in the oxygen-sensing pathway and regulates hypoxia-induced genes which lead to proliferation of endothelial cells and pericytes [28]. Among VHL patients, 3.6–16% develop ELSTs, and one third of ELSTs are related to the VHL disease [29, 30].

Previous studies have attempted to standardize the treatment of ELSTs [22, 31]; however, reviewing the literature, many recurrences emerge, revealing our limited knowledge of the tumor and doubting the appropriateness of how we handle it.

The objective of this study was to analyze the cases of ELST treated at our institution and compare the results to the literature, in order to identify the critical points that lead to a lack of radicality.

Materials and methods

The study was approved by the institutional review board, and all subjects gave informed consent on the use of their data, in accordance with the Declaration of Helsinki.

A retrospective analysis of all patients with a histologically confirmed ELST or low grade adenocarcinoma of the ELS, managed at our institution, between December 1991 and January 2020, was performed. Paragangliomas, middle ear adenomas and adenocarcinomas, as well as metastatic adenocarcinomas, were excluded from the analysis. After a thorough evaluation, 13 patients were included in the study.

The presenting symptoms and signs of each patient were analyzed. All patients underwent preoperative audiologic examination by pure-tone audiometry and speech audiometry. Pure-tone average (PTA) was calculated as the mean of 500 Hz, 1 kHz, 2 kHz and 4 kHz thresholds. Bone and air conduction data were considered, as well as the resulting air–bone gap. The preoperative and postoperative facial nerve function was graded according to the House–Brackmann scale (HB) [32]. All patients underwent gadolinium-enhanced magnetic resonance imaging (MRI) with angio-MRI, and temporal bone high-resolution computed tomography (CT) without contrast administration. Patients were screened for VHL disease mutations by genomic studies.

Preoperative angiography and embolization was indicated in some patients. All patients were eventually treated by microsurgery, and the approach was selected according to the extension of the disease.

Intraoperative facial nerve monitoring was conducted in all patients. The extent of the tumor, its resection and the sacrifice of important structures were collected from the surgical charts.

Follow-up consisted of clinical evaluations and yearly MRI scans.

Finally, a review of the literature was conducted, and data on VHL germline mutation, radical excision, recurrences and use of other complementary or (co-) adjuvant treatments (embolization and radiotherapy) were compared to the collected data of this series. Single case reports were excluded, and only case series with at least 10 cases were considered for comparison.

Statistical analysis was performed using Graphpad Prism software (GraphPad Software, Inc, San Diego, CA, USA). Data collected from each patient were analyzed using descriptive statistics; continuous variables were expressed as mean ± SD (standard deviation); categorical variables were expressed as percentage (frequency). Fisher's exact test was used when comparing populations. Comparison of means between groups or values among groups was made with two-tailed Student's *t* test. Values were considered significant at $P < 0.05$.

Results

Thirteen consecutive ELST cases were reviewed, in thirteen different patients, eight female patients and five male (Table 1). The mean age at diagnosis and surgery was 37 years old ± 16.5 (ranging from 17 to 62, median 32). In seven cases, the tumor was located at the right temporal bone.

Symptomatology at onset affected mostly hearing, with five patients presenting progressive hearing loss and one presenting a sudden sensorineural hearing loss. Three patients presented rotatory vertigo without menieriform characteristics. Two patients complained pulsating tinnitus. Finally, two patients presented a progressive facial palsy. Seven to sixty months passed between onset of symptomatology and indication to surgery, with a mean of 26 ± 17 months. At the time of surgery, 10 patients had hearing loss (77%), 8 tinnitus (61.5%), 5 vertigo (38.5%) and 3 instability (23%). Three patients complained also otalgia (23%). A retrotympanic mass was detected in 6 patients (46%). Eleven patients presented a grade I HB facial nerve, whereas one patient had a grade III facial palsy and another a grade V. None of the patients had other cranial nerves affected. Three patients had a sensorineural hearing loss, whereas seven patients presented a mixed hearing loss. The other three patients presented preoperative anacusis (non-measurable thresholds). Ipsilateral air conductive PTA had a mean of 51 dB ± 22, whereas bone conduction was 43 dB ± 16. The difference between air and bone conduction was not statistically significant (paired *t* test, $p = 0.0535$), with a mean value of air–bone gap of 18 ± 29. Speech discrimination scores varied from 0 to 100%, with a mean of 51% ± 46.

Table 1 Preoperative characteristics

PT	Age (age at revision)	Sex	Presenting symptoms	Time to diagnosis (months)	PTA AC	PTA BC	SDS (%)	Facial Nerve (HB)	Tumor Size (mm)	VHL
1	17 (30)	F	Vertigo	36	62.5	51.25	100	I	20	N
2	23	F	SSNHL	60	–	–	0	I	15	N
3	53	M	PHL	54	65	41.25	100	I	30	N
4	25	F	facial palsy	20	–	–	0	III	50	Y
5	20	F	PHL	12	76.25	61.25	0	I	40	N
6	32	F	puls. tinnitus	36	31.25	27.5	100	I	43	N
7	18	M	PHL	24	–	53.75	0	I	30	N
8	62	M	vertigo	28	20	20	100	I	25	N
9	28	F	PHL	7	65	65	50	I	10	N
10	59 (61)	M	facial palsy	8	–	30	50	V	10	N
11	44	F	puls. tinnitus	18	25	25	100	I	30	N
12	51	F	vertigo	12	61.25	53.75	60	I	20	N
13	49	M	PHL	24	–	–	0	I	30	N

PT patient, *F* female, *M* male, *SSNHL* sudden sensorineural hearing loss, *PHL* progressive hearing loss, puls. tinnitus: pulsating tinnitus, *PTA AC* pure-tone average air conduction, *BC* bone conduction, *SDS* speech discrimination score, *HB* House–Brackmann scale, *VHL* von Hippel-Lindau, *N* no, *Y* yes

Based on the clinical evaluation and imaging, initial diagnosis was only correctly hypothesized in half of the cases (6 cases). In three cases, a paraganglioma was initially suspected, and in another case, a teratoma. One patient had undergone surgery elsewhere for cholesteatoma; therefore, a recurrent cholesteatoma was presumed in this case. Patients with suspected preoperative ELST were referred to a geneticist. The others were indicated genetic consultation only after histological diagnosis. The results of seven patients were brought to our attention. One of these patients had a VHL germline mutation. She later developed a pons hemangioblastoma. The rest of the patients may have had a genetic consultation, but we are not aware of the result. None of them developed any typical VHL-associated manifestation, although some may have had a too short follow-up.

Tumor size was calculated according to imaging, the maximum diameter measured 27.2 mm ± 12.3 (median 30, range 10–50 mm).

Preoperative angiography and concurrent embolization was performed in three cases, two days before surgery. The indication was given according to the preoperative MRI. Evidence of strong vascularization and the presence of intratumoral flow voids were evocative of a vascular component. Three patients underwent angiography, and they were preoperatively diagnosed as paragangliomas due to their strong vascularization.

In total, fifteen surgeries were performed in thirteen patients (Table 2). Twelve were primary surgeries, and one was a revision in a patient treated elsewhere for a presumed temporal bone cholesteatoma. Two were revision surgeries in patients operated at our center. A translabyrinthine approach was conducted in five primary cases, with cul-de-sac external auditory canal closure in one case. Two patients underwent a transotic approach. These approaches allow a direct access to the posterior cranial fossa. Four patients underwent surgery by a combined approach: a translabyrinthine with either a middle cranial fossa approach or an infratemporal fossa approach type A, or a transotic with infratemporal fossa approach type A in one, two and one cases, respectively. In four cases, the sigmoid sinus or jugular bulb was infiltrated and was therefore ligated and resected. Finally, one patient underwent a subtotal petrosectomy. The patient with a presumed recurrent cholesteatoma underwent revision surgery through a transcochlear approach. A translabyrinthine approach was indicated in two patients with no intracranial extension and no invasion of the inner ear or IAC, due to their poor preoperative hearing (pt. 9 and pt. 13). Moreover, in one case (pt. 9), a middle cranial fossa extension was done in order to preserve and avoid injuring an anterior and dominant sigmoid sinus.

The labyrinth was infiltrated in 8 cases (57.1%), with the posterior semicircular canal being the most frequently involved location; however, cases of cochlear infiltration were also present. Only three cases had an intact fallopian canal; however, one had a recurrence and presented an infiltrated fallopian canal in the revision surgery. The facial nerve was infiltrated in only one case, at the stylomastoid foramen. The patient underwent simultaneous tumor removal and primary facial nerve repair with end-to-end anastomosis. The sigmoid sinus was infiltrated in two cases. Similarly, two patients had an infiltrated jugular bulb. In 7 cases (46.7%), the tumor eroded the carotid canal, with cases extending to the vertical portion of the carotid, whereas the carotid artery was never infiltrated (Fig. 1). An internal auditory

Table 2 Intraoperative characteristics

PT	Approach	Intraoperative tumor extension								GTR/STR	Recurrence	Location residual / recurrence
		Inner ear	Facial nerve	SS: e/i	JB: e/i	CC	IAC	Dura	Intradural			
1	TLA	Y	N	N	N	N	N	N	N	GTR	Y	
	TLA	TL revision	Y-c	N	Y-e	Y	N	N	N	GTR	N	CC
2	TL + ITFA-A	Y	Y-c	N	Y-i	Y	Y	Y	N	GTR	N	
3	TO + ITFA-A	N	Y-c	Y-i	N	Y	N	Y	Y	GTR	N	
4	TC	Y	Y-c	N	N	Y	Y	Y	Y	GTR	N (first surgery other center)	
5	TO	Y	Y-c	Y-e	Y-e	N	Y	Y	N	GTR	N	
6	TO	N	Y-c	Y-e	N	Y	N	Y	Y	GTR	N	
7	TLA	Y	Y-c	N	Y-i	N	N	Y	N	GTR	N	
8	TLA	Y	Y-c	Y-e	Y-e	N	N	Y	Y	STR	Persistence	Intradural
9	TL + MCFA	N	N	N (anterior)	N	N	N	N	N	GTR	N	
10	STP	N	Y-c	N	N	N	N	N	N	STR	Persistence	CC
	STP revision	N	Y-c	N	N	Y	N	N	N	GTR	N	
11	TL + ITFA-A	Y	Y-nerve	Y-i	Y-e	Y	N	Y	Y	GTR	N	
12	TLA	Y	Y-c	N	Y-e	N	N	Y	Y	GTR	N	
13	TLA	N	N	N	N	N	N	N	N	GTR	N	

PT patient, *TLA* translabyrinthine approach, *ITFA-A* infratemporal fossa approach type A, *TC* transcochlear, *TO* transotic, *MCFA* middle cranial fossa approach, *STP* subtotal petrosectomy, *Y* yes, *N* no, *c* fallopian canal, *SS* sigmoid sinus, *e* erosion, *i* infiltration, *JB* jugular bulb, *CC* carotid canal, *IAC* internal auditory canal, *GTR* gross tumor resection, *STR* subtotal tumor resection

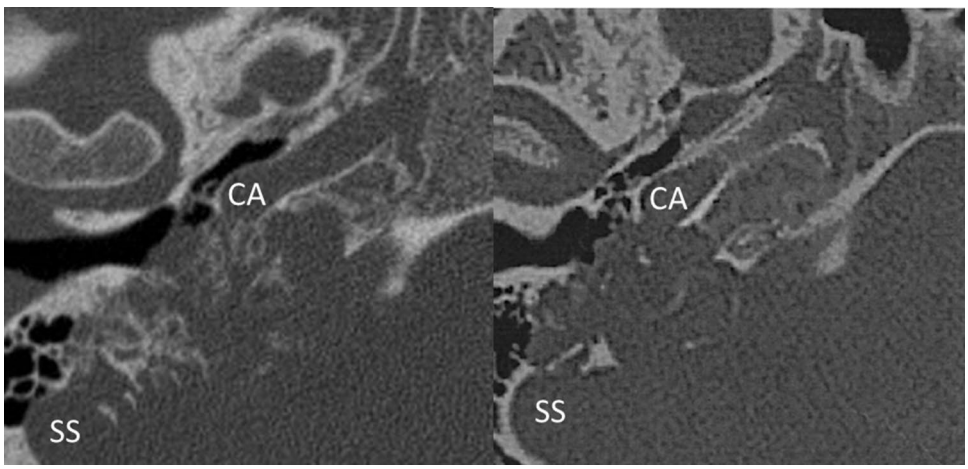

Fig. 1 CT scan of cases 6 (left) and 11 (right) evidencing the anterior extension of the tumor and erosion of the bony carotid canal. Both cases had pulsating tinnitus at the onset of symptoms and intraoperative evidence of carotid canal erosion without infiltration of the carotid artery (CA). *SS* sigmoid sinus

canal or intradural extension was considered when the tumor was located in the internal auditory canal or surpassed the dura, respectively. Dural infiltration was considered when the tumor was adherent to the dura and there was no cleavage plane between tumor and dura. The internal auditory canal was occupied by tumor in 3 cases (20%). The dura was infiltrated in 9 cases (60%), and an intradural extension was present in 6 patients (40%). Finally, in one case, the tumor extended up to the clivus.

The patients were subdivided in two groups according to the involvement or not of the labyrinth. Hearing loss or vertigo was not statistically associated with labyrinthine infiltration (Fisher's exact test, $p = 0.5227$ and $p = 0.5758$, accordingly), and there was no statistically significant difference between the air conduction of the two groups (unpaired t test, $p = 0.3162$, mean 84 ± 28.3 vs 60 ± 47.5, respectively), nor the bone conduction (unpaired t test, $p = 0.097$, mean 69 ± 31.1 vs 37 ± 4.3, respectively). However, speech discrimination scores of patients with a labyrinthine infiltration were significantly lower than those without an inner ear infiltration (unpaired t test, $p = 0.0413$, mean $27\% \pm 43$ vs. $80\% \pm 27$, respectively).

The inner ear was sacrificed in twelve patients because of labyrinthine infiltration, unserviceable hearing and/or necessity to adequately access the intracranial extension. The patient treated with a subtotal petrosectomy maintained hearing after both primary and revision surgeries. The facial nerve in the immediate postoperative period was grade I after eight in 15 surgeries, and the rest presented a grade II, III and IV in one case each. Finally, after four in 15 surgeries, the patients presented a grade VI. At the last follow-up of each patient, 9 patients (69.2%) presented a grade I, whereas one (7.7%) and three (23.1%) patients presented a grade II and III facial palsy, respectively. Two patients had an improvement of their facial nerve palsy: The patient with a grade III improved to I, and the patient with V improved to II. Three patients had a worsening of their preoperative facial function (all grade III at the last follow-up): In one case, the facial nerve was infiltrated by tumor, whereas in the other two cases, an infratemporal fossa approach type A with anterior facial nerve rerouting was done in order to eradicate the tumor undermining the facial nerve and reaching the internal carotid artery.

A gross total resection (GTR) was initially believed in twelve cases. However, a persistence was evident at the first postoperative MRI of one patient (after 2 months), and he underwent a revision of subtotal petrosectomy. In another case, profuse bleeding impeded a complete removal. The patient underwent a subtotal resection (STR), with indication to revision after embolization. Finally, more than 30% of the patients needed embolization prior to adequate removal. (Three patients underwent embolization prior to their primary procedure and one patient prior to the revision procedure.) None of the patients underwent adjuvant radiotherapy. The patient with a clival extension (pt. 11) had a GTR, 27 months of follow-up and no recurrence to date; therefore, no adjuvant treatment was considered.

Follow-up had a mean duration of 61.3 months ± 63 (ranging from 5 to 186 months, median 37). One patient continued follow-up, and a recurrent disease emerged after 146 months. The cavity was revised, tumor had extended toward the carotid artery and eroded the carotid canal. In total, there were two residual tumors and one recurrence (23.1%).

Literature review

Thirty papers of ELST case series were published and reviewed, describing 242 cases, with a majority of sporadic tumors and 93 VHL disease-associated cases [2, 4–26]. Tumor size ranged from 0.2 to 6.4 cm. A mean of 22.8% of recurrent or residual tumors are described (ranging from 0 to 40% according to the article).

Case series with at least ten ELSTs treated were analyzed further (Table 3). These seven articles constitute more than half of the total cases, presenting 147 patients with 152 ears treated. Among them, 57 were associated with VHL disease. Most of the cases described were primary surgeries, whereas in nearly 5% of the cases, the tumors were recurrent or residual diseases treated in other centers, ranging from 0 to 21.2% according to the series. Preoperative embolization was performed in 9.4% of the patients, varying according to the articles from 0% to 63.6% (23% in our series). A STR was done in at least 23 cases presented. Postoperative radiotherapy

Table 3 Endolymphatic sac Tumors case series with at least 10 cases

Paper	Number of patients	Number of ears	VHL	Tumor size (cm) mean (range)	Revision from other center[a]	Pre-op embolization	Post-op RT	Recurrent /residual[b]	STR	FU (months)
Heffner DK [2]	20	19	0	4–6	0	0	4	12	7	–
Hou et al. [6]	11	11	0	–	0	7	1	3	2	61.5
Kim et al. [8]	31	33	30	1.3 (0.2–5.2)	7	2	2	4	3	49.9
Carlson et al. [11]	13	14	5	2.76 (0.9–4)	2	0	2	5	4	65.4
Friedman et al. [12]	18	18	2	2.4 (1–3.3)	1	0	4	3	1[c]	67
Nevoux et al. [13]	14	14	8	2.42 (1.1–5)	0	1	0	6	1	42
Le et al. [17]	14	15	3	3.65 (1.05–6.76)	0	3	2	3	3	–
Thompson et al. [18]	26	27	9	2.9 (0.4–8)	0	1	0	4	≥ 1	74.4
Present study	13	13	1	2.72 (1–5)	1	3	0	3	2	61.3

VHL von Hippel-Lindau, *Pre-Op* preoperative, *Post-Op RT* postoperative radiotherapy, *STR* subtotal tumor resection, *FU* follow-up

[a]The column refers to the number of patients who underwent primary surgery in another center, and therefore, revision surgery might involve recurrent or residual disease. In order to avoid biases, they are considered separately from recurrences or residual tumors resulting from the series presented in each article

[b]Recurrent/residual tumors resulting from treatment of the tumors in each series, each recurrence/residual tumor in the same patient is counted separately

[c]Multiple operations

was conducted in 10.1% of the cases described, ranging from 0% to 22.2% of the cases according to the series (0% in our series). Follow-up varied from 1 to 285.6 months, with a mean of 60 months (61.3 months in our series). In total, 29.3% of the cases of these larger series presented a residual tumor or a recurrent disease (23.1% in our series), nearly 35% if the revisions of tumors treated previously in other centers are also considered.

Discussion

Since it was first described as a "low-grade adenocarcinoma of probable endolymphatic sac origin," Heffner revealed the difficulty of accomplishing a GTR [2]. More than half of the residual/recurrent tumors were a consequence of STR, both in the literature reviewed and our series (Table 3).

To begin with, patients describe symptoms for a long period of time before diagnosis is made, allowing the tumor to expand [17], without any significant difference between patients with and without documented VHL disease [18]. Moreover, its rarity leads to inaccurate preoperative diagnosis, which might influence therapeutical decisions. Hou et al. present a series where an ELST was considered in less than 10% of the patients preoperatively [6]. ELSTs on MRI appear either solid or cystic-solid, with flow voids and heterogeneous gadolinium enhancement [17]. When the tumor is centered on the endolymphatic sac and retrolabyrinthine region, diagnosis is eased; however, larger lesions extend into adjacent regions, resembling different diseases, in particular paragangliomas which are frequently suspected instead [12, 18]. However, cases of erroneous diagnosis are described also after multiple surgeries, with inaccurate histological evaluations [12].

Our department is not associated with a department of genetics; therefore, patients referred to our center do not have a previous diagnosis and we suspect this also explains the low incidence of VHL-associated tumors of this series. However, a meticulous preoperative evaluation and diagnosis should lead to a proper planning, with genetic evaluation or identification of other clinical manifestations, in order to identify a VHL-disease association. VHL-associated tumors tend to affect younger patients [18], even though our series included many young non-VHL-related patients. Although VHL-associated tumors tend to be less aggressive and recurrent, they confer the risk of bilaterality; therefore, surgery should be performed as soon as possible with an attempt to preserve hearing [13]. Moreover, in case of positivity, metastatic clear cell renal carcinoma should also be excluded [18], and different areas affected by VHL-associated tumors should be studied.

Renal cell carcinoma and hemangioblastomas tumor cells have demonstrated VHL loss of function and up-regulation of hypoxia inducible factor-1 (HIF-1) [33]. Studies are carried out to identify possible drugs that can target the tumor on a molecular and cellular level (34). Although a study affirms that sporadic and VHL disease-associated ELSTs have normal VHL-mediated HIF-1 regulation [35], it is largely accepted that the basis of VHL-associated tumors is a constitutive expression of HIF-1 which controls and promotes angiogenesis [28, 33]. This pathogenesis can explain why ELSTs are hypervascular and bleed easily. In our series, the three cases with preoperative embolization were initially misdiagnosed paragangliomas. However, similar to one of the residual cases of this series, other authors were obliged to perform a STR because of severe intraoperative bleeding [6, 13, 17]. Although the blood supply derives mainly from external carotid artery branches, larger intracranial tumors may also be nurtured from branches of the vertebral artery [6, 8]. Furthermore, this profuse vascularization limits the use of narrow approaches. We now consider angiography also in suspected ELSTs with evidence on the MRI of strong vascularization and the presence of intratumoral flow voids. This examination should be especially performed in larger tumors, with or without an intracranial extension, in order to proceed with embolization when possible.

There have been no reports of distant metastasis, except from isolated "drop metastasis" [36, 37]. However, they are locally aggressive, eroding the mastoid cells, infiltrating the petrous bone and adjacent structures. Large tumors can extend inferomedially, via the retrofacial route to the hypotympanum, jugular bulb and anteriorly toward the carotid canal, or posteriorly, infiltrating the posterior fossa dura and invading the cerebellopontine angle. STR has been described in cases where noble structures are infiltrated or surrounded [8]. Transpetrous approaches allow an adequate control of all structures, frequently in expense of hearing. Even though according to the preoperative audiologic results, labyrinth invasion could not have been predicted, the inner ear was frequently interested, so a translabyrinthine or transcochlear approach was necessary in order to eradicate the tumor. Other authors have described cases with GTR by a retrolabyrinthine approach [11], which could be preferred in smaller tumors with permissive anatomy and serviceable hearing. Some authors propose a retrosigmoid approach in order to preserve hearing; however, most affected structures are not visualized with this approach limiting its possible indications in ELSTs [38].

Unfortunately, these tumors tend to be extensive before patients seek medical care. If the tumor extends anteriorly toward the fallopian canal, a subtotal petrosectomy with external auditory canal closure should be indicated. When hearing is compromised, a TLA in general permits an adequate exposure of the endolymphatic sac area, with the possibility to access the IAC and intradural extension, and remove any dural involvement. Jugular bulb infiltration was

controlled through an ITFA. In order to control an anterior extension involving the carotid canal, a transotic or transcochlear approach can be performed. When an ITFA is combined to a TLA, then both the retrolabyrinthine area and carotid canal are controlled.

We always try to achieve a GTR given the borderline nature of the tumor. Moreover, being an aggressive and hypervascular disease, immediate eradication of the disease should be preferred instead of risking a more complicated reoperation. Tumors with an intracranial involvement and profuse bleeding can be extremely dangerous, which convinced us to suspend surgery in one case and prefer a STR. Our tendency is now to embolize most larger tumors in order to avoid intraoperative uncontrolled bleeding and eventual STR. This attitude is evident by the fact that the only case with intraoperative evidence of persistent disease was secondary to uncontrolled bleeding. The second case with STR appeared intraoperatively as a GTR even though persistence/recurrence was evident on the postoperative MRI.

Tumor was never left on the facial nerve in order to avoid a postoperative facial palsy. Facial nerve infiltration was rarely encountered, whereas the fallopian canal was frequently eroded and infiltrated by tumor, and its dissection allowed an improvement of the facial function in two cases which suggests a symptomatology secondary to compression or inflammation.

A case that has been previously published recurred 13 years after surgery [10]. Although most recurrences appear within 5 years from surgery [6, 9, 12], it is imperative to continue follow-up for longer periods.

Recurrence after GTR can usually be efficiently treated with revision surgery, whereas residual tumor after STR is prone to sizeable or multifocal disease [11]. One residual disease and one recurrence were located at the carotid canal. Although ELSTs are generally centered at the retrolabyrinthine area, they tend to erode and invade the petrous bone and frequently extend anteriorly. This should warrant an adequate evaluation and exposure of the area in larger tumors.

Recurrences and residual disease occur more frequently than in other petrous bone tumors [39, 40], but are equivalent to those developing in petrous bone chondrosarcomas [41, 42]. The similarity among petrous bone chondrosarcomas and ELST is bone infiltration, which strongly affects tumor removal. Recurrence after GTR most probably depends on the difficulty to identify the extension due to bone tumor infiltration.

The use of postoperative radiotherapy remains under debate with some authors advocating postoperative radiotherapy in patients who undergo STR or present local recurrence [11, 43, 44], whereas other authors find no benefit [2, 8, 45]. Radiotherapy should only be proposed to patients unable to undergo surgery or for non-resectable tumors [21, 24].

Conclusions

Although ELSTs are slow growing tumors, they are locally aggressive with infiltration of noble structures. They should therefore be treated with extensive surgery aiming at GTR. Radicality must be achieved at the expenses of the inner ear and hearing when necessary. Accurate diagnosis and correct preoperative planning, with embolization when possible, will facilitate surgery and avoid STR due to intraoperative bleeding. Given their similarity to paragangliomas, we suggest that all patients with extended disease should be studied with angiography and eventual embolization. Moreover, all adjacent structures should be studied before considering the surgical approach, which must provide an adequate exposure. Finally, patients must be informed of the importance of long follow-ups in order to avoid insidious recurrences due to the high infiltrative nature of the tumor.

Compliance with ethical standards

Conflict of interest The study was done at the Gruppo Otologico, a quaternary referral center for neurotology and skull base surgery. There is no conflict of interest involved, and the present work has not received any funding from any sources.

Ethical statement This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent The study was approved by our Institutional Review Board. Additional informed consent was obtained from all individual participants for whom identifying information is included in this article. However, the article does not contain any direct information regarding patient identity.

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