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Advanced Techniques in the Management of Complex Head and Neck Paragangliomas

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Original article

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Abstract

Head and Neck paragangliomas (HNPs) are tumors of the skull base which pose a challenge to surgeons due to the fact that these tumors are vascular, locally aggressive and involve important neurovascular structures like the jugular bulb, internal carotid artery, the facial and the lower cranial nerves. We have identified a set of HNPs that can be considered as complex cases based on certain clinical parameters. The identification of such high-risk complex cases is necessary for logical decision making, proper pre-operative planning and intraoperative management. Of a total of 284 HNPs, 66 were considered as complex cases. We did a retrospective review of these cases and analyzed the outcomes of the**se cases.**

Key words: Head & Neck Paraganglioma (HNP), Tympanojugular Paraganglioma (TJP), Vagal Paraganglioma (VP), Internal Carotid Artery (ICA), Vertebral Artery (VA), Lower Cranial Nerves (LCN), Facial Nerve (FN), Infratemporal Fossa Approach–Type A (ITFA–A)

Introduction

Head and Neck Paragangliomas (HNPs) are slow growing neuroendocrine tumours arising from the parasympathetic autonomic nervous system with a strong vascularization. HNPs include tympanojugular paragangliomas (TJPs), vagal paragangliomas (VPs), and carotid body tumours (CBT). Tympanomastoid paragangliomas (TMPs), earlier called glomus tympanicum or tympanic body tumour, are another set of similar tumours limited to the middle ear, and hence can be excluded from HNPs [1]. Their slow growth and discreet location make it difficult to detect them early. Likewise, their close proximity to important neurovascular structures like the jugular bulb, internal carotid artery (ICA), vertebral artery (VA), lower cranial nerves, the facial nerve (FN) and the hearing apparatus make them very difficult to treat. Surgery remains the mainstay of treatment for such tumours. However, it was not until Ugo Fisch[2] standardized the surgical approaches to reach these tumours by way of the Infratemporal Fossa Approaches (ITFA) types A, B, C, and D that these tumours could be dealt with effectively. Simultaneous improvements neuroradiology and neuroanesthesia enabled surgeons to map the skull base to get optimal surgical results. At our centre, we developed upon the earlier techniques and systematized the management of the ICA in HNPs by introducing stenting of the ICA [3]. It can be said that lateral skull base surgery evolved with the evolution of techniques to deal with HNPs. Nevertheless, surgery in this area is still complicated and consistent results have been achieved only in a few reputed centers of excellence across the world.

The object of this article, based on some of our earlier scientific publications, is to present our management protocols in the treatment of HNPs, specifically the more complex tumours involving the skull base including the cranio-cervical neuro vasculature.

Materials and Methods

Charts of all patients with HNPs were studied retrospectively. At the Gruppo Otologico, all

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patients with HNPs undergo routine ENT examination PTA and a clinical photograph of the otoscopy findings. We also document the FN using the House Brackmann grading system by taking pictures of four facial postures during each visit of the patient. All patients were subjected to high resolution CT scans, gadolinium enhanced MRI and four-vessel angiography. The facial nerve monitor was used intra-operatively in all cases. All TJPs and VPs were classified according to the Modified Fisch classification including the Vertebral artery (V) classification developed at our center. The CBTs were classified according to the Shamblin's classification. The surgical approach used most commonly was the ITFA–A [4, 5]. Other approaches used were the Transcervical approach and the Transmastoid-infralabyrinthine approaches. Intracranial extensions were dealt with using the Petro-occipito-trans-sigmoid approaches (POTS) or by the Extreme Lateral Approaches. Post-operatively, patients were usually discharged within seven days and followed up annually for three years and then biannually for the next decade.

Tumours were considered complex under the following conditions: Large size, large intradural extension, extension to the foramen magnum, clivus or the cavernous sinus, involvement of the ICA or the presence of a single ICA on the site of the lesion, involvement of the VA, presence of a dominant sigmoid on the site of the lesion, bilateral or multiple tumours, post-irradiated or recurrent tumours.

All cases in which tumours were found to be encircling, infiltrating, or kinking the ICA were managed pre-operatively using a stent. In cases where the stenting was not possible due to severe stenosis or kinking a permanent balloon occlusion was performed.

Results and observations

A total of 284 HNPs, 237 TJPs, 28 VPs and 19 CBTs were treated at the Gruppo Otologico, Piacenza, Italy from 1988 to 2015 and 66 (23.23%) of these were considered to be complex tumours. The description of the tumours is in Table 1. Sixty of the tumours were TJPs, 2 VPs and 4 CBTs. Thirty six (54.5%) of the tumours were complex due to their size, 46 (69.7%) of them due to the presence of an intradural extension and 33 (50%) of them due to involvement of vital vasculature of the skull base (ICA, VA and SS). Multiple or bilateral tumours were encountered in 14 (21.2%) of the cases. The surgical approaches applied in all the cases are shown in Table 2. ITFA-type A was the most favoured approach for TJPs and the Trans-cervical approaches for VPs and CBTs.

Table 1: F eatures of complex HNPs in our series

Features	No. of Cases
Large tumours	
C3 TJPs	27
C4 TJPs	5
De2 TJPs	3
Type III VP	1
Intradural extension	
Di1 TJPs	25
Di2 TJPs	18
	2
Type III VP	1
Extension to	
Cavernous sinus	2
Foramen magnum	3
Clivus	8
Serious involvement of	
ICA	24
VA	4
A single ICA on the lesion side	2
Unilateral sigmoid sinus on the lesion side	2
Dominant sigmoid sinus on the lesion side	1
Malignancy (or very aggressive case)	1 (or 1)†
Bilateral HNPs	3
Multiple HNPs	11
History of previous treatment	13
Total	**66**

Table 2: Surgical Approaches for HNPs

	TJPs	VP	CBT
ITFA-A	32		
ITFA-A + TT-TC	16		
ITFA-A + POTS	6		
ITFA-A + ELA	2		
ITFA-A + ILA	4		
TCA		1	3
TCA + ITFA-A		1	
TCA + TMA			1
Total	**60**	**2**	**4**

ITFA-A: Infratemporal Fossa Approach type A, TT-TC: Transtubercular transcondylar extension, POTS: Petro-occipito-trans-sigmoid Approach, ELA: Extreme Lateral Approach, ILA: Infralabyrinthine Approach, TCA: Transcervical Approach, TMA: Transmastoid Approach, TJP: Tympanojugular Paraganglioma, VP: Vagal Paraganglioma, CBT: Carotid Body Tumour

Table 3 – Use of intra-arterial ICA stents for HNPs

No.	Tumour class	Previous treatment	Multiple tumours	Encasement in degrees as seen in MRI	Angiogram feature	Stent (cervical)	Stent (petrous)	Surgical removal
1	C3	Surgery/ VA occlusion	No	360	stenosis	Xp	Xp	Subtotal
2	C4	Surgery	No	360	stenosis	Xp	Xp	Subtotal
3	C3	-	Yes	180	stenosis	Xp	Xp	Total
4	C3	-	Yes	360	stenosis	Xp	NF	Total
5	C3	Surgery/ contralateral ICA occlusion	Yes	270	stenosis	Xp	Xp	Total
6	C2	Surgery	Yes	270	stenosis	Xp	NF	Total
7	C2	-	No	180	stenosis	NF	NF	Total
8	C3	Surgery	Yes	270	-	LEO	LEO	Subtotal (but not related to ICA)
9	C3	Surgery	No	360	-	Xp	NF (2 stents)	Total after PBO
11	CBP	-	No	270	-	Xp	-	Total
12	VP	-	Yes	270	-	Xp	-	Total
10	C2	Surgery	Yes	180	-	Xp	NF (2 stents)	Waiting for surgery
11	CBP	-	No	270	-	Xp	-	Total
12	VP	-	Yes	270	-	Xp	-	Total

ICA - Internal Carotid Artery, VA – Vertebral Artery, Xp – Xpert stent, NF – Neuroform 3 stent

The ICA was stented in 12 cases and the details are in Table 3. Ten cases of TJPs and one each of VP and CBT were stented. Eight (66.7%) of them resulted in a total tumour clearance. In all cases, tumours were encircling the ICA by 180 degrees or more. In all cases of TJPs, both the cervical and the petrous portions of the ICA were stented. The VA was involved in eight cases, all of them TJPs (Table 4). A definitive VA management was required in all cases, two of which were occluded permanently. Total tumour clearance was achieved in six (85.7%) of the seven cases.

Blood transfusion was required in only two cases. There was no mortality in the series. Complications included two cases of hematoma, one case of wound dehiscence and one case of transient CSF leak into the neck. One of the cases underwent a cochlear implantation on the operated site for hearing rehabilitation. Eight cases resulted in a subtotal resection, one of which was referred for radiotherapy. The rest of them are all on follow-up.

Discussion

HNPs represent the pinnacle of difficult in lateral skull base surgeries. Although surgery has remained as the mainstay of TJPs, successful outcomes in terms of total tumour clearance and minimal morbidity achieved in a few centres of excellence have not been replicated elsewhere. The reason for this is that HNPs are tumours that have a trans-cranio-temporo-cervical extension and to get optimal results in such tumours, the surgeon needs to possess a thorough knowledge of skull base anatomy as well as complex surgical techniques. However, surgical management of HNPs has yielded good results over the last few decades with the introduction of the ITFA and the introduction of techniques like the intra-arterial stenting of the ICA. This has made surgery feasible in cases previously considered in-operable. Nevertheless, surgery is still fraught with complications and pre-operative assessment plays an important role in the successful outcome in the management of these tumours. To ensure that difficult cases are recognized and dealt with in a systematic way we have classified them as complex cases based on certain parameters as mentioned earlier and discussed below.

Large size – As HNPs grow in the skull base, the pathways of extension include the carotid canal, the

Table 4 – Results of Vertebral Artery treatment

Case No.	Age/ Gender	Site	Class of TJP	Surgical approach for VA involvement	Definitive VA procedure	Results of definitive procedures	Residual tumour location	Reasons for residual tumour	Follow-up (months)
1	56/F	L	C2Di2Vi	MTCA	tumour dissection	subtotal removal from VA	VA & PICA	vessel encasement	30
2	24/F	R	C4Di2Vi	ELA	tumour dissection	total removal from VA	CS	risk of ophthalmoplegia	156
3	59/M	R	C2Di2Vi	TC	tumour dissection	total removal from VA	-	-	13
4	51/F	R	C3Di2Vi	TD-TB-TCo-TC	tumour dissection	total removal from VA	-	-	96
5	42/M	L	C2Di2Vie	EL	PBO & resection of the VA with tumour	total removal from VA	-	-	30
6	41/M	R	C3Di2Ve	ITFA-ELA	coil insertion & tumour dissection	total removal from VA	-	-	24
7	30/M	L	C2Di2Vi	TD-TB-TCo-TC	tumour dissection	total removal from VA	-	-	30
8	38/M	L	C3Di2Vi	2nd-stage surgery is planned	-	-	-	-	24

Vi = Tumour involvement of intradural VA; Ve = tumour involvement of extradural VA; Vie = tumour involvement of intra and extradural

VA; TD-TB-TCo-TC = transdural-transbulbar-transcondylar-transclival approach; MTCA = Modified Transcochlear approach;

ELA = extreme lateral transcondylar approach; PBO = preoperative permanent balloon occlusion; CS = Cavernous Sinus; ITFA = Infratemporal fossa approach.

jugular bulb and the sigmoid sinus, the petrous apex or intradural into the posterior cranial fossa wherein they involve the lower cranial nerves. A large size obviously brings into play the other factors mentioned above that complicates the presentation of TJPs discussed below. According to the modified Fisch classification, class C3 & C4 are considered as large tumours. We managed 35 patients with tumours considered to be of a large size of which 27 were Fisch C3, five were C4, and three were De2. ITFA-A can be used for class C2 and ITFA-A with extensions like the ITFA-B or the transtubercular transcondylar (TT-TC) extensions can be used for class C3/C4 tumours. In case of involvement of the clivus, the condyle of the occipital bone or the foramen magnum, the modified transcochlear or the extreme lateral approach are necessary and were performed at our centre.

A large intradural extension – Although some authors prefer a single staged surgery [7], we feel that in the case of an extensive dural involvement, a second-stage resection of the intradural component can be considered. We managed 45 patients with IDE; 25 with Fisch Di1, 18 Di2, and 2 Di3. In 14 of them, a staged surgery was performed. The advantage of a staged surgery is that in a few months after the first surgery, a definite cleavage plane would be established between the tumour and the brain stem due to the devascularization of the tumour during the first surgery that would result in a shrinkage of the intradural component (Figure 1A, B, C, and D). Another consideration is that in tumours involving LCNs, their sacrifice may result in severe aspiration and continuous cough, which in turn could increase the intracranial pressure resulting in increased incidence of CSF leaks[8]. We prefer to perform a staged resection for tumours with more than two centemetre intradural extension[5]. The approach of choice during the second stage depends upon the site and size of the residual tumour and the hearing status of the patient. Procedures of choice include the petro-occipital trans-sigmoid (POTS) approach and the extreme lateral approach.

Foramen magnum, clival or the cavernous extensions – Tumours with a foramen magnum or a clival extension can be effectively tackled using a modified transcochlear approach (Type D) or an extreme

lateral approach [9]. It is important to drill out the involved bone of the clivus to prevent recurrence. We had 13 patients including two with tumour involving the cavernous sinus, three involving the foramen magnum and eight involving the clivus. In two of them, the tumour involved the cavernous sinus the tumour was left behind to avoid compromising the functionality of cranial nerves VI, IV, and III. Both patients were subjected to gamma knife. We had three cases involving the foramen magnum. Complete removal was not feasible in one of them due to bleeding.

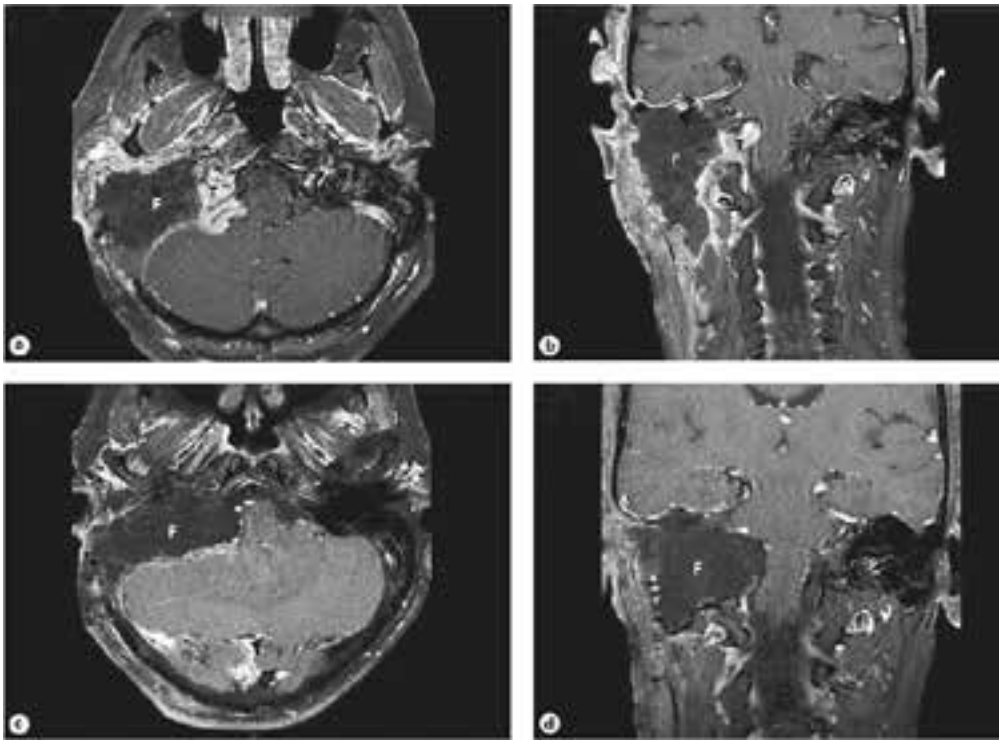

Figure 1: **A, B -** MRI, axial and coronal views after the first-stage surgery. The residual intradural tumour can be identified. The surgical cavity is filled with abdominal fat. T = Intradural tumour; F = fat. **C, D -** MRI, axial and coronal views after the second-stage surgery. After the surgery, there is no residual tumor.

ICA involvement – HNPs have a high propensity to involve the ICA due to their close anatomical proximity to the structure[4]. Separation of the tumour can be achieved by sub-periosteal/adventitial dissection of the ICA in the carotid canal (horizontal portion) or sub-adventitial dissection in the vertical portion[10]. In case of complete encirclement of the ICA by the tumour and in cases of stenosis, handling of the artery without adequate pre-operative endovascular treatment could result in intra-operative damage to the artery, incomplete resection or a cerebral vascular accident due to arterial spasm[2]. When the tumour infiltrates the ICA, a pre-operative PBO is indicated if the cerebral blood flow is compensated by the contralateral arterio-venous system. However, sacrifice of the artery can be avoided in most cases by using an intra-arterial stent (Figure 2A, B, C, D and Figure 3). The Gruppo Otologico in the clinical and surgical management of complex HNPs since early 2003 as a method to avoid pre-operative closure of the ICA, high-risk arterial bypass and to protect the integrity of the artery intra-operatively stenting of the cervical and petrous segments of ICA was introduced as a pre-operative management protocol. Stenting is indicated in cases in which the collateral blood supply into the circle of Willis is deemed insufficient[11, 12, 13].

Twenty-one pre-operative ICA stenting procedures were performed at our centre on 19 patients (Table 2). Stenting of the ICA allows reinforcement of the artery, reducing the risk of intra-operative injury of its wall while performing a more aggressive carotid dissection in the sub-adventitial plane. The stent permitted a safe mobilization of the artery

when indicated. Hence, stenting allows aggressive surgery aiming at total tumour resection in cases where previously, only a sub-total resection could be achieved. English literature mentions only one other case of stenting of the intratemporal segment of the ICA in the surgical management of TJPs [7].

An ICA only on the side of the lesion – Most cases of skull base paragangliomas require pre-operative management of the ICA. However, the presence of one-and-only ICA on the side of the lesion is a unique challenge. However, this situation is not very uncommon as paragangliomas tend to occur bilaterally and in such cases it is common for the ICA to be sacrificed on one side if involved. In such cases, the presence of a second tumour on the contralateral side involving the ICA is considered a complex case. In case of a one-and-only ICA involved by the tumour, traditional management options included 'wait-and-scan', subtotal resection and radiotherapy. Carotid bypass procedures run a high risk of cerebral ischemia. With the advent of stenting of the ICA, such patients have a chance at complete tumour clearance with surgery [12]. At the Gruppo Otologico two patients with a single ICA have been operated upon after stenting wherein we achieved total tumour clearance without any adverse consequences.

Vertebral artery involvement – Involvement of the VA by HNPs is very uncommon. Eleven cases have been reported worldwide, of which eight cases belong to our series, all of them TJPs. VA management in HNPs presents the most complex challenge in management of HNPs. Seven of the eight patients underwent surgery and the results are summarized (Table 3). In two patients, pre-operative occlusion was performed. In one of our articles, we have presented the radiological and surgical findings of VA involvement by TJPs to emphasize the importance of VA assessment, which led us to propose a 'V' class to the existing Fisch classification[14]. In large tumours, the VA system must always be studied in addition to the ICA systems. In addition to determining infiltration of the VA, it also helps in detecting anastomosis between the VA and the external carotid systems, which can be potentially hazardous during embolization [15]. Surgically, when the third segment of the VA is involved, addition of an extreme lateral extension to the standard ITFA will ensure adequate exposure of the area. Involvement of the fourth segment of the VA is associated with large intradural components. A two-stage surgery is indicated in such cases (Figure 4A-F).

Unilateral or dominant sigmoid on the side of the lesion – The sigmoid sinus often need to be obliterated and the jugular vein ligated during resection of HNPs, especially in TJPs. However, ligation of the sigmoid sinus of the dominant or the presence of unilateral sinus on the side of the lesion is most likely to result in intracranial hypertension and venous congestion leading to fatal brain edema[9]. Therefore, it is important to evaluate pre-operatively the drainage of the cerebral venous systems, with special emphasis on the mastoid emissary vein and the condylar veins of the tumour side. In case of large emissary or condylar veins all attempt must be made to preserve them. In cases where the collateral venous drainage cannot be preserved or when the patient has insufficient collateral venous drainage, aggressive surgery must be abandoned in favour of a more conservative option like subtotal resection (with preservation of the sigmoid/other dominant veins), radiotherapy or a wait-and-scan approach.

Multiple or bilateral tumors – In the management of bilateral HNPs, the possibility of bilateral deficits of important LCNs looms large and hence neural preservation is very important to achieve a good quality of life for the patient post-operatively. We had 11 patients with multiple HNPs. According to our management protocol, the tumour with LCN deficits are operated upon first leaving the opposite tumour to be followed up or irradiated. A subtotal resection is attempted sparing the LCNs followed by radiation or the patient may be irradiated primarily if the opposite side has a large tumour, which is growing. If the tumours on both sides do not show evidence of growth, both tumours can be approached with a wait-and-scan.

Recurrence after previous surgery, previously irradiated tumors – Revision surgery or previously irradiated tumours pose a specific problem as surgery in such

cases is extremely difficult due to lack of cleavage planes and due to bleeding. In addition, previous surgery or radiation increases the risk of CSF leak and damage to the LCNs and FN and injury to the carotid as the scarring around the carotid makes it particularly vulnerable to damage during surgery[2,9]. Pre-operative treatment of the ICA by stenting or PBO plays a vital role in such cases. In our present series, 13 cases had undergone previous treatment and all three of them underwent total resection.

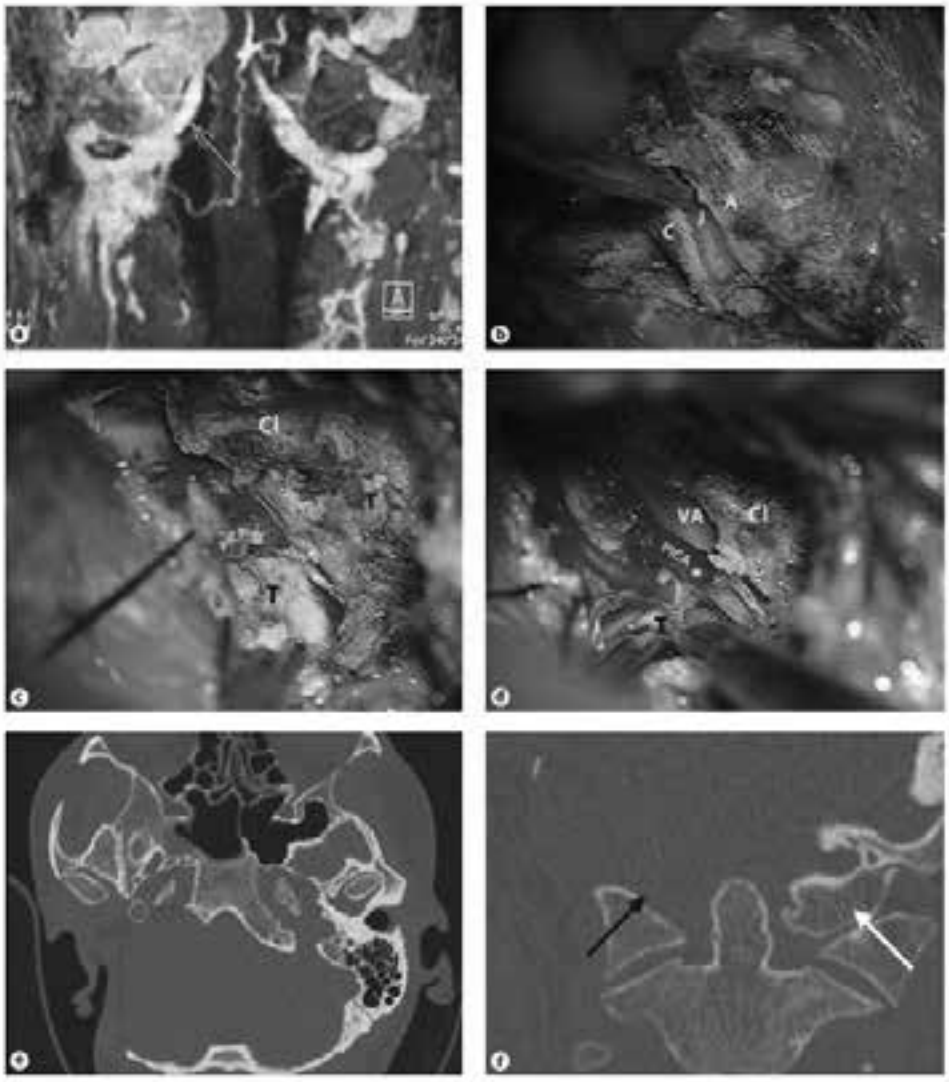

Figure 4 : **A -**A class C4Di2Vi tumour. MRI coronal image demonstrating tumour encasement of the VA. **B-F –** Surgical steps of extreme lateral approach. **B -** The transverse process of the atlas (A) is drilled out and the atlanto-occipital joint (J) is removed. C = Condyle. **C -** The tumour (T) is attached to the vertebral and posterior inferior cerebellar arteries infiltrating the clival (Cl) bone, which is partially drilled out. **D -** The tumour is separated from the PICA. **E -** CT scan. Axial view showing the stent in the ICA and the extent of bone removal. **F -** CT scan coronal view showing resection of occipital condyle (black arrow) compared to non-operated side (white arrow).

Vagal paragangliomas (VPs)

VPs are less common than CBT and TJP, occurring in the 4th and 5th decades of life, and are more common in females[16]. We managed 22 patients with VP from 1988 to 2009[17]. Our policy is to offer surgery as the treatment choice for patients with VP, whether or not there exists a paralysis of the vagus whereas in older patients with no serious complications, a wait-and-scan policy is adopted. For bilateral lesions, if the patient has an abnormal vagus nerve function on one side, surgical removal is considered on that side, and a more conservative management is applied to the contralateral side. The commonly used approaches are the transcervical, transcervical-transmastoid and the ITFA-A.

Conclusion

HNPs are a complex set of tumours of the skull base. The cases that we have identified in this report as complex were most often considered inoperable in the past. However, owing to advances in lateral skull base surgical techniques, neuroradiology, and neuroanaesthesia even the complex cases can be effectively tackled with minimal morbidity.

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