CLINICAL STUDY

SURGICAL MANAGEMENT OF HEAD AND NECK PARAGANGLIOMAS: REVIEW OF 55 CASES

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SUMMARY

Objective: The aim of the study is to review a single institution's experience regarding the sites of origin, clinical manifestations and surgical treatment results of head and neck paraganglioms (PGs).

Methods: Fifty one patients who were operated due to head and neck paragangliomas between 2000 and 2012 were included in the study. Retrospective evaluation of the records in means of diagnostic tools, surgical findings and outcomes yielded 55 PGs in 51 patients. Seventeen patients had 20 carotid body tumors (CBT) while 12 had jugulotympanic PG (JTP), 1 had isolated jugular PG (JP), 18 had tympanic PG (TP) and 4 had vagal PG (VP).

Results: CBT: Ballon occlusion test was applied to 10 of 17 excised CBTs. Internal carotid artery was not able to be preserved in 3 patients. No other neurological or vascular deficit was encountered in CBT patients. Complete resection was achieved in all patients. JTP and JP: Preoperative embolization was applied in all JTP's (n=12). Postoperatively, cerebrospinal fluid leakage leading to meningitis was observed in 1 JTP. Complete resection was provided to the JP patient.

TP: Out of 18 patients, 16 were operated through endaural and 2 were through endomeatal incision and complete resection was obtained in all.

VP: Out of 4 VP patients, 3 were undergone balloon occlusion test. Incomplete resection was performed in 1 patient. Cranial nerve palsies were observed in 2 patients postoperatively.

Conclusion: In management of head and neck PGs, choice of treatment modality should be determined according to patient's age, tumor size and location, existence of cranial nerve deficits and experience of the surgeon. For CBTs and TPs, surgery is still the prefferedtreatment of modality in our clinic. In management of VPs, due to possible morbidities, surgery might be reserved until the mass becomes symptomatic. For JTPs, decision of surgery should be individualized.

Keywords: Paragangliom, carotid body tumor, jugulotimpanicum, vagal paragangliom

BAŞ VE BOYUN PARAGANGLİYOMLARININ CERRAHİ TEDAVİSİ: 55 OLGUNUN GÖZDEN GEÇİRİLMESİ

ÖZET

Amaç: Çalışmanın amacı, baş ve boyun paragangliyomları (PG) ile ilgili tek bir merkezin, tümörün köken aldığı bölge, klinik bulgular ve cerrahi tedavi sonuçları açısından deneyimini gözden geçirmektir.

Gereç ve Yöntemler: Çalışmaya 2000- 2012 yılları arasında, baş ve boyun PG nedeni ile ameliyat edilen 51 hasta dahil edildi. Kullanılan tanısal yöntemler, cerrahi bulgular ve sonuçlar açısından kayıtlar retrospektif olarak incelendiğinde 51 hastada toplam 55 PG tespit edildi. Çalışmadaki 17 hastada 20 karotis cisimciği tümörü (KCT), 12 hastada jugulotimpanik PG (JTP), 1 hastada izole juguler PG (JP), 18 hastada timpanik PG (TP) ve 4 hastada vagal PG (VP) mevcuttu.

Bulgular: KCT:.Eksize edilen 17 KCT'nin 10'una balon oklüzyon testi uygulandı. Üç hastada internal karotis arter korunamadı. KCT hastalarında başka herhangi bir vasküler ya da nörolojik defisite rastlanmadı Tüm tümörlerde tam rezeksiyon sağlandı..

JTP ve JP: Tüm JTP'lerde (n=12) ameliyat öncesi embolizasyon uygulandı. Ameliyat sonrasında 1 JTP'de menenjite yol açan beyin omurilik sıvısı kaçağı izlendi. JP hastasında tam rezeksiyon sağlandı.

TP: On sekiz hastanın 16'sında endaural, 2'sinde endomeatal insizyon ile cerrahi uygulandı ve hepsinde tam rezeksiyon sağlandı.

VP: Dört VP hastasının 3'üne balon oklüzyon testi uygulandı. Bir hastada tam rezeksiyon yapılamadı. Ameliyat sonrasında hastaların2'sinde kraniyal sinir paralizileri gözlendi.

Sonuç: Baş ve boyun PG'lerinde, tedavi yönteminin seçimi, hastanın yaşı, tümörün boyutu ve yerleşim yeri, kraniyal sinir paralizilerinin varlığı ve cerrahın deneyimine göre belirlenmelidir. KCT'ler ve TP'ler için kliniğimizde tercih edilen tedavi yöntemi cerrahidir. VP'lerde olası morbiditeler nedeniyle, cerrahi, kitle semptomatik hale gelene kadar ertelenebilir. JP'lerde ise cerrahi kararı her olgu ayrı değerlendirilerek alınmalıdır.

Anahtar Sözcükler: Paragangliyom, karotis cisimciği tümörü, jugulotimpanikum, vagal paragangliyom

INTRODUCTION

Paragangliomas are neuroendocrine tumors derived from extra-adrenal paraganglionic tissue[1]. In the head and neck region, they compromise a rare group of highly vascularized tumors which are originated from chromaffin cells of parasympathetic paraganglia and named according to their site of localization[2]. They most commonly occur at the carotid bifurcation where they are named as carotid body tumors (CBT). The jugular bulb (jugular paraganglioma; JP), the tympanic plexus on the promontory (tympanic paraganglioma; TP) and the

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vagal nerve (vagal paraganglioma; VP) are the other common sites of origin of head and neck paragangliomas (HNP)[3]. Most of the HNP are benign lesions with malignancy incidences of 4%, 6% and 16% for JP, CBT and VP respectively[4]. The majority of these neoplasms are solitary, except the lesions within the multiple endocrine neoplasm (MEN) syndromes, type II A and type II B, and Carney complex. Multiple paragangliomas may occur in up to 40% of familial paragangliomas and in up to 10% of sporadic tumors[5,6]. Although all paragangliomas contain cytoplasmic neurosecretory granules, only a minority of paragangliomas demonstrate clinical hypersecretory symptoms. Patients with clinical signs and symptoms of catecholamine secretion should be evaluated for blood levels and multiple tumors[7].Symptoms change according to tumor localization; ranging from a neck mass to hearing loss, vertigo or cranial nerve palsy. One or more of the diagnostic imaging tools including ultrasonography (USG), computed tomography (CT), magnetic resonance imaging (MRI) or angiography are always mandatory in order to plan the management approach[8]. Among non-invasive techniques, MRI has the advantage of providing multiplanar imaging of tumor extension and vessel encasement. In large PGs, areas of high and slow flow may yield the typical "salt and pepper appearence"[9]. On the other hand, the gold standard for detection of small PGs is still digital subtraction angiography (DSA)[10].Contrast enhanced MR angiography might be used to study tumor hemodynamics of PGs which show rapid and homogenous enhancement[11].

CT is mostly utilized in TPs and JTPs. In TPs, CT provides visualization of the tumor extension through bony structures such as ossicular chain, facial nerve canal and/or cochlear promontory[12].

When the diagnosis is not clear with the mentioned non-invasive imaging modalities, diagnostic angiography can show the specific vascular supply of PG as well as leading to differential diagnosis. High vascular supply of these tumors may lead to profuse intraoperative bleeding. In order to avoid both blood loss and surgical difficulties related to bleeding, preoperative embolization is recommended for vagal and jugulotympanic PGs In these tumor localizations, an occlusion test is also usually necessary to check the possibility to sacrifice internal carotid artery during radical surgery. Benefit of embolization is poor for carotid body tumors and tympanic PGs[13,14]. Recently, CT and/or MR angiography are the alternatives to conventional angiograhy. However, when the vascular supply pattern is not well determined, an occlusion test is required or embolization is planned, their utilization is limited.

Balloon occlusion test is indicated when VPs or JTPs encase internal carotid artery or resection bares the risk of injury to the artery. During occlusion, test should be terminated if neurological signs appear, which is encountered in 5% of cases. These patients are considered to be at high risk for stroke and non-surgical treatment options, subtotal resection together with preservation of the artery or re-vascularisation previous to resection should be considered. Patients with diminished perfusion, who constitute 25%, are at mild to moderate risk in terms of stroke. Preoperative grafting of the internal carotid artery is recommended for such cases. The occlusion test itself bares risk of neurological sequelae in 4%, therefore it should be reserved only for the mentioned patients[13,15].

Surgery,radiotherapy and embolization or combinations of these are the treatment options of HNPs, on which debate still exists in the literature. Size, extension and localization of the tumor are important determinants for the possibility of surgery with acceptable morbidity. The most important determinant is considered to be increase in size or cranial nerve deficit[10]. The decision to treat or not to treat should be made multidisciplinary together with otolaryngologist, neuroradiologist, vascular surgeon and neurosurgeon, if necessary. Morbidity related to resection of CBTs, mainly depends on Shamblin classification; for type III CBTs, cerebrovascular complications occur in less than 5% and permanent cranial nerve deficits in approximately 20%; and incidence is lower in type I and II lesions[16]. Morbidity related to resection of vagal and jugular PGs is significantly higher compared to CBTs. For complete removal of a VP, sacrifice of vagal nerve is almost always required[17]. The morbidity rate is also high for large JTPs. Therefore, surgery of VPs and JTPs is only indicated if the tumor is small enough to allow total resection with low risk of morbidity or when the cranial nerve defect has already been established by the tumor itself. In cases of multicentric disease the aim should be to prevent development of cranial nerve deficit and to preserve at least one vagal nerve.

When the mentioned risks are high, alternative traetment modalities, such as conventional radiotherapy and stereotactic radiosurgery should be considered.[9]. When the slow rate of growth is taken into account, "wait and scan" policy is another option for certain cases. Follow up with MRI scans and

intervals up to 2 years seems suitable fort he stable cases[10].

The aim of this retrospective study is to review our experience in the surgical management of HNPs and evaluate the outcomes and complications in our series. Therefore it would be possible to track weak and strong points of approaches to HNPs and re-organize them.

MATERIAL and METHODS

A retrospective review of medical records of patients who were operated due to a HNP between January 2000 and June 2012 was performed. There were 51 patients with 55 craniocervical paragangliomas. This study was approved by the institutional review board. There were 11 male (22%) and 39 (78%) female patients with a mean age of 46.9 (range 16-72 years).

Surgery was the treatment of choice for all the patients included in the retrospective review. Preoperative embolization together with conventional angiography was performed in all of the jugulotympanic paragangliomas (JTPs). However, only diagnostic angiography was performed for CBTs. Seventeen CBTs, 1 JP, 12 JTPs, 18 TPs and 4 VPs were operated. At least two of the imaging techniques among CT, MRG or angiographic scanning were performed for all the patients preoperatively. Mean follow-up time was 12.62 months (range 1-84 months).

RESULTS

Carotid Body Tumors

Being the most incident PG, there were 17 patients with 20 CBTs among 55 PGs (36%) , 17 of which were excised. All of the patients demonstrated the complaint of painless neck mass. According to the Shamblin classification, there were five type I, five type II and seven type III excised lesions, respectively(19). Balloon occlusion test, which was tolerated well except in one case, was performed in 10 (%59) of the patients. The standard attitude of the clinic is to utilize occlusion test in CBTs however, rest of the patients had refused to have the test due to probable neurological risks. Preoperative embolization was performed in one patient whom had significantly more abundant vascular supply to the tumor. Otherwise, embolization was not routinely applied to CBTs with the basic opinion that it leads to certain amount of fibrosis which makes surgical dissection more difficult leading to possible intraoperative complications. All tumors were removed completely without any local recurrence in their follow-up. The mean follow- up period was 29.9 months (6-84 months), with a median of 27 months. External carotid artery was sacrificed in three patients in whom the vessels were entirely surrounded by the lesions. Internal carotid artery damage occurred in three cases. In the first case, internal carotid artery was adhesive to the CBT at the upper and lower poles of the lesion and dissection was not possible without sacrificing the artery where an end to side anastomosis of common carotid artery with internal carotid artery was performed with the saphenous vein graft prior to excision of the paraganglioma. In the other two cases internal carotid artery was damaged during surgical dissection; it was sutured primarily in one patient and repaired with goretex vascular graft in the other one. Two of the patients had temporary vagus nerve paralysis leading to vocal cord paralysis which recovered after first postoperative year in both. No other postoperative vascular or neurological complications were observed in the patients.

Tympanic Paragangliomas

The second most common PGs were TPs. There were 18 patients with TPs, among 55 HNPs (32%) which were also resected. Endaural incision was preferred in 16 patients while endomeatal incision was sufficient in the rest two. Hearing loss was not seen in any of the patients postoperatively. One patient had recurrence and had revision surgery in his follow-up at the 9th month postoperatively. The only major complication encountered was the postoperative cerebrospinal fluid leakage in one patient within the mastoidectomy cavity. Re-exploration of the cavity did not yield the exact localization of the leakage, yet obliteration with the adipose tissue eliminated the problem.

Jugular and Jugulotympanic Paragangliomas

There were twelve JTPs (22%) and one isolated JP (2%)operated in our series. Patients' complaints were tinnitus, hearing loss or bleeding at the admission; except the JP with a complaint of neck mass. CT and MRI were used in diagnostic work up of all the patients. Preoperative embolization was performed in all the JTPs. Three patients developed cranial nerve deficits (cranial nerves 7 and 11 paralysis), one patient had cerebellar infarct and one had cerebrospinal fluid leakage and meningitis postoperatively. One of these patients was operated due to recurrence of the JPT who had the previous surgery four years ago in another institution. One of the patients with JTP had also two CBTs concomitantly, one of which was dissected simultaneously.

Vagal Paragangliomas

Four patients with four VPs (8%) were operated. All patients had CT and MRI's and three patients had balloon occlusion tests prior to intervention. One of the patients who had a revision surgery due to a recurrent lesion, operated primarily in another center, had residual tumor postoperatively that was stable for three years in his follow up. cranial nerve 10 was sacrificed in this patient due to the invasion of the nerve by the tumor. The other three patients had complete resection of their lesions. Lower cranial nerve deficits were observed postoperatively in another patient with cranial nerves 9 and 10 paralysis. No other vascular or neurological complications were encountered in these four patients.

DISCUSSION

HNPs are rare lesions comprising about 0.6% of head and neck tumors and about 0.03% of all tumors[20]. CBT is the most common type of HNPs accounting about 60% of the cases[21]. The middle ear is the next most common site for HNPs, and JTPs are the second most common paragangliomas of the head and neck. VPs are rare tumors, accounting less than 5% of all HNPs[8]. In our series, there were 20 CBTs (36%) among all 55 HNPs while TPs represented 32%, JTPs 22%, JP 2% and VPs 8% of the total number of tumors. Although number of CBTs is somehow lower than the incidences in the literature, CBTs and TPs are the most common localizations just like the previos series. Multiple cervical paragangliomas account for 11-22% and familial cases constitute 10-50% of these cases in the literature[22]. The majority of HNPs are benign lesions with overall malignancy rate of 6% for CBTs, 2% to 5% for JTPs and 16% and 19% for VPs[20]. It is not always possible to predict malignant behavior based on histologic features alone. There are some studies that have undertaken the task of identifying histologic criteria for malignancy Some histologic features include necrosis, extensive capsular or vascular invasion, increased mitotic activity, atypical mitotic figures, loss of a well-differentiated zellballen pattern with loss of the S-100 positive sustentacular cell population and tumor cell spindling. But there are no accepted histopathological criteria for malignancy though and the diagnosis of a ‘malignant paraganglioma' can only be made when there is metastasis to non-neuroendocrine tissue[23,24]. As far as malignancy is not frequent in these rare tumors, there were no cases of malignant paragangliomas in our series.

Paragangliomas are located in different sites of the head and neck region, such as CBTs and TPs. Although they have similar histopathological characteristics, the management approaches are diverse, particularly when they are treated with surgery. CBTs and VPs are the lesions of the neck while TPs are located solely in the tympanic cavity. JTPs are mainly the lesions of the jugular bulb with or without extension into the middle ear or mastoid regions. Although the main goal of the surgery is complete removal of the lesion without giving rise to complications or recurrences, different surgical approaches are required in each type of these tumors.

In CBT surgery, routine preoperative tests and embolization are topics of discussion, and avoiding postoperative complications may be difficult in certain cases. In our clinic, we perform preoperative laboratory tests for serum and urine norepinephrine, epinephrine and vaniylmandelic acid routinely and abdominal USG only in patients who have hypertension, bilateral lesions or familial history in order to detect existence of multiple and active lesions. In our series, there were three patients with bilateral CBTs; two of them had familial history. One of these two patients was found to be the only active secreting paraganglioma case in the series. Challenging topics about CBT surgery are avoiding vascular injury and preserving nerve functions. Mortality after CBT excision due to ICA rupture was reported between 0 % - 7.4 % in different series[25]. No morbidity or mortality was seen in our three cases in which we encountered ICA damage and repaired primarily, with vein graft and goretex. It is important to perform balloon occlusion test preoperatively and to work with a team that is competent for vascular anastomosis and grafting in CBT surgery to avoid morbidity and mortality. On the other hand, we do not recommend preoperative embolization for CBTs due to the fact the procedure does not provide an advantage in terms of dissection or bleeding intraoperatively. There were also 1 JP and 4 VPs in our series. JP was not invading the tympanic cavity and excised through the neck without any complications. One of the patients with VPs had cranial nerves 9 and 10 paralysis postoperatively, and one had cranial nerve 10 paralysis and residual tumor which was stable for three years in his postoperative follow-up. Recently, the idea of watchful waiting without performing surgery is predominating due to the high risk of neurological morbidity related to surgery of VPs[8]. The authors' of this paper agree with this opinion taking into consideration that the slow growing pattern of these lesions do not necessitate surgery in most of the VP cases. Surgery might be the choice of treatment in selected cases; otherwise it is not reasonable to encounter the risk of neurological deficits.

Paragangliomas originating from the jugular bulb might require simultaneous approach both through the ear and neck for total excision. In our series there were 12 JTPs, all of which were embolized preoperatively and surgically removed. Surgical success is measured by total excision without recurrence which is shown to be between 0 - 14 % in the literature[26,27]. There was one patient of recurrent JTP (8%) in our series who was referred to our clinic with the recurrent tumor after the initial surgery performed in another institution. Three year follow-up revealed a stable residual lesion postoperatively. Recent reports advocates radiotherapy as the first choice of treatment for HNPs. Hinerman et al.[28] declared overall local control rate of 95 % after radiotherapy treatment for 121 HNP patients. Lightowlers et al.[29] reported a 5-year actuarial local control rate of 87% for 21 HNPs patients treated with fractionated external beam radiotherapy. In their study aiming to evaluate the local control effect of CyberKnife on HNPs, Bianchi et al.[30] reported no local recurrence for approximately 20 months follow-up for eight patients. In a review comparing outcomes and complications of conventional surgery and radiosurgery, Gottfried et al.[31] found that surgery was associated with higher morbidity rates with 92.1% control and 3.1% recurrence rate (88.2% total resection) while radiosurgery provided 2.1% recurrence rate with 8.5% morbidity rate. However, radiation treatment assesses treatment efficiency by growth inhibition and provide stable lesion in radiographical studies during follow-up. It is shown that chief cells are not affected as much as the distinctive vascular structure which may create malignant potential[32]. Moreover, radiosurgery might lead to serious complications causing morbidity such as inflammation of external auditory canal and middle ear, osteoradionecrosis, cranial nerve neuropathies and direct injury to the brain tissue[21]. Also, conventional surgery after radiosurgery, when indicated, is a very complicating procedure.

TPs originate from the glomus bodies located along the Jacobson's nerve (tympanic brach of the cranial nevre 9) and the Arnold's nerve (auricular branch of cranial nerve10)[33]. There are different classification systems described for TPs, most widely accepted ones are defined by Fisch and Mattox and the one reported by Glasscock and Jackson[34]. There were 16 type A and 2 type B lesions in our series according to Fisch and Mattox classification which defines four classes in regard to location and extension of the tumor. Most important diagnostic work up for TPs is to differentiate it from JTPs which can be performed with high resolution computed tomography which provides useful information about tumor extension in relation to bone and involvement of adjacent structures. Preoperative angiography is not performed as far as embolization is not necessary for these lesions. In the management of TPs, surgery is the first choice rather than radiosurgery when the lesion is limited to middle ear and mastoid regions. In our clinic, mostly endaural incision is preferred as it enables the required surgical exposure. Among our TP cases, the only major postoperative complication was the cerebrospinal fluid leakage which was controlled immediately with re-exploration. Recurrence rates after TP surgery has been reported between 0% and 5% in the literature[35,36]. Hearing was preserved in all patients and there was only one patient with reccurence which occurred in the 9th month of the follow-up and was managed with surgery again.

CONCLUSION

In conclusion, surgery is still the preferred treatment modality in the management of the CBTs and TPs in our clinic. It enables complete removal of the tumors with low rates of recurrence and morbidity in experienced hands. On the other hand, although the number of VPs are limited in this series, authors consider surgical intervention only in selected cases of VPs in order to avoid neurological complications; clinical and radiological follow up might be sufficient in most of the patients. The decision between surgery and radiotherapy should be made individually according to tumor and patients characteristics for JTPs.

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