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ORIGINAL ARTICLE

Primary tumours of the parapharyngeal space. Our experience in 51 patients

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KEYWORDS
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Abstract
Introduction and objectives: Tumours of the parapharyngeal space are rare, representing only 0.5% of head and neck oncology. The aim of this study is to present our experience with the diagnosis and therapies for these tumours.
Patients and method: This study is a retrospective review of 51 patients diagnosed as having tumours of the parapharyngeal space and treated surgically between 1984 and 2006. Tumours originating in the deep lobe of parotid gland were excluded.
Results: Seventy percent of the parapharyngeal space neoplasms were benign and thirty percent malignant. Pleomorphic adenoma was the most common neoplasm (37%), followed by miscellaneous benign tumours (34%), paraganglioma (21%), and neurogenic tumours (8%). Surgery was chosen in all cases, with the transcervical approach used in 32 cases, the cervical-transparotid approach in 13 cases, the transmandibular approach in 4 cases (with mandibulectomy in 1 patient), the transoral approach in 1 case, and the infratemporal fossa approach in 1 case. The most common complications were those deriving from damage to nerve structures.
Conclusions: Most parapharyngeal space tumours can be removed surgically with a low rate of complications and recurrence. The transcervical approach is the most frequently used.

PALABRAS CLAVE
Espacio parafaríngeo;
Tratamiento quirúrgico;
Tumores parafaríngeo;

Tumores primarios del espacio parafaríngeo. Nuestra experiencia en 51 pacientes

Resumen
Introducción y objetivos: Los tumores originados en el espacio parafaríngeo son poco frecuentes, y representan el 0,5% de la enfermedad oncológica de cabeza y cuello. El objetivo de este estudio es presentar nuestra experiencia en el diagnóstico y el tratamiento de estos tumores.

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Tumores de glándulas salivales;
Paragangliomas;
Neurinomas

Pacientes y método: Realizamos un estudio retrospectivo de 51 pacientes, diagnosticados y tratados quirúrgicamente de una tumoración parafaríngea, durante el período comprendido entre 1984 y 2006. Se excluyeron los tumores originados en el lóbulo profundo de la parótida.
Resultados: El 70% de las neoplasias del espacio parafaríngeo fueron de naturaleza benigna y el 30%, maligna. El adenoma pleomorfo fue el tumor más frecuente (37%), seguido por un grupo de tumores de origen misceláneo (34%), los paragangliomas (21%) y los tumores de origen neurogénico (8%). En todos los casos el tratamiento fue quirúrgico. Se realizó un tratamiento transcervical en 32 pacientes, un tratamiento cervical-transparotídeo en 13 pacientes, un tratamiento transmandibular en 4 pacientes (sólo se precisó de mandibulectomía en un caso), un caso de tratamiento transoral y un caso de tratamiento infratemporal tipo A. Las complicaciones más frecuentes fueron las derivadas de lesiones de estructuras nerviosas.
Conclusiones: La mayoría de los tumores localizados en el espacio parafaríngeo son subsidiarios de tratarse de forma quirúrgica, con una tasa baja de complicaciones y recurrencias. El más utilizado es el tratamiento transcervical.

Introduction

The parapharyngeal space is a virtual anatomic region in the shape of an inverted triangular pyramid, extending from the skull base to the hyoid bone. It is possible to define a base, a vertex, and 3 walls. Its upper limit, or base, is the petrotympanic region of the temporal bone, and its lower limit, or vertex, the greater horn of the hyoid bone. An external wall formed by an aponeurotic muscle bundle comprising the sternocleidomastoid muscle and its aponeurosis, the superficial cervical aponeurosis lining the parotid, and the ascending branch of the lower jaw, with the pterygoid and masseter muscles. The medial wall is formed by the lateral face of the pharynx. The posterior wall is formed by the aponeurosis, the prevertebral muscles and the cervical transverse apophyses. This space is divided into 2 compartments by a styloid diaphragm or osteomuscular aponeurotic sheath originating in the styloid apophysis, and following a top-down angled plane running from back to front and lateral to medial location. The anterior or pre-styloid compartment is occupied by the deep lobule of the parotid, fat, and lymph nodes, the internal maxillary artery and the inferior, lingual and auriculotemporal alveolar nerves. The posterior or retro-styloid compartment contains the neurovascular axis, comprising the carotid artery, the jugular vein, the cervical sympathetic chain and the IX, X, XI, and XII nerve pairs.[1] After this complex anatomical description, it is easy to understand the great histological diversity of tumours that may have their origin in the parapharyngeal space.[2]

Parapharyngeal tumours, also known as pharyngomaxillary, pterygomandibular, pterygopharyngeal, or lateropharyngeal tumours, are infrequent in head and neck oncology, representing only 0.5%[3] Nonetheless, the parapharyngeal space is of particular importance, both for the diversity of structures it houses and for the varied nature of the tumours it can contain. The anatomical characteristics of these tumours hinder early diagnosis with a standard physical examination. Complementary imaging studies, particularly computerized tomography (CT), and, above all, magnetic resonance imaging (MRI), are greatly reducing these limitations in the diagnosis and planning of surgical treatment. The benign nature of most of these tumours and their surreptitious anatomical setting require a surgical treatment capable of ensuring the complete extirpation of the lesion with minimal morbimortality. The most common treatments of choice are the transparotid approach in pre-styloid tumours and the transcervical treatment in retro-styloid tumours.

Material and method

We report here a retrospective study of 51 patients with tumours in the parapharyngeal space undergoing surgical treatment at our hospital between 1984 and 2006.

The method used was to review their clinical and pathology records, analyzing patient data such as age, gender, clinical presentation, examination, treatment, and follow-up.

Patients were excluded from this study if their tumours were not primary but only invaded this region from an adjacent area or if they originated in the deep lobe of the parotid, as were lymph node metastases.

Results

The age range of our study group was very large, going from months to 81 years of age; the mean was 45 years and the median, 43 years. There was a predominance of males: 30 (60%) versus 21 females (40%).

The most common reasons for coming to see a doctor was the emergence of a mass, either in the cervical area, as presented by 13 patients (25%), or in the oropharynx area, presented by 10 patients (20%). A common symptom was upper dysphagia, present in 10 patients (20%). Other less frequent symptoms included respiratory failure through the nose, dysphonia, earache, neck pain, and ageusia. We should point out that there is a group of 9 patients (18%) in our series where the illness coursed asymptomatically and diagnosis was an accidental finding after imaging study was required for other reasons.

The most common findings on physical examination were swelling of the posterior wall of the oropharynx and the

amygdaline region in 26 patients (51%); in 18 patients (35%), the palpation of a cervical mass was observed. Other less frequent signs were paresias or paralysis of the low cranial pairs. Examination was unremarkable in 3 patients (6%).

Once the suspected existence of a parapharyngeal tumour has been established, diagnosis is essentially based on imaging tests. The radiological study most often used in our series was CT, in 48 patients (94%), followed by MRI, in 24 patients (47%). In patients with tumours presenting an intense uptake of contrast agent, or signs of increased vascularization, an arteriography was indicated in 9 cases (18%).

From the perspective of the pathologist's report, a pre-surgical study was performed using a fine-needle aspiration biopsy (FNAB) in 8 patients (16%). The result agreed with the definitive pathology result in 3 cases; therefore, we obtained 65% false positives. Surgical biopsy was performed in 7 patients (14%), of which 5 were done cervically and the other 2 transorally.

In our series, there is a clear predominance of benign tumours, in 36 patients (70%), with respect to malignant tumours in 15 patients (30%). Among the benign tumours, the most frequent was pleomorphic adenoma (14 patients), followed by paragangliomas (10 patients) and Schwannomas (3 patients). The rest of the benign tumours have been grouped under the heading Sundry, as their origins are very varied; they are infrequent if analyzed individually, but overall their volume in our series is quite considerable (Table 1).

The histological distribution of the 15 malignant neoplasms diagnosed was mixed malignant tumours of the salivary gland (5 patients), malignant Schwannoma (1 case), neuroblastoma (1 case), and finally, a Sundry group (8 patients) (Table 2).

All of the patients underwent surgery. In 8 cases (15%), they had previously been operated on at their originating hospital but, due to incomplete resection or relapse, they came to our centre for a subsequent therapeutic assessment.

With respect to the procedure performed, the most frequent treatment was transcervical in 32 cases (63%). In 13 patients, a transcervical-transparotid approach was used; in 5 cases, a partial parotidectomy was performed to ensure tumour-free surgical margins or due to tumorous involvement of the parotid gland. In 4 patients, a transmandibular approach was applied and in only 1 case was mandibulectomy required. Finally, 2 patients (the oldest ones) were subjected to a transoral treatment and one other patient had an infratemporal type A treatment (Table 3).

Resection of the tumour was complete in 44 cases and incomplete in 7 cases: a chordoma, a malignant salivary gland tumour, a malignant fibrohistiocytoma, a neurinoma of the cervical sympathetic nerve, pleomorphic adenoma, a rhabdomyosarcoma, and an angiosarcoma. Complementary treatment with radiation therapy, chemotherapy or a combination of both was applied in these 7 patients.

In 2 patients, it was necessary to perform a temporary tracheotomy. Both cases involved malignant tumours: a neuroblastoma with medium-grade malignancy and a minor salivary gland carcinoma. A nasogastric tube was fitted in 7 patients with a high possibility of developing post-

Table 1 Histological distribution of benign tumours

Benign tumours	Patients
Pleomorphic adenoma	14 (39%)
Vagal paragangliomas	10 (28%)
Schwannomas	3 (8%)
Vagal	2
Cervical sympathetic	1
Sundry	9 (25%)
Ameloblastoma (2)	
Angiomyoma	
Angiofibroma	
Haemangiopericytoma	
Hyaline cyst	
Branchial cyst	
Lymphangioma	
Mesenchymal tumour	

Table 2 Histological distribution of malignant tumours

Malignant tumours	Patients
Salivary glands	5 (34%)
Malignant Schwannoma	1 (6%)
Neuroblastoma	1 (6%)
Sundry	8 (54%)
Chordoma	
Malignant fibrohistiocytoma	
Melanoma	
Angiosarcoma	
Malignant solitary fibrous tumour	
Rhabdomyosarcoma	

Table 3 Distribution of patients by surgical treatment

Treatments	Patients	Total
Transcervical	11 salivary gland tumours 0 vagal paragangliomas 4 neurinomas 7 sundry	32
Cervical-transparotid	7 salivary gland tumours 1 vagal paraganglioma 5 sundry	13
Transmandibular	1 salivary gland tumour 3 sundry	4
Transoral	1 salivary gland tumour	1
Infratemporal tipe A	1 malignant fibrous tumour	1

surgical dysphagia, either during the surgical procedure itself or in the immediate post-operative phase. All cases involved tumours of neurogenic origin (paragangliomas or neurinomas) involving the vagus nerve. Only 1 patient required gastrostomy due to persistence of her disphagia.

We should highlight the absence of intra-operative and peri-operative mortality. As for complications, the most frequent were paresias or paralyses of low cranial pairs in 10 cases (20%). In 5 patients, paralysis of the X nerve was observed, 3 patients presented Horner's syndrome due to involvement of the cervical sympathetic nerve and 2 cases had facial palsy. Three of these 10 cases already presented neurological involvement prior to the surgery performed at our hospital: they were 2 patients previously operated on for a vagal paraganglioma and one patient diagnosed as having a neurinoma of the cervical sympathetic nerve.

The mean hospital stay was for 13 days and the median was 9.5 days. After discharge from hospital, the patients were followed up regularly at our out-patient clinics.

At the end of the study follow-up period, 43 patients were alive and tumour-free. Of the 8 patients who developed a recurrence of their tumour, 6 died and 2 were still alive with tumour. The relapses presented in patients diagnosed as having malignant tumours in which it was impossible to perform complete surgical resection of the mass, except for one case of pleomorphic adenoma, where the patient is still alive.

Discussion

The parapharyngeal space is a virtual anatomic region classically compared to an inverted triangular pyramid extending from the skull base to the hyoid bone.

A high percentage of the tumours arising in this space present a silent, asymptomatic course and so are frequently diagnosed by chance during a general examination or in a radiological study including this region.[4,5] The growth or dissemination of the tumours in this space occurs through their direct extension into the adjacent spaces with the least resistance, such as: the parotid gland, the sub-maxillary gland, the retropharyngeal space, the chewing space, the amygdaline region, the carotid sheath. For this reason, it was very common in the clinical examination to detect the presence of a cervical mass by performing a bimanual palpation or a swelling of the pharyngeal walls on inspection. In general, cervical growth translates into a long prior course and a large tumour size. Intra-oral growth requires differential diagnosis vis-à-vis tumorous and inflammatory illnesses of the amygdaline region, and even carotid aneurysms. It is subsequently important to perform a systematic neurological examination to detect neural deficits that might help in the differential diagnosis of the mass.[6] The presence of pain, trismus (caused by the infiltration of the tumour into the internal pterygoid muscle) and the paralysis of cranial pairs must alert us to the presence of a malignant tumour, neurinomas or paragangliomas.[7] We have seen that both the presenting symptoms and the systematic physical examination of these tumours are very non-specific.

For this reason, it is essential to perform complementary imaging studies, basically CT and/or MRI, to confirm the diagnosis of a parapharyngeal tumour, as well as the topographical diagnosis that will subsequently help us choose the surgical treatment.[8] This radiological study provides us with information on the mass's pre-styloid or retro-styloid location, its relationship with the parotid gland, the large vessels and the radiological characteristics of the tumour.[9]

Both the CT scans and the MRI images can be used as the first choice. Most patients would not require both types of study; generally speaking, MRI provides us with more information. The only advantage of CT scans over MRI images is the better definition of bone involvement; nonetheless, it is the most widely used in this series due to its lower cost and greater accessibility at our centre. In those cases where the tumour was retro-styloid, a vascular origin was suspected or signs of malignancy were present, an MRI test was performed. An angiographic study was indicated in tumours where the CT indicated a tumour of neurogenic or vascular origin.[10] In the oldest cases, conventional arteriographies were performed; nowadays angiographic MRI scans are used, except for highly vascularized tumours requiring embolization prior to surgery, or the performance of an occlusion test, should the resection of the internal carotid artery be necessary. In those cases where it was necessary to perform embolization, the arteriography has to be carried out 23 days prior to surgery. An additional delay implies an increase in the inflammatory phenomena or even repermeabilization.

The radiological characteristics of the tumour mass and the displacement its growth causes in the fat and the carotid artery[11] are extremely useful for the differential diagnosis of parapharyngeal neoplasms. Thus, pleomorphic adenomas and neurinomas have a very similar appearance in MRI results; however, the former displace vessels to the posterior area (Figure 1) while the latter displace them to the anterior area (Figure 2). Unlike neurinomas, paragangliomas present areas devoid of flow in MRI images. Vagal glomi produce anterior and medial displacement of the carotid arterial system (Figure 3). Most neurinomas arising from the vagus nerve or the cervical sympathetic nerve are significantly highlighted in gadolinium-enhanced MRI scans, and they tend to produce displacement in anterior and lateral directions to the internal carotid artery.

Our experience in cytological diagnosis using FNAB is limited and not very useful. It was performed in 8 patients, and only in 3 of them was it possible to find a correlation with the pathology report results corresponding to the surgical specimen. These were 2 cases of pleomorphic adenomas and 1 case of neuroblastoma. In this latter case it was necessary to perform a subsequent biopsy to determine the degree of malignancy. These results contrast somewhat with those obtained in other series,[12] where the pre-surgical histological diagnosis of these tumours was highly specific. In 2 patients, the earliest ones in our series, biopsy samples were obtained transorally, in the full knowledge that this technique is now contraindicated. This is due to the fact it presents a greater risk of bleeding, there is worse control over the parapharyngeal vascular structures, a greater risk of local recurrence due to dissemination in the pharyngeal mucosa and, finally, fibrosis in the incision area that increases the risk of an oropharyngeal fistula in subsequent surgery.[6]

Therefore, the diagnostic strategy to be followed in view of a clinical suspicion of a parapharyngeal mass must

be: first of all, to request an imaging study (MRI provides more information) and, after ruling out vascular origin, we will proceed with a cervical approach in one of its many variations, leaving intra-operative biopsy as an option. Where the suspicion points to a vascular tumour (generally, vagal paragangliomas), additional tests such as and angiographic MRI or arteriography and perhaps embolization may be ordered.

In this study, as in the majority of papers reviewed,[6,7,9,13] there is a clear predominance of benign tumours (70% in our series), and the most frequent histological type is pleomorphic adenoma of the minor salivary glands (all those originating in the deep lobe of the parotid were excluded). Neurogenic tumours constitute the second group in terms of frequency, and the most common among these is paraganglioma. Because of the wide variety of structures contained in the space, there is an extensive group of infrequent tumours, as in our case: chordomas, mesenchymomas, haemangiopericytoma,[14] malignant fibrohistiocytoma, and angiosarcoma.

Different approaches have been described for the complete resection of these tumours: transcervical, cervical-transparotid, transmandibular, and transoral. The choice depends on the location of the tumour, its relation with regard to the large vessels and the suspicion of malignancy.[6,9,15] The pre-operative importance of identifying, using radiological signs, whether it is a benign or malignant tumour lies in the fact that the former, despite their larger size, are generally much more elastic than malignant ones, and therefore easier to remove. The transcervical approach was the treatment most frequently applied in our series, was adequate and sufficient for complete complication-free exeresis of most parapharyngeal tumours. In some patients with pre-styloid masses, where there was suspected involvement of the deep lobe of the parotid or large retro-styloid masses, it was necessary to extend treatment by using a cervical-transparotid approach. The main problem with the transcervical route is that, in large masses, it may be difficult to control the skull base. Occasionally, dissecting the tumour may make it easier to perform the extraction manoeuvre and, in other cases, it could be necessary to perform a mandibulotomy. For malignant tumours requiring an extensive surgical field to ensure free margins, transmandibular approaches were applied in 4 patients. In these cases, in order to reduce the sequelae of the mandibulotomy, a visor flap has to be provided and, if possible, the mandibulotomy has to be medial at the exit from the mentonian orifice, seeking a favourable region between 2 teeth. A transoral approach was only needed in one patient, and infratemporal type A treatment in one other.

As in the literature reviewed,[16] the largest number of sequelae in our series were of neurogenic origin, paresias or paralyses of low cranial pairs related with resections of paragangliomas and neurinomas. The existence of post-surgical complications depends on the type of tumour, the relationship between the mass and the large vessels and the intra-operative lesions on anatomical structures located in the parapharyngeal space. The most frequent finding is a transient or permanent lesion of a nerve stem. Thus, the facial nerve may be affected in parotid treatments or malignant tumours infiltrating the gland. Low cranial pairs (IX, X, XI, XII) may be affected in neurogenic tumours. An isolated lesion of the vagus nerve produces dysphonia, but rarely aspirations; however, when it is affected simultaneously with pairs IX and XII, there are problems

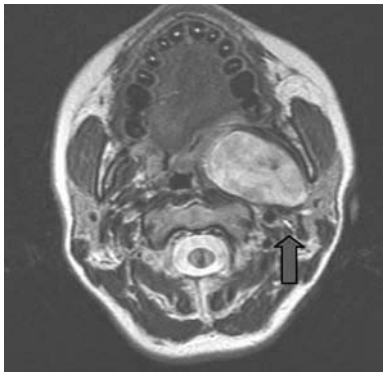

Figure 1 Cervical magnetic resonance in the axial plane, showing a pleomorphic adenoma located in the pre-styloid producing a posterior displacement of the vascular axis (arrow).

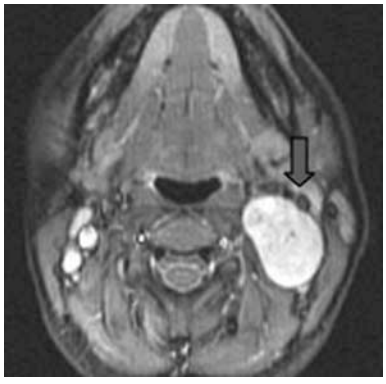

Figure 2 Axial magnetic resonance, showing a cervical sympathetic neurinoma located in the retro-styloid space displacing the vascular axis anteriorly (arrow).

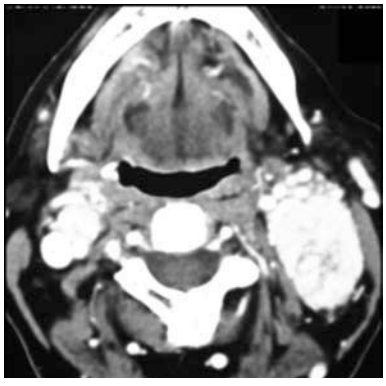

Figure 3 Cervical computerized tomography in the axial plane, showing a right vagal paraganglioma and left carotid paraganglioma.

with swallowing, potentially requiring the placement of a nasogastric tube and, in very rare cases, the performance of a gastrostomy, until contralateral compensation is achieved. Techniques for the medialization of the paretic vocal cord can be used, such as type I thyroplasty. Lesions to the XI or spinal pair produces motor deficits, and a lesion to the cervical sympathetic plexus gives rise to the well-known Horner's syndrome.[17] We have noted that in elderly patients presenting prior palsy (X, XII, IX) after extirpation of a parapharyngeal neurinoma or paraganglioma, without the presence of additional nerve lesions after surgery, aspiration and poor swallowing ensued and worsened.

In our series, there is no case of intra-operative or immediately post-operative mortality. As a result of the tumour, the follow-up revealed the death of 6 patients (11%) diagnosed as having a malignant tumour who developed locoregional recurrences. This percentage is high if we compare it with other published series presenting no mortality at all.[9] The presence of a larger number of malignant tumours in our study may explain these results. With benign diseases, we only recorded one case of recurrence corresponding to a pleomorphic adenoma.

In our series, the use of complementary treatments involving radiation therapy[6,9] was limited to patients with malignant tumours, or benign ones (one case of pleomorphic adenoma) where complete resection was not possible.

Conclusions

Parapharyngeal tumours are infrequent in the population and initially present with asymptomatic behaviour, due to their peculiar anatomical location. Clinical suspicion tends to appear incidentally, in the course of a systematic physical examination, or else following the onset of a neck tumour on the lateral wall of the pharynx, the 2 most common forms of presentation. Other possibilities are the presence of pain, trismus or paralysis of low cranial pairs.

Diagnosis is essentially based on radiology, CT or MRI, and in certain cases we will need to perform conventional angiographies. Biopsies are not indicated except in the context of extirpation surgery.

The design of the surgical approach depends on the location and dimensions of the tumour; the transcervical or cervical-transparotid route is valid for most pre-styloid and retro-styloid tumours. Transoral treatment is not indicated due to the high number of complications and the high recurrence rate associated with this technique.

Post-surgical morbidity with parapharyngeal tumours basically revolves around (mostly transient) neuropathies in the lower cranial pairs which arise in the resection of neurogenic or malignant tumours.

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