Chapter 21: Parapharyngeal space tumours

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Anatomy

The parapharyngeal space is a potential space located on both sides of and parallel to the naso- and oropharynx. It is filled with loose connective tissues, arteries, veins, lymph glands, nerves, muscles, tendons, glomus bodies and salivary gland tissue. It has roughly the shape of an inverted five-sided pyramid with its base towards the sphenoid bone and its apex directed inferiorly towards the minor horn of the hyoid bone (Heeneman, Gilbert and Rood, 1979).

Much of the confusion concerning head and neck spaces in general, and the parapharyngeal space in particular, can be explained by the inconsistent nomenclature relating to these anatomical entities. The parapharyngeal space is known in the literature under the names of pterygomaxillary space, pharyngomaxillary space (Mosher, 1929), lateral pharyngeal space and pterygopharyngeal space (Coller and Yglesias, 1935). The term 'parapharyngeal space' seems most appropriate and is commonly used in the current literature.

Anteriorly, the space is bounded by the pterygoid muscles with their interpterygoid fascia and those fasciae directed laterally towards the buccinator muscle and angle of the mandible. Laterally, the space is limited by the ascending ramus of the mandible, while posterolaterally the deep lobe of the parotid gland and retromandibular fossa can be identified. Medially, there is the pharynx with the tonsillar fossa inferiorly and eustachian tube superiorly. The posterior border is limited by the cervical spine covered by prevertebral muscles and fascia.

Tumours originating within the parapharyngeal space exert pressure on neighbouring structures and expand towards those areas that offer the least resistance, namely the naso- and oropharynx medially, the upper neck between the tail of the parotid and the submandibular gland inferiorly, and the retromandibular fossa posterolaterally.

The retropharyngeal space is connected with the parapharyngeal space in an area just medial to the carotid sheath and its contents. Situated at the junction of these two spaces is the superior lateral lymph node (node of Rouvière, 1927) normally draining the nasopharynx, upper oropharynx and sinuses. The retropharyngeal space provides a pathway towards the mediastinum (Lincoln's highway), while anteriorly and laterally there are connections to other spaces located about the oral cavity and salivary glands.

The parapharyngeal space is divided into anterior (prestyloid) and posterior (poststyloid) compartments by the styloid process and the three muscles and two tendons attached to it (Riolan's bouquet). Table 21.1 summarizes the structures lying in these compartments.

Of special interest is the deep lobe of the parotid gland between the mandible laterally, the medial pterygoid muscle medially and the masseter muscle anteriorly. The sternocleidomastoid and posterior belly of the digastric muscles as well as those structures
arising from the styloid process are in a posterior position. Patey and Thackray (1956-157) coined the term 'stylomandibular tunnel' formed by the posterior margin of the ascending ramus of the mandible anteriorly, the styloid process and stylomandibular ligament behind and the base of the skull above. This tunnel resists pressure so that tumours of the deep lobe of the parotid gland assume a dumb-bell shape as they grow.

Table 21.1 Structures located in the compartments of the parapharyngeal space and in the retropharyngeal space

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| Tumours of the parapharyngeal space originate from the various types of cells and tissues present within this space, by direct extension from neighbouring structures or through lymphogenous or haematogenous spread. Numerous primary benign and malignant tumours have been described, the group of salivary gland tumours being most prevalent (50%) followed by the neurogenic tumours (30%). The remaining 20% is made up of a wide variety of tumours, the list of which is getting longer as the limitations of light microscopy, with its inherent shortcomings in distinguishing the relationships of the various structures to one another, are overcome by electron microscopy techniques and special stains to identify cell structures. Tumours originating outside the parapharyngeal space arise from surrounding structures such as parotid gland, mandible and maxilla, nasopharynx, tonsils, sinuses and intracranial cavity.

The parapharyngeal space is richly endowed with lymphatics that drain the sinuses, pharynx and thyroid gland (Robbins and Woodson, 1985). The nodes of the upper deep cervical chain are located in this space. They are connected superiorly to the node of Rouvière, while inferiorly they flow towards the jugulodigastric node, the node most commonly involved with metastatic disease from head and neck tumours. This node lies just outside and inferior to the parapharyngeal space.

While lymph usually flows away from a tumour towards the big veins, under certain conditions the flow is in the opposite direction, for example, when distal lymph channels are obstructed by tumour emboli, previous irradiation or previous surgery. This explains why the parapharyngeal space can be involved secondarily by primary tumours from the oral cavity and elsewhere after previous treatment.
Salivary gland tumours

Two types of salivary gland tumours occur in the parapharyngeal space. The first type arises de novo from salivary gland tissue in the parapharyngeal space and has no connection with the parotid gland. As the tumour grows it pushes a compressed layer of fibroadipose tissue ahead of itself, which might be visible on the newer higher resolution type of computerized tomography (CT) scans. The second type is the 5% of parotid tumours that arise within the deep lobe of the parotid gland (Conley and Clairmont, 1978) and it is this type that has an intimate relationship with the gland. The histology and incidence of the tumours of the deep lobe are similar to tumours originating in the superficial lobe of the gland; most are benign pleomorphic adenomata while the most common malignant tumour is adenoid cystic carcinoma (Hanna et al, 1968; Work and Gates, 1969; Johns, 1977). Discussion of the classification of salivary gland tumours and their biological behaviour is described elsewhere (see Chapters 19 and 20).

Neurogenic tumours

Nerve sheath tumours

Schwannomata

All peripheral motor and sensory axons are covered by Schwann cells throughout their length. Tumours arising from these cells are called schwannomata and are the most common neurogenic tumours in the parapharyngeal space. They are also more common in the head and neck than elsewhere in the body. The terms neurinoma, neurilemmoma and neuroma should no longer be used. Schwannomata are generally solitary and are seen in relation to nerve trunks in that they can readily be dissected from the nerve of origin, most often the vagus nerve.

On cutting the tumour the heterogeneous surface can be seen with solid areas, cysts, haemorrhage, and yellow spots representing areas of lipid deposition.

Microscopic examination reveals that the tumour is composed of alternating areas, some organized and compact (Antoni type A) and some of loosely arranged, relatively acellular tissue (Antoni type B). Occasionally, one pattern may predominate, but the tumours usually are composed of both. The cells are spindle shaped, with elongated and ovoid nuclei. The term Verocay bodies refers to a special arrangement of the cells in an interwoven pattern, producing pallisades with fibrillary zones. There may be macrophages containing lipid and deposition of haemosiderin. Occasionally lymphocytic infiltration around blood vessels is seen. There may be pleomorphism and irregularity of the nuclei with mitotic figures not necessarily associated with malignancy. Axons are found in the capsule and not within the bulk of the tumour.

Neurofibromata

Neurofibromata arise from the Schwann cell and from the perineurium, which is composed of specialized cells called perineurial fibroblasts. In marked contrast to schwannomata, neurofibromata encompass their nerve of origin. It is virtually impossible to
dissect the tumour away from the parent nerve without sacrificing the nerve. These tumours often originate from small subcutaneous peripheral sensory nerve trunks. They are usually solitary although they can be multiple, and are not necessarily associated with neurofibromatosis.

The cut surface of a neurofibroma is usually homogeneous, grey, frequently gelatinous and without haemorrhage and cyst formation. Microscopically, the cells are spindle shaped and are arranged in groups. Special stains show many axons throughout the tumour.

Plexiform neurofibromata appear as multiple nodules or fusiform swellings along the course of the nerve of origin, frequently a cranial nerve. These tumours are characteristic of neurofibromatosis, and under the microscope they show patterns reminiscent of both schwannomata and neurofibromata.

**Malignant schwannomata**

A malignant schwannoma is a malignant neoplasm of nerve sheath origin that infiltrates locally and also metastasizes. The tumours are rare in the general population but occur with higher frequency in patients with neurofibromatosis. Microscopically they are whorls of spindle cells with interlacing fascicles. There is pleomorphism, hyperchromatism, increased cellularity and frequent mitoses. There may be focal areas of chondroid, osteoid or even rhabdomyoblastic metaplasia present. This tumour is known in the literature as fibromyxosarcoma of nerve, fibrosarcoma or myxosarcoma of nerve sheath, neurilemmal sarcoma or secondary malignant neuroma. These terms should no longer be used.

**Nerve cell tumours**

The terms neuroblastoma and ganglioneuroma indicate the cell of origin. Although these tumours usually occur in the adrenal medulla, they occasionally develop along peripheral nerves elsewhere in the body including the head and neck. They may produce catecholamines (Glenner and Grimley, 1974).

**Paragangliomata**

The parapharyngeal space contains vagal bodies closely associated with the ganglion nodosum of the vagus nerve. These bodies contain clusters of chemoreceptor cells and make up a part of the chemoreceptor or glomus system of the body (Lore, 1973). The system consists of minute extra-adrenal paraganglia located along major arteries such as the carotid, pulmonary and mesenteric arteries. Tumours originating from glomus bodies are called glomus tumours, chemodectomata or paragangliomata. At one time the tumours were divided into chromaffin or non-chromaffin, according to the presence of a brown reaction product after the application of dichromate solution, the brown stain representing oxidation products of catecholamines. These findings appear to be inconsistent and today the tumours are classified by site without other qualifying names. In the head and neck, glomus tumours are seen in the jugular bulb, in the crotch of the carotid artery, in the supraglottic larynx where they originate from the glomus laryngicum superior (Greenway and Heeneman, 1975), and from the vagal body (glomus intravagale). Tumours originating from these extramedullary receptor cells rarely produce catecholamines.
Paragangliomata have a familial tendency. They occur more often in females and are often multicentric particularly in people living at high altitude (Heeneman and Maran, 1979). They are generally encapsulated but may be ill defined, with a variegated, rubbery consistency, and are intimately bound to associated vessels and nerves. The cut surface may be smooth and homogeneous and is often yellow to grey with areas of necrosis and haemorrhage. Under the microscope the typical tumour shows reproduction of the architecture of the normal paraganglia. The cells are organized into groups, cords, ribbons, and rosettes and have a uniform polygonal outline, with eosinophilic cytoplasm. Nuclei may be hyperchromic and bizarre. Mitoses are unusual and the cells can be shown to contain brown, granular pigment which represents the catecholamines. There is an alveolar pattern, with clusters of cells surrounded by a delicate fibrovascular stroma (Zellballen). Reticulum staining will show the cell mass surrounded by the stroma.

Histologically, paragangliomata are benign. It is difficult to determine malignancy on histological grounds alone. Correlation with clinical findings such as rapid growth, fixation, bone destruction and local invasion is essential. Since these tumours are often multicentric it is sometimes hard to distinguish between metastases and multiple foci. Malignancy occurs in less than 10% of cases (Conley, 1965).

Other tumours

Sarcomata are rare in the parapharyngeal space and take on features of sarcomata found elsewhere. Their identification depends on careful electron microscopic analysis. Involvement of the parapharyngeal space by osteogenic chondrosarcoma is secondary, resulting from expansionary growth of these tumours when they originate from neighbouring structures, for example, base of the skull, maxilla, mandible, and eustachian tube.

A neck mass is the initial manifestation in 30% of lymphomata and involvement of the lymph nodes located in the parapharyngeal space is not rare. Occasionally a primary lymphoma with no involvement of other neck nodes is encountered.

Table 21.2 indicates other primary tumours that may be found in the parapharyngeal space as encountered in the literature. The biological behaviour of these tumours is the same as tumours of similar histology found elsewhere in the head and neck.

Diagnosis

Most tumours of the parapharyngeal space are benign, slow growing and produce symptoms by exerting pressure on neighbouring structures and those within the space. The malignant tumours also invade the surrounding bones: maxilla, mandible, pterygoid plates and base of skull. Often symptoms are long-standing and have been treated unsuccessfully until the tumour becomes manifest. Sometimes the diagnosis is made incidentally during a routine head and neck examination by inspection and palpation of the submandibular trigone, retromandibular fossa and pharynx. Parapharyngeal space tumours expand to these areas as they do not offer the same resistance as surrounding bony structures. Bimanual ballottement of a tumour in the lateral pharyngeal wall differentiates a parapharyngeal space growth from a primary tumour in the soft palate and also provides information as to extent and degree of fixation.
Hearing loss resulting from middle ear effusion caused by pressure on the eustachian tube is the most common symptom. Symptoms of a dull or neuralgia-like pain or a chronic sore throat are next in frequency. Although more common in malignant tumours these symptoms do not necessarily indicate malignancy.

Motor nerve palsies in the distribution areas of the vagus, spinal accessory and hypoglossal nerves are caused by direct pressure on the nerve. When there is ipsilateral vocal cord paralysis, shoulder weakness and a deviation of the tongue, then the jugular foramen (Vernet) syndrome is complete. Horner's syndrome has been reported. Sensory deficits of the mandibular division of the trigeminal nerve or its branches are caused by perineural invasion invariably due to adenoid cystic carcinoma.

Trismus and narrowing of the pharynx leading to airway obstruction, speech defects and dysphagia can be explained by mass effect.

Once a primary parapharyngeal space tumour is suspected and a careful examination of the upper aerodigestive tract has ruled out a primary tumour then an accurate radiological evaluation is indicated. Plain sinus films confirm the presence and size of most soft tissue tumours and demonstrate bone erosion. A chest X-ray to determine the presence of metastases of involvement of the chest cavity with malignant lymphoma is part of the preoperative examination.

The new generation of CT scanners with better resolution power not only accurately delineate the extent of the tumour, but also give information as to whether it arises from the deep lobe of the parotid or de novo. In the latter case there may be a lucent line representing the compressed layer of fibroadipose tissue between the tumour and the deep lobe of the parotid (Som, Biller and Lawson, 1981). Computerized tomographic scanning may indicate the degree and extent of bone erosion. Where there is any question of erosion, particularly in important areas such as the base of skull region, tomography may provide further information.

Enhancement indicates increased vascularization and, as most parotid tumours are relatively avascular, most parapharyngeal space tumours are hypodense. The most common enhancing tumour is the schwannoma followed by the paraganglioma. Haemangiomas and tumours with haemorrhagic degeneration also enhance. When there is enhancement, carotid arteriography is indicated not only to determine the degree of vascularization, but also to identify the feeding vessels of the tumour, to detect a vascular abnormality and to determine whether there is displacement of the carotid arterial system. Tumours arising in the deep lobe of the parotid when entering the prestyloid compartment of the parapharyngeal space displace the internal carotid artery posterolaterally. The site of neurogenic tumours is less constant and the displacement is variable. Widening of the carotid bifurcation (so-called lyre sign) is seen in carotid body tumours.

Magnetic resonance (MR) imaging may well become an important tool in the preoperative evaluation of parapharyngeal space tumours.

Experienced histopathologists may be able to arrive at a reasonably accurate histological diagnosis in about 80% of cases on the basis of material supplied by a fine needle
biopsy. Only when a tissue diagnosis is required before definitive treatment (for example, in tumours of advanced size or when malignancy is suspected necessitating wide extirpative surgery and/or irradiation) should an incisional biopsy be performed. This should preferably be carried out by an external approach rather than intraorally in view of the risk of seeding of tumour and uncontrollable bleeding.

The method of choice in arriving at a proper histological diagnosis is an excisional biopsy.

**Treatment**

**Surgical management**

The management of tumours of the parapharyngeal space is primarily surgical. The surgical approach to the space is transoral, transparotid, via the upper neck or the retromandibular fossa, transpharyngeal, or by any combination of the above. Exposure can be enhanced by mandibulotomy (Bass, 1982), which is reported to be necessary in fewer than 10% of cases (Stell, Mansfield and Stoney, 1985).

Transoral delivery of the tumour through an incision in the lateral pharyngeal wall is unsafe and to be discouraged unless the tumour is superficial or less than 2 cm on palpation, in which it is hard to identify on a CT scan. Attempted removal of larger tumours causes undue pressure on the capsule with an inherent danger of rupture and seeding. Immediate control of the carotid artery and its branches in cases of massive haemorrhage is impossible.

Deep lobe tumours of the parotid that have not yet entered the stylomandibular tunnel and therefore do not involve the parapharyngeal space, are best dealt with through the transparotid or retromandibular approach. After formal removal of the normal outer lobe of the parotid, the facial nerve and its branches are often found to be stretched by the tumour depending on its size. These branches must be dissected free from the tumour which is readily done if it is benign and has a capsule. Adherence of the tumour to the facial nerve and its branches may indicate malignancy, but it is advisable not to take the nerve or any one of its main branches without histological confirmation and without prior consent from the patient. If the pathologist is unable to supply a tissue diagnosis on frozen section, then it is prudent to abandon the operation at this time, close the wound and return a few days later when the results of permanent sections are available and the patient has been duly informed about the likelihood of postoperative facial nerve dysfunction.

It should be remembered that with deep lobe tumours, a formal *en bloc* removal with a cuff of healthy tissue as is achieved with outer lobe tumours of the parotid gland, is not possible. The tumour can be dissected free from the deeper tissues by blunt dissection and, depending on its location, can be delivered from between the cervicofacial and cervicoparietal division of the facial nerve (transparotid) or posteroinferior to the main stem and cervicofacial division (retromandibular).

Large parotid tumours involving the parapharyngeal space are palpable in the retromandibular fossa, and when large enough, also in the lateral wall of the pharynx, pushing it medially. Superficial parotidectomy allows for identification of the main stem of the facial
nerve and the branches in greatest danger of being unduly stretched during tumour removal. The tumour can be exposed and bluntly dissected by pulling the mandible forward, cutting the stylomandibular ligament and fracturing the styloid process. If necessary, additional exposure can be obtained by performing an osteotomy at the level of the angle of the mandible, preferably angulated to promote postoperative stabilization. The inferior alveolar nerve is severed causing anaesthesia of the ipsilateral lower lip and chin, a major disadvantage of this technique.

A tumour of the parapharyngeal space presenting as a mass in the upper neck, between the tail of the parotid and the submandibular gland, is probably not a deep lobe tumour but rather a neurogenic one. These presentations are best approached through a horizontal neck incision and dissection upward toward the skull base. Additional exposure can be obtained by removal of the submandibular gland and dissection of the tail of the parotid. The great vessels are readily seen and controlled if necessary.

When the tumour is very large, malignant, or extends way up towards the base of skull area and maximum exposure is required for vessel control and adequate tumour removal, the parapharyngeal space is opened up through a transpharyngeal approach. A median lip splitting incision is extended laterally towards the anterior border of the sternocleidomastoid muscle 3 cm below the inferior margin of the mandible. After clearing the submandibular trigone, the external and internal carotid arteries are identified, and tapes placed around these vessels for control. A stepped mandibulotomy in the area of the symphysis or just anterior to the ipsilateral mental foramen to preserve sensory innervation to the chin and lower lip is carried out. The mucosa of the floor of the mouth is incised lateral to the submandibular duct and 2 cm parallel to the mandible to preserve sufficient mucosa for closure. The incision is extended upward along the anterior tonsillar pillar to the level of the upper pole of the tonsil. The parapharyngeal space is exposed by swinging the mandible outward after division of the muscles of the floor of the mouth, taking care not to injure the lingual and hypoglossal nerves. Further soft tissue dissection upward will provide a reasonably good exposure to the base of skull and tumours in that area.

Paragangliomata require special consideration because of their vascularity. Proximal and, if possible, distal control of major arteries has to be established. In about 10% of cases major vessels will have to be resected with the tumour and preoperative consultation with a vascular and/or neurosurgeon is strongly advised. Preparations will have to be made for potentially massive intraoperative bleeding, particularly in those cases when adequate distal control at the skull base cannot be readily achieved. In these cases the internal carotid artery cannot be grafted.

Glomus tumours often adhere to surrounding tissues including vessels and base of skull. Sharp dissection and good exposure are required. The transpharyngeal approach is the safest for these tumours.

Smaller carotid body tumours lying in the upper neck in the crotch of the carotid artery are best exposed through a large horizontal neck incision over the tumour. They can be readily dissected using the adventitia as the plane of resection.
Larger tumours not only grow between the bifurcation but also surround it forming a readily dissectable line where the two sides meet. This line invariably lies posterolateral to the carotid artery system, and because the tumour is here at its thinnest, it is the easiest area to dissect and identify the adventitial plane of dissection. Massive tumours must be divided to identify the carotid artery bifurcation and to find the adventitial dissection plane.

Paragangliomata are usually benign, slow-growing tumours causing minimal morbidity unless they are large enough to cause pressure symptoms. The risks of surgical resection and postoperative complications, particularly neurological deficits, are high and many elderly patients may die from other causes before treatment for these tumours is necessary. Tumours of the glomus system in patients who live in high altitude areas rarely require resection.

An ipsilateral neck dissection is indicated when the tumour in the parapharyngeal space is malignant and neck nodes are palpable. There is no scientific support for the necessity of leaving the specimen containing primary tumour attached to the neck specimen.

Postoperative care

After surgery to the parapharyngeal space most patients can be routinely extubated immediately. After posterior mandibulotomy when postoperative pharyngeal oedema is to be expected, keeping the endotracheal tube in place for a period of 24 hours followed by supervised extubation is invariably adequate. With the transpharyngeal approach, when the floor of the mouth is incised, a tracheostomy is safest and therefore mandatory.

Suction drainage is required. Antibiotic coverage to prevent wound infection is not necessary so long as the pharynx is not opened. Only then is it advisable to cover the patient with third generation cephalosporins for a period of 3 days, starting one day before operation.

With good knowledge of the anatomy and with sound surgical techniques, the postoperative complications are kept to a minimum. The major problems are related to sensory and motor deficits in the distribution area of those nerves removed or injured during the operation. Overstretching of the facial nerve will cause a temporary paresis, most commonly of the submandibular division. Ipsilateral vocal cord paralysis is to be expected following removal of schwannomata of the most frequently involved nerve, the vagus. Glossopharyngeal and hypoglossal nerve palsies and Horner's syndrome are not rare following the removal of paragangliomata.

Cerebrovascular accidents, particularly in the elderly, may result from surgery for paragangliomata after manipulation of the common and internal carotid arteries or after grafting procedures.

The incidence of salivary fistulae should not be any higher than seen following parotidectomy for tumours of the superficial lobe and certainly not as frequent as after surgery for chronic parotitis. Frey's syndrome (gustatory sweating) is troublesome in about 10% of cases requiring some form of management. Again, the incidence is no higher than in parotidectomy for other reasons.
The role of radiotherapy

Anatomical relations prevent *en bloc* resection of malignant tumours with a wide margin of healthy tissue. Even if the tumour has been removed grossly, it is prudent to treat patients with high grade malignant tumours with a full course of postoperative radiation to the primary site and the ipsilateral neck. Radiotherapy as primary treatment for malignant tumours should be used in patients who appear to have unresectable tumours and should be offered to those patients who refuse surgery. Stage I malignant lymphoma also requires radiotherapy.

A beneficial response of paragangliomata to radiotherapy is explained by intimal thickening of the feeding vessels leading to a decrease in size of these vessels. Diminished tumour opacification and decreased venous shunting is sometimes noted (Myers et al, 1971; Handel et al, 1977). This method has a place in the treatment of elderly patients with large tumours or in patients who refuse surgery.

Malignant neurogenic tumours are radiosensitive but cures have been recorded only with neuroblastomata.