PARAPHARYNGEAL SPACE TUMORS

Review Article

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State of Art

BY

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JUNE 2003

PARAPHARYNGEA L SPACE TUMOURS

Parapharyngeal space (PPS) is one of potential fascial planes of head and neck, that may become involved by various pathological processes: infectious, inflammatory and neoplastic which represents less than 1% of all head and neck tumours ***(5)***.

Parapharyngeal space resembles an inverted triangular pyramid with concave faces. The base is the skull base and apex is the greater cornu of hyoid bone, whereas the space is further divided into prestyloid and poststyloid compartments by styloid process and its attached muscles and fascia ***(28)***.

The boundaries of this space have probably been described with more variation in literature than those of any other space. As mentioned, the PPS is a potential fascial space, so it is mainly composed of deep fascia of the neck.

The medial wall is the buccopharyngeal fascia, or visceral fascia, as it extends from the skull base caudally, covering the pharyngobasilar fascia and outer aspect of the pharyngeal constrictor muscles. The constrictor muscles meet the buccinator muscle at the pterygomandibular raphe. This linear fascial condensation extends from a cranial margin at the hamulus of the medial pterygoid plate to a caudal attachment on the lingual surface of the mandible near the posterior margin of the mylohyoid line. The buccopharyngeal fascia covers both the pharyngeal constrictors and the buccinator muscles, while fusing the intervening pterygomandibular raphe, ***the anterior boundary*** of the PPS is usually considered to be the pterygomandibular raphe. ***Caudally***, the PPS has been described as extending down to the hyoid bone. However, in actuality the fascia around the submandibular gland, the sheaths of the styloid muscles, the fascia over the posterior belly of digastric muscle, the fascia on the lingual surface of the mandible, and the visceral fascia all fuse near the level of the angle of the mandible, functionally obliterating the PPS. Thus effectively the styloglossus muscle can be considered to be ***the inferior boundary*** of the PPS ***(23)***. ***The lateral boundary*** is the fascia on the medial surface of parotid gland, which is derived from the superficial layer of the deep cervical fascia. ***The posterior boundary*** is the most controversial because some authors have placed the carotid sheath in the PPS, while others have referred the sheath as the carotid space. Today, most surgical and anatomic opinions in the literature place the cranial portion of the carotid sheath

within the PPS ***(47)***. The superior, anterior, lateral, posterolateral and posterior boundaries are somewhat rigidly bounded by bone or thick fascia, therefore masses arising within the PPS tend to enlarge medially and inferiorly ***(33)***.

The terminology used in descriptions of the various compartments of the PPS is at least as variable as that used to describe the fascial layers ***(48)***. ***Compartmentalization*** is accomplished by the tensor-vascular-styloid fascia, the stylopharyngeal aponeurosis *(aileron),* and the sagittal partition *(cloisosagittale).* According to most authors, a well-defined fairly thick fascial sheet arises directly from postero-inferior edge of the tensor veli palatini muscle. This distinct fascia extends along the skull base towards the medial pterygoid plate, and caudally and posterolaterally from this muscle to the styloid process and styloid musculatures. Fusing inferiorly with the fascia covering the styloglossus muscle, the fascial sheet closes the gap between the tensor veli palatini, the skull base (from the sphenoid spine on the medial side of the foramen ovale to the root of the medial pterygoid plate), and the styloid process and its associated musculature. Anteriorly, the fascia reaches the pterygomandibular raphe and fuses with it, the interpterygoid fascia, and the buccopharyngeal fascia ***(46)***.

Further continuation of the tensor- vascular-styloid fascia from the styloid process to the posterior border of the mandibular ramus ***(20),*** a thickening in the lower portion of this stylomandibular fascia is the stylomandibular ligament. The deep portion of the parotid gland protrudes through the stylomandibular tunnel, which is the space between the back of the mandible and the stylomandibular ligament and the skull base. This stylomandibular fascia may also be thought of a fusing of the superficial layer of the deep cervical fascia as it covers the medial aspect of the parotid gland and the fascia of the styloid musculature. There are two more layers of fascia that are in relation to tensor- vascular- styloid fascia and which further subdivide or partition this region. One is described variously as extending medially from either the vascular fascia or the styloid musculature to the buccopharyngeal fascia lying in a roughly coronal plane near the lateral pharyngeal recess or fossa of Rosenmüller ***(42)***. This fascia has been described in the literature as the stylopharyngeal aponeurosis and some French anatomists refer it as the "*aileron*" ***(20)***.

The last fascial layer positioned approximately in the sagittal plane and extends from the buccopharyngeal fascial aponeurosis to the alar fascia and prevertebral fascia near their attachments to transverse processes of the

cervical vertebrae. This fascia is referred to by ***Charpy*** as the cloison sagittale *(sagittal partition)* ***(9,20)***.

The compartmentalization has become more important because of sophisticated imaging techniques have allowed more precise preoperative diagnosis based on the anatomy of the subdivisions of the PPS resulting in large part from more precise imaging techniques, surgical advances have allowed easier and safer access to the tumors in this area ***(13)***.

The three fascial planes described before, divide the PPS into three compartments. The *first compartment* is lateral to the tensor-vascular-styloid fascia and deep to the medial boundary of what is called "***masticator space",*** which is formed by splitting of the superficial layer of the deep cervical fascia when reaches the inferior margin of the mandible, to envelope the pterygoid, temporalis and masseter muscles. This area contains a small amount of fat and has the deep portion of the parotid gland protruding into its lateral margin. *The second compartment* is a very thin slit like region between the buccopharyngeal fascia medially and the tensor- vascular- styloid fascia laterally.

There is only a small amount of loose connective tissue in this second compartment, which is bounded posteriorly by the stylopharyngeal aponeurosis *(aileron). The third* and final compartment of the parapharyngeal region is posterior to the stylopharyngeal aponeurosis and separated from the retropharyngeal space by the sagittal partition. Deep layer of the deep cervical fascia makes up the posterior boundary of this compartment. It contains the internal carotid artery, internal jugular vein, and at various levels cranial nerves IX, X, XI, XII. Thus this third compartment is the carotid sheath and its contents. Almost all descriptions of this area include some or all of these compartments, and a variety of names ***(48)***. ***Som*** referred to the *prestyloid* and *retrostyloid* compartments of the PPS as being separated by the fascia stretching from the styloid process and its related musculature to fuse with that enveloping the tensor palatini muscle ***(46)***. They mentioned fascia extending from this tensor-vascular- styloid fascia to the prevertebral fascia, separating the *retrostyloid* compartment from the *retropharyngeal* space. This fascia is similar to the cloision sagittale *(sagittal partition)* described by ***Charpy(9)***. Thus ***Som and Curtin,***combined the spaces on either side of the stylopharyngeal aponeurosis and the second and third compartment just described, into one compartment called the *(retrostyloid space),* the first compartment which is lateral to the tensor- vascular- styloid fascia and

into which protrudes the deep portion of the parotid gland called the *(prestyloid space*) ,in some recent literatures the terminology of *prestyloid* and *retrostyloid* compartment is used ***(48).*** Supported by opinions come from some surgeons***(1,2,3,7,18)*** who noted that in their operative approach to the PPS, the plane of tensor -vascular-styloid fascia acts as an important landmark, with the great vessels and cranial nerves lying deep to the plane. In this sense, this fascia, the styloid process, and its musculature act as a protective barrier to these vital structures. In other recent literature, the terminology of *prestyloid compartment* and *poststyloid compartment* is used ***(10,32,44).Figure (1),showing the Compartmentalization of the PPS.***

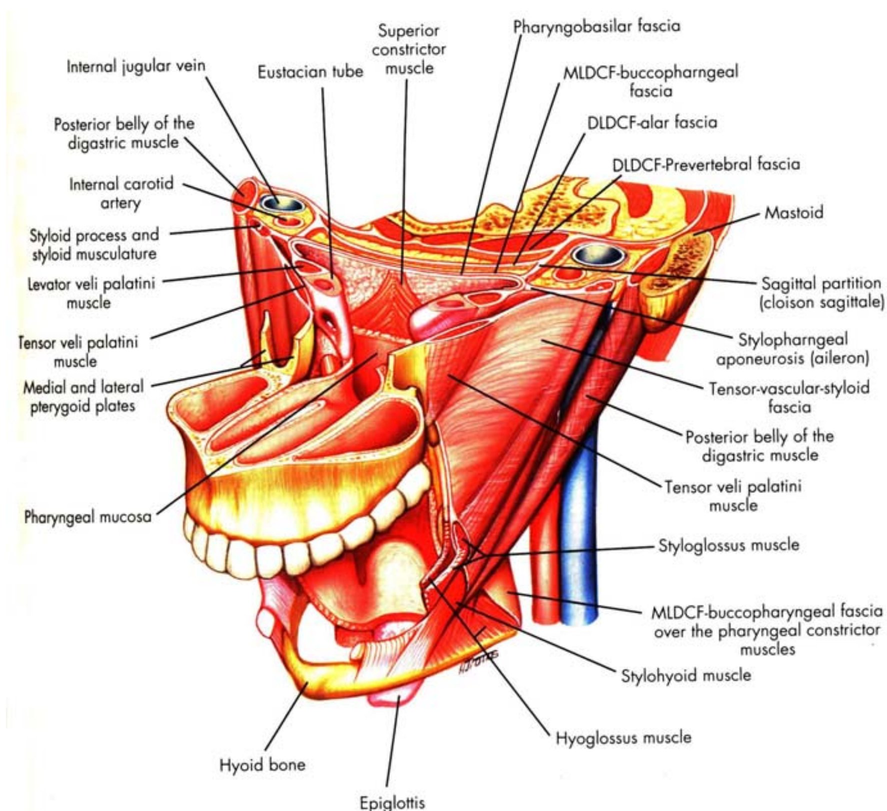

Figure 1: Drawing at the level of the face and upper neck. This diagram showing tensor-vascular-styloid fascia.
MLDCF: middle layer of deep cervical fascia, DLDCF: deep layer of deep cervical fascia (from Som PM, Curtin HD. Normal Anatomy of the Neck. In: Head and Neck Imaging: 1996: 730).

The Contents Of The PPS:

The *poststyloid compartment* (posteromedial compartment) contains the internal carotid artery, which runs in carotid sheath to reach the carotid canal at the base of the skull. The internal jugular vein also runs in *poststyloid compartment* and it is deeply situated to the internal carotid

artery. The cranial nerves from the glossopharengeal nerve to the hypoglossal nerve they are also present in *poststyloid space*. The sympathetic nerve chain and numerous lymph nodes they are present in *poststyloid space.* This space also called the vascular space.

The *prestyloid compartment* (anterolateral compartment) contains the internal maxillary artery and vein, inferior alveolar, lingual and auriculotemporal nerves. Other contents include fat, medial and lateral pterygoid muscles, the deep portion of the parotid gland and numerous lymph nodes. Pathological conditions in this area can cause trismus by involvement of pterygoid muscles, bulging of the tonsillar fossa and depression of the soft palate and motor and sensory involvement of the third division i.e mandibular branch of trigeminal nerve ***(44)***. Some authors consider the deep lobe of the parotid gland, the fat and the lymph nodes are the only content of the *prestyloid compartment* excluding the other contents which belongs to the *masticator space*(*32*)***.Figure (2),showing the contents of the PPS.***

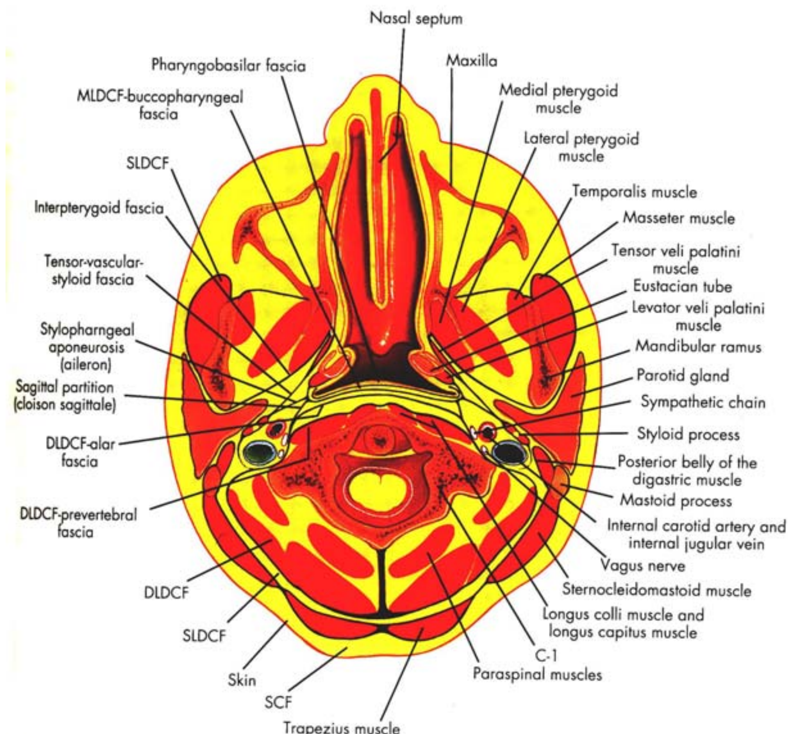

Figure 2: Axial diagram through the level of C-1. This diagram showing the contents of PPS.
DLDCF: deep layer of deep cervical fascia, SLDCF: superficial layer of deep cervical fascia , SCF: subcutaneous fat (from Som PM, Curtin HD. Normal Anatomy of the Neck. In: Head and Neck Imaging: 1996: 727).

Almost all tumors that occur in the PPS arise either from the deep portion of the parotid gland anterolateral to the tensor- vascular -styloid fascia or from the cranial nerve elements traveling with the internal carotid artery and internal jugular vein, posterior to the stylopharyngeal aponeurosis and the tensor vascular styloid fascia. In the opinion of most authors***(3,14,27),*** the PPS is considered a closed space that is surrounded by a number of other spaces. These include the pharynx, the submandibular space, the masticator space, the parotid gland space, the retropharyngeal space, the danger space which is located between the two layers of the prevertebral fascia and the prevertebral space. In some people portions of these fascia are weak or incomplete. Because of this, a few authors believe that the PPS freely communicates with other spaces such as sub-mandibular space and retropharyngeal space ***(48)***.

Another important structure relating to the PPS is the stylomandibular ligament, which extends from styloid process to the inferior part of posterior border of mandibular ramus ***(12)***. The "*stylomandibular tunnel*" is thus formed between the ligament, the skull base and the ramus of the mandible. Tumors arising in the deep lobe of the parotid gland can have one of two shapes, depending on whether they originate medial or lateral to this tunnel. Lateral tumors become constricted as they grow medially through the tunnel resulting in "*dumbbell shape*". Tumors arising medial to the stylomandibular ligament will be round, pushing the soft palate medially as they enter the PPS ***(48)***.

TYPES OF THE PPS TUMORS

-Tumors of the parapharyngeal space are uncommon, comprising 0.5- 1% of all head and neck neoplasms***(16).*** Both benign and malignant tumors may arise from any structure contained within the PPS. Of PPS tumors, 70-80% are benign and 20-30% are malignant. Most PPS tumors are of salivary gland tumors, neurogenic tumors especially Schwannomas and paragangliomas, lymphoreticular lesions comprise nearly 80% of PPS tumors. The remainder includes a wide variety of lesions, including lipoma, liposarcoma, hemangioma,heamangiopericytoma ,hemangioendotheliomas, meningioma rhabdomyosarcoma, chondrosarcoma, malignant fibrous histocytoma and metastatic lesions. ***(49).***

Metastatic lesions must be suspected when pain is a prominent clinical feature and radiological findings demonstrate a characteristic lesion with central leucency and an enhancing rim, especially when these are encountered in a patient with a known primary carcinoma elsewhere in the body. When the primary lesion is not apparent or suspected, the diagnosis cannot be made with certainty until a tissue sample has been obtained. ***(36).***

Salivary Gland Neoplasms

A- Benign Neoplasms include the following:

1- Pleomorphic adenoma.
2- monomorphic adenoma.
3- Oncocytoma.
4- Warthin`s tumor.
5- Benign lymphoepithelial disease.

B- Malignant neoplasms include the following:

1- Mucoepidermoid carcinoma.
2- Adenoid cystic carcinoma.
3- Adenocarcinoma.
4- Carcinoma ex pleomorphic adenoma.
5- Malignant Warthin’s tumor.
6-Acinic cell carcinoma.
7- Salivary duct carcinoma.
8- Squamous cell carcinoma.
9- Undifferentiated carcinoma.

The most common tumors arising in the PPS are of salivary gland origin, which accounts for 40-50% of PPS lesions and are located in the prestyloid PPS. These tumors may originate either in deep lobe of parotid gland, ectopic salivary gland nests, or minor salivary glands of the lateral pharyngeal wall. The incidence of neoplasms that occur within the deep lobe of the parotid gland is identical to that of the superficial lobe. However, only a small percentage of deep lobe parotid tumors involve PPS. The most common prestyloid PPS lesion is “pleomorphic adenoma”, which represents 80-90% of salivary neoplasms in the PPS. Other benign salivary lesions, including Warthin’s tumor and oncocytomas, occur in the prestyloid PPS, as do malignant salivary lesions.

Carcinoma ex. Pleomorphic adenoma i.e carcinoma on top of pleomorphic adenoma, and adenoid cystic carcinoma are the most

frequently reported salivary malignancies of the PPS. Approximately 20% of all salivary lesions in the PPS are malignant ***(5).Figure (3) showing MRI imaging of the deep lobe of the parotid tumor.***

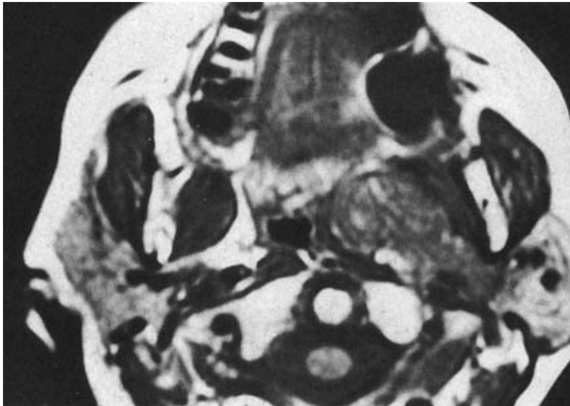

Figure 3a

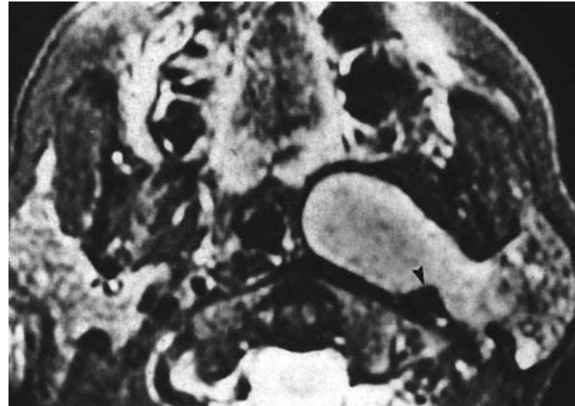

Figure 3b

Figure 3: Axial T1W (a) and T2W (b) MR scans show a slightly dumbbell-shaped left deep lobe parotid begin mixed tumor. The mass lies anterior to the internal carotid artery (arrow-head). Note that there is no fat plane between the posterolateral margin of the tumor and the parotid gland (from Som PM, Curtin HD. Parapharyngeal space. In: Head and Neck Imaging: 1996: 921).

Neurogenic Neoplasms

Neurogenic tumors account for 25-30% of PPS lesions and are the most common tumors of the poststyloid compartment. Neurilemomas are the most commonly encountered lesions, followed in frequency by paragangliomas and neurofibromas. These three neoplasms account for the majority of the neurogenic lesions of PPS ***(16).*** Neurogenic lesions may be benign or malignant including the following:

A- Benign lesions

.Neurilemomas (Schwannomas).
.Neurofibroma.
.Paraganglioma.
.Ganglioneuroma.

B-Malignant lesions

.Malignant paraganglioma.
.Neurofibrosarcoma.
.Schwannosarcoma.
.Ganglionblastoma.

Paragangliomas are benign vascular neoplasms that arise from the paraganglia or extraadrenal neural crest tissue. Paraganglia function as

chemoreceptors and are associated with the carotid body,the jugular bulb, and the vagus nerve in the poststyloid PPS. Carotid body tumors, glomus jugulare, and glomus vagale are slow-growing paragangliomas that may be asymptomatic but cause cranial nerve deficits, bone erosion, or intracranial extention as they increase in size.

Approximately 2% of head and neck paraganglioma secrete catecholamines and may cause paroxysmal symptoms of catecholamins excess. Ten percent of paragangliomas are multiple, associated with paragangliomas at other locations.Ten percent of paragangliomas are hereditary, associated with paraganglioma syndrome. In patients with hereditary paraganglioma, the incidence of of multicentricity is 35%.

Hypertension and flushing are suggestive of either a functioning paraganglioma or an associated pheochromocytoma. Neurilemomas are the most common neurogenic tumor and arise from any nerve surrounded by Schwann cells. In the PPS,the most commn sites of origin are the vagus nerve and sympathetic chain***(43)Figure (4,5), showing CT of neurogenic tumors of the PPS.***

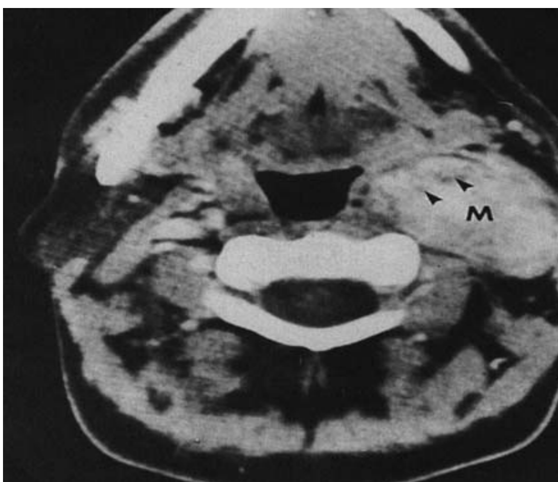

Figure 4: Axial contrast CT shows a large enhancing left PPS glomus vagale tumor (M) (from Som PM, Curtin HD. Parapharyngeal space. In: Head and Neck Imaging: 1996: 928).

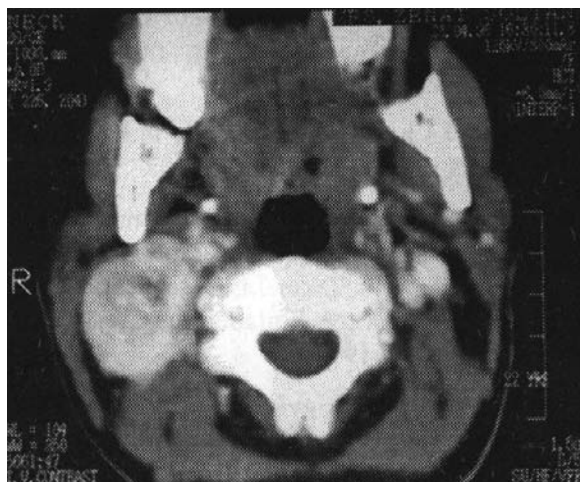

Figure 5: Axial contrast CT shows right carotid body tumor (from Som PM, Curtin HD. Parapharyngeal space. In: Head and Neck Imaging: 1996: 929).

Lymphoreticular Lesions

Lymphoreticular lesions comprise 10-15% of PPS lesions. The lymphatics may be involved by primarily or secondarily by carcinoma, or infectious or inflammatory processes may involve them ***(5).***

The PPS and retropharyngeal nodes drain the oronaso, hypopharyngeal area, posterior nasal cavity, and paranasal sinuses as well the posterior oral cavity. These are two groups, a superior lateral group (nodes of Rouviere) and an inferior medial group ***(30).*** Lymphoma is the most common malignant lymphoid process, but metastases from thyroid cancer, and sqamous cell carcinoma, and renal cell carcinoma and osteogenic sarcoma may present in the nodes of the PPS ***Figure (6), showing metastatic renal cell carcinoma in the PPS.***

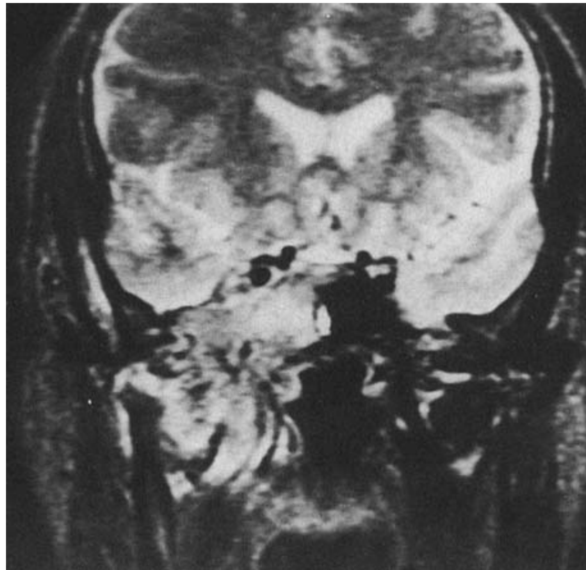

Figure 6: Coronal T2W MR scans show an infiltrating right PPS tumor (metastatic renal cell carcinoma) eroding the skull base and invading the cavernous sinus and the pterygoid muscles (from Som PM, Curtin HD. Parapharyngeal space. In: Head and Neck Imaging: 1996: 937).

Other rare lesions of the PPS

A variety of more unusual lesions may present in the PPS, and these lesions comprise 10-15 % of the PPS lesions. While the pathologists usually makes the final determination and diagnosis in such cases, it is important to recognize that vascular lesions, such as hemangiomas, arteriovenous malformations, and internal carotid artery aneurysms, may present in the PPS. Imaging studies of this region must be obtained before

attempting biopsy or excision ***(16). Figure (7) showing rhabdomyosarcoma of left PPS.***

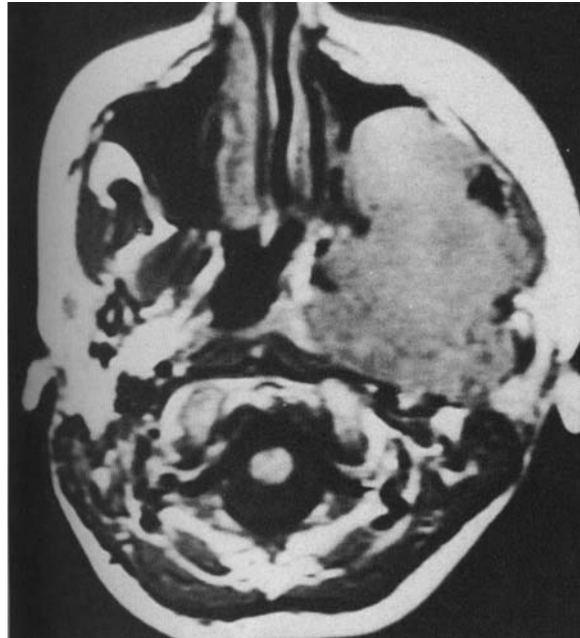

Figure 7: Axial T1W MR shows a homogeneous, infiltrating rhabdomyosarcoma in the left PPS. The tumor has destroyed the left mandible, posterior maxillary sinus wall, and skull base (from Som PM, Curtin HD. Parapharyngeal space. In: Head and Neck Imaging: 1996: 943).

They include:

Vascular (Hemangiopericytoma, angiosarcoma)

Muscle (Rhabdomyoma, Leiomyoma, rhabdomyosarcoma)

Connective tissue (Lipoma, fibroma, fibosarcoma, chondrosarcoma)

Meningioma, Meningiosarcoma.

Congenital (Branchial cleft cyst, dermoid, hemongioma, lymphangioma, arteriovenous malformation).

Pseudotumor sclerosing cervicitis, myositis, abscees, aneurysm.

Malignant invasion from surrounding structure

Distant metastases

(Curtin,1987).

CLINICAL MANIFESTATIONS

PPS tumors most commonly present as asymptomatic masses in the neck or palatal region found on routine physical examination. In series reported by ***Carrau ,Mayer, Johnson ,***nearly 50% of patients had a neck mass***.(8).***

PPS tumors palpable in both lateral neck and oropharynx often pass through the relatively constricted area termed the stylomandibular tunnel.This tunnel causes these neoplasms to be dumbbell in shape ***(32).***Dumbbell tumors encountered in the PPS are almost always benign pleomorphic adenomas that have originated in the deep lobe of the parotid gland***. (40).***

“Unilateral Eustachian tube dysfunction” may result from significant medial extension causing soft palate and nasopharyngeal swelling which results in obstruction of the pharyngeal opening to middle ear, also there is “serous otitis media” which can be accompanied by a “conductive deafness”. ***(27).***

Oropharyngeal bulging from underlying PPS may cause significant displacement of the ipsilateral tonsil and may give the appearance of a primary tonsillar lesion. Patients may complain of a “chronic sore throat”. Symptoms of dysphagia, dyspnea, and obstructive sleep apnea may result from distortion of the lateral pharyngeal wall by PPS lesions. In such cases, tracheostomy has been recommended for relief of airway obstruction***(36).***

Most neoplasms arising within the PPS are benign. These lesions rarely produce pain early in the course of the disease ***(8).*** Neurological dysfunction tends to be a late finding that occurs only when massive lesions compress contiguous neural structures. Neuropathies encountered in the course of the disease may reflect the site of origin of the neoplasm. The tumor can arise from the nerve or the nerve can be affected by pressure from a lesion arising in the immediate vicinity ***(40).*** Patients with neurofibroma involving the vagus nerve may present with vocal cord paralysis. Involvement of the hypoglossal nerve resulting in deviation of the tongue to the side of the nerve involvement with ipsilateral tongue weakness. Weakness of the trapezius muscle with shoulder drop characterizes spinal accessory nerve paralysis. Glossopharyngeal nerve paralysis results in reduction or absence of gag reflex; however, this finding may be subtle and difficult to establish. Horner’s syndrome, characterized by myosis, anhydrosis, and ptosis, characterize the clinical

triad of the involvement of the cervical sympathetic chain. Involvement of the mandibular branch of the trigeminal nerve results in hypothesia in the distribution of the nerve. ***(21).***

Tumor involvement of the skull base and associated jugular foramen may produce jugular foramen syndrome with neuropathy involving the 9th, 10th, 11th cranial nerves (Vernet's syndrome***(21).*** Voice changes unrelated to nerve involvement are similar to these seen in patients with peritonsillar abscesses who demonstrate a "hot potato voice". This dysphonia is secondary to palatal displacement and involvement of the lateral pharyngeal wall by the mass. Medial displacement of the oropharyngeal wall and adjacent tonsil and soft palate may be associated with dysarthria and dysphagia ***(27).*** Pain may result from glossopharyngeal neuralgia or carotodynia with compression of glossopharyngeal nerve or the carotid artery. Occasionally, pain may be associated with hemorrhage into a benign lesion. However, pain and neurological dysfunction are more often indicative of malignancy with infiltration of skull base. Under these circumstances, facial nerve may be involved ***(45).*** Trismus results from malignant involvement of the medial and lateral pterygoid muscles, or involvement of the coronoid process of the mandible ***(8).*** Another presenting symptom may be an ill-fitting maxillary denture caused by displacement of the soft palate by tumor. Hearing loss may be encountered when cartilaginous part of the Eustachian tube is compressed resulting in middle ear effusion ***(40).***

Symptoms of catecholamine excess include hypertension, palpitations or tachyarrhythmias; flushing, headaches and nausea are suggestive of a catecholamine-secreting paraganglioma or an associated pheochromocytoma ***(43).***

Physical Examination

Physical examination may suggest the origin and nature of the tumor. The most common physical finding is a painless oropharyngeal or neck mass. Careful attention should be paid to the oropharynx, tonsillar area, pharynx and neck. Using "bimanual palpation" may localize lesions arising from deep lobe of the parotid. Benign tumors within the PPS may also be bimanually ballotable. Performing a full cranial nerve evaluation, including laryngoscopy, to test the motor and sensory innervations of the larynx is essential. A postnasal examination may be needed to show the lateral nasopharyngeal wall including the Eustachian tube orifice.

The vagus nerve is the most commonly involved cranial nerve, and vagal palsy is suggestive of either a paraganglioma or a malignancy. A neck mass that is pulsatile or has a thrill to auscultation suggests a vascular tumor, though carotid pulsations may be transmitted through an overlying mass and may be misleading. Paragangliomas are classically compressible and mobile in anteroposterior direction but not in a vertical direction ***(46).***

INVESTIGATIONS

Although most PPS neoplasms are benign, but the variety of neoplasms and complex anatomy present unique diagnosis and treatment challenges. To investigate a case of PPS tumor, the physician should do imaging study ***(36)***. Other investigations include fine needle aspiration biopsy and special investigations such as 24-hour urinary catecholamines in cases of paragangliomas ***(24)***.

Radiological Study

Radiological studies are essential in the evaluation of a patient with a suspected PPS mass. It is important that these studies be obtained prior to consideration of biopsy, because given the differential diagnosis of PPS lesions, one often can make a diagnosis on the basis of imaging without the need for fine-needle aspiration biopsy (FNAB) or open biopsy. Imaging studies should answer the following questions: Is the mass prestyloid or poststyloid? What is the relationship to the parotid gland? What is the relationship to the great vessels? What are the soft tissue characteristics of the tumor?

The differential diagnosis of a PPS mass can be greatly narrowed by determining whether the mass arises from the deep lobe of the parotid and whether the mass originates in the prestyloid or poststyloid space. The parapharyngeal fat pad is located in the prestyloid space. Prestyloid lesions cause medial displacement of the parapharyngeal fat pad and are located anterior to the great vessels. Poststyloid lesions displace the parapharyngeal fat pad anteriorly and laterally, between the mass and the pterygoid muscles. Computed tomography (CT) scans and magnetic resonance imaging (MRI) studies have equal efficacy in localizing the lesion to the prestyloid or poststyloid space ***(46).*** Both studies have advantages and disadvantages over each other. CT scans or MRI studies are used as a starting point in the evaluation of a PPS mass, and sometimes, one may be the only investigation needed. Angiography is reserved for enhancing

lesions. Ultrasonography does not provide adequate resolution of the PPS and is not indicated in the workup of PPS lesions ***(36).***

CT Scan versus MRI Study:

CT scanning can localize a PPS to the prestyloid or poststyloid space. It also may demonstrate whether the mass arises from the deep lobe of the parotid, a fat plane between the parotid and the mass suggests an extraparotid origin. Also, CT scanning is superior to MRI in demonstrating the presence of calcifications and bony involvement, with contrast infusion the relationship of the mass to great vessels may be appreciated, though enhanced poststyloid lesions may be difficult to separate from carotid artery, CT scanning is inferior to MRI in delineating soft tissue characteristics of the tumor, particularly in large lesions in which the tumor margin may be difficult to distinguish from the fascia of adjacent musculature ***(32)***.

CT scanning also carries the risk of exposure to ionizing radiation and intravenous contrast. Nevertheless, CT scanning remains widely used because of its wide availability and lower cost. CT scanning may be the only study required since the majority of PPS masses will be prestyloid lesions arising from parotid gland. Because of its superior soft tissue and vascular resolution, a subsequent MRI is recommended to further evaluate all poststyloid masses or, if malignancy is suspected, to evaluate the extent of malignancy and to rule out intracranial extension ***(47)***.

MRI is superior to CT scanning in its ability to ascertain the soft tissue characteristics of PPS tumors. MRI can differentiate between the tumor and muscle, and it has greater resolution in defining the great vessels and their relationship to the tumor. Intracranial extension is better delineated on MRI. The diagnosis can often be made on the basis of characteristic MRI findings. Paragangliomas have been described as having a salt and pepper appearance on MRI because of numerous flow voids within the lesion. Schwannomas show greater enhancement on T2-weighted images, enhanced with gadolinium, and lack flow voids. MRI scanning probably the screening test of choice to evaluate a PPS lesion because of the greater soft tissue resolution and vascular information obtained.

However, the cost is significantly greater, determination of bone involvement is poor, and it may be contraindicated in certain patients (e.g. those with pace makers, those who have claustrophobia). The information

obtained from both CT scanning and MRI is complementary and both should be obtained in evaluation of extensive lesions or when there is suspicion of malignancy ***(27)***.

Role of Angiography in diagnosis of the PPS tumors:

Angiography is recommended in the workup of all enhancing lesions. Angiography also is used if malignancy is suspected and there is a possibility of carotid sacrifice during resection. If carotid resection is considered, it is combined with balloon occlusion testing to measure cerebral blood flow (see balloon occlusion test later) ***(46).***Angiography is useful in the evaluation of poststyloid lesion to demonstrate their relationship to the great vessels and to distinguish between neurogenic and vascular lesions; however, this distinction can usually be made on MRI ***(8)***.Angiography may be diagnostic of neurogenic lesions. Carotid body tumors are usually located at the bifurcation and cause splaying of carotid bifurcation, called the lyre sign. Glomus vagale tumors, because of their association with the vagus nerve, lie laterally and posteriorly to the carotid system, displacing this anteriorly and medially. Schwannomas appear as avascular masses displacing the carotid system anteriorly. Metastases (e.g. renal cell carcinoma) often appear quite vascular if they take their blood supply from the external carotid. All vascular lesions should be evaluated with angiography to delineate their extent and blood supply; feeding vessels may be identified and may be embolized preoperatively to facilitate resection. CT angiography and MR angiography are emerging as alternatives to arteriography. These tests are not widely used, but they may relegate conventional arteriography to those instances in which the blood supply remains in question or embolization is being considered ***(47)***.

Biopsy

Under most circumstances, a presumptive diagnosis can be made on the basis of the imaging studies. Under no circumstances should biopsy of a PPS mass be performed prior to obtaining the radiologic studies. Complete surgical excision is the mainstay of treatment and is recommended for both diagnostic and therapeutic purposes. Fine needle aspiration biopsy (FNAB) must be considered adjunct to clinical diagnosis. Aspiration may be easily undertaken in patients with tumor palpable in the neck. Deeply seated parapharyngeal masses may be aspirated percutaneously employing CT guidance. FNAB provides useful information if a diagnosis of malignancy is suspected. When clinical findings such as pain, rapid growth, and

fixation, together with radiographic evidence of bone destruction, suggest malignancy, the FNAB may aid in confirming the clinical impression and afford valuable information for the treatment planning. If imaging studies suggest vascular tumor paraganglioma, however, FNAB may provide little information and is best avoided because of risk of bleeding. However, when the FNAB produces results that do not confirm with clinical picture, the physician should be suspicious that the sampling error may have occurred. This serves as further indication of excision of the lesion and complete histological evaluation. Incisional biopsy should only be considered if the patient is not an operative candidate and FNAB is inconclusive and if a diagnosis of malignancy or lymphoma is strongly suspected. Transoral open biopsy has been described but carries a significant risk of hemorrhage and a contamination of pharyngeal mucosa by tumor, which requires excision of that site during subsequent definitive resection. Most surgeons condemn this practice ***(15,41)***.

Special Investigations

After performing the proceeding evaluation, one should have a reasonably good idea of the nature of the tumor and the surgical approach. If paraganglioma is suspected, 24-hour urine collection of catecholamines including vanillyl mandelic acid (VMA), metanephrines. If catecholamines levels are positive, then do a metaiodinated benzyle guanidine (MIBG) scan. This radioisotope has a similar molecular structure to norepinephrine and is used to trace catecholamine uptake and storage. If a failure of a diagnosis of such secreting tumor with appropriate prophylactic therapy may result in serious intraoperative arrhythmia and hypertension. Also, there is a possibility of multicentric paragangliomas and those should be actively sought (e.g. by performing MRI, CT, and if indicated, bilateral carotid angiography). Evaluation of patients with multiple paraganglioma syndrome should always include CT evaluation of the adrenal gland ***(26).***

The Balloon Occlusion Test measures the effect of internal carotid artery occlusion on cerebral blood flow (CBF) and the adequacy of the contralateral circulation. It is indicated when imaging studies suggest carotid involvement or when resection of the lesion carries a high risk of intraoperative carotid artery injury. Angiography is performed and the internal carotid artery is occluded using a balloon-tipped catheter for 10-15 minutes. In patients who develop neurologic symptoms, the test is abandoned and no further evaluation is performed. Those patients are

considered at high risk for stroke and should undergo non-operative therapy, subtotal resection with carotid preservation, or revascularization prior to resection. In patients without neurological symptoms during the test, Xenon-enhanced CT scanning is performed to quantitate CBF. CBF is evaluated both before and after balloon occlusion, xenon gas is inhaled, it diffuses rapidly into blood stream, and perfused areas on xenon-enhanced CT scanning are considered to mild to moderate risk of stroke with prolonged carotid occlusion. Interposition grafting of the internal carotid artery is recommended if the artery is to be sacrificed. There is 4% incidence of neurologic sequelae from the balloon occlusion test itself, so the procedure is reserved only for cases in which the carotid is suspected to be involved or at risk ***(25)***.

If a metastatic lesion is suspected, the primary tumor should be sought by performing a full clinical examination, panendoscopy, a full metastatic work up including CT scan of chest and abdomen and bone scan as directed by clinical evaluation ***(29)***.

TREATMENT OF THE PPS TUMORS

Surgery

Surgery is the mainstay of the treatment for tumors of the PPS. The choice of surgical approach is dictated by the size of the tumor, its location, its relationship to the great vessels, and suspicion of malignancy ***(16)***. Because most of these tumors are benign, the approach chosen should minimize surgical morbidity, as well as the risk of surgical recurrence.

Surgical morbidity can be minimized, or at least anticipated by careful attention to pre-operative evaluation, so there are no surprises encountered in the operating room and the patient is adequately prepared ***(11)***.

Functioning tumors must be identified prior to resection, as manipulation of a catecholamine-secreting tumor may cause intraoperative cardiac arrhythmias and hypertensive crisis.Preoperatively alpha-adrenergic and beta-adrenergic blockade with phenoxybenzamine and propranolol must be given.Patients with multiple paragangliomas should undergo CT scanning of the adrenal glands to search for an associated pheochromocytoma preoperatively ***(36)***.

The Surgical Approaches:

The surgical approach best applied to the PPS tumors is an external one, which affords adequate visualization, control of bleeding, and identification of major vessels and nerves. Internal approaches are to be discouraged, except perhaps in the rare circumstance of an extremely small lesion localized to the medial aspect of the space that can clearly be defined as such ***(46)***.

1- Transoral Approach

This approach has been described by some surgeons for the removal of small benign neoplasms that originate in prestyloid compartment and present as an oropharyngeal mass and not palpable in the neck. However, it gives very limited exposure, inability to visualize the great vessels, and increase in injury of facial nerve. Most surgeons reserve this approach for only very small mixed salivary gland tumors arising from minor salivary glands of lateral pharyngeal wall or hard palate. Others believe that this is not an acceptable approach for PPS tumors because of possibility of tumor spillage or incomplete removal, vascular injury with resultant uncontrollable hemorrhage, increased risk of infection, potential risk of facial nerve injury. The transoral approach may be combined with an external approach to mobilize lesions with significant oropharyngeal component. This is not the approach of choice for most PPS lesions ***(25.33)*** .

II. Transcervical (Submandibular) Approach

Most authors favor the transcervical approach as the preferred method for removal of most poststyloid PPS tumors *(8)*. This has been used ideally in patients with extraparotid lesions such as paragangliomas and other poststyloid PPS tumors of relatively small size (3 to 4 cm). An incision is made which is transverse curvilinear placed in a skin fold at level of hyoid bone, subplatysmal flaps are elevated, with preservation of submandibular gland and marginal mandibular nerve which are reflected superiorly. Some authors described another incision that is made approximately two fingers breadths below the angle of mandible. After identification of marginal mandibular nerve, the submandibular gland is removed. If preservation of submandibular gland is done, so division of styloglossus muscle and stylohyoid ligament allows entrance for PPS. If submandibular gland is removed so direct access to PPS occurs. The PPS is entered from below, and the lesion is dissected free and removed. Sharp and blunt dissection are often possible and allow under direct visualization

the prevention of injury of major structures such as common carotid artery and internal jugular vein.

Because of the relatively limited exposure medially, superiorly, and posteriorly, blunt dissection is necessary for tumor removal. Exposure may be improved as much as 50% by transecting the stylomandibular ligament and dislocating of mandible anteriorly. A useful variation of intermaxillary fixation, use of primary loops to secure the mandible after anterior dislocation. Disadvantages include limited exposure medially, superiorly and posteriorly. Complete control of vascular structures particularly at the skull base is not possible. If further exposure becomes necessary, osteotomy techniques must be used. Transcervical approach without mandibulotomy may be adequate for paragangliomas and other relatively avascular extrapartoid tumors less than 5 cm in diameter. Tumor larger than this results in significant carotid artery displacement with the added risk of vessel injury through this limited exposure approach ***(44)***.

Some authors differentiate between the approach needed to excision of paragangliomas and other small poststyloid PPS tumors and that used to excision of the prestyloid PPS lesions. The former called *"transcervical approach"* is done without entrance of submandibular triangle ***(33)***. The latter called *"transcervical submandibular"* approach is done with dissecting the submandibular triangle by retraction of posterior belly of digastric muscle, permitting division and ligation of facial artery, then removal of submandibular gland, division of digastric tendon may be required if large tumors are encountered ***(1).***

III. Transcervical-Transparotid Approach

This approach is served for lesions arising from the deep lobe of the parotid. Small lesions of deep lobe of parotid with or without minimal involvement of the PPS may be removed by transparotid approach only without dissecting the submandibular space. For lesions of large size arising from deep lobe of parotid with involvement to the PPS. The usual transparotid approach accompanied with transcervical approach by using the usual incision used for parotidectomy extending to the neck anteriorly to the submandibular space. Some authors called this approach *"transparotid submandibular approach"* ***(1)***.

In *transparotid - transcervical approach*, superficial parotidectomy with facial nerve dissection is done in the usual manner and the specimen is removed. The facial nerve is then dissected free of the underlying deep lobe

of the parotid gland and the tumor is exposed. The submandibular gland is displaced; the tumor is then mobilized in a three-dimensional manner from the parotidectomy wound, as well as the submandibular space, and removed. The cervical incision allows access to the PPS component of the tumor ***(36)***.

In some instances the styloid process may be sectioned and the mandible dislocated anteriorly ***(1).***

IV. Transcervical-Transmandibular Approach

Some surgeons have recommended mandibulotomy to facilitate exposure to the PPS to remove these tumors ***(7)***. Some authors described the mandibulotomy approach as "*transmandibular approach*". The following situations need mandibulotomy to improve the exposure, which are very large tumors, vascular tumors with superior PPS extension, malignant tumors to facilitate oncologic resection, and cases in which distal control of the carotid at the skull base is required ***(46)***. Combinations of this technique with the transparotid approach are possible in large deep lobe tumors as well. Tracheostomy is required for airway management in the immediate postoperative period, because of the degree of postoperative oropharyngeal edema and potential for airway obstruction. ***Attia, Bentley,*** have not found this technique necessary in the removal of benign tumors ***(2)***. Most of benign tumors can be successfully dissected and delivered through the submandibular space without resorting to mandibulotomy. In cases of large tumors requiring sharp dissection and close careful anatomical dissection of important structures, anterior dislocation of the condyle out of the glenoid fossa or mandibulotomy may be necessary to facilitate a lateral approach to the PPS and skull base.

A- Midline Mandibulotomy

A lip splitting incision communicating with the previously described cervical incision is used. This is done through extension of medial limb of the transverse incision superiorly in the midline to the inferior border of the mandible and curves laterally around the contour of the chin back toward the midline of the lower lip, the incision is then extended to split the lip. The anterior lip flaps are not elevated more than 2 cm off the midline, after which a midline mandibular osteotomy is made. A midline or paramedian mandibulotomy between the lateral incisor and canine is performed. The lip splitting incision is extended in the floor of the mouth along the lateral gutter between the alveolus and tongue to the superior aspect of the anterior tonsillar pillar. Care is taken to avoid injury to the lingual and hypoglossal

nerves. After division of musculature of floor of mouth, the mandible is retracted laterally, allowing exposure to great vessels, severing the pterygoid attachments also adds in the exposure. The internal and external carotid arteries may then be identified and secured with vascular tapes. The external carotid artery may be ligated and divided. Exposure of the PPS for removal of the tumors is now optimal. The facial nerve may be identified carefully from below without complete superficial parotidectomy in selected cases ***(46)***.

Biller, Shugar, Krespi described an anterior approach for wide field exposure of the base of skull ***(7)***. Following elevation of skin flap, the digastric and stylohyoid muscles are detached from the hyoid bone and reflected superiorly. Mylohyoid muscle is divided. Anterior mandibulotomy is then undertaken, an osteotomy is preferred for preservation of inferior alveolar nerve function. Greater exposure can be afforded through the development of a posteriorly based palatal flap dividing the palatine artery and nerves on the side of the dissection. Removal of the posterior aspect of the hard palate further facilitates exposure of the nasopharynx and skull base ***(52)***. ***Attia and Bentley,*** described a combined paramedian osteotomy with horizontal ramus osteotomy to improve access to inferior aspect of PPS while sparing the inferior alveolar nerve ***(2).***

B. Lateral Osteotomy (Manibulotomy)

The osteotomy is performed in the region of angle of the mandible, after the masseter muscle has been cut from the mandible and retracted superiorly. The osteotomy transects the inferior alveolar nerve. The mandibular segments are distracted, and often part of medial pterygoid muscle must be separated to increase exposure. Further distraction is limited by the attachments of the stylomandibular ligament and the ligaments surrounding the temporomandibular joint as well as the temporalis tendon attachment to the coronoid. Severing attachment of stylomandibular ligament often creates significantly increased exposure. With traction maintained to separate the mandibular fragments, the tumor can be both bluntly and sharply dissected with control of the major neurovascular structures. This technique may be used with, superficial parotidectomy or without it, although exposure is more limited. The submandibular gland can be removed or retracted, and the parotid can be reflected superiorly alone with the masseter muscle from the inferior border of mandible prior to osteotomy. The facial nerve may be temporarily paralyzed, secondary to the traction of adjacent soft tissues. The osteotomy

is repaired using an osteosynthesis eccentric dynamic compression plate, thus averting the need for prolonged intermaxillary fixation ***(3,19).***

Several variations in the mandibulotomy have been advocated. Most have been designed to avoid or minimize injury to the inferior alveolar nerve, lingual nerve, and dentition or to improve the surgical access to the PPS. There is some disagreement concerning the morbidity of sectioning the inferior alveolar nerve with lateral osteotomy. ***Pinsolle,*** reported the inferior alveolar nerve function returns within one year using lateral stair-step osteotomy with miniplate fixation ***(39)***. Others, advocate use of inverted L osteotomy or C-shaped osteotomy just posterior to mandibular foramen to avoid damage to the inferior alveolar nerve altogether ***(19).***

V-Infratemporal fossa approach

A preauricular infratemprolar fossa approach, as described by ***Fisch (18),*** can be utilized for malignant tumors involving the skull base or jugular foramen. This approach can be combined with frontotemprolar craniotomy for removal of tumors with significant intracranial extention. A parotidectomy incision with cervical extention and described above is extended superiorly into a hemicoronal scalp incision. The temporalis muscle is elevated to expose the glenoid fossa, which is removed laterally, the tempromandibular joint can be displaced inferiorly, or the mandible condyle can be transected for improving the exposure. Orbitozyygomatic osteotomies are performed and the infratempolar skull base and distal carotid exposed. The fascial nerve and vascular structures in the neck are identified through the cervical and preauricular approaches ***(36).***

The Non Surgical Treatment

Non-operative management of PPS lesions may be considered for patients who are poor surgical candidates because of combined disease, who are elderly patients, who fail balloon occlusion test, who have unrespectable lesions, and who have benign slow-growth tumors that would carry a significant risk of sacrifice of multiple cranial nerves if resected. The risks and benefits of surgery must be weighted in every case ***(8)***. Alternatives to surgery consist of observation or radiation therapy ***(37)***.

Observation

For group consists of patients who are poor surgical candidates and elderly patients with asymptomatic paragangliomas. Observation may be appropriate in patients with multiple paragangliomas who have preexisting

contralateral cranial nerve deficits resulting from resection of a contralateral paraganglioma. Elderly patients do not fare as well following loss of cranial nerve function and the natural course of an asymptomatic paraganglion may be associated with less morbidity than surgical resection ***(31)***.

Radiotherapy

Radiation therapy favored in specific circumstances. Included are those patients with multiple paragangliomas in whom surgical removal of all tumors could result in significant morbidity such as bilateral vocal cord paralysis or cranial nerve XII palsies. ***MaCaffery, Meyer, Michels ,*** reviewed a series of 18 patients with vagal paragangliomas and found 40% incidence of multiple tumors ***(31)***.

Radiation therapy may be considered in patients who are poor surgical candidates but require treatment. These include elderly patients who are symptomatic, patients with internal carotid artery involvement who fail balloon occlusion, or patients with contralateral cranial nerve deficits in whom resection would result in a significant reduction in quality of life. Most surgeons for malignant tumors recommend radiation therapy as an adjunct to surgery in patients with high-grade malignancies, inoperable tumors and when adequate oncologic resection margin cannot be obtained ***(37).***

Follow up care

All patients with PPS masses should undergo routine follow up, regardless of whether treatment is non-operative or surgical. The frequency of follow up examinations varies according to the tumor histology. Patients managed non-operatively should be monitored for tumor growth and development or progression of symptoms. Following surgical excision, patients with benign histology are routinely followed to rule out recurrence, patients with malignancies require closer observation and monitoring. Adjunctive radiation therapy is appropriate for high-grade malignancies and in cases where an adequate resection margin cannot be obtained ***(10).***

Complications following Treatment

In addition to the intraoperative complications mentioned before, injury to lingual and hypoglossal nerves may result from the transcervical approach, when the submandibular triangle is entered. Patients should be notified preoperatively that injury to any or all branches of the facial nerve may result from nerve resection or traction injury; in addition, the ramus mandibularis branch is at risk during cervical approaches. Transection of the facial nerve intraoperatively is best managed by performing nerve grafting at the time of surgery. Eye protection is required in the postoperative period ***(40).***

Injury to cranial nerves IX, X, XI and XII and the cervical sympathetic chain may result from surgery of the PPS. The incidence of postoperative cranial nerve deficits ranges from 11-57%, with higher incidences seen in studies with proportionately great numbers of malignancies or neurogenic lesions. An isolated nerve injury usually is well tolerated in an otherwise healthy patient ***(36).***

Injury to the hypoglossal nerve usually does not significantly impair swallowing function. Injury to the vagus nerve results in vocal cord paralysis and if injury occurs above the level of the nodose ganglion, laryngeal sensation also is affected. Thyroplasty or Teflon injection may be performed intraoperatively or at a later date. The advantage to delaying vocal cord medialization procedures is the patients often will accommodate and the extent of medialization required can be better assessed after this has occurred ***(40)***.

Elderly patients or patients with multiple cranial nerve deficits will be expected to have greater difficulty with swallowing, and medialization as well as cricopharyngeal myotomy should be performed concomitant with resection. If swallowing rehabilitation is prolonged or unsuccessful, gastrostomy tube placement may be necessary. Patients with difficult handling oral secretions may require tracheotomy for airway protection ***(21)***.

Injury to spinal accessory nerve results in weakening of the trapezius muscle, winging of the scapula, and adhesive capsulitis from disuse. An active range of movement physical therapy program can manage this postoperatively. Transection of cranial nerve XI is best managed by nerve grafting, when recognized intraoperatively, to achieve some recovery of

function. Horner’s syndrome may result from injury to the cervical sympathetic chain. The resulting anhydrosis is managed symptomatically.

Vascular complications are more common with removal of neurogenic or vascular lesions. The incidence of intraoperative vascular injury and of perioperative stroke has been reported at 4% for poststyloid lesions. Morbidity may be reduced by avoidance of undue traction on the carotid artery, which may result in intimal tears. Primary repair or vein grafting should be performed for all vessel lacerations ***(37)***.

Complications of mandibulotomy include infection, temporomandibular joint dysfunction, non-union, plate extrusion, and tooth loss. When the osteotomy site is through dental sockets rather than between them, tooth loss is more common. Malocclusion may occur following mandibulectomy in dentate patients ***(46).***

Complications of radiation therapy, whether used primarily or as adjunct to surgery, include xerostomia, tissue fibrosis, acceleration of dental caries, and osteoradionecrosis. Osteoradionecrosis is managed by debridement, antibiotics for secondary infection, and hyperbaric oxygen when it is available. Dental caries may be prevented by the use of fluoride trays. Teeth in poor condition should be extracted. Xerostomia is a life-long problem, but it can be alleviated by treatment with pilocarpine (Salagen, 5 mg orally tid), or artificial saliva applications ***(10)***.

Outcome and Prognosis

The recurrence rate of benign PPS neoplasms following surgical extirpation ranges from 0-9%. The rate of recurrence of parotid pleomorphic adenomas following lateral lobectomy or total parotidectomy, as indicated by the position of the tumor, varies from zero to 2%, in contrast to the much higher recurrence rate seen after enucleation of the tumor***(34).***Malignant transformation of Warthin’s tumor is exceptional.Carcinomas ex. Warthin’s tumor account for 0.3% of all lymphadenomas***(4).***Some of these carcinomas may be radiation induced. Recurrence rates for mucoepidermoid carcinoma are rather high in most series. ***Nascimento, Ameral, Prado,*** reported a 30% recurrence rate ***(35)***. The 15-year cure rate varies according to the grade of the tumor. The 15-year “cure” rate was 48% for patients with low-grade carcinomas and 25% for patients with intermediate and high-grade carcinomas***(50).***In a study of adenoid cystic carcinomas it was found that the most important factor influencing prognosis was the presence or absence of tumor at the margins

of the resection***(38).***The same authors calssified adenoid cystic carcinomas according to their predominant histologic pattern- tubular, cirbriform, or solid. Tumors containing many tubular structures had the most favorable prognosis, and those consisting, predominantly of solid nests had the worst ***(4).***

As a group, acinic cell carcinomas behave like low-grade malignant tumors, in that they tend to recur locally (35%) yet seldom metastasize (6% to 16%)***(17).*** Thus, patients with this tumor should be followed up for long periods of time.In patients with invasive carcinomas the extent of invasion, as measured in millimeters, is a valuable guide to prognosis and biologic behavior; carcinomas that invade less than 8mm carry a 5-year survival of 100%, whereas those that invade more than 8mm have a 5-year survival rate of lesss than 50%. Carcinosarcom is highly lethal and has a 5-year survival of 0%***(51).*** Paragangliomas recur in approximately 5%, and because 10% are multicentric, there remains a risk of development of a second tumor. Patients with a familial paraganglioma syndrome have a 35% incidence of multicentricity. In addition, patients with paragangliomas who are being managed non-operatively need to be alerted to the incidence of malignant degeneration, which is approximately 10% and usually associated with rapid growth. Thus, patients with paragangliomas require lifetime follow up. Malignant tumors of the PPS have a much higher rate of recurrence (25-77%) depending on histology, extent of resection, and duration of follow-up. Postoperative radiation therapy for PPS malignancies is recommended to prevent the recurrences. However, because of the relative scarcity of these lesions, no large series available to demonstrate a survival benefit ***(10)***.

In future, genetic screening of patients at risk for hereditary paraganglioms should be possible. The gene responsible for transmission of hereditary paragangliomas, termed **PGL**, has been mapped to chromosome 11, in large pedigree analysis, loci at 11q23 (PGL 1) have been shown to be most commonly associated with or mutant PGL gene, which is inherited from carrier fathers in an autonomic dominant fashion subject to maternal imprinting. There are no affected offspring from affected mothers. Genetic manipulation of a mutant PGL gene may one day prevent or interrupt the development of these tumors ***(6)***.