Our experiences with parapharyngeal space tumors and systematic review of the literature

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Abstract

Objectives To find out the geographical distribution, age, sex, mode of presentation, diagnostic modalities, surgical approaches, postoperative complications, follow-up and histopathology of parapharyngeal space tumors (PFT) through world wide web search (WWWS) and PFT of our series.

Materials and methods A retrospective study of all PFT seen and treated in S.R.N Hospital, Allahabad between 1990 and 2006 was done. A systematic review of the literature was done through WWWS.

Results PFT were commonest in the Asian zone. Incidence was highest in the 3rd and 4th decade. Oropharyngeal (100%) and cervical (91.6%) swelling were the commonest presentation. MRI is better than CT scan in evaluating fat plane. Transcervical approach was the commonest. In our series, benign tumors (83.4%) were common, constituting 50% of neurogenic and 16.6% of salivary gland origin.

Conclusion PFT were more prevalent in the Asian zone. Neurogenic tumors were commonest in our study which contradicts the WWWS of having maximum PFT of salivary gland in origin.

Keywords Parapharyngeal space · Salivary glands · Schwannoma · Imaging · Surgery

Introduction

Parapharyngeal space tumors (PFS) present a diagnostic challenge. It constitutes less than 0.5% of head and neck tumors [1]. Previously many such space occupying lesions were dealt with swelling of the neck and pharynx with half-hearted attempt in their surgical ablation. Because the PFS is located deep within the neck, the role of clinical examination is limited. With popularization of cross-section imaging by CT and MRI scanning and interpretation of imaging data based on a combination of these systems, it is possible to precisely locate a lesion and to even give a clue to the probable nature of the tumor. In this study an endeavor was made to find out the epidemiology of PFS tumors through a WWWS and to see whether there is any difference in tumors, that we see and the tumors found in web search.

Materials and methods

The case records of all patients presenting with a diagnosis of PFT who were treated in ENT, Head and Neck Surgery Department, SRN Hospital, Allahabad between 1990 and 2006 were reviewed retrospectively. The study included consideration of geographical distribution, age, sex, clinical presentation, imaging techniques, cytology, surgical approach, postoperative complications, and follow-up of cases. Percentages were used for nominal variables and comparisons. A systematic review of the literature was done through WWWS. Information about the PFT was obtained by subject or journal title, title abbreviation, the NLM ID (NLM's unique journal identifier) and by author names indexed in PubMed and Google search. The database includes non-paid articles and abstracts in Entrez Pubmed and Google sites irrespective of the time period.

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Results

From Jan 1990 to Sept 2006, 12 patients of PFT were identified in our institution and reviewed. This proves the rarity of the neoplasm. In WWWS, 580 cases were found to have PFT. Most of the cases studied were from Asia (China, Japan and Southeast Asian countries like India, Indonesia and Thailand). About 318 cases were found in Asia, 204 cases from North America, 54 cases from Europe and 4 cases from Africa. So it is most rare in Africa and South America (Fig. 1). Age varied from 17 to 70 years. The highest incidence was found in the 3rd and 4th decade (25% each) in our hospital and in the 3rd (18.4%) and 4th (24%) decade in WWWS (Fig. 2). Out of the 12 patients, eight were female. So female preponderance was observed in our study where as in WWWS male to female ratio was 1.5:1.

In our cases, the most mode of presentation was oropharyngeal swelling (100%, Fig. 3) causing odynophagia (58.3%) and difficulty in breathing (33.3%), cervical swelling (91.6%, Fig. 4), neurological deficit (33.3%) like hoarseness of voice, slurring of speech, weakness of shoulder, blurring of vision and multiple cranial nerve palsy. On detailed analysis of clinical presentation of PFT in WWWS, we observed oropharyngeal swelling (74.2%) causing odynophagia (70%) and difficulty in breathing (25%), cervical swelling (61.2%), neurological symptoms (22.3%) and multiple cranial nerve (CN) palsy (9, 10 and 11) in 22.3% cases. Some patients, particularly malignant tumors of

childhood, presented with ear symptom like diminished hearing, tinnitus and ear discharge.

Investigations

As per records the investigations, which had been done, were routine blood and urine examinations, imaging studies like plane X-ray, CT scan and MRI. All patients in our institution underwent high resolution CT scan. MRI was done in 5 patients. MRI was found to be better than CT scan in evaluating fat plane. Figure 5 (A&B) shows MRI of the patient of pleomorphic adenoma diagnosed by fine needle aspiration cytology (FNAC). In CT scan, the fat plane between the deep lobe of parotid and tumor was not very clear whereas in MRI scan it could be seen clearly. It helped in planning the surgical approach. Hence, this tumor could be easily removed by transcervical approach through finger dissection. It was found to be minor salivary gland pleomorphic adenoma. By studying CT and MRI characteristics and displacement of vessels in carotid sheath, the probable nature of tumor could be ascertained. Figure 6 (A & B) shows the CT scan of poststyloid schwannoma with characteristic non-homogeneous patchy appearance with displacement of internal carotid artery (ICA) anteriorly. Another CT scan of rare tumor of fibrohistiocytoma shows homogenous mass in poststyloid area. In WWWS, paragangliomas were found to have salt and pepper appearance on MRI because of numerous voids within the lesion whereas schwannomas showed greater enhancement on T2-weighted images, enhanced with

Fig. 1 PFT cases geographical distribution (WWWS) $n = 580$.

Fig. 2 Comparison of age distribution of PFT in WWWS and our study

Fig. 3 Oropharyngeal swelling in PFT

Fig. 4 Cervical swelling in PFT

gadolinium and lack of voids. The other modalities of investigations, which have been done in web search, were digital subtraction angiography (DSA), carotid angiography and immunological markers. Twenty-four hour urine analysis for vinyl mandelic acid (VMA) helped in diagnosing chromaffin producing paragangliomas. FNAC was found to be 75% accurate in diagnosing PFT through web search. In rest of the cases final diagnosis could be ascertained only after complete excision biopsy.

Surgery

Out of the 12 cases, 8 cases could be removed surgically by transcervical approach only. One case of deep lobe parotid

tumor was removed by cervicofacial approach. Three out of the 12 patients required lateral mandibulotomy for complete exposure and extirpation of tumor. One patient who was initially diagnosed as a case of ectopic pleomorphic adenoma was found to have lot of adhesions during surgery. It was difficult to remove this tumor even after mandibulotomy. The final diagnosis after complete excision biopsy was metastatic squamous cell carcinoma. After six months, primary was detected in the right main bronchus and the patient died of hemoptysis. In one patient metastatic lymph nodes in PFS from occult primary after open biopsy were found. He was subjected to radiotherapy. All benign tumors could be dissected out easily. However, there was difficulty in removing a carotid body tumor and another angiomatoid

Fig. 5 MRI showing fat plane in minor salivary gland tumor

variant of benign fibrohistocytoma where ligation and excision of external carotid artery was required for complete excision. Hypoglossal nerve was retracted during excision of fibrohistocytoma. In another patient of poststyloid fibromyxoma of PFS, the internal carotid artery (ICA) was engulfed by the tumor itself. This patient required ligation of ICA and packing of internal jugular vein (IJV) during extirpation of tumor. However, this patient died after two weeks due to multiple cranial nerve palsy which lead to septicemia due to aspiration pneumonia. From this, we learn that such patients should have undergone balloon occlusion

test combined with brain scan in the preoperative period to measure the amount of blood flowing to the brain. If balloon test is inadequate, such benign tumors may be left as such. In postoperative period, right vocal cord paresis was found in one schwannoma patient on second postoperative day, which improved in six weeks after a course of steroids. One patient of neurofibroma presented with 9th, 10th and 11th cranial nerve (CN) paresis, which improved after 8th week of surgery. In WWWS search, the major surgical approach was transcervical (82%) followed by transparotid (20%), preoral (15.75%), combined (11.75%), swing (7.4%), postaural (3%) and lateral base skull approach in 2.7% cases. Mandibulotomy was combined in 20.3% cases. WWWS showed involvement of cranial nerves (6, 7, 9, 10, 11 and 12) in 19 % cases during postoperative period. The histopathological diagnosis of PFT in present series and WWWS is illustrated in Table 1.

The period of follow-up in benign tumors varied from 6 months to 10 years except one patient who died in post operative period due to multiple cranial nerve palsy. There was no recurrence in benign tumors. Prognosis remained singularly poor in malignant tumors. Recurrence was seen after 6 months in one patient of metastatic lymph nodes in PFS from occult primary in bronchus lung. Another patient, who was subjected to radiotherapy showed regression of tumor in follow-up. However, he was lost to follow-up after two months.

Discussion

The parapharyngeal space is an inverted pyramid shaped potential space which extends from the base of the skull superiorly to the greater cornua of the hyoid bone inferiorly. It is bounded medially by the parapharyngeal wall and buccopharyngeal fascia, laterally by the medial pterygoid and ascending ramus of mandible in the anterior portion and parotid gland with its fascia in the posterior portion. Because the space is limited above and laterally by the rigid bones of base of skull and mandible respectively, the natural expansion of tumors in majority of cases will be medially towards the pharynx causing smooth bulge in the lateral pharyngeal wall pushing tonsil anterior-medially. The space not only contains fascia and muscles which are of little pathological interest but also the bifurcation of the common carotid artery, the internal and external carotid arteries, last four cranial nerves, cervical sympathetic chain and few lymph nodes. Clinically, the parapharyngeal space should be considered in two spaces: prestyloid space and poststyloid space. Fascia from the styloid process to the tensor veli palatine muscle divides the parapharyngeal space into these two compartments. The prestyloid space is anterolateral and contains cervical portion of the deep lobe of the parotid gland, minor or ectopic salivary gland, a small branch of the CN V to the tensor veli palatine muscle, ascending

Table 1 Histopathology of PFT

Histopathology	SRN Hospital, Allahabad (in %)	World wide web search (in %)
Neurogenic	50.0	33.6
(a) Schwannoma	25.0	16.8
(b) Neurofibroma	16.6	8.4
(c) Paraganglioma	8.3	8.4
Salivary gland tumors (Pleomorphic adenoma)	16.6	41.2
(a) Deep lobe parotid	8.3	18.6
(b) Minor salivary gland	8.3	22.6
Miscellaneous (teratomas, giant cell tumors, lipomas, fibromatosis)	16.6 (fibrohistocytoma and fibromyxoma 8.3 each)	3.2 (rhabdomyomas – 0.7)
Malignant	16.6	21.8
(a) Secondary from occult primary	8.3	
(b) Secondary from bronchogenic carcinoma	8.3	

pharyngeal artery and pharyngeal venous plexus. The majority of the prestyloid space is actually fat. The poststyloid compartment is posteromedial and contains ICA, IJV, CN IX to XII, cervical sympathetic chain, lymph nodes and glomus bodies. Lesion may arise from any of these structures [2, 3].

We have done a WWWS through PubMed and Google search. Our study included geographical distribution, age, sex, mode of presentation, diagnostic modalities, surgical approach, postoperative complications, follow-up and histopathology. Through web, we found that most of cases were from Southeast Asian countries such as China, Japan, Thailand, Singapore and India. Instances of sporadic cases reports are there but a good series is lacking. “In the series reported by Work and Gates [4] and WWWS, the commonest tumors were benign mixed salivary gland tumors (33.3% and 41.2% respectively) and neurilimmomas (27.7% and 30.4% respectively). Hughes found that pleomorphic adenoma was the most common neoplasm (40%), followed by paraganglioma (20%), neurogenic tumor (14%), malignant salivary gland tumor (13%), miscellaneous malignant tumors (7%), and miscellaneous benign tumors (6%) [5]. However, in our series neurogenic tumors (50%) were most frequent entities. In one of the most recently published study on primary parapharyngeal tumors, Luna-Ortiz et al. from Mexico reported neurogenic tumors to be 57% of all tumors [6]. We also encountered two rare cases of fibrohistocytoma and fibromyxoma of PFS.

Neural tumors are derived from neural crest cells. They can be divided into two main groups: the nerve sheath tumors and tumors derived from the sympathoblast. The normal nerve fiber is ensheathed by schwann cells and by loosely distributed endoneural fibroblasts. The schwann cell is the parent cell of both common clinical tumors, the schwannoma (neurilemmoma) and the neurofibroma [2]. In the present series, 6 patients had tumors of neurogenic ori-

gin, i.e. two schwannoma of vagus nerve and two neurofibroma, one schwannoma of cervical sympathetic chain and one neurofibroma of hypoglossal nerve. In one case fibers of the 10th nerve were found stretched over the capsule of the tumor from which tumor could be dissected easily. The patient had postoperatively right vocal cord paresis, which improved subsequently. In CT scan, schwannoma usually appeared as non-homogenous patchy mass with displacement of vessels anteriorly (Fig. 6 A&B). In WWWS, schwannoma constituted about 16.8% of PFT, hence, the most common type of neurogenic tumor. In WWWS, schwannomas were heterogeneously hypodense before contrast enhancement and at least partially hyperdense after contrast enhancement with displacement of adjacent vessels at CT, if they were vagal in origin, antero-medially displacement of ICA. Because most PFS neurogenic tumors arise primarily from vagal nerve (less commonly arising from the sympathetic chain or one of the other local nerves) which is positioned posterior to the ICA, these neurogenic tumors tend to displace this vessel anteriorly [7]. They may have a deceptive post contrast enhancement on MRI, apparently due to extravascular accumulation of contrast material. The tumor arises from solitary nerve fiber. Paralysis of the associated nerve is thus unusual. Malignant change is also very unusual and may not occur at all [2].

The present study includes three neurofibromas of PFS. In other case of neurofibroma, patient had 9th, 10th, 11th cranial nerve palsy preoperatively which recovered at 8th week postoperatively. Neurofibroma has an origin from perineurium and is thus linked inseparably from the nerve of origin. It usually presents as slowly enlarging painless neck mass developing over a period of years. Angiography is needed to differentiate these tumors from paragangliomas, but the final diagnosis must usually wait until excision. The nerve from which the tumor arises is evident in one in three operations. It may be stretched over the capsule of the

Fig. 6 CT scan of poststyloid schwannoma of Xth nerve showing non-homogenous patchy appearance and displacement of internal carotid artery anteriorly (arrow)

tumor, or the tumor can be in the central core of the nerve with the fibers spread around it. All simple tumors should be excised and an attempt made to rejoin or graft the nerve [2].

In WWWS, paragangliomas constitutes 8.2% of PFT. Genetic susceptibility plays a part in the etiology of paragangliomas. The gene responsible for transmission of hereditary paragangliomas has been mapped to chromosome 11. In large pedigree analysis loci at 11q23 (PGL1) has been shown to be most commonly associated with mutant PGL gene which is inherited from carrier father in an autosomal dominant fashion subject to maternal imprinting [8].

Paragangliomas usually were homogeneously hyperdense after contrast enhancement with incorporation of adjacent vessels on CT, if they were of carotid origin, lateral displacement of ICA. Presence of internal flow voids on MRI in a mass that is greater than 2 cm is suggestive of paraganglioma, rather than schwannoma. Flow voids are not helpful in distinguishing between these two lesions when their mean diameter is less than 2 cm [9]. Oslen et al. described chronic appearance of paraganglioma, that is, a salt pepper appearance in all lesions larger than 2 cm in diameter [10]. The paragangliomas arise from chemoreceptor bodies. At imaging, the three sites of origin may be distinguished. Glomus vagale and jugulare tumors tend to displace the ICA anteriorly. Splaying of internal and external carotids and Lyre's sign suggests the diagnosis of carotid body tumor [11]. Glomus vagale tumors have smaller intracranial extensions and better developed capsules than glomus jugulare tumors. Vagal paragangliomas arise from nests of paraganglionic tissue within the perineurium of the vagus nerve at its ganglion nodosum, i.e. just below the skull base. The carotid body tumor has a much more prominent surface vasculature than the glomus vagale and can be deeply embedded in the vessel wall, resection extremely painstaking. Patients present with long history of the slowly enlarging painless lump in the region of the carotid bulb. About 30% patients present with parapharyngeal mass [2]. Patients may present with bruit, blackout and increased carotid sinus sensitivity. Nerve involvement is rare. The investigation mandatory is carotid angiogram which demonstrates the tumor circulation, extent of tumor and cross circulation if any. Investigations of urine catecholamines and metabolites rule out functional chemodectomas, because the patient may suffer from hypotensive shock after removal of functional chemodectomas. Treatment of choice is surgical excision. Radiotherapy can be given to those who refuse surgery, in poor risk patients or in metastatic disease. Prognosis is good [12].

In the present series, two patients had salivary tumors. These were pleomorphic adenoma originating each from deep lobe parotid and minor ectopic salivary glands. In one case tumor arose from minor salivary gland because MRI scan clearly showed the fat plane between deep lobe parotid and tumor and the tumor was enucleated easily by finger dissection as it was free from parotid gland. The other case originating from deep lobe parotid which was removed by cervicofacial transparotid approach. Salivary gland tumors are the most common primary lesions (40% of all primary PFS masses) [5, 13] These may cause swelling in one of 3 ways – dumble tumor from the stylomandibular process of deep lobe of parotid, tumor from the cervical process of deep lobe and minor salivary gland tumor [2, 3]. There is no consistent physical finding that allows a clinician to differentiate confidently between a deep lobe parotid mass and an extraparotid lesion [14]. The best method for making this distinction is still the visualization of a fat plane

between the deep lobe and the posterolateral aspect of the mass. This fat plane represents the compressed fibrofatty supporting matrix of the parapharyngeal space and, when it is seen; undoubtedly the mass is extraparotid in origin. When the fat plane is not seen between the mass and the parotid gland, the lesion is probably a parotid tumor. Thus an absent fat plane sign correctly identified a tumor as being intraparotid [15].

In one patient metastatic lymph nodes in PFS from occult primary after open biopsy was found. He was subjected to radiotherapy. One patient presented with benign PFT (pleomorphic adenoma) but after surgical excision, he had reoccurrence and later was diagnosed as metastatic squamous cell carcinoma from bronchogenic carcinoma of lung. The patient died of hemoptysis. The enlarged lymph nodes in carotid space with areas of decreased central accentuation may be either due to neoplastic and inflammatory cause [9]. Parotid lesions (mucoepidermoid carcinomas, adenoid cystic carcinomas and acinar cell carcinoma) are uncommon and mostly arises from the minor pharyngeal submucosal glands. Most malignant tumors of peripheral nerve arise from the schwann cell. Neuroblastomas are tumors of childhood and in the head and neck may be secondaries from an abdominal tumor or may arise primarily from the cervical sympathetic chain [2].

The goal of PFT surgery is to provide adequate tumor visualization to achieve complete tumor removal, while preserving the surrounding nerves and vessels and control of any hemorrhage. Overall, transcervical and transparotid approach are the two main approaches. They have also been used with mandibulotomy to increase exposure. Transcervical approach is usually used for poststyloid tumors and transparotid approach for prestyloid tumors. They have also been used with mandibulotomy to increase exposure. In the present series, eight cases were removed surgically by transcervical approach only. One case of deep lobe parotid tumor was removed by cervicofacial approach. Three out of 12 patients required lateral mandibulotomy for complete exposure and extirpation of tumor. One patient who was initially diagnosed as a case of ectopic pleomorphic adenoma was found to have lot of adhesion during surgery. It was difficult to enucleate this tumor even after mandibulotomy. However tumor, was freed from all around and removed in a single piece. Transcervical approach starts with a transverse incision at the level of the hyoid bone. The submandibular gland is often removed or retracted anteriorly. An incision through the fascia deep to the submandibular space allowed for entry into the parapharyngeal space and blunt dissection of the tumor. Many modifications have been reported. Some surgeons divide the digastric, stylohyoid and styloglossus muscles from the hyoid bone to improve exposure. The styloid process and the stylomandibular ligament can also be divided to elevate the mandible anteriorly to improve access. This approach frequently involves blind finger dissection. Transcervical approach can be combined

with mandibulotomy. Various locations for osteotomy have been reported, including mandibular body, angle ramus, and parasymphysis. The key is to try to limit injury to the inferior alveolar nerve while providing access to the parapharyngeal space. The risk of mandibulotomy includes inferior alveolar nerve anesthesia, loss of dentition, malocclusion, mandibular malunion or non-union, and possibly requires a tracheotomy. Olsen recommended mandibulotomy for vascular tumors extending into the superior parapharyngeal space, solid tumors that are confined to the superior aspect of the parapharyngeal space and malignant tumors invading the skull base [16]. Transparotid approach is commonly used for deep lobe parotid tumors. It starts with a superficial parotidectomy with facial nerve preservation. The facial nerve is then separated from the deep lobe of the parotid gland and retracted. The dissection continued posteriorly and inferiorly around the mandible.

Many surgeons prefer the transcervical-transparotid approach. A standard parotidectomy incision is made and carried into the lateral neck. The main trunk and lower division of the facial nerve are identified. The posterior belly of the digastric and stylohyoid muscle are divided, allowing for visualization of the internal and external carotid arteries, internal jugular vein, CN IX, X, XI, XII, and sympathetic chain. The styloid process and stylomandibular ligament may be transected to give a wide opening into the parapharyngeal space. Olsen reported using this technique in 80% of his case series. He recommended this approach for all deep lobe parotid tumors, extraparotid salivary tumors and most of the poststyloid neurogenic tumors [16]. Hughes also reported that transcervical-transparotid approach to be the preferred procedure for removal of most parapharyngeal tumors [5]. For vascular tumors that extend into the superior portion of the parapharyngeal space, Olsen recommended cervical-parotid approach with midline mandibulotomy [16]. Midline lip splitting is used to expose anterior mandible. Then the mandible is divided in the midline. An intra-oral incision is then made in the floor of the mouth extending back to the anterior tonsillar pillar and up to the level of the hard palate. The hypoglossal nerve and lingual nerve are preserved. The styloglossus and stylopharyngeus muscles are divided. The mandible is retracted laterally and superiorly to give wide exposure to the parapharyngeal space. Tracheotomy is necessary for this approach. Since primary PFT are increasingly rare, few large scale studies are available. Shahab recently published his review of PFT for over 27 years of experience, the second largest study in literature [17]. The 5 and 10-year survival for benign parapharyngeal tumor is 100%. For malignancies the 5 year survival was 93%, but fall to 57% at 10 years. This study showed that a patient is highly unlikely to die of a benign parapharyngeal space tumor, therefore careful consideration of surgical treatment and discussion with the patient are crucial. While surgery is the mainstay of the treatment for parapharyngeal tumor, radiation therapy should be considered in elderly

patients with paragangliomas. Also isolated asymptomatic parapharyngeal schwannomas in elderly patients with no nerve deficit should probably be observed.

Conclusion

Anatomy of PFS is complex with important neurovascular structures. In the present series, most common age of presentation was 3th and 4th decade. There was predominance of females in our study as compared to males in web search. WWWS has shown highest prevalence of PFT in South East Asian zone. Oropharyngeal and cervical swelling were the commonest mode of presentation. FNAC was found to be diagnostic in 75% of cases in web search. CT scan is helpful in deciding the site, extent, relationship to styloid process, parotid gland, vessels and the probable nature of the neurogenic tumors. MRI was proved to be better than CT scan in evaluating fat plane in prestyloid compartment. Benign tumors of neuroectodermal origin were commonest in our study which contradicts the WWWS of having maximum PFT of salivary gland in origin. Prognosis remained favorable for PFT.

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