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The Importance of Imaging and Fine Needle Aspiration Biopsy in Primary Benign Parapharyngeal Space Tumors

Primer Benign Parafarengeal Boşluk Tümörlerinde Görüntüleme ve İnce İğne Aspirasyon Biyopsisinin Önemi

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ABSTRACT Objective: The purpose of this study is the comparison of the radiological pre-diagnosis with the cytopathological results acquired from fine needle aspiration biopsy (FNAB) and the post-operative final histopathological results in operated patients diagnosed to have primary benign parapharyngeal space (PPS) tumors. **Material and Methods:** In our study, 20 patients who were considered to be benign with preoperative imaging and FNAB between 2011 and 2017 were observed retrospectively. Patients suspected of malignancy with preoperative imaging or FNAB were excluded from the study. **Results:** From a total of 20 patients, 11 were female while 9 were male, and the mean age was 54 (21-78). In post-styloid region (n=10), the pre-operative radiological diagnosis was reported as paraganglioma (n=6), and peripheral nerve sheath tumors (n=4). In pre-styloid region (n=10), the preoperative radiological diagnosis was reported as deep lobe parotid tumor (warthin and pleomorphic adenoma) (n=6), lymphadenitis (n=1), minor salivary gland cyst (n=1), lipoma (n=1) and branchial cleft cyst (n=1). Compared to specimen results, preoperative imaging results of 20 patients were consistent with specimen in 18 patients, while specimen results were reported as malignant in 2 patients, although imaging was benign. FNAB was performed in 13 patients without vascular tumor suspicion, and results consistent with specimen results were obtained in 11 patients. Although FNAB results were reported as benign in 2 patients, the specimen result was reported as malignant. **Conclusion:** In our study, we found that, even if imaging and FNAB in PPS benign masses reported largely accurate results, it is rarely not able to rule out malignancy. These possibilities should be kept in mind when approaching the benign tumors of the parapharyngeal region.

Keywords: Parapharyngeal space; biopsy; fine-needle

ÖZET Amaç: Çalışmamızda primer benign parafarengeal boşluk (PPS) tümörü tanısı ile opere edilen hastalarda, ince iğne aspirasyon biyopsisinden (İİAB) elde edilen sitolojik sonuçlarla, radyolojik ön tanı ve postoperatif son histopatolojik sonuçların kıyaslanması amaçlanmıştır. **Gereç ve Yöntemler:** Çalışmamızda, 2011-2017 yılları arasında preoperatif görüntüleme ve İİAB ile benign olduğu düşünülen 20 hasta retrospektif olarak izlendi. Preoperatif görüntülemede veya İİAB ile malignite şüphesi olan hastalar çalışma dışı bırakıldı. **Bulgular:** Toplam 20 hastanın 11'i kadın, 9'u erkek olup ortalama yaş 54 (21-78) idi. Poststiloid bölgede (n=10) ameliyat öncesi radyolojik tanı paraganglioma (n=6) ve periferik sinir kılıfı tümörleri (n=4) olarak rapor edildi. Prestiloid bölgede (n=10), ameliyat öncesi radyolojik tanı derin lob parotis tümörü (warthin ve pleomorfik adenom) (n=6), lenfadenit (n=1), minör tükürük bezi kisti (n=1), lipom (n=1) ve brankial yarık kisti (n=1) olarak raporlandı. Cerrahi sonrası spesmen sonuçlarıyla karşılaştırıldığında, 20 hastanın preoperatif görüntüleme sonuçları 18 hastada örnekle tutarlıyken, 2 hastada görüntüleme iyi huylu olmasına rağmen örnek sonuçları malign olarak bildirildi. Vasküler tümör şüphesi olmayan 13 hastaya, cerrahi öncesi İİAB uygulandı ve 11 hastada biyopsi sonuçlarıyla spesmen sonuçları uyumlu olarak izlendi. İki hastada, İİAB sonuçları benign olarak bildirilmesine rağmen spesmen sonucu malign olarak rapor edildi. **Sonuç:** Çalışmamızda, parafarengeal bölge benign tümörlerinde görüntüleme ve İİAB büyük ölçüde doğru sonuçlar bildirmiş olmasına rağmen nadiren maligniteyi ekarte edemediğini gördük. Parafarengeal bölgenin, benign lezyonlarına yaklaşımda bu yanılma payının da akılda tutulması uygun olacaktır.

Anahtar Kelimeler: Parafarengeal boşluk; biyopsi; ince iğne

The parapharyngeal space (PPS) is a deep potential space shaped like an inverted pyramid that originates form the skull base and extends to the greater cornu of the hyoid bone. This space is divided

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into pre-styloid and post-styloid areas by the fascial structure called tensor veli palatini, lying between styloid process and lateral pterygoid plate. While the retro mandibular part of the parotid gland, some fibro-adipose tissues, internal maxillary artery and vein and lingual, inferior alveolar and auriculotemporal nerves are located in pre-styloid compartment; carotid artery, internal jugular vein, cranial nerves (IX,X,XI,XII), cervical sympathetic chain and many lymph nodes are located in post-styloid area. The separation of the PPS into pre and post-styloid areas is important for the possible diagnosis and for structuring the differential diagnosis of a tumor located in this area.[1-5]

Imaging techniques have a key role in the evaluation and the differential diagnosis of the tumors of this region. Magnetic resonance imaging (MRI) and computed tomography (CT) with contrast agents provide information about the localization and extension of the mass and border relations with the nearby tissues, the presence of enlarged lymphadenopathies, shifting direction of neighboring structures, and the vascularization degree of the mass.[1,4-6]

In PPS tumors, the determination of cytopathological diagnosis with fine needle aspiration biopsy (FNAB) technique provides crucial information for the surgeon in determining the correct preoperative plan. However, being localized deep inside the neck, being a reservoir for many types of tumors, and also the morphological similarity of these tumors in this region makes it difficult to obtain an accurate diagnosis. Hence, the diagnosis is frequently determined by the post-operative histopathological and immunohistochemical evaluation.[3,4]

The best treatment choice is the surgical removal of the tumor. By trans-oral approach (TOA), trans-cervical approach (TCA), trans-parotid approach (TPA), trans-mandibular approach (TMA), infratemporal approach, or the combination of all these approaches, the tumor can be totally excised.[1] With the development of robotic surgeries in recent years, transoral robotic approaches have also been reported.[7]

The purpose of this study is the comparison of the radiological prediagnosis with the cytopathological results acquired from FNAB and the post-operative final histopathological results in operated patients diagnosed to have primary benign PPS tumors.

MATERIAL AND METHODS

Our study was conducted in accordance with the principles of Helsinki's Declaration and was approved by the local ethics committee of our hospital (05.04.2017 03/33). Twenty patients who were operated in our clinic between 2011 and 2017 and whose preoperative radiological evaluations came out as benign tumors originating from the PPS, were reviewed retrospectively. Only the patients who were operated by the surgeons in this study group were included in this study. Patients suspected of malignancy with preoperative imaging or FNAB were excluded from the study.

Patients' medical history, detailed physical and neurological examination findings of head and neck and endoscopic examination findings of the nasopharynx, larynx and hypopharynx, radiological imaging techniques and their reports, cytopathological results of FNABs, operation notes, postoperative histopathological results of the specimen and follow-up information were gathered from clinical/laboratory records. Patients first underwent MRI with contrast agent; and upon cases MRI could not be performed or an evaluation of bony structures was required, CT imaging was used. MRI was performed with 1.5 Tesla MRI systems with a gantry opening of 60 cm (Signa HDi, GE Healthcare, Milwaukee, WI, USA) or 70 cm (Magnetom Aera, Siemens AG, Erlangen, Germany). Upon tumors of vascular origin, or if the presence of a close relationship between the tumor and vascular structures was suspected, MR/CT angiography was performed. In carotid body tumors; balloon occlusion test and pre-op embolization were performed when necessary.

Cytopathological examination with FNAB was performed in all cases could technically reached and apart from masses of vascular origin. FNAB was performed either by the surgeon or the radiologist under the guidance of ultrasound through transcervical or transoral route. FNAB was performed with 25 gauge

needles in 10-ml plastic injectors by standard aspiration procedure. Aspirations were repeated if FNAB results were not clear or malignancy was suspected.

The localization, dimension and features of the tumor, radiological and FNAB prediagnoses, surgical procedures, postoperative final histopathological results are presented in Table 1.

RESULTS

From a total of 20 patients, 11 patients were female while 9 patients were male, and the mean age was 54 (21-78). The most common physical examination finding was a lump in the neck. In 15 patients the mass was located in the neck, in 1 patient in the preauricular region and in 1 patient it was located in side of the oral cavity. Masses were detected coincidentally in 3 other patients upon imaging for different complaints. The dimensions of the masses varied between 2.3 and 6.2 cm. (3.62 in average). The mean postoperative follow up period was 3 years.

In 10 patients (%50), the mass was located in post-styloid region. The preoperative radiological diagnosis was reported as paraganglioma in 6 patients, and peripheral nerve sheath tumors (schwannoma and

TABLE 1: Clinical, radiological and pathological data of patients.

N	Location	Dimention and features	Radiological diagnosis	FNAB cytological diagnosis	Final histopathological diagnosis	Surgical approach
1	Post-styloid	27x21x17 mm hyper vascular,semi-solid	Cystic schwannoma	-	Papillary thyroid carcinoma metastasis	TCA+TMA
2	Pre-styloid	24x18x22 mm cystic	Cyst (minor salivary gland origin)	Cystic	Retantion cyst (minor salivary gland origin)	TCA
3	Post-styloid	35x22x18xmm hyper-vascular	Paraganglioma	-	Paraganglioma (GC)	TCA
4	Post-styloid	36x25x24 mm hyper-vascular	Paraganglioma	-	Paraganglioma (GC)	TCA
5	Post-styloid	32x21x19 mm solid	Schwannoma	Schwannoma	Schwannoma (vagal)	TCA
6	Pre-styloid	40X14X12 cystic	Cystic (Branchial cleft, -necrotic LAP)	Cystic	Branchial cleft cyst	TCA
7	Pre-styloid	33x22x19 heterogenous solid	Parotid deep lobe (warthin)	Warthin	Warthin	TPA
8	Post-styloid	30x35x20 mm solid	Nerve sheath tumor	Non-diagnostic	Neurofibroma (vagal)	TOA
9	Post-styloid	40x30x25mm hyper-vascular	Paraganglioma	-	Paraganglioma (GC)	TCA
10	Post-styloid	29x20x18mm solid	Schwannoma	Schwannoma	Schwannoma (cervical sympathetic chain)	TCA
11	Pre-styloid	50x30x20 mm solid	Pleomorphic adenoma	Benign cytology (non-specific)	Pleomorphic adenoma	TPA
12	Pre-styloid	45X20X30 mm solid	Pleomorphic adenoma	Pleomorphic adenoma	Pleomorphic adenoma	TPA
13	Pre-styloid	32X23X20 mm cystic / necrotic	Warthin	Cellular pleomorphic adenoma or low grade tumor)	Acinic cell carci noma (low grade)	TPA
14	Pre-styloid	27X25X22 mm solid	Pleomorphic adenoma	Pleomorphic adenoma	Pleomorphic adenoma	TPA
15	Pre-styloid	43X37X22 mm solid	Lipoma	Lipoma	Lipoma	TCA
16	Post-styloid	45X30X40 mm hyper-vascular	Paraganglioma	-	Paraganglioma (GC)	TCA
17	Post-styloid	62X40X40 hyper-vascular	Paraganglioma	-	Paraganglioma (Vagal)	TCA+ TMA
18	Pre-styloid	23X17X25mm cystic / necrotic	Lymphadenitis	Reactive Lymphadenitis	Lymphadenitis	TCA+ TPA
19	Post-styloid	54x30x20 mm hyper vascular	Paraganglioma	-	Paraganglioma (GC)	TCA
20	Pre-styloid	32x22x18 mm solid	Pleomorphic adenoma	Pleomorphic adenoma	Pleomorphic adenoma	TCA

TCA: Trans-cervical approach; TMA: Trans-mandibular approach; TPA: Trans-parotid approach; TOA: Trans-oral approach.

neurofibroma) in 4 patients. Imaging results in 9 of 10 patients in the post-styloid region were consistent with specimen results. A semi-solid mass which was located in the right post-styloid region, detached from the surrounding tissues with smooth borders, and involved hyper-intense, hyper-vascular and cystic components with significant contrast uptake in T2 MRI images was reported as cystic schwannoma in one patient (Figure 1). This mass was completely removed with TMA (midline mandibular osteotomy with labial incision) and TCA (Figure 2). However, it was surprising that the specimen diagnosis was reported as papillary thyroid cancer metastasis. It was discovered that the patient had underwent superficial parotidectomy because of nodular sialoadenitis in previous years. After 3 weeks from this surgery, total thyroidectomy and neck dissection (level 2-6) were performed. The pathology of the specimen was reported as follicular variant papillary thyroid cancer with no lymphatic involvement. After post-operative radioactive I-131 treatment, no relapse was detected in the 6 year follow-up.

In 10 patients (%50) the mass was located in prestyloid region. The preoperative radiological diagnosis was reported as a parotid tumor of deep lobe origin (warthin and pleomorphic adenoma) in 6 patients, a minor cyst of salivary gland origin in 1 patient, a branchial cleft cyst in 1 patient, lipoma in 1 patient, and lymphadenitis in 1 patient. In the prestyloid region, the radiological and specimen diagnoses were compatible except for the patient with radiological prediagnosis of warthin's tumor, and specimen diagnosis of low grade acinic cell tumor. In this patient's case, frozen sections were taken intra-operatively; and total parotidectomy was performed since it could not be differentiated whether it is benign or malignant. No further treatment was applied due to negative surgical margins and the absence of vascular and lymphatic involvement; and no recurrence was observed during the 2-year follow-up.

FNAB was not applied to patients who were considered paraganglioma due to the hyper-vascular nature of the mass. In these patients, specimen results and imaging results were compatible, and no unexpected results were encountered. While the results of the specimens were consistent with FNAB in 11 of the 13 patients, the results of the specimen were reported as malignant, although the FNAB was benign in 1 patients. In 1 patient whose imaging results were benign, FNAB results were reported as nondiagnos-

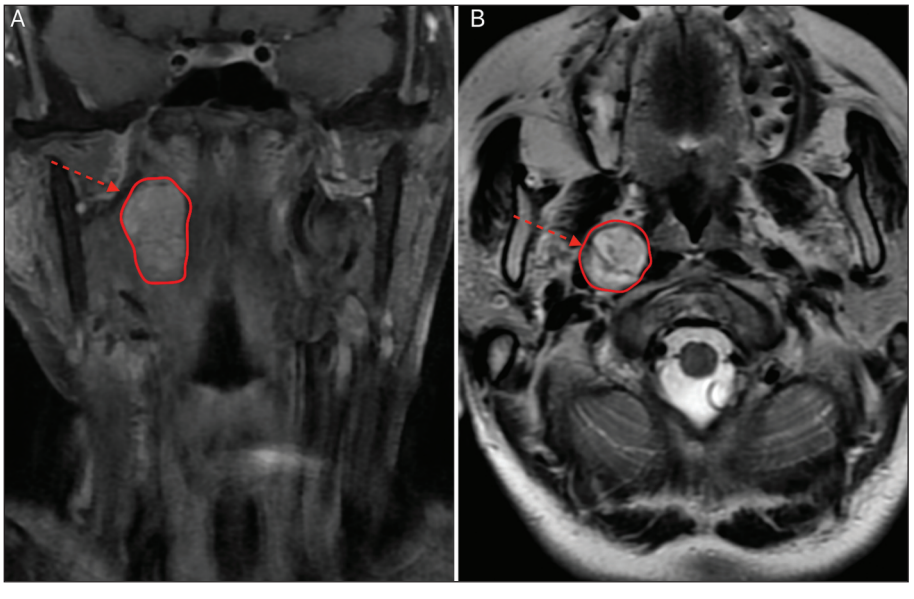

FIGURE 1: Coronal and axial view of the post-styloid parapharyngeal mass. A) Coronal fat suppressed TSE T1 weighted image of parapharyngeal mass; B) Axial fat suppressed TSE T2 weighted image with lobulated margins.

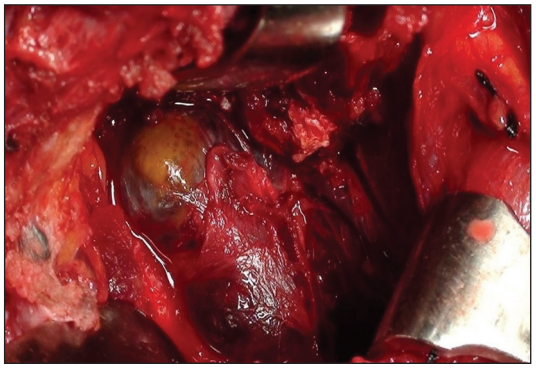

FIGURE 2: The intra-operative image of the papillary thyroid carcinoma metastasis.

tic. The specimen result of this patient was observed in benign character in accordance with the imaging.

In 2 of the 20 patients included in our study, although the imaging or FNAB results were benign, the specimen result was reported as malignant. This fallibility should be kept in mind in the treatment plan of PPS benign tumors.

DISCUSSION

The PPS is an anatomically and functionally complex part of the neck. The fact that the PPS is surrounded by muscles, the mandible, and the parotid gland makes the examination of the tumors in this region difficult; in other words, it creates a difficult region to reach or enter for the clinician. Because of the difficulties in reaching this region, MRI and CT are milestones in initial evaluation of PPS tumors.[4-6]

With MRI and CT scanning, the goal is to determine the tumor's localization, anatomic structure that it originates from, its malignant and benign features, and in the light of all mentioned above, to make the differential diagnosis.[6] In that, the shifting direction of the greater vascular structures and the adipose tissue, which is predominant in the PPS, the vascularization of the tumor, the characteristics and degree of contrast uptake are all important markers in imaging.[5]

In this study, %80 of the radiological prediagnoses were confirmed with final histopathological diagnoses; apart from two patients operated as a result of preoperative radiological assessment, who were considered to have primary benign PPS tumors. The patient whose final histopathological diagnosis came out as metastatic papillary thyroid carcinoma was radiologically misdiagnosed as cystic schwannoma because of the solid-cystic appearance and hyper-vascular features. As a result, the patient was operated with an incorrect diagnosis and the surgical plan lacked the surgical treatment of the thyroid gland and the neck apart from the primary excision of the mass.

Papillary thyroid cancer metastasis may present characteristic imaging features like cystic appearance and punctuate calcifications. The reason of the cystic appearance is the tendency of the thyroid carcinoma to produce colloidal material (thyroglobulin), and the existence of spontaneous intralesional hemorrhages. The existence of spontaneous intralesional hemorrhages causes them to be evaluated as vascularized tumors. Punctate calcifications have been shown only in a few lymph node metastases. While it is easy to identify these with CT, it is difficult to do so with MRI.[8] In the differential diagnosis of a cystic tumor in the post-styloid area; cystic schwannomas, neurofibromas, inflammatory lymphadenopathies, necrotic nodal metastases, lymphomas and cystic hygromas should be considered.[8]

The use of FNAB technique is limited due to the region-specific difficulties. The PPS is a region that can harbor tumors of great variability and number, where more than 70 histologically different tumors can be originated.[9] The difficulties in reaching deeply located tumors, the high frequency of hyper-vascular tumors and the existence of vital structures that may be harmed are the other reasons that restrict the use of the in addition. The high ratio of nondiagnostic samples (the lack of cellular material, blood aspirates) is another factor that prevents obtaining an accurate diagnosis.[1,5]

Although the diagnoses of PPS tumors are generally based on final histopathological reports, there are some studies about the use of FNAB in preoperative diagnosis of these lesions. Only in few of those both surgery and imaging techniques were evaluated in order to confirm the tumor. Mondal and Raychoudhuri reported the reliability of per-oral FNAB as %88.2 in a study performed on a mixed group of 63 patients who had malignant-benign tumors and in-

flammatory lesions in PPS. In this study, imaging was not used to confirm the location of the lesion.[10] In a study group which consisted of 21 patients with primary benign PPS tumors, Caldarelli et al. performed FNAB only in 5 pre-styloid tumor cases after imaging. The authors reported that they could not perform FNAB in post-styloid area tumors because of major risks and nondiagnostic samples.[11] In a study performed by Arnoson et al. on 27 patients whose benign-malignant PPS tumors were confirmed with both surgery and imaging techniques, specific diagnosis were only obtained from 36% of all FNAB samples. In this study, the reliability of FNAB was reported as %92 in the diagnosis of positive and negative malignancy, and nondiagnostic sample rate was reported as %31.[12]

In our study, FNAB was performed in all patients could reached to mass with FNAB and without vascular lesions. Compared to postoperative histopathological diagnosis, the competence of FNAB was determined in 11 patients (%84.6), in our study for determining the absolute diagnosis. Nondiagnostic results were observed in 1 patient. In 1 patient, conflicting results obtained from imaging techniques and FNAB, and being unable to differentiate between benign and malignant features in frozen sections during surgery have strengthened the possibility of malignant tumor. Consequently, total paratidectomy was performed. The accurate diagnosis of the patient could only be obtained from the postoperative histopathological examination.

While acinic cell carcinoma was thought to be a benign tumor in the past, it was considered to be malignant with understanding tumor's metastatic ability and high local recurrence rate. Because of low frequency, poor malignant behavior potential and the fact that it has no specific characteristics, FNAB and imaging have low sensitivity value in pre-operative diagnosis. It is not uncommon that these tumors are misdiagnosed as pleomorphic adenoma or as Whartin's tumor.[13]

CONCLUSION

Although expressing an optimal opinion is difficult in our study due to the limited number of patients, it can be suggested that PPS benign tumors can be widely recognized by imaging methods and FNAB. However, it should be kept in mind that the possibility of not being able to eliminate malignancy. Otherwise, surgical approach and treatment modality may be significantly affected.

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During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Sevim Aslan, Münir Demirci, Zeynep Kızılkaya Kaptan;* ***Design:*** *Sevim Aslan;* ***Control/Supervision:*** *Münir Demirci;* ***Data Collection and/or Processing:*** *Sevim Aslan, Hasan Yiğit, Hatice Ünverdi, Burak Numan Uğurlu;* ***Analysis and/or Interpretation:*** *Sevim Aslan, Zeynep Kızılkaya Kaptan;* ***Literature Review:*** *Sevim Aslan, Burak Numan Uğurlu;* ***Writing the Article:*** *Sevim Aslan, Burak Numan Uğurlu;* ***Critical Review:*** *Münir Demirci;* ***References and Fundings:*** *Hatice Ünverdi, Hasan Yiğit;* ***Materials:*** *Sevim Aslan.*

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