

Neurogenic Tumors of the Neck: A 20 Year Review

Boynun Nörojenik Tümörleri: 20 Yıllık Seri

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ABSTRACT Objective: To investigate the clinical presentation, diagnostic strategy, treatment approach, and postoperative morbidity of neurogenic tumors in the neck region, which are rarely observed and cannot be easily separated from other masses of this region. **Material and Methods:** A retrospective analysis of the medical data of patients with histopathologically confirmed neurogenic tumors who underwent surgery at the otorhinolaryngology department over the 20 years from 2000 to 2019. **Results:** Twenty-one patients were evaluated. Fifteen (71%) of them were women and 6 (29%) were men, with ages of 0-75 years. Out of 21 cases, 19 (90%) were benign, while 2 (10%) cases had malignant histology. Of the patients, 14 (67%) were diagnosed with peripheral nerve sheath tumors, 5 (24%) with ganglion cell tumors, and 2 (9%) with paraganglion cell tumors. The most common presentation symptom was neck swelling. Other symptoms included pain and numbness in the arm, dyspnea, dysphagia, and snoring. Postoperative morbidities included Horner's syndrome, vocal cord palsy, and motor weakness of the upper limb. Fine-needle aspiration cytology was not diagnostic in any of the patients who underwent the procedure; core needle biopsy was diagnostic in all patients who underwent. **Conclusion:** Neurogenic tumors located in the neck are extremely rare. Differential diagnoses of these tumors are critical to provide patients with information about possible postoperative neurological deficits and other morbidities. Neither imaging methods nor preoperative biopsies can provide clear information about the definitive diagnosis.

Keywords: Neck; neurogenic tumor; neurinoma; schwannoma

ÖZET Amaç: Bu çalışmanın amacı, boyun bölgesinde nadir görülen ve bu bölgedeki diğer kitlelerden kolaylıkla ayrılamayan nörojenik tümörlerin klinik tablosunu, tanı stratejisini, tedavi yaklaşımını ve postoperatif morbiditesini araştırmaktır. **Gereç ve Yöntemler:** 2000 yılından 2019 yılına kadar 20 yıl boyunca kulak-burun-boğaz bölümünde ameliyat edilen, histopatolojik olarak doğrulanmış nörojenik tümörleri olan hastaların tıbbi verilerinin retrospektif analizi yapıldı. **Bulgular:** Toplamda 21 hasta değerlendirildi. Yaşları 0-75 arasında olan hastaların 15'i (%71) kadın, 6'sı (%29) erkekti. Yirmi bir olgunun 19'u (%90) benign, 2'si (%10) ise malign histolojiye sahipti. Hastaların 14'üne (%67) periferik sinir kılıfı tümörü, 5'ine (%24) ganglion hücreli tümör, 2'sine (%9) paraganglion hücreli tümör tanısı konuldu. En sık başvuru semptomu boyunda şişlikti. Diğer semptomlar; kolda ağrı ve uyuşma, nefes darlığı, yutma güçlüğü ve horlamaydı. Ameliyat sonrası morbiditeler arasında Horner sendromu, vokal kord paralizisi ve üst ekstremitelerde motor güçsüzlük vardı. İnce iğne aspirasyon sitolojisi uygulanan hastaların hiçbirinde tanısal değildi, kalın iğne biyopsisi yapılan hastaların tamamında tanı koydurucuydu. **Sonuç:** Boyunda yerleşen nörojenik tümörler son derece nadirdir. Bu tümörlerin ayırıcı tanısı hastalara postoperatif olası nörolojik defisitler ve diğer morbiditeler hakkında bilgi verilmesi açısından oldukça önemlidir. Ne görüntüleme yöntemleri ne de ameliyat öncesi biyopsiler kesin tanı konusunda net bilgi verememektedir.

Anahtar Kelimeler: Boyun; nörojenik tümör; nörinoma; şivannoma

Neurogenic neoplasms represent approximately 9-10% of all soft tissue neoplasms, and nearly 14%-15% of them are located in the head and neck region.^{1,2} These tumors, which develop from the

embryonic neural crest, can be classified into 3 groups: peripheral nerves-sheath tumors, ganglion cell tumors, and paraganglion cell tumors, depending on the cells from which they originate.³

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The presenting symptoms of neurogenic neoplasms can vary according to the subtype, size, and location of the tumor. Palpable mass in the neck is the most common presentation of neurogenic tumors of this region.⁴ Dysphagia, dyspnea, cranial nerve palsy, and extremity neurological deficits are other symptoms that can be observed. Permanent or temporary neurological deficit may develop not only as a presenting symptom but also because of surgical treatment.

It is important to distinguish neurogenic tumors from each other and other neoplasms of the neck. But it is not always easy. Preoperative biopsy and imaging studies may be useful in the differential diagnosis of neurogenic tumors. Knowing the tumors in which region cause which symptoms can guide the surgeon in terms of diagnosis, and it is important to know the postoperative problems that may be encountered in terms of informing patients.

This retrospective study was performed to investigate the clinical presentation, diagnostic method, treatment approach, and postoperative management of neurogenic tumors in the neck region, which are rarely observed and cannot be easily separated from other masses of this region.

MATERIAL AND METHODS

This study was approved by Baskent University Institutional Review Board (Date: March 30, 2021, no KA21/172), and written informed consent for surgery was obtained from all patients. This study was conducted in accordance with the Declaration of Helsinki of the World Medical Association. After approval from the Institutional Ethics Committee, we performed a retrospective analysis of the medical data of patients with histopathologically confirmed neurogenic tumors who underwent surgery at the otorhinolaryngology department over the 20 years from 2000 to 2019.

We excluded patients with intracranially located neurogenic tumors. Although acoustic neuromas, esthesioneuroblastomas, and neurogenic tumors of the paranasal sinus fall within the scope of otorhinolaryngology, they have different presentation symptoms and specific diagnostic and therapeutic

problems; therefore, they will not be discussed in the present study. We included only patients with neurogenic tumors located in the neck region.

The data of the patients' age, gender, and presenting symptoms were collected from the hospital archive. Tumor pathology, localization, size, and if it can be determined, the involved nerve were analyzed. If present, neurological deficits at presentation and postoperative neurological deficits were also analyzed. All patients underwent at least one imaging method, and preoperative biopsy was performed in some patients. The role of imaging methods and preoperative biopsy in the diagnosis was also examined.

Tumors were grouped into three different localizations: suprahyoid-parapharyngeal region, carotid bifurcation level, and infrahyoid-supraclavicular region to determine which localization caused which symptoms more. In tumors localized in more than one region, the area where the majority of the mass was found was accepted as the main localization. In addition to general evaluations, patients with specific conditions related to diagnosis and treatment were mentioned separately and discussed in light of the literature.

RESULTS

General characteristics of all patients: Twenty-one patients with histopathologically confirmed neurogenic tumors located in the neck region were evaluated. Fifteen (71%) of them were women and 6 (29%) were men, with ages of 0-75 years (mean 34 yr). Out of 21 cases, 19 (90%) were benign, whereas only 2 (10%) cases had malignant histology. When classified according to embryological origin, 14 (67%) were diagnosed with peripheral nerve sheath tumors [11 schwannomas, 2 neurofibromas, 1 malignant peripheral nerve sheath tumor (MPNST)], 5 (24%) with ganglion cell tumors (4 ganglioneuromas, 1 neuroblastoma), and 2 (9%) with paraganglion cell tumors (2 carotid body tumors). The characteristics of all the patients are shown in Table 1.

Localization of tumors: The tumor was located in the parapharyngeal-suprahyoid region in 4 (19%) patients, in the carotid bifurcation level in 12 (57%) patients, and in the infrahyoid-supraclavicular region

TABLE 1: Properties of 21 patients and tumors.

No	Sex	Age (year)	Side	Size (mm)	Morphology	Nerve of origin	Presenting symptom	Pre-op biopsy	Localization	Embol embolization	Comp complication
1	F	48	Right	34x27	Schwannoma	Hypoglossus	Dysphagia	NP	SH-PP	Yes	
2	F	21	Left	30x30	Schwannoma	Brachial plexus	Neck swelling w/ UL pain, numbness	NP	IH-SC		Dys of UL
3	F	25	Left	40x40	MPNST	?	Neck swelling w/ UL pain, numbness	CNB (Diagnostic)	IH-SC		
4	M	0	Right	80x65	Neuroblastoma	Cer symp ch	Congenital neck mass	NP	Entire neck		
5	F	33	Left	25x17	Carotid body	Paraganglionic cell	Asymptomatic	NP	CBL	Yes	
6	F	1	Left	42x38	Cellular schwannoma	?	Stroring	Punch biopsy (wrong diagnosis)			SH-PP
7	M	19	Left	90x55	Ganglioneuroma	Cer symp ch	Neck swelling w/ dyspnea	CNB (Diagnostic)	SH-PP		
8	F	6	Right	30x30	Ganglioneuroma	Cer symp ch	Neck swelling	NP	CBL		Homer's
9	M	23	Right	65x40	Neurofibroma	Cer sen	Neck swelling	NP	IH-SC		
10	F	13	Right	45x30	Neurofibroma	Vagus	Neck swelling	NP	CBL		VC palsy
11	F	75	Left	40x30	Schwannoma	Vagus	Neck swelling	CNB (Diagnostic)	SH-PP		VC palsy
12	M	66	Right	20x20	Schwannoma	Brachial plexus	Neck swelling	FNAC (Nondiagnostic)	CBL		Dys of UL
13	F	47	Left	45x20	Schwannoma	Cer sen	Neck swelling	FNAC (Nondiagnostic)	CBL		
14	M	25	Left	40x30	Schwannoma	Vagus	Neck swelling	NP	CBL		YesHomer's
15	F	38	Left	80x40	Schwannoma	Cer sen	Neck swelling w/ UL pain, numbness	FNAC (Nondiagnostic)	CNB (Diagnostic)		CBL
16	F	74	Left	73x55	Ganglioneuroma	Cer symp ch	Neck swelling	NP	CBL		
17	M	71	Right	24x18	Carotid body	Paraganglionic cell	Neck swelling	NP	CBL	Yes	
18	F	27	Right	30x25	Schwannoma	Brachial plexus	Neck swelling	NP	IH-SC		
19	F	45	Right	55x30	Schwannoma	Vagus	Neck swelling	FNAC (Nondiagnostic)	CBL		
20	F	17	Right	85x50	Schwannoma	Cer sen	Neck swelling	NP	CBL		
21	F	39	Left	120x100	Ganglioneuroma	Cer symp ch	Neck swelling	NP	CBL		

MPNST: Malignant peripheral nerve sheath tumor; UL: Upper limb; w/ with; NP: Not performed; CNB: Core needle biopsy; FNAC: Fine needle aspiration cytology; cer symp ch cervical sympathetic chain; SH-PP: Suprahoid-parapharyngeal region; IH-SC: Infrahoid-supradavicular region; CBL: Carotid bifurcation level; VC: Vocal cord, cer sen cervical sensitive; Dys: Dysfunction.

in 4 (19%) patients. In a patient with neonatal neuroblastoma, the mass extended from the skull base to the clavicle and covered the entire neck.

Clinical presentation: Nineteen patients (90%) had at least one clinical symptom at admission, one had an incidental diagnosis, and one was diagnosed by prenatal ultrasonography. Seventeen patients (81%) presented with neck swelling. Of the patients with neck swelling, 13 (76%) had isolated swelling, 3 (18%) were accompanied by pain and numbness in the arm, and 1 (6%) was accompanied by dyspnea. One patient had only dysphagia and one patient had only snoring. In a patient with no symptoms, the mass was incidentally detected by an imaging method performed for another reason.

On physical examination, displacement of the pharynx mucosa or ipsilateral tonsil toward the lumen was observed in 4 (19%) patients. One of these patients was a patient with isolated dysphagia, one was a patient with isolated snoring, one was a patient with dyspnea accompanied by swelling in the neck, and one was a patient with isolated neck swelling. In all of these patients, the mass was located in the parapharyngeal suprahyoid region.

In 2 of the 3 patients who had pain and numbness in the arm, the mass was located in the infrahyoid supraclavicular region. The other patient with this symptom had a huge mass (8x4 cm) located at the carotid bifurcation level.

Physical examination findings in 4 patients provided information about the mobilization of the mass. Three of them did not move in the vertical direction and one was mobile in all directions. While all masses that did not move vertically were vagal schwannoma, the mobile mass was a schwannoma originating from the cervical sensitive nerve.

The imaging study: At least one imaging study was conducted in all patients. In 13 patients magnetic resonance imaging (MRI) were performed and in 11 patients computed tomography (CT) were performed (both MRI and CT performed in 3 patients). On MRI, most tumors display low-to-intermediate signal intensity on T1WI and heterogeneous hyperintensity on T2WI. On CT, tumors showed variable attenuation

patterns (hypo-, iso-, or hyper attenuated) with different patterns of contrast enhancement.

Preoperative biopsy: Preoperative diagnostic biopsy was performed in eight patients [3 fine-needle aspiration cytology (FNAC), 3 core-needle biopsies (CNB), 1 FNAC followed CNB, 1 punch biopsy]. The results of FNAC for all 4 patients were non-specific. The results of all patients who underwent CNB were the same as those for postoperative definitive diagnosis.

A 9-month-old female patient who complained of snoring since birth underwent a punch biopsy under general anesthesia from the mass displaced the pharynx wall and left tonsil medially. Surgical excision was recommended to the patient because the pathology result was a low-grade MPNST, but her family refused. Because the patient who received chemotherapy did not benefit from the treatment, surgical excision was performed 2 months later. Interestingly, the postoperative definitive pathologic diagnosis was cellular schwannoma.

Preoperative embolization: Preoperative embolization was performed in 4 patients. Two of them were patients with carotid body tumors. One of the other patients had a pulsatile mass in the neck at the level of the carotid bifurcation that did not move in the vertical direction. The mass with intense contrast enhancement on CT and MRI was considered to be radiologically compatible with the carotid body tumor. Successful embolization was performed for the mass fed by the occipital and pharyngeal branches of the external carotid artery. Intraoperatively, it was seen that the mass originated from the vagus, and the definitive pathological diagnosis was schwannoma. The other patient had isolated dysphagia, and a pulsatile mass that pushed the tonsil and pharynx mucosa to the midline was detected on physical examination. Preoperative embolization was planned for the mass that was radiologically thought to be glomus. At the beginning of the embolization, the patient developed dysarthria, suggesting vertebrobasilar embolism, and the procedure was terminated. The patient was taken to the intensive care unit and died on the fifth day. The mass excised during autopsy was a schwannoma originating from the hypoglossus.

Postoperative morbidity: Two patients developed Horner's syndrome and one recovered over a 6-month period. Vocal cord palsy occurred in 2 patients. Two patients developed motor weakness in the upper limb, and both recovered over time with physical therapy.

Pathological analysis: Out of 21 cases, only 2 (10%) cases had malignant histology. A patient with malignant histology (MPNST) was lost to follow-up in the postoperative period. In the other patient, a giant mass was detected on the neck by prenatal ultrasonography. Considering that the mass could obstruct the airway by compression, we decided to perform the ex utero intrapartum treatment procedure. The patient was intubated before cutting the umbilical cord, after which tomography was performed and the mass was removed. The pathology result was compatible with neuroblastoma. The patient had no postoperative morbidity or recurrence in the second postoperative year.

DISCUSSION

Tumors arising from peripheral nerves or nerve sheaths, ganglion cells, and paraganglion cells have been classified together under the heading of neurogenic tumors. Of these, peripheral nerves or nerve sheath tumors include neurofibromas and schwannomas; ganglion cell tumors include ganglioneuromas and neuroblastomas; and paraganglion cell tumors include pheochromocytoma and carotid body tumor.

Neurogenic tumors are most commonly located in the posterior mediastinum. Most of the tumors in this area are asymptomatic and are detected incidentally on routine chest X-rays, but this is not the case for neurogenic tumors in the neck region.⁴ Neurogenic tumors in the neck region present with symptoms such as palpable mass, dysphagia, neural deficit, and dyspnea.^{3,5} Of these symptoms, palpable mass is the most common as in our study.

In fact, these symptoms are not symptoms specifically related to neurogenic tumors. These are symptoms encountered in other masses in the neck area. The main issue is not which symptoms are encountered in neurogenic tumors, but rather neuro-

genic tumors in which localization caused which symptoms more. In most of our patients with complaints of pain and numbness in the arm, the mass was located in the infrahyoid-supraclavicular region. In all of our patients with upper aerodigestive tract symptoms, the mass was located in the parapharyngeal-suprahyoid region. While one patient had only neck swelling at the first admission, a complaint of difficulty in breathing was added 2 months later, and the patient had to be operated without wasting too much time. The treatment of benign neurogenic tumors is surgery; however, patients without obvious complaints can be followed up. It will be useful to inquire about complaints such as difficulty in breathing or swallowing in patients with tumors located in the parapharyngeal-suprahyoid region and complaints such as pain and numbness in the upper extremity in patients with tumors located in the infrahyoid-supraclavicular region at follow-up.

Although the size, localization, and relationship with surrounding structures of neurogenic tumors can be evaluated by imaging methods, it is not sufficient to distinguish tumors in this group from each other.⁶ It is not surprising that neurogenic tumors, which are difficult to distinguish from each other even pathologically, cannot be distinguished from each other by imaging methods because of their many common features. On MRI, neurogenic tumors show hypointense to isointense signals on T1WI and heterogeneously hyperintense signals on T2WI with variable contrast enhancement. CT imaging shows variable attenuation patterns (hypo-, iso-, or hyperattenuated) with different patterns of contrast enhancement. According to the study of Matsumine et al., intratumoral lobulation and the presence of T1-hyperintense areas on MRI invoke the possibility of a malignant neurogenic tumor.⁷ Imaging methods are more helpful in distinguishing malignant and benign neurogenic tumors from each other.

It is important to distinguish carotid body tumors from other neurogenic tumors because of the high risk of bleeding. But it is not always easy. Although classically carotid body tumors are known as pulsatile masses that can be moved from side to side but not in a vertical direction (fontaine sign), these characteristics can also be found in other neurogenic tumors.

Vagal or cervical sympathetic chain schwannomas located in the carotid neighborhood can be mixed with carotid body tumors because they do not move in the vertical direction, and the pulsation reflected from the carotid may be thought to be caused by the tumor during examination.^{8,9} In our study, 3 of 4 patients diagnosed with vagal schwannoma had no movement in the vertical direction, whereas 1 patient had no information about mobilization. Schwannomas are sometimes indistinguishable from carotid body tumors using imaging methods because of their hypervascular nature.¹⁰ The characteristic “salt and pepper” appearance on T1-weighted MRI of carotid body tumors can also be seen in some hypervascular schwannomas.¹¹ In two of our cases, embolization decision was made with suspicion of carotid body tumor because of physical examination and imaging methods. In one of them, after successful embolization and surgery, it was understood that the mass was a vagal schwannoma. In the other patient, complication developed during embolization and the patient died. The pathology of the mass excised during the postmortem autopsy was reported as schwannoma.

Similar to other neck masses, preoperative biopsy may be useful in the diagnosis of neurogenic tumors. Ahn et al. investigated the diagnostic usefulness of CNB and compared this technique with FNAC.¹² According to their study, the diagnostic accuracy of CNB was 96.6% and that of FNAC was 19.2%. In our patients, FNAC results were not diagnostic in any patient, whereas CNB was consistent with definitive diagnosis in all patients. It is important to distinguish between malignant and benign neurogenic tumors because of differences in treatment approaches. While treatment options such as chemotherapy are important in malignant tumors, surgical excision is sufficient in benign tumors. However, it is not always possible in some cases to achieve a definitive diagnosis until the tumor has been excised. Cellular schwannoma is a diagnostically challenging and unusual variant of benign schwannoma. Because of its high cellularity, nuclear pleomorphism, and increased mitotic activity, it may be mistaken for MPNST, as seen in this study. The presence of a well-defined peritu-

moral capsule, subcapsular lymphocytes, and macrophage-rich infiltrates favor the diagnosis of cellular schwannoma, whereas the presence of perivascular hypercellularity, tumor herniation into vascular lumens, and necrosis favor MPNST.¹³ In addition to these factors, immunohistochemistry is useful in the differential diagnosis of MPNST and cellular schwannoma.

Neurological deficits and pain can be seen both as a presentation symptom and as postoperative sequelae. Preoperatively, this may be due to the nerve from which the tumor originates or to the neighboring nerve from which the mass presses, whereas postoperatively, this may be due to damage to the nerve from which the tumor originates during surgery or damage to the neighboring nerves because of traction during surgery.¹⁰ Preoperative neurological deficits and pain are known to be more common in malignancies.^{3,14} In our series, there were 2 malignant pathologies, one of which was congenital neuroblastoma, and the surgery was performed immediately after birth; therefore, the pre-operative neurological examination could not be evaluated, while the other MPNST patient had numbness and pain in his arm during application. Of the 3 patients with neurological complaints, the other 2 had schwannomas originating from the brachial plexus.

CONCLUSION

In conclusion, neurogenic tumors located in the neck are extremely rare. Differential diagnoses of these tumors are critical to provide patients with information about possible postoperative neurological deficits and other morbidities. Neither imaging methods nor preoperative biopsies can provide clear information about the definitive diagnosis. Therefore, one should be prepared for different things intraoperatively, and while informing the patients, it should be clearly explained that a pathology different from the pre-operative predictions may be encountered.

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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: Ömer Vural, Cem Özer; **Design:** Ömer Vural, Cem Özer; **Control/Supervision:** Cem Özer, Fulya Özer, İsmail Yılmaz; **Data Collection and/or Processing:** Ömer Vural, Fulya Özer; **Analysis and/or Interpretation:** Cem Özer, İsmail Yılmaz; **Literature Review:** Ömer Vural, Cem Özer; **Writing the Article:** Ömer Vural, Cem Özer, Fulya Özer, İsmail Yılmaz; **Critical Review:** İsmail Yılmaz, Fulya Özer; **References and Fundings:** Ömer Vural, Cem Özer; **Materials:** Ömer Vural, Cem Özer.

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