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Thoracic neurogenic tumors: A clinicopathologic evaluation of 42 cases

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Abstract

Background & Objective: Neurogenic tumors typically originate from the peripheral nerves, paraganglionic nerves, or the autonomic nervous system. Tumors arising from peripheral nerves are classified as schwannoma, neurofibroma, and malignant peripheral nerve sheath tumors while tumors arising from the sympathetic chain ganglion cells are classified as ganglioneuroma, ganglioneuroblastoma, and neuroblastoma. Tumors arising from the parasympathetic chain ganglion cells are classified as paraganglioma. Neurogenic tumors of the thorax are uncommon and originate from large airways, lungs, the mediastinum, or the chest wall. In this study, we report the clinical and histopathological features of 42 patients diagnosed with neurogenic tumors of the thorax. *Methods:* A retrospective review of the medical records of 42 patients diagnosed with intrathoracic neurogenic tumors and treated in Uludag University between 2002 and 2012 was conducted. All pathology specimens were examined by a pathologist experienced in the examination of soft tissue tumors. The patients were evaluated according to age, gender, location and histological characteristics of the tumor. *Results:* The study group included 42 patients diagnosed thoracic neurogenic tumors, including 31 female (74%) and 11 male (26%). The sex ratio was 2.8 (female/male) and the mean age of the study population was 38.52 years. The age of patients ranged from 3 to 73 years. The neurogenic tumor was located in the posterior mediastinum in 31(74%) patients, anterior mediastinum in 2 (5%) patients, and in the chest wall in 9 (21%) patients. The origin of the neurogenic tumor was the peripheral nerve sheath in 31 (74%) patients, and the ganglion cells in 10 (24%) patients, and the paraganglion system in 1 (2%) patient. The study group also included 20 (48%) patients diagnosed with schwannoma, 6 (14%) patients diagnosed with malignant peripheral nerve sheath tumor , 5 (12%) patients diagnosed with neurofibroma , 5 (12%) patients diagnosed with ganglioneuroma, 4 (10%) patients diagnosed with neuroblastoma , 1 (2%) patient diagnosed with ganglioneuroblastoma and 1 (2%) patient diagnosed with paraganglioma. Our study group comprised 36 adults and 6 children. Of the adult patients, 20 (55%) had schwannomas, 6 (17%) malignant peripheral nerve sheath tumor, 5 (14%) neurofibroma, 4 (11%) ganglioneuromas, and 1 (3%) paraganglioma. Four of the six children (66%) included in our study group were diagnosed with neuroblastoma, 1 (17%) child was diagnosed with ganglioneuroma, and 1 (17%) child was diagnosed with ganglioneuroblastoma. The malignancy rate was 83% in children and 17% in adults.

Conclusion: Age is an important clinical parameter in terms of histological type and malignancy rate. In our study group, malignancy rate in children was much higher than adults. The most common thoracic neurogenic tumor in adults and children was schwannoma and neuroblastoma, respectively.

INTRODUCTION

Neurogenic tumors typically originate from the peripheral nerves, paraganglionic nerves, or the autonomic nervous system. Tumors arising from peripheral nerves are classified as schwannoma, neurofibroma, and malignant peripheral nerve sheath tumors (MPNST) while tumors arising from the sympathetic chain ganglion cells are classified as ganglioneuroma, ganglioneuroblastoma, and neuroblastoma. Tumors arising from the parasympathetic chain ganglion cells are classified as paraganglioma.[1] Neurogenic tumors of the thorax are uncommon and originate from large airways, lungs, the mediastinum, or the chest wall.[2] Neurogenic tumors represent 15-25% of mediastinal tumors, generally occurring in the posterior paravertebral area.[2]

In this study, we report the clinical and histopathological features of 42 patients diagnosed with neurogenic tumors of the thorax.

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METHODS

A retrospective review of the medical records of 42 patients diagnosed with intrathoracic neurogenic tumors and treated in Uludag University between 2002 and 2012 was conducted. All pathology specimens were examined by a pathologist experienced in the examination of soft tissue tumors. The patients were evaluated according to age, gender, location and histological characteristics of the tumor.

The study protocol was reviewed and approved by the Ethics Committee of university. An informed consent form for the use of pathological specimens for scientific purposes is provided to patients as part of the standard procedure prior to the pathological examination.

RESULTS

The study group included 42 patients diagnosed thoracic neurogenic tumors, including 31 female (74%) and 11 male (26%). The sex ratio was 2.8 (female/male) and the mean age of the study population was 38.52 years. The age of patients ranged from 3 to 73 years.

The neurogenic tumor was located in the posterior mediastinum in 31 (74%) patients, anterior mediastinum in 2 (5%) patients, and in the chest wall in 9 (21%) patients.

The origin of the neurogenic tumor was the peripheral nerve sheath in 31 (74%) patients, and the ganglion cells in 10 (24%) patients, and the paraganglion system in 1 (2%) patient. The study group also included 20 (48%) patients diagnosed with schwannoma (Figure 1A), 6 (14%) patients diagnosed with MPSNT (Figure 1B), 5 (12%) patients diagnosed with neurofibroma, 5 (12%) patients diagnosed with ganglioneuroma, 4 (10%) patients diagnosed with neuroblastoma, 1 (2%) patient diagnosed with ganglioneuroblastoma, and 1 (2%) patient diagnosed with paraganglioma.

The group of 20 patients diagnosed with schwannoma consisted of 6 men and 14 women. Four of 6 patients (67%) diagnosed with MPNST and four of five patients (80%) diagnosed with neuroblastoma were female. The mean age of patients suffering from peripheral nerve sheath tumor was 43.54 years and the mean age of patients diagnosed with tumors of neural origin was 19.8 years. The mean age of patients diagnosed with schwannoma was 47.75 years, the mean age of patients diagnosed with neurofibroma was 34 years, the mean age of patients diagnosed with MPNST was 37.5 years, and the mean age of patients diagnosed with neuroblastoma was 5.8 years. The age, sex and location distribution according to histological subtypes is shown in Table 1.

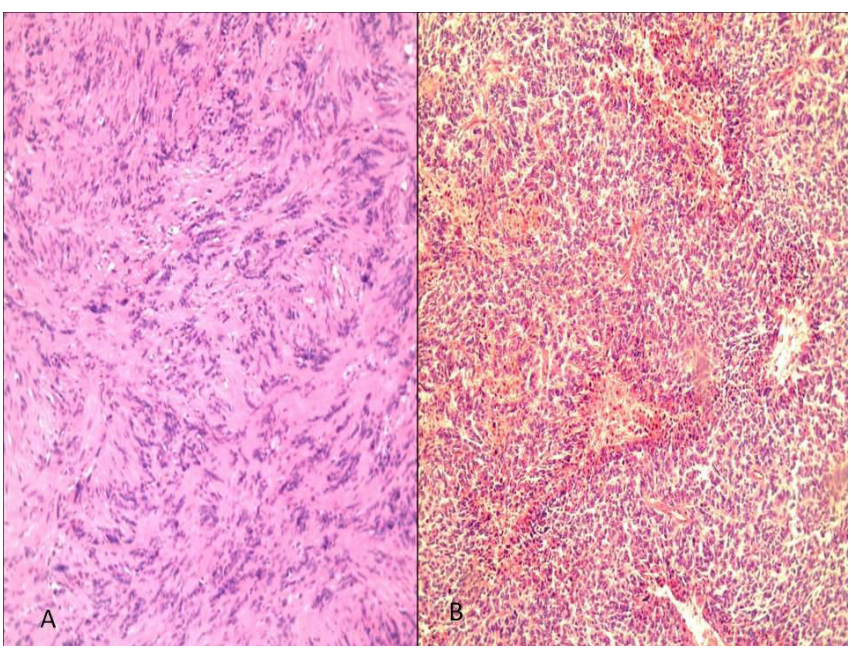

Figure 1A. Schwannoma; Wavy nuclei are dense in hypercellular areas (Anthony A) and sparse in hypocellular areas (Anthony B). (Hematoxylin-Eosin staining X200). 1B. Malignant peripheral nerve sheath tumor; Fascicles by the spindle cells, and the presence of bizarre cells and necrotic tissue. (Hematoxylin-Eosin staining X200)

Table 1: The age, sex and location distribution according to histological subtypes.

Diagnosis	Number of cases (%)	Age: Range (mean)	Sex: Female/male	The most common location
Schwannoma	20 (48%)	21-70 (47.75)	14/6	Posterior mediastinum (13/20, 65%)
MPNST	6 (14%)	24-53 (37.50)	4/2	Posterior mediastinum (5/6, 83%)
Neurofibroma	5 (12%)	21-57 (34.00)	3/2	Posterior mediastinum (3/5, 60%)
Ganglioneuroma	5 (12%)	9-73 (35.00)	5/0	Posterior mediastinum (5/5, 100%)
Neuroblastoma	4 (10%)	3-7 (5)	3/1	Posterior mediastinum (4/4, 100%)
Ganglioneuroblastoma	1 (2%)	3	female	Chest wall
Paraganglioma	1 (2%)	60	female	Posterior mediastinum

MPNST: malign peripheral nerve sheat tumor

Three patients diagnosed with schwannoma, neurofibroma and MPNST were diagnosed with neurofibromatosis type 1 (Table 1). These 3 patients (2 male and 1 female) had multiple cutaneous neurofibromas and café-au-lait spots.

Our study group comprised 36 adults and 6 children. Of the adult patients, 20 (55%) had schwannomas, 6 (17%) MPNSTs, 5 (14%) neurofibromas, 4 (11%) ganglioneuromas, and 1 (3%) paraganglioma. Four of the 6 children (66%) included in our study group were diagnosed with neuroblastoma, 1 (17%) child was diagnosed with ganglioneuroma, and 1 (17%) child was diagnosed with ganglioneuroblastoma. The malignancy rate was 83% in children and 17% in adults. Schwannoma was the most common tumor in adult patients (20 cases, 48%).

DISCUSSION

Thoracic neurogenic tumors are generally located on the mediastinum or on the chest wall. Neurogenic tumors originating in the lungs are extremely rare. A study conducted by Takeda *et al*.[3] included 146 patients diagnosed with thoracic neurogenic tumor. The location of the neurogenic tumor was the posterior mediastinum in 136 (93%) of these patients. In our study, 31 patients (74%) had a tumor originating in posterior mediastinum, and 9 (21%) patients exhibited tumors originating in the intercostal nerve of the chest wall. The location was the anterior mediastinum in 2 (5%) patients. None of the patients in our study was diagnosed with neurogenic tumor originating from the lung parenchyma.

The malignancy rate of the thoracic neurogenic tumors is higher in children than adults.[3,4] Topcu *et al*.[4] published a study of 60 patients diagnosed with thoracic neurogenic tumor, reporting that 48 of these patients (80%) had benign tumors while 12 patients (20%) had malignant tumors. The malignancy rate was 61.5% in children and 8.5% in adults (4). Takeda *et al*.[3] have reported that 5.8% of neurogenic tumors occurring in adulthood are malignant, although the proportion of malignancy may be as high as 41.7% in childhood. Further, the malignancy rate was higher in infants and young children, at 100% under 2 years of age, 71% for patients 2–4 years of age, and 16% for those 5–14 years of age. They also reported that nerve sheath tumors were more common in adults (78%) than children (3.3%). Schwannoma was the most common neurogenic tumor seen in adults, and it was not observed in any patients under 15 years of age.[3] In our study group, we observed that the majority of patients had benign tumors (31 cases, 74%) while the minority, 11 cases (26%), had malignant tumors. Our study group comprised 36 adults and 6 children. Of the adult patients, 20 (55%) had schwannomas, 6 (17%) MPNSTs, 5 (14%) neurofibromas, 4 (11%) ganglioneuromas, and 1 (3%) paraganglioma. Four of the 6 children (66%) included in our study group were diagnosed with neuroblastoma, 1 (17%) child

was diagnosed with ganglioneuroma, and 1 (17%) child was diagnosed with ganglioneuroblastoma. The malignancy rate was 83% in children and 17 % in adults. Schwannoma was the most common tumor in adult patients (20 cases, 48%).

Schwannoma is a benign peripheral nerve sheath tumor and is the most common thoracic neurogenic tumor in adults. This type of tumor is typically well-circumscribed and encapsulated with a slow growth profile. Schwannoma exhibits an immunophenotype and ultrastructural features identical to schwann cells. Tumors with wavy nuclei are dense in hypercellular regions (Antony A) and sparse in hypocellular areas (Antony B).[5] The 20 schwannoma patients, including 14 females, included in our study group range in age from 21 to 70 years, and mean age is 47.75 years.

MPNST is a rare malignant tumor of the peripheral nerve sheath. This tumor accounts for 5%–10% of all soft-tissue sarcomas and usually affects adult patients 20–50 years of age. MPNST arises from major nerve trunks such as the paraspinal nerve, sacral plexus, brachial plexus, sciatic nerve, or neurofibroma.[6] Microscopic examination of MPNST reveals the formation of fascicles by the spindle cells, and the presence of bizarre cells and necrotic tissue. MPNST has high mitotic activity.[5] In our study group, 6 (14%) patients were diagnosed with MPNST, 2 males and 4 females. The 6 MPNST patients varied in age from 24 to 53 years old, with a mean age of 37.5 years.

Neurogenic tumors originating from nerve cells are classified as neuroblastoma, ganglioneuroblastoma, or ganglioneuroma. These tumors typically occur in childhood. The characteristic features of neuroblastoma are small, round hyperchromatic nuclei and narrowed cytoplasm. These tumors occur in young children, with an average age of 22 months at diagnosis. Ganglioneuroblastoma consists of neuroblast, ganglion, and intermediary cells. Patients diagnosed with ganglioneuroblastoma are typically less than 10 years old.[5] Four of the 6 children included in our study group were diagnosed with neuroblastoma, one child was diagnosed with ganglioneuroma, and one child was diagnosed with ganglioneuroblastoma.

Ganglioneuroma rarely occurs in the elderly, but is commonly seen in children and young adults.[7] In our study, the mean age of patients diagnosed with ganglioneuroma was 35 years, much older than expected. One of these four patients was 73 years old was and another was 56 years old. Only one published case of ganglioneuroma involved a patient over 70, a female patient reported by Maruyama *et al*.[7] aged 74 years.

Von Recklinghausen (VRH) disease is a rare genetic disorder associated with multiple types of neurogenic tumor. Bıcakcıoglu *et al.*[8] published a report of 149 patient diagnosed with thoracic neurogenic tumors, including seven who were also diagnosed with Von Recklinhausen (VRH) disease. Ribet *et al*.[9] reported the incidence of Von Recklinhausen (VRH) disease as 14%. Five of these patients were diagnosed with neurilemmoma, five were diagnosed with neurofibroma, four were diagnosed with ganglioneuroma, one was diagnosed with ganglioneuroblastoma, and one was diagnosed with malignant schwannoma. Topcu *et al*.[4] observed only 3 patients diagnosed with Von Recklinhausen (VRH) disease out of a cohort of 60 patients. Two of these patients were diagnosed with neurofibroma and one was diagnosed with MPNST. The two patients that had been diagnosed with neurofibroma experienced recurrence of the disease. In our study, only three patients were diagnosed with neurofibromatosis type 1; these patients had disease that was classified as schwannoma, neurofibroma and MPNST.

In conclusion, we report a group of 42 patients diagnosed with and treated for thoracic neurogenic tumor in Uludag University Faculty of Medicine. These patients were evaluated according to their clinical and histopathological features. Thoracic neurogenic tumors were more frequent in women. (F/M: 2.8). The posterior mediastinum was the most common location of tumors. The malignancy rate was 83% in children and 17 % in adults. Age was an important clinical parameter in terms of histological type and malignancy rate. Schwannoma was the most common thoracic neurogenic tumor (20 cases, 48%). The most common thoracic neurogenic tumor in children was neuroblastoma. The malignancy rate was 83% in children and 17% in adults.

DISCLOSURE

Conflict of interest: None

REFERENCES

1. Lee JY, Lee KS, Han J, et al. Spectrum of neurogenic tumors in the thorax: CT and pathologic findings. *J Comput Assist Tomogr* 1999; 23:399-406.
2. Woo OH, Yong HS, Shin BK, Oh YW, Kim HK, Kang EY. Wide spectrum of thoracic neurogenic tumours: a pictorial review of CT and pathological findings. *Br J Radiol* 2008; 81:668-76.

3. Takeda S, Miyoshi S, Minami M, Matsuda H. Intrathoracic neurogenic tumors—50 years' experience in a Japanese institution. *Eur J Cardiothorac Surg* 2004; 26:807-12.
4. Topcu S, Alper A, Gulhan E, Kocyigit O, Tastepe I, Cetin G. Neurogenic tumours of the mediastinum: a report of 60 cases. *Can Respir J* 2000; 7:261-5.
5. Husain AN. Thoracic Pathology. Philadelphia: Elsevier, 2012:444-9
6. Murphey MD, Smith WS, Smith SE, Kransdorf MJ, Temple HT. From the archives of the AFIP. Imaging of musculoskeletal neurogenic tumors: radiologic-pathologic correlation. *Radio Graphics* 1999; 19:1253-80.
7. Maruyama R, Tanaka J, Maehara S, Saeki H, Kinjo M, Higashi H. Intrathoracic ganglioneuroma in an elderly patient over 70 years of age. *Gen Thorac Cardiovasc Surg* 2007; 55:437-9.
8. Bicakcioglu P, Demirag F, Yazicioglu A, Aydogdu K, Kaya S, Karaoglanoglu N. Intrathoracic Neurogenic Tumors. *Thorac Cardiovasc Surg* 2013; 23. DOI: 10.1055/s-0033-1343898
9. Ribet ME, Cardot GR. Neurogenic tumors of the thorax. *Ann Thorac Surg* 1994; 58:1091-5.