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Histologic Types of Chest Wall Tumors—Nine Years' Single Center Experience

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ABSTRACT

Background: Chest wall tumors are rare and mostly malignant. More than half of the malignancies are primary and the remainder are metastatic. Many studies have reported that metastatic lesions occur with about the same frequency as primary tumor. We evaluate common histological types of chest wall tumors in a tertiary center for respiratory and thoracic diseases (National Research Institute of Tuberculosis and Lung Disease). Method: We performed a retrospective study of chest wall tumors at National Research Institute of Tuberculosis and Lung Disease (NRITLD) from April 2001 to March 2010. The pathology slides of patients were retrieved from the pathology archive of NRITLD and reviewed by two pathologists. The lesions were classified as primary or metastatic according to the relevant clinical data and imaging findings. Result: A total of 124 chest wall tumors were identified in patients with a mean age of 47.7 years (range 4 - 90 years). The male/female ratio was 2:1. The most commonly affected side was the right (42.7%). There were 105 malignant tumors (84.7%), out of which 49 (46.2%) were primary and 57 (53.8%) were metastatic in origin. The majority of the metastatic lesions were epithelial tumors (36/57) (63.1%). The metastatic origin was clear in 51 cases, mostly arising from the lungs (35.7%). The most common types of primary chest wall tumors were primitive neuroectodermal tumor (15/49, 30.6%), chondrosarcoma (7/49, 14.3%), and malignant fibrous histiocytoma, undifferentiated pleomorphic sarcoma (5/49, 10.2%). The most common benign tumor was lipoma (5/18, 35.7%). Conclusion: Most common tumors of chest wall in this study were malignant, mostly metastatic epithelial neoplasms.

KEYWORDS

Chest Wall; Histology; Immunohistochemistry; Primary; Metastatic Tumor

1. Introduction

Chest wall tumors constitute less than 1% of all tumors. A little more than half the lesions are primary tumors of the chest wall and the remainder are metastatic. It is a relatively frequent location for metastasis from distant organs but extension of underlying lung tumors into the thoracic wall may also occur. Many studies have reported that metastatic lesions occur with about the same frequency as primary tumors [1,2] .

Chest wall tumors, benign or malignant, are catego-

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rized into eight main diagnostic categories of muscular, vascular, fibroblastic/myofibroblastic and fibrohistiocytic, peripheral nerves, osseous and cartilaginous chondro-osseous, adipose, hematologic and cutaneous origins. However, there are some malignant tumors that arise from the chest wall but do not fit well in any of these categories, called uncertain differentiation tumors, like Ewing sarcoma and synovial sarcoma [3,4].

Review of literature reveals that most of the primary chest wall tumors are malignant [5], and benign chest wall tumors are uncommon lesions although there are some reports that show them as the most common type [6].

Clinically, malignant chest wall tumors manifest as painful, rapidly growing, large palpable masses but sometimes they are incidentally detected on chest X-rays [7].

We performed a retrospective study of chest wall tumors at NRITLD, between 2001 and 2010 to show the morphological variants of tumors of this site in a tertiary and referral center and compare them with the relevant data available in the literature.

2. Materials and Methods

A retrospective study of patients presented with chest wall tumors was conducted in a tertiary center, NRITLD, from April 2001 to March 2010. Two pathologists reviewed all patients' slides retrieved from the archives of the pathology lab and an additional Immunohistochemistry (IHC) study was performed, if necessary, for definitive diagnosis. Clinical data were obtained through a review of hospital records of these patients. Tumor classification was done according to the histopathological and IHC findings as well as clinical data to determine the origin of tumors as primary or secondary.

The lesions were subdivided into different groups as: 1) malignant or benign, 2) primary or secondary, and 3) epithelial, soft tissue, bone and cartilage, or hematologic tumors. The study protocol was approved by the human subjects review committee of NRITLD. All participants signed written informed consent.

3. Results

The mean age of patients was 47.7 years (range 4 to 90 years). There were 85 males (68.5%) and 39 females (31.5%). Male to female ratio was 2.1. The presenting symptom was a painful and/or rapidly growing mass in 88 patients (70.9%). Twenty patients (16%) were asymptomatic and detected incidentally. Specimens were obtained either from surgical resection (excisional biopsy in 75 patients) or biopsy (incisional biopsy in 40 and CT-guided biopsy in 9 patients). Most tumors (42.7%) were located at the right side.

Table 1 shows the distribution of patients according to the histologic subtypes.

Eighteen from 124 Patients (14.5%) had benign tumors; 13 were males (72.2%) and 5 were females, with a mean age of 37.8 years (range 4 - 64 years). The majority of benign tumors were lipoma (35.7%) followed by schwannoma and benign spindle cell tumor (two cases each, 14.3%). The others are listed in **Table 1**.

One hundred and six out of 124 patients (85.5%) had malignant tumors; 67 were males (63.2%) and 39 were females (36.8%), with a mean age of 48.7 years (range 6 - 90 years). The mean age of patients with a malignant tumor (48.7 ± 20) was older than that of patients with a benign lesion (37.8 ± 16) ($p < 0.000$). The rate of malignancy in males and females was 83.7% and 88.6%, respectively. The mean age of patients with a malignant tumor was older than that of patients with a benign lesion (mean age of 48.7 vs. 37.8 years, respectively).

The majority of benign tumors were lipoma (35.7%), followed by schwannoma and benign spindle cell tumor (two cases each, 14.3%). Based on the histopathological examination and clinical findings, the malignant tumors were divided into two subgroups of primary or secondary. Forty-nine patients (46.2%) had primary tumors of chest wall and 57 had secondary tumors, mostly originating from the lungs and pleura.

Overall, the most common primary malignant tumors were primitive neuroendocrine tumor (15 cases, 30.6%), chondrosarcoma (7 cases, 14.3%), malignant fibrous histiocytoma (5 cases, 10.2%), sarcoma, NOS and malignant peripheral nerve sheath tumor (4 cases each, 8.2%). Plasmacytoma (6.1%), leiomyosarcoma (4.1%), rhabdomyosarcoma (4.1%), synovial sarcoma (4.1%), and dermatofibrosarcoma protuberans (4.1%) ranked consecutively and the last three were osteosarcoma, giant cell tumor of bone and liposarcoma (2% or one case each).

Over half the malignant tumors (57 patients, 53.8%) were metastases from distant organs or direct invasions from adjacent structures. The primary sites were determined in 51 cases either clinically or by immunohistochemical staining; mostly originating from the lungs (35.7%) and adjacent pleura (22.8%). The common histologic types were carcinomas (63.1%) and malignant mesotheliomas (22.8%). In addition, among metastatic tumors, there were 6 patients with hematologic neoplasms (10.5%), one metastatic gastrointestinal stromal tumor (GIST) and one malignant fibrous histiocytoma.

4. Discussion

Chest wall neoplasms can be classified based on their tissue of origin and their benign or malignant nature. They may be either primary or secondary; the latter mostly result from direct invasion of the lung, pleural,

Table 1. Demographic data and distribution of histologic types of chest wall tumors.

Histology	Number	%	Age range (Female: Male) (Mean age)
MALIGNANT	**106**	**85.5**	**6 - 90 (39:67) (48.7 yr)**
Secondary tumors	**57**	**54.3**	**16 - 90 (18:39) (57.5 yr)**
Carcinoma	**36**	**63.1**	**31 - 90 (9:27)**
Mesothelioma	**13**	**22.8**	**34 - 74 (3:10)**
Soft tissue tumors			
Malignant fibrous histiocytoma	1	1.7	44 (0:1)
Gastrointestinal stromal tumor	1	1.7	40 (0:1)
Hematologic neoplasms			
B cell Lymphoma	**5**	8.7	16 - 78 (5:0)
Hodgkin's Lymphoma	**1**	1.7	21 (1:0)
Primary tumors	**49**	**46.2**	**6 - 85 (21:28) (38.5 yr)**
Soft tissue tumors	**37**	**75.5**	**6 - 85 (16:21)**
Primitive neuroectodermal tumor/Ewing	15	30.6	6 - 54 (5:10)
Malignant fibrous histiocytoma	5	10.2	28 - 85 (2:3)
Sarcomas, not otherwise specified	4	8.2	36 - 46 (3:1)
Malignant peripheral nerve sheath tumor	4	8.2	19 - 78 (3:1)
Leiomyosarcoma	2	4.1	18 - 55 (1:1)
Rhabdomyosarcoma	2	4.1	38 - 58 (1:1)
Synovial Sarcoma	2	4.1	37 - 58 (1:1)
Dermatofibrosarcoma	2	4.1	31 - 43 (0:2)
Liposarcoma	1	2.0	68 (0:1)
Bone and cartilaginous tumors	**12**	**24.5**	**20 - 72 (5:7)**
Chondrosarcoma	7	14.3	24 - 72 (3:4)
Plasma cell neoplasm	3	6.1	46 - 70 (0:3)
Osteosarcoma	1	2.0	20 (1:0)
Giant cell tumor of bone	1	2.0	23 (1:0)
BENIGN	**18**	**14.5**	**4 - 64 (5:13) (37.8 yr)**
Soft tissue tumors	**14**	**77.8**	**18 - 64 (5:9)**
Lipoma	5	35.7	49 - 55 (1:4)
Schwannoma	2	14.3	18 - 64 (1:1)
Benign spindle cell tumor	2	14.3	35 - 41 (2:0)
Hemangioma	2	14.3	29 - 49 (0:2)
Angiolipoma	1	14.3	24 (0:1)
Fibromatosis	1	7.1	21 (1:0)
Neurofibroma	1	7.1	45 (0:1)
Bone and cartilaginous tumors	**4**	**22.2**	**4 - 37 (0:4)**
Langerhans cell histiocytosis	1	0.2	15 (0:1)
Osteoblastoma	1	0.2	4 (0:1)
Osteochondroma	1	0.2	33 (0:1)
Osteochondral hamartoma	1	0.2	37 (0:1)

mediastinal, or breast tumors to the adjacent chest wall. Moreover, primary tumors can be classified according to their tissue of origin into soft tissue, and bone and cartilage.

Most of the neoplasms in this study were malignant (85.5%); of which, slightly more than half (53.8%) were metastatic, mostly from the lung and pleural tumors. Soft tissue tumors ranked first followed by tumors of bone and cartilage in our series, among which PNET/Ewing sarcoma was the most common malignancy (30.6%) followed by chondrosarcoma (14.3%). There are different reports on variable distribution of chest wall tumors with soft tissue and bony origin according to age and tumor categorization [3,4,8-10]. In our study, chondrosarcoma was the most malignant chest wall tumor with bone origin which is also the most common malignancy in other studies [10]. However, ES/PNET family of tumors are reported to be the most common chest wall tumor in children and young adults and overall, it is the third most common malignant chest wall tumor [10,11]. Furthermore, our patients with ES/PNET were young adults (mean age: 19 years).

Nowadays, soft tissue tumors are classified according to the line of differentiation rather than the type of tissue of origin. However, a more recent classification classified them into fibroblastic/myofibroblastic, lipomatous, smooth muscle, skeletal and extra gastrointestinal stromal tumors, tumors of blood and lymph vessels, perivascular, synovial and mesothelial tumors, peripheral nerve sheath and primitive neuroectodermal tumors and extraskeletal osseous and cartilaginous tumors [12].

The most common primary soft tissue tumor in our series was Ewing sarcoma/primitive neuroectodermal tumor (ES/PNET). However, most of such cases occurred in younger age groups, children and adolescents with a mean age of 19 years (range 6 - 54 years). PNETs are members of Ewing family of tumors and when localized to thoracopulmonary region, they are called Askin tumor. They are usually diagnosed by the shared abnormal cytogenetic of t (11; 22) (q24; q12), cellular morphology, immunophenotyping and clinical response and are categorized in the Ewing sarcoma family of tumors (ES/PNET). They are the most frequent soft tissue tumors of children and young adults, mostly arising from deep soft tissues of extremities; however, they may be found anywhere in the body. Their prevalence in chest wall is reported to be 15% [9] named as Askin tumor in the thoracopulmonary region. Pathologic diagnosis is usually made by light microscopy and immunohistochemistry study. They are malignant small round cell tumors with immunoreactivity for MIC2 (CD99) and negative cytokeratin. Sometimes molecular studies are required to find the mentioned translocation [12].

In our study, chondrosarcoma was the most common tumor with bone and cartilage origin, similar to other studies [3,4,10,11]. All 7 cases were low grade, including two clear cell types and all arose from rib or strnum. Well differentiated chondrosarcoma may morphologically resemble chondroma, although chondroma in the chest wall area is extremely rare. It is recommended that all cartilaginous tumors with chondroma-like features that are larger than 2 - 3 cm in diameter be considered as well differentiated chondrosarcoma due to their local recurrence and requirement for wide local excision [13].

Malignant fibrous histiocytoma (MFH) which is the most common soft tissue sarcoma [12] has been reported to be rare in the chest wall [4]. But it was the most common soft tissue tumor and first in adults in our study. MFH/undifferentiated high grade pleomorphic sarcoma is the most frequently observed soft tissue tumor in adults occurring in ages 50 - 70 years. They mostly arise from soft tissue of lower and upper extremities. It is rarely localized within the thorax [14]. Histologically, they are divided into storiform pleomorphic, myxoid, giant cell type and inflammatory type some of which having prognostic importance. Among the mentioned types, storiform pleomorphic subtype is more frequent. There were 6 cases of MFH, 4 of which were men. Five were primary tumors and one was metastatic originated from larynx. Patients' mean age was 55.3 years. It was the most frequent soft tissue tumor of this area among adults. Four were storiform pleomorphic, one was giant cell type and one case was myxoid type. Diagnosis of MFH is commonly made by exclusion based on morphology and IHC. They are actually pleomorphic sarcomas without any line of differentiation [12].

Recent studies have shown that MFH is not a distinct tumor type; instead, it should be considered as an undifferentiated pleomorphic sarcoma (NOS) (so-called MFH) [15,16].

Fibrosarcoma is a diagnosis of exclusion using immunohistochemical, ultrastructural and molecular studies. Nowadays this diagnosis has significantly decreased. For example, pleomorphic spindle cell tumors with fibroblastic differentiation are grouped as MFH and molecular studies also classified some of sarcomas as monophasic synovial sarcoma [12]. We reviewed all spindle cell tumors reported as "sarcoma, not otherwise specified", without pleomorphic features. After morphologic evaluation and IHC staining, two of them reclassified as synovial sarcoma and two as sarcomatoid mesothelioma. Finally, four cases (8.2%) of sarcomas were diagnosed as NOS compared to 1.8% in Gross *et al.*, series [16]. Others estimated the prevalence of unclassified sarcomas as about 1% of sarcomas of the chest wall in adults and 10% in infants and children [17,18]. Molecular studies may exclude other mesenchymal tumors and suggest these tumors as fibrosarcoma.

Malignant peripheral nerve sheath tumor (MPNST) which accounts for 5% - 10% of all soft tissue sarcomas is malignant counterpart of nerve sheath tumors; arising from a peripheral nerve or a preexisting neurofibroma; half of them arise in the setting of neurofibromatosis type1, Von-Recklinghausen disease [12]. The most common anatomic sites include major nerve trunks and proximal portions of the upper and lower extremities and the trunk [12,15]. We had four MPNSTs (8.2% of primary chest wall tumors); only one of the patients was a young girl who had neurofibromatosis.

In our study, plasma cell neoplasms accounted for 6.1% of all primary chest wall tumors; these tumors result from clonal expansion of plasma cells. In the chest wall, they can be part of plasma cell myeloma in which a multifocal plasma cell neoplasm is associated with the presence of an M-protein in serum and/or urine accompanied by bone marrow involvement or may present as a localized bone tumor called solitary plasmacytoma. There was one case of solitary plasmacytoma and two cases with monoclonal protein and bone marrow involvement of plasma cell myeloma in our series. They may be solitary or multiple. Skull and vertebra are principle locations of multiple myeloma followed by ribs, clavicle and scapula in a descending order of frequency. Solitary plasmacytoma is rare in these locations [19]. We had three cases diagnosed by CT-guided core biopsy showing bone marrow involvement with multiple myeloma. One case was diagnosed as solitary myeloma without bone marrow involvement.

We had two cases of primary leiomyosarcomas of chest wall. Of all soft tissue sarcomas, approximately 1% - 4% was leiomyosarcomas which is a tumor of adult life [20]. While histologically similar, soft tissue leiomyosarcoma has been subdivided into four site-related groups for prognostic and treatment purposes: retroperitoneal/abdominal leiomyosarcomas, leiomyosarcoma of somatic soft tissue, cutaneous leiomyosarcoma, and leiomyosarcoma of vascular origin [12]. Once located in extremities and trunk, they are grouped as leiomyosarcoma of somatic soft tissue which is far less common and affects both sexes equally [21].

Rhabdomyosarcomas arise from skeletal muscle progenitor cells with a histologic classification as embryonal, alveolar and pleomorphic (sometimes named adult type). They are the most common soft tissue sarcomas in children, adolescents and young adults. They rarely occur in older patients but if so, they are mostly of pleomorphic subtype. We had two pleomorphic rhabdomyosarcomas. The most common anatomic location of these tumors is head and neck followed by trunk [12].

We found two cases of synovial sarcomas. They are malignant soft tissue tumors of uncertain type and account for 2.5% - 10.5% of all primary malignant soft-tissue neoplasms. A consistent specific translocation, most commonly a balanced reciprocal translocation, t (X; 18) (p11.2; q11.2), is found in more than 90% of all synovial sarcomas .In most series, the most affected sites are extremities [22]. About 5% - 7% of them arise in the trunk, thorax, and chest wall [23,24]. These tumors were positive for CD99, CK and EMA.

Metastatic malignancies are not unusual and are often seen at the terminal stages of a malignant disease, associated with a poorer outcome. In most studies they comprise most of the malignant chest wall tumors [25]. In our study more than half of the cases (53.8%) were metastatic malignancies mostly originated from the direct invasion of lung, pleural and breast tumors.

Other malignancies can also metastasize to the chest wall like one case of clear cell carcinoma of the kidney, as well as soft tissue sarcomas including one GIST of stomach and one MFH with larynx as the primary origin in our series.

Hematologic neoplasms may also manifest as a soft tissue mass, and are mostly secondary neoplasms. The most common type of lymphoma in our series was diffuse large B cell lymphoma.

The most common hematopoietic tumors manifesting as chest wall tumors in our study were: five large B cell lymphomas including one plasmablastic variant of B cell lymphoma and one case of Hodgkin lymphoma, which was soft tissue manifestation of recurrence in a 21-year-old known case. There are rare cases of non-Hodgkin's lymphoma presenting as a large chest wall mass as the only site of disease [26].

In most studies, benign tumors are less common than malignant ones in the chest wall. Osteochondromas, chondromas, fibrous dysplasia and desmoid tumors are the most common ones [25]. In our review, lipoma was the most frequent (35.7%) benign tumor. Lipomas are the most common soft tissue tumors with numerous case reports documenting their presence in other rare locations [27]. Lipomas of the chest wall are deep and tend to be less well-circumscribed. They are often detected at a relatively late stage of development thus being larger [28]. Schwannomas comprised 14.3% of benign tumors. They are tumors of peripheral nerves that originate from the nerve sheath. Thoracic schwannomas are frequently located in the posterior mediastinum (75% - 90%) or in the chest wall [7,12,29].

5. Conclusion

The most common tumors of chest wall in this study were malignant, mostly metastatic epithelial neoplasms.

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