Pleuropulmonary Blastoma: A Case Report

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INTRODUCTION

Pleuropulmonary blastoma (PPB) is a lung cancer (1, 2) that is very uncommon in children. Manivel et al. (1) firstly described the presence of PPB in children in 1988 that is different from the classical adult type biphasic epithelial-stromal morphology. PPB is observed in children of different ages varying from one month to twelve years. The incidence rates for PPB between genders are similar. Initial findings are usually flu-like symptoms with or without fever (3).

Dehner (4) described three different types of PPB morphologically according to gross and microscopic features. The prognosis is strongly correlated with the histological type. Five-year survival rate was 80-90% in patients with type 1, while 50% in type 2 and 3. In this report we present a case of type 3 PPB in order to discuss the clinical, histopathological, immunohistochemical features and the differential diagnosis of the disease.

CASE REPORT

A three-year-old boy presenting with fever and symptoms of upper respiratory tract infection was admitted to the hospital. A solid tumoral lesion filling the right hemithorax and accompanying by the pleural fluid was observed radiologically (Figure 1).

Core needle biopsy of the lesion demonstrated histologically small tissue fragments consisting of primitive round embryonal cells in a loose myxoid stroma (Figure 2). Although these cells were predominantly monotonous, some showed eosinophilic cytoplasm and larger nuclei (Figure 3). These morphological findings were suspicious for PPB.

ÖZ

Pleuropulmoner blastom bebeklik ve erken çocukluk dönemine ait, sıklıkla akciğer, daha ender olarak plevra kaynaklı nadir görülen embriyonel bir tümördür. Burada bu antite; insidansına bağlı olarak yeterli sistematik literatür verisi bulunmaması nedeni ile, klinik, histopatolojik ve immuhistokimyasal özelliklerini tartışmak içindir. Üç yaşında bir erkek çocuk yüksek ateş ve üst solunum yolu enfeksiyon bulguları ile başvurmuştur. r adyolojik incelemede sağ hemitoraksı dolduran solid kitle saptanmıştır. Biyopsi ve cerrahi materyal histopatolojik olarak incelenmiştir. Tümör başlıca solid alanlardan oluşmakta olup, miksoid bir stroma içerisinde iğsi, poligonal ve yuvarlak hücreler içermekte idi. İmmunohistokimyasal boyamada tümör hücreleri vimentin ve desmin pozitif idi. mIB-1 labeling index was above 90%. Histological diagnosis was pleuropulmonary blastoma type 3. The surgically sampled adjacent diafragma was also infiltrated with the tumor. The patient was treated with chemotherapy and showed no signs of recurrence in the follow-up of 9 months. Pleuropulmonary blastoma is a very rare childhood cancer that needs to be kept in mind in the pathological differential diagnosis of thoracic tumors in the children.

Key Words: Lung neoplasms, Child, Pleuropulmonary blastoma

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A surgical biopsy was also performed later by thoracotomy. On histopathological evaluation, predominantly solid partially necrotic tumor tissue was observed. The tumor tissue also contained a few cystic areas. The tumor cells present in the myxoid stroma were round or fusiform in shape and their nuclei were hyperchromatic. These blastomatous looking tumor cells were organised in some areas resembling the cambium layer of the rhabdomyosarcomas. Immunohistochemically the tumor cells were stained diffusely positive with vimentin, weakly positive for desmin and negative Mic-2 (CD99) and actin. MIB-1 index was over 90%.

After debulking of the tumor by four cycles VAC (Vincristine, actinomycin-D, cyclophosphamide) chemotherapy, a right upper lobectomy was performed. Macroscopically the lobectomy specimen showed the tumoral lesion of 7x9 cm with solid tan-coloured cut surface (Figure 4). Histopathological diagnosis was type 3 PPB characterized by solid areas consisting of rhabdomyosarcomatous cells. These cells appeared primitive and atypical but some showed large eosinophilic cytoplasm. Immunohistochemical staining revealed positive immunoreactivity with desmin and vimentin (Figure 5). The final pathological diagnosis was PPB type 3. A diaphragmatic tissue sampled surgically also revealed a tumoral infiltration that was similar histopathologically.

The hilar lymph nodes were negative. ICE (ifosfamide, carboplatin, etoposide) treatment protocol was started and...
the overall prognosis in the 9 months follow-up is very good without any evidence of recurrence.

**DISCUSSION**

Although intrathoracic neoplasia and neoplasms of the chest wall are not common, pulmonary metastases are the most frequent intrathoracic neoplastic lesions in children (2). Pleuropulmonary blastoma (PPB) is an aggressive tumor that includes less than 1% of all primary malignant pulmonary tumors in the pediatric population. A family history is evident in 25-30% of the cases usually presenting with cystic lesions and childhood cancers (5). There are presently over 100 cases registered with The Pleuropulmonary Blastoma Registry (www.ppbregistry.org). Initial symptoms are usually flu-like illness with or without fever (3). Some patients with type 2 and 3 PPB may present with lung cysts. The radiologic findings of a PPB include different patterns of masses lesions and/or cysts such as unilateral, rarely bilateral, localized air-filled cysts or a purely solid mass. Rarely, PPB is diagnosed when metastatic involvement of brain, bone, lymphoid tissue, liver, pancreas, renal and surrenal tissue occurs (6,7).

Dehner (4) defined three types of PPB morphologically. Type 1 was characterized as multicellular cystic tumors surrounded by ciliated columnar respiratory type benign metaplastic epithelium separated by fibrous septa (6). Beneath the respiratory epithelium a continuous or interrupted cell layer including immature or primitive tumor cells morphologically varying from small round to fusiform-shaped cells resembles the cambium layer of botryoid rhabdomyosarcoma (6).

Histopathologically, solid areas of type 2 and type 3 tumors show the characteristics of both blastomatosis and sarcomatosis. In type 2 lesions cysts are observed macroscopically, however there are some solid areas including anaplastic cell clusters, cartilage, and nodules of blastoma. Type 3 lesions seem like type 2 lesions; however they include predominantly solid areas. Features like nodules of cartilage with malign appearance, cellular aggregates of anaplastic and pleomorphic cells, areas like fibrosarcoma, foci of rhabdomyosarcomatosis, liposarcomatosis, or chondrosarcomatosis and areas that seem like condensed blastoma separated with loose fusiform cells can be seen alone or combined (6).

Most of the neoplastic cells were immunoreactive for vimentin. It is positive in focal areas of rhabdomyoblastic cell population, cartilage, fibrosarcoma, or histiocytoma and foci of blastomatosis. Only respiratory epithelial cells are cytokeratin (CK) positive, smooth muscle actin and desmin are positive mainly in rhabdomyoblastic cells; on the other hand they can be positive focally in primitive cells (6, 9). S100 expression in nodules of cartilage may be helpful to distinguish cystic lesions of lung and chest wall from synovial sarcomas. Moreover, negative CD99, EMA (epithelial membrane antigen) and CK are also useful in the differential diagnosis from synovial sarcoma (9).

In differential diagnosis there are other tumors that contain mainly small round cells (10). Primitive neuroectodermal tumors that appear in the thoracic soft tissue show more cellular areas including rosette formation. The differential diagnosis of PPB also includes rhabdomyosarcoma, metatstastic neuroblastoma, extrarenal rhabdoid tumor, desmoplastic small cell tumor, congenital infantile fibrosarcoma, metastatic myxoid chondrosarcoma and other biphasic childhood tumors that may affect the chest (8). Rhabdomyosarcomas are treated with a different protocol, therefore the differential diagnosis is important. In PPBs of the mediastinum lymphoblastic lymphomas should be kept in mind in the differential diagnosis. Pulmonary blastoma, which is important in differential diagnosis, is a rare congenital lung tumor, but it is usually seen in adults. Malignant epithelial cells are not seen in PPB and this morphology is an important key point to distinguish it from pulmonary blastoma (8).

Although present symptoms are similar, the clinical prognosis depends the histological type and five-year survival appears better in type 1 patients, while it is worse in type 3. In type 1, besides a better prognosis, recurrences can occur locally. Central nerve system is the major area for metastasis. Spinal cord and skeletal system also carry risk of metastasis. Ocular and pancreatic metastases have also been reported (2). The management of PPBs is a multimodal
approach including chemotherapy, radiotherapy, and transplantation of autologous hematopoietic stem cells, however an effective treatment has not been defined yet (11-13). Indolfi P et al. reported (14) that extrapulmonary invasion is the parameter of worse prognosis and neoadjuvant chemotherapy for 9-10 weeks should be followed by a successful total resection.

In conclusion PPB is a very rare childhood cancer that needs to be considered in the pathological differential diagnosis of thoracic tumors in the children. This case is reported also because of its diagnosis performed by needle biopsy.

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