Biphasic pulmonary blastoma in a child

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Pulmonary blastoma (PB) is a rare malignant pulmonary tumor composed of immature mesenchyme and/or epithelium that resembles an embryonic lung at 10-16 weeks gestation. PBs constitute only 0.25 to 0.5 percent of all primary malignant lung tumors. Approximately 20 percent of the reported cases have occurred in pediatric patients. A seven-year-old girl presented with fever, cough, respiratory distress and chest pain on the left side. An x-ray, ultrasonography and a computed tomographic scan of the chest showed a large mass consisting of solid and cystic components almost completely occupying the left hemithorax associated with pleural effusion. The diagnosis of biphasic PB was established by histological examination of thoracotomy material. The patient was considered inoperable due to tumor involvement of the mediastinum, and she died two days after the initiation of chemotherapy. We report this case of PB to raise attention to the clinical, radiological and pathological features of PB in childhood because of its rarity.

Key words: pulmonary blastoma, biphasic, child.

Pulmonary blastoma (PB) is a rare malignant pulmonary tumor composed of immature mesenchyme and/or epithelium. It was first described by Barret and Barnard in 1945[1-4]. The tumor was later named "pulmonary embryoma" by Barnard[5] in 1952 because of its microscopic resemblance to an embryonic lung at 10-16 weeks gestation. In 1961, Spencer[6] reported three cases and first used the term "pulmonary blastoma" believing that the tumor was the pulmonary analogue of nephroblastoma. PBs constitute only 0.25 to 0.5 percent of all primary malignant lung tumors[7]. However, 20 percent of the patients reported in the literature were younger than 20 years of age and 15 percent were younger than 10 years of age[2,4]. In 1988, Manivel et al.[8] described pleuropulmonary blastoma (PPB) in 11 children as a distinctive intrathoracic/pulmonary neoplasm whose blastematous and sarcomatous features differentiated it from the biphasic epithelial-stromal morphology of the classic adult type PB. We report a seven-year-old girl with PB because of its rare occurrence in childhood.

Case Report

A seven-year-old girl presented with fever, cough, difficulty in breathing and chest pain on the left side of one week duration. She had been hospitalized in a local hospital and administered nonspecific antibiotic therapy prior to her reference to our clinic, but she did not respond. During the physical examination her body temperature was 37.7°C, she was dyspneic and malaised. She had a respiratory rate of 42 breaths per minute, absence of breath sounds on the left chest and dullness to percussion on the left, and clubbing. Heart beats could be heard on the right chest. Laboratory investigation revealed Hb 10.3 g/dl, Htc 36%, MCV 76 fl, WBC 11,300/mm^3 with 72% neutrophils and 28% lymphocytes, platelet count 478,000/mm^3, ESR 68 mm/h, and CRP 24 mg/dl. PPD was negative, serum LDH level was 8,900 U/L, ALT 14 IU/L, and AST 26 IU/L. A chest x-ray showed complete opacification of the left lung field with rightward shift of trachea and mediastinum (Fig. 1). Ultrasonography (USG) demonstrated a mass consisting of solid and cystic components almost completely occupying the left hemithorax

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associated with pleural effusion. A computed tomographic (CT) scan of the chest showed a large mass consisting of heterogeneous hyperdense and hypodense areas representing solid and cystic components associated with pleural effusion within the left chest region (Fig. 2). Skeletal survey, brain CT and abdominal USG findings were normal. The pleural fluid which was obtained by thoracentesis was serohemorrhagic; cytologic examination of pleural fluid revealed fluid revealed erythrocytes, and polymorphonuclear and mononuclear cells along with sparse plasma cells and mesothelial cells, but no malignant cell was observed. Pleural fluid density was 1026, protein concentration 7.5 g/dl, and LDH 139 U/L. No microorganism was seen with Gram staining; culture was negative.

Percutaneous needle biopsy of the left lung was performed, and a focal area suggesting a tumor consisting of blastematous features was seen microscopically. The patient then underwent a left thoracotomy. A large mucinous, fragile, necrotic and hemorrhagic tumor almost completely occupying the left hemithorax, invading the mediastinum and compressing the trachea was found. Pleura was thickened. The patient was considered inoperable and only a biopsy was performed. Histologically, the tumor included both epithelial and mesenchymal components. The epithelial component included tubular glands which were lined by pseudostratified ciliated cells; some were lined by columnar cells with clear cytoplasm (Fig. 3).

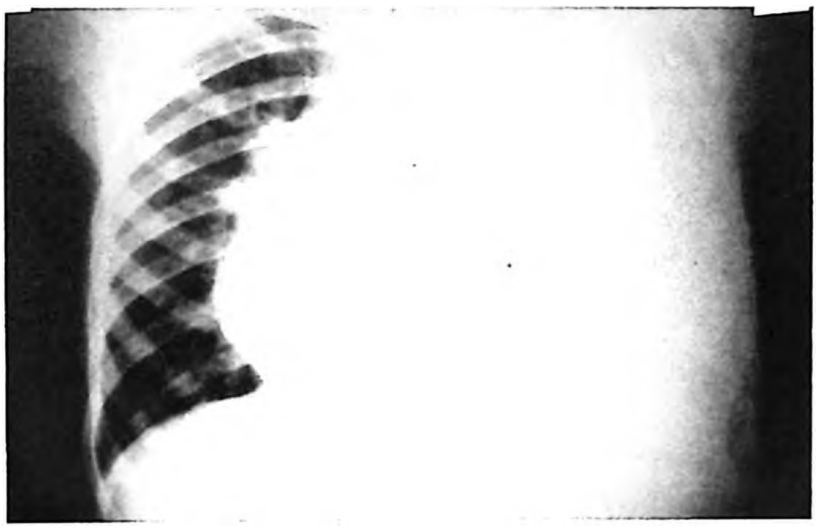

Fig. 1. Chest x-ray shows complete opacification of the left hemithorax, with rightward shift of the mediastinum.

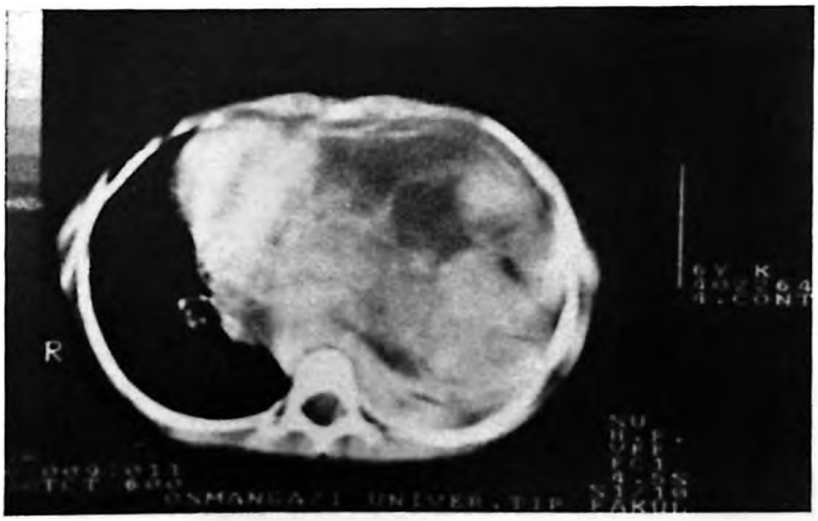

Fig. 2. CT scan of the chest shows a large mass consisting of heterogeneous hyperdense and hypodense areas representing solid and cystic components within the left chest region.

The stroma was embryonic or primitive blastematous with small, oval and spindled stromal cells and included the areas of immature striated muscle, cartilage and fascicles of fetal type smooth muscle (Fig. 4). A diagnosis of biphasic PB was made. Immunohistochemically, vimentin was negative, and desmin was positive in areas of rhabdomyoblastic differentiation. The patient was referred to an oncology center for chemotherapy and radiotherapy, but died two days after the initiation of chemotherapy.

Discussion

Most often PB in adults occurs in the fourth decade of life[2,7]. The age range at presentation for the pediatric population is newborn to 15 years[8-11]. No apparent gender difference has been observed in childhood PPB cases[9]. Recently, Priest et al.[12] reported that approximately 25 percent of PPB cases have a constitutional and familial predisposition to dysplastic or neoplastic conditions. Trisomy 2 and trisomy 8 were detected in some PPB cases and so were believed to be related to the development of PPB[13,14].

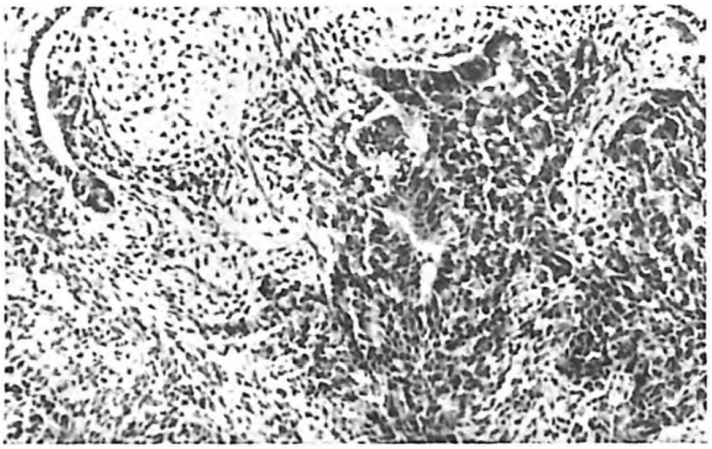

Fig. 3. Biphasic pulmonary blastoma. Tubular glands lined by pseudostratified columnar epithelial cells, some with clear cytoplasm are surrounded by embryonic and primitive blastematous stroma (H.E.x200).

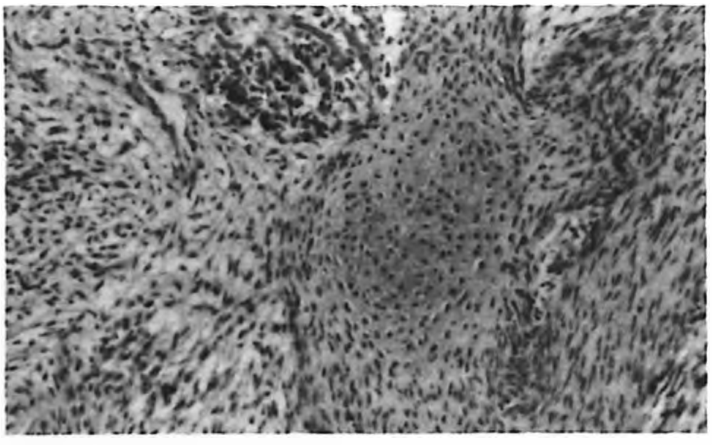

Fig. 4. Mesenchymal areas displaying rhabdomyoblastic, smooth muscle and cartilaginous differentiation (H.E.x200).

Forty-one percent of the patients are asymptomatic, and the tumor is generally found by routine chest radiography. The most common presenting symptoms in PB are respiratory distress, nonproductive cough, fever, and chest or abdominal pain[2,8,9]. Although our patient presented with cough, fever, chest pain and respiratory distress of one week duration, the presence of clubbing suggested that the tumor had been asymptomatic for a long time. Generally, the initial presentation suggests a respiratory infection unresponsive to antibiotic therapy[8,9].

Chest radiographs reveal a partial or total opacification of a lung field and mediastinal deviation to the contralateral side in almost all instances. A pleural effusion may be associated[2,3,8]. Noninvasive diagnostic tests and bronchoscopy have a low value in detecting blastomas. Percutaneous needle biopsies can establish the diagnosis, especially in the peripheral lesions[2,9,15]. Histological examination of the thoracotomy material is the most valuable method for definitive diagnosis[2,3,8,9]. Although the chest radiogram, USG and CT scan revealed a mass and a pleural effusion in the left chest region, and percutaneous needle biopsy suggested a blastematous tumor, the definitive diagnosis of PB was established in our patient by histological examination of the thoracotomy material. Cytologic examination of the pleural effusion did not assist in the diagnosis.

Pulmonary blastomas (PBs) are generally single tumors, well circumscribed and round, but sometimes are lobulated and multiple[2,3,7-9]. Tumors have well-delineated, gray to light yellow, solid, firm, friable areas which are focally rubbery or gelatinous with irregular foci of hemorrhage and necrosis[2,3,7-9]. At thoracotomy, a solitary, mucinous, fragile, necrotic and hemorrhagic tumor completely occupying the left hemithorax, invading the mediastinum and compressing the trachea was found in our patient.

In 1988, Manivel and associates[8] proposed that PPB -the so-called pulmonary blastoma of childhood- is a distinctive clinicopathologic entity from PB in adults because of its variable anatomic location, primitive embryonic-like blastema and stroma, absence of a carcinomatous component, and potential for sarcomatous differentiation, in contrast to PB in adults which consists of a mixture of immature mesenchymal and epithelial elements. These neoplasms may be intrapulmonary, mediastinal or pleural-based masses in contrast to PB in adults[7-9]. Because of the extensive nature of the tumor in the chest, it may not be possible to determine the precise site of origin in some instances[8,9], and pleural effusion may contribute[2,7-9] as in our patient. Manivel et al.[8] questioned whether truly biphasic pulmonary tumors occur in children, and they proposed that the previously reported cases of "pulmonary blastoma" in children were probably examples of the same tumor[8]. But in 1991, Koss et al.[2] reported that biphasic PBs do occur in children, although infrequently. Our patient is also a case of biphasic PB, since histologically the tumor included both epithelial and mesenchymal components. Koss et al.[2] suggested the separation of PBs into two major histological groupings, i.e., those composed solely of well-ordered neoplastic glands (well-differentiated fetal adrenocarcinoma -WDFA-) and those composed of a mixture of neoplastic glands and malignant stroma (biphasic PB). They reported that WDFA also occurs in children infrequently.

Pleuropulmonary blastoma (PPB) cases were subclassified into PPB type I, II, or III by Dehner et al.[16] based on the cystic (type I), cystic and solid (type II), or solid (type III) character of the tumor. The tumor of our case included both solid and cystic areas. Histologically, multiloculated cysts, separated by thin fibrous septa and lined by ciliated columnar respiratory epithelium is the characteristic feature in type I PPB. Beneath the respiratory epithelium, there is a continuous or discontinuous zone of condensed small, round-to-spindle-shaped immature or primitive tumor cells with the cambium layer-like appearance of sarcoma botryoids. Solid areas in type II and type III PBs consist of blastemal stromal cells, arranged in alternating bands of compact and loose cells in a myxoid matrix. There may be anaplastic and pleomorphic mesenchymal cells with numerous mitoses. Areas of chondrosarcoma, rhabdomyosarcoma, and smooth muscle-like spindle cells may be found[2,7-9]. In our case, the tumor also included rhabdomyoblastic, smooth muscle and cartilaginous differentiation areas within the malignant stroma.

Immunohistochemically, blastomas show expression of cytokeratin, epithelial membrane antigen, carcinoembryonic antigen, and often chromogranin in their epithelial elements;

however, the blastematous elements demonstrate vimentin, keratin, and actin expression[2,3,7,9]. In our case, vimentin was negative, and desmin was positive in areas of rhabdomyoblastic differentiation.

The association of PPBs with cystic lung lesions, including congenital cystic adenomatoid malformation, extralobar sequestration and bronchogenic cysts, has been reported, but it remains uncertain whether PPB arises in an uderlying malformation of the lung or whether longstanding lung cysts are themselves an initial manifestation of PPB[9,12].

Surgical excision, ranging from wedge excision to pneumonectomy, is the treatment of choice[2,3,8,9,11,17]. The duration of survival is quite different in operated cases, ranging from a few months to 24 years[2,3,8,9,17]. Chemotherapy and radiotherapy have been employed as either adjuvant to surgical treatment, or in patients whose condition is inoperable and in those with tumor recurrence. However, the effectiveness of these treatment modalities remains uncertain[3,8,9]. The most frequently used chemotherapeutic agents are vincristine, actinomycin D, cyclophosphamide, 5-fluorouracil, doxorubicin, and cisplatin[8,9]. Unusual therapeutic interventions such as intracavitary cisplatin and intracavitary ^{32}P appear worth considering[9]. Our patient was considered inoperable and died two days after the initiation of chemotherapy. recurrence of tumor may develop at the ipsilateral or contralateral lung, and distant metastases may occur chiefly to the central nervous system, involving brain and spinal cord, bone, liver, and soft tissue[3,8,9]. There was no distant metastasis in our patient.

Childhood blastomas especially have a very poor prognosis[8,9]. Priest et al.[9] reported that event free survival at two years from diagnosis was 49 percent, overall survival at two years 63 percent, and overall survival at five years 45 percent, even after multimodality therapy, in pediatric patients. A number of reports suggest that the presence of metastasis at initial presentation, tumor size greater than 5 cm, mediastinal or pleural involvement and tumor recurrence adversely effect the survival[2,4,9,17]. Koss et al.[2] reported that the prognosis of WDFA is better than for biphasic blastomas. However, Francis and Jacobsen[4] noticed that the prognosis of PBs is unpredictable based on their histological findings. In our patient, tumor size was greater than 5 cm, it was invading the mediastinum, there was no distant metastasis and the patient had a poor outcome.

We reported a seven-year-old PB case to give attention to the clinical, radiological and pathological features of PB in childhood because of its rarity. PB should be considered in differential diagnosis of patients who present with respiratory tract infection findings and whose symptoms do not improve with nonspecific antibiotic therapy in the presence of radiograms showing opacification of partial or total lung fields. Thorough family histories are essential on presentation of a child with a PB, and early surgical intervention is indicated for any pulmonary abnormalities in children from these families, in light of the literature knowledge[9,12].

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