A rare primary pulmonary tumor of childhood

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Pleuropulmonary blastoma (PPB) is known to be the pulmonary blastoma of childhood. It has a range of macroscopic and microscopic features which appear to correlate with eventual prognosis. Type 1, presenting as a multicystic lesion, occurs at an earlier age and has a more favorable prognosis than other types.

The presented case of type 1 PPB had a microscopic focus of rhabdomyosarcoma. Although this patient was disease-free one year after the initial diagnosis without chemotherapy, he presented at 14 months with local dissemination and cardiac metastasis, revealing the inevitable chemo-radiotherapy need in PPB.

Key words: blastomas, childhood tumors, histopathology, pleuropulmonary blastoma, prognostic factors.

Primary pulmonary neoplasms are rare in children and there are only sporadic examples of basically adult-type pulmonary tumors. Most neoplasms are metastatic in nature; more commonly there are some non-neoplastic conditions that may simulate a tumor, i.e. an abscess, intrapulmonary bronchogenic cyst, or solid adenomatoid malformation[1].

In the lung, mesenchymal tumors, with a clear antecedence of or concomitant with cystic lesions, have frequently been reported[2-4]. Rhabdomyosarcoma is the most common type of mesenchymal tumor associated with lung cysts[3,5,7]. We present a case of embryonal rhabdomyosarcoma arising within a pre-existing congenital lung cyst, namely a type 1 pleuropulmonary blastoma (PPB).

Case Report

A three-year-old boy was admitted to the hospital for tachypnea and shortness of breath. He had two previous similar attacks, the first at the age of three months and both resolving after chest tube placement. On these previous admissions, operation was recommended as chest X-rays suggested congenital lobar emphysema or adenomatoid cystic malformation, but the family refused. At the last admission, he was found to be afebrile and dyspneic. Breath sounds could not be heard on the upper sides bilaterally. A chest X-ray showed complete opacity in this area. The placement of a chest tube yielded partial expansion of the right lung but symptoms were not relieved. Culture from the outlet of the chest tube was negative. Thorax computerized tomography (CT) scan showed pneumothorax in the left lung field, and air-filled areas between the parietal and visceral pleura (Fig. 1). Thus, some kind of parenchymal or bronchial congenital abnormality characterized by a large cystic mass with questionable septa was proposed. Thoracotomy revealed a huge cyst based on the mediastinal surface of the left upper lobe and largely situated in the anterior mediastinum. The cyst could not be removed en masse and disintegrated when handled. The child was discharged two weeks later as both lungs expanded.

The surgical specimen was reddish-brown, fragmented, fibrotic and irregular tissue measuring 6x5x1 cm; some resembling cyst walls. The cuboidal epithelium could barely be seen lining the cyst wall with fibrosis, congestion and chronic inflammation. Neighboring lung tissue was unremarkable. Thorough sampling revealed that the cysts were mostly lined by respiratory epithelium and, in two examples, the cambium layer was present beneath the

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epithelium with deeply situated rahbdomyoblastic cells and rare bizarre giant cells (Fig. 2). Immunohistochemical staining using PAP method with anti-desmin and smooth muscle actin (SMA) antibodies (BioGenex) showed strong reactivity with desmin in most of the deeply situated cells, but no reactivity with SMA The pathologic diagnosis was type I PPB.

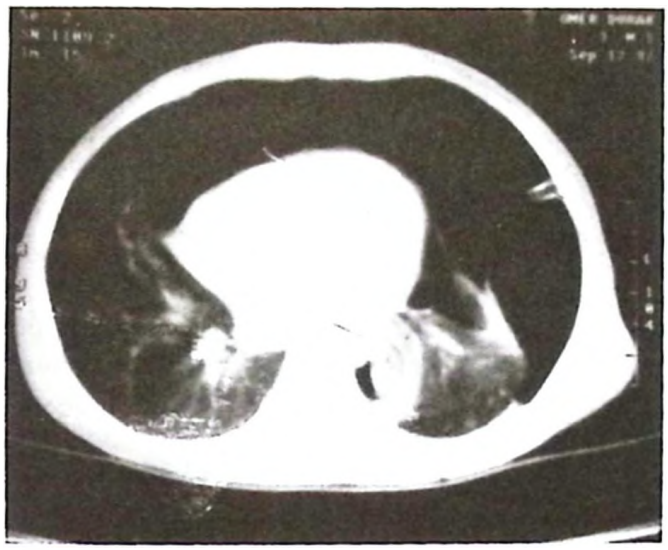

Fig. 1. Thorax CT image showing pneumothorax and air-filled areas between the parietal and visceral pleura in the left lung field.

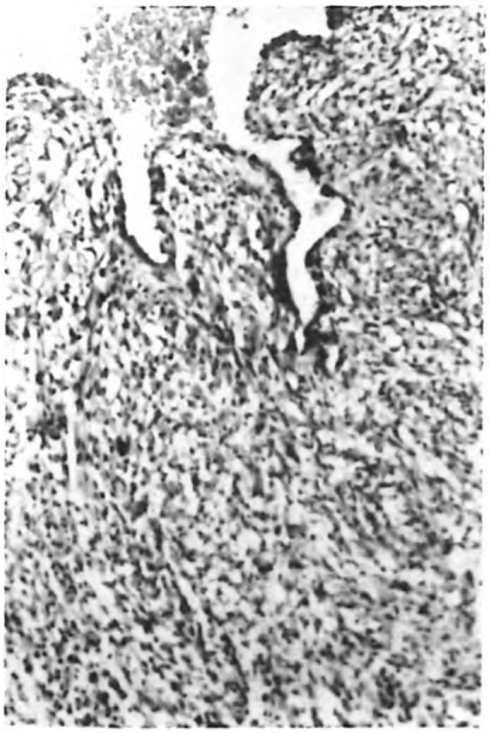

Fig. 2. Cells with rhabdomyoblastic differentiation beneath the surface epithelium of the cyst (H&E, x20).

After the pathologic diagnosis, thorough evaluation for metastases was negative and chemotherapy was planned. However, the family refused the medication. He was well 12 months later, but 14 months after the diagnosis, he presented with dyspnea, facial edema, prominence of jugular veins and a mass of 4x5 cm on the thoracic wall. The clinical picture was consistent with a superior vena cava syndrome. A chest X-ray and a CT of the thorax revealed the presence of a mass measuring 11.8x12x7.8 cm in the middle lobe of the right lung and pericardial effusion.

Echocardiogram showed a 1.5x1.5x1 cm mass in the vicinity of the tricuspid valve without disturbing its function. Investigations for metastases at other sites were negative. With these findings, he was accepted as PPB with tricuspid valve metastasis, and vincristine, Actinomycin D, cyclophosphamide polychemotherapy protocol was started. After five courses of chemotherapy, the tumor in the lung shrank to 6x5.3x4 cm and pericardial effusion regressed, but the mass in the heart remained the same. He then received radiation therapy to the primary tumor site, but died with disseminated metastasis 20 months after his initial diagnosis.

Discussion

Rhabdomyosarcoma (RMS), although a common mesenchymal tumor of childhood, rarely occurs as a primary pulmonary tumor[8]. Indeed, primary tumors of the lung are very uncommon in children. In a series of 43 childhood cases, Cohen and Kaschula[1] eight primary pulmonary tumors (18.6%), two (4.6%) of which were PPB, second only to plasma cell gronuloma.

In children, 10% or less of pulmonary blastomas (PB) have classic histological features with epithelium, blastema and stroma. PPB is accepted to be the PB of childhood and occurs in various anatomical locations in the thoracic cavity (intrapulmonary, mediastinal or pleural based), whereas classical PB is usually located in the lung parenchyma. In PPB only mesenchymal cells are neoplastic in contrast to classical PB defined as a distinctive group of carcinosarcoma[7,9-11]. There are also reported childhood cases of pulmonary adenocarcinomas of fetal type, but this entity bears no relationship to PPB[11].

Twenty-five percent of PPB occur in a constitutional/familial setting in which PPB patients themselves or young family members

have other dysplastic or neoplastic conditions, leading to the hypothesis that the PPB may arise in a precursor developmental abnormality[1]. There is preliminary evidence that PPB may be associated with loss of heterozygosity on chromosome 11p 15.5 in the region of Wilms' tumor gene; the rare association between PPB and Wilms' tumor has been implicated in RMS[7,12]. Cytogenetic findings suggest common genetic mechanisms between embryonal RMS and PPB[13,14]. We could not perform any cytogenectic investigations in our case. On the other hand, the child had an elder healthy sister, but the family history was questionable about presence of a similar disorder because another sister had died at the age of 40 days with cyanosis.

Pleuropulmonary blastomas (PPB) have a range of macroscopic and microscopic features which appear to correlate with eventual prognosis. Type 1 is the least complex pattern presenting as a multicystic lesion, occurring at an earlier age and having a more favorable prognosis than other types. Type 2 tumors have grossly visible cysts but also solid foci of blastematous islands; nodules of malignant appearing cartilage; small or large clusters of pleomorphic, anaplastic cells; and spindle cell sarcoma. Type 3 are exclusively solid tumors which are among the largest masses and are associated with the greatest degree of friability, hemorrhage and necrosis[9]. The macroscopic and microscopic features of our case were consistent with type 1 PPB with a focus of embryonal RMS.

There is a significant relationship between pulmonary cystic disease and PPB. In a series of 50 PPB cases, pulmonary cysts and/or pneumothorax had at some time been present in 19 cases (48%), and intracystic masses developed in 41.7% of the cysts observed before one month of age[7]. However, considering only congenital malformations, the frequency of pulmonary cyst-related PPB is not as high as expected[16,17]. It remains uncertain whether PPB arises in an underlying malformation of the lung or PPB has itself the potential to induce the formation of epithelial-lined cysts and to elicit cystic transformation as an initial manifestation of the neoplasm[7]. The presented case had two previous attacks of pneumothorax. The presence of cyst was first observed at the age of three months but it was probably congenital.

The probability of finding malignancies microscopically justifies prompt resection of pulmonary cysts shortly after diagnosis[16,17]. Other malignancies such as bronchoalveolar carcinoma, arising in congenital cysts, have also been infrequently reported[4,16].

Pleuropulmonary blastoma PPB is a disease with poor prognosis[3,5,7,10,11,18]. In a series of 50 PPB cases, event-free survival at two years was 83% for type 1, 49% for type 2 and 42% for type 3, and the overall survival at five years was 45%. Despite aggressive chemotherapy[18], and sometimes radiotherapy[3,7], some of the patients die with metastases especially to the brain[3,7,18], bones[7] and lymph nodes[3,5]. Local recurrences were also experienced[6,7].

The presented case was disease-free one year after the diagnosis despite no chemotherapy having been given. We were aware that this follow-up period was short for a distinct outcome, because recurrence after 60 months has been reported[7]. In fact, 14 months later local dissemination and cardiac metastasis were detected in this patient. Although CT and radiotherapy seemed to reveal the clinical symptoms and limit the disease, the patient died of disseminated metastasis at 20 months after the initial diagnosis.

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