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A female case of pleuropulmonary blastoma type 1 whose pulmonary cystic lesion was followed since neonate

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ABSTRACT

Pleuropulmonary blastoma (PPB) is a rare malignant mesenchymal tumor. It is classified into 3 subgroups, and PPB type 1 is known to be a cystic lesion with good prognosis. Here, we report a case of PPB type 1 seen in a 1-year-old girl whose pulmonary cystic lesion had been followed-up as a congenital pulmonary airway malformation since neonate. The cyst had been diagnosed as congenital pulmonary airway malformation before surgery but the final diagnosis was type 1 PPB. The tumor had a somatic mutation in exon 25 of the *DICER 1* gene whereas no germline mutation was found.

1. Introduction

Pleuropulmonary blastoma (PPB) is a rare intrathoracic tumor, which occurs in children less than 5 years old [1,2]. PPB was first described by Manivel et al., in 1988 as intrathoracic neoplasms with a blastematous and sarcomatous pattern that arose from a cystic lung lesion [3]. PPB accounts for less than 1% of all malignant lung tumors in pediatric patients [4,5]. The treatment strategy of PPB is surgical complete resection, if possible, but in advanced cases it is very difficult and the prognosis of advanced disease is very poor.

PPB type 1 is a completely cystic lesion diagnosed by histology of the resected specimen and the prognosis is better than for other advanced types. However, it is often difficult to distinguish type 1 PPB from congenital pulmonary airway malformation (CPAM). Constitutional or familial PPB was reported to be associated with a germline mutation in *DICER 1*. We report the case of 1-year-old girl with a cystic lung lesion in the left upper lobe that was pathologically diagnosed as PPB type 1 with a *DICER-1* gene mutation after surgical resection.

2. Case report

A 1 year and 4 months old girl was referred to our center with a CPAM on her chest roentgenogram (Fig. 1A), which was first observed at neonatal age. There was a radiolucent lesion located in the left lung. Computed tomography (CT) showed the main large cyst on the lingula of left lung (Fig. 1B). The cyst had been checked by periodic chest CT since neonatal age at another hospital, and it gradually grew in size and its diameter was 25 × 57 × 61 mm at referral. A contrast medium bronchogram and bronchoscopy

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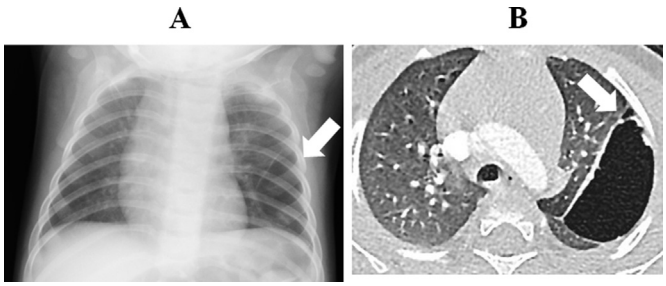

Fig. 1. Chest roentgenogram and chest CT. (A) A chest roentgenogram demonstrated a large air-filled hyperlucent lesion in the left lung (arrow). (B) Axial chest CT with contrast enhancement showed a cyst in the lingula of the left lung. There was a small septum (arrow) and the cyst contained no fluid.

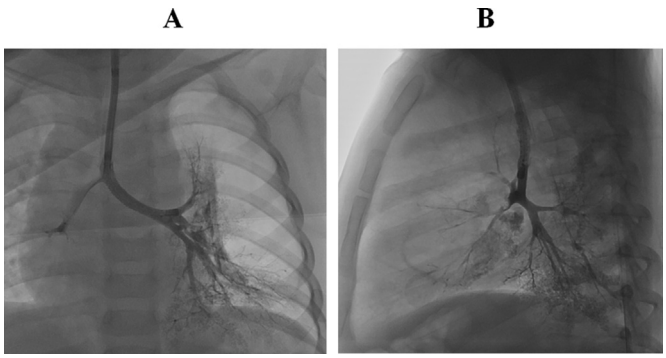

Fig. 2. Bronchogram of the case study. (A) Bronchography demonstrated a contrast medium free area caused by compression from the cyst. (B) The sagittal section showed all the branches of the left lung.

demonstrated all left bronchial branches present and the cyst had compressed normal bronchial branches (Fig. 2A and B). Aortography showed no aberrant artery from the systemic circulation. She had no respiratory symptoms and her laboratory data was within normal limits. She had no family history about PPB and the other malignant diseases such as thyroid tumor, ovarian tumor and Wilms tumor.

The differential diagnosis of this cystic lesion included CPAM type 1, large bronchogenic cyst, and PPB type 1, although this is a rare disease.

The patient underwent left thoracotomy to resect the cystic legion. The cyst protuberated from the pulmonary surface of the left lingula (Fig. 3A and B). A left upper lobectomy was performed to resect the lesion completely.

The pathological findings demonstrated the lesion was a multiloculated cyst but some parts of the cystic wall were thicker, where spindle-shaped primitive tumor cells proliferated at the subepithelial space forming a cambium layer (Fig. 4A, B, C). Some cells showed differentiation to striated muscle fiber, and desmin and Myo-D1 were positive on such primitive tumor cells (Fig. 4D and E). From these pathological findings, the cyst was finally diagnosed as PPB type 1. Potential germline and somatic gene mutations in *DICER 1* gene were investigated using formalin fixed paraffin embedded samples of tumor and normal tissues with target deep sequencing for the coding exon using a next generation sequencer, as previously described [6]. A somatic heterozygous mutation, c.5425G>A (p.G1890R), in exon 25 of the *DICER 1* gene was present in tumor cells only. No germline mutation was found in her normal tissues.

The lesion was completely resected and no metastatic legion was found by image examinations after surgery. Our oncology multidisciplinary team (MDT) decided not to treat the patient with chemotherapy and to follow her at the outpatient clinic with careful monitoring for tumor recurrence by every three months ultra low dose chest CT until 60 months of age according to the recommendation of the International PPB registry (IPBR). After eight months follow-up, she had no recurrence.

3. Discussion

PPB is classified into three groups based on the proliferation process. Type 1 PPB only has a cystic component, type 2 PPB has both cystic and solid components, and type 3 PPB is a completely solid mass that suggests it is the most advanced phase [7]. The clinical features of the three types correlate with age at diagnosis and prognosis. Type 1 PPB is diagnosed at 10 months of age (median), which is younger than that of type 2 (median, 34 months of age) and type 3 (median, 44 months of age) [8]. The overall survival rate of type 1 PPB is 80–85%, for type 3 it is 45–50% [8] and for type 2 it is an intermediate value between that of type 1 and type 3.

It is difficult to make a correct diagnosis of type 1 PPB before surgery because it has no solid component and therefore the cystic lesion can only be observed by diagnostic images. Clinical and radiological findings in our case could not clearly distinguish the lesion from CPAM type 1 and other congenital lung diseases, such as bronchogenic cyst. However, in our case the cystic lesion was followed since a neonatal age and periodic chest CT revealed that the cyst increased in size with age. Feinberg et al. identified clinical and radiological findings that may distinguish between CPAM and PPB [9]. They proposed a diagnostic algorithm and the management of congenital cystic lesions based on symptoms, germline mutation of *DICER 1* gene, and radiological features. This algorithm was very useful for us when deciding on surgery, but the correct diagnosis of PPB finally depended on the pathological findings of the surgical specimen. In our case the patient had been followed for 1 year and 4 months in another hospital and chest CT was taken for three times there. The operation should be done earlier if possible to prevent the overinvestigation and to get the correct diagnosis.

Histologically, PPB is a multilocular cystic lesion with a discontinuous layer of spindle shaped primitive tumor cells beneath a benign epithelium [10]. This subepithelial layer resembles the cambium layer of rhabdomyosarcoma and rhabdomyoblastic differentiation is present in some cases, such as the case presented here. Sometimes cystic lesions of the lung are misdiagnosed as CPAM even after surgery and retrospective pathological analysis of the lesion has disclosed type 1 PPB after tumor recurrence. Therefore, we propose a careful pathological survey for

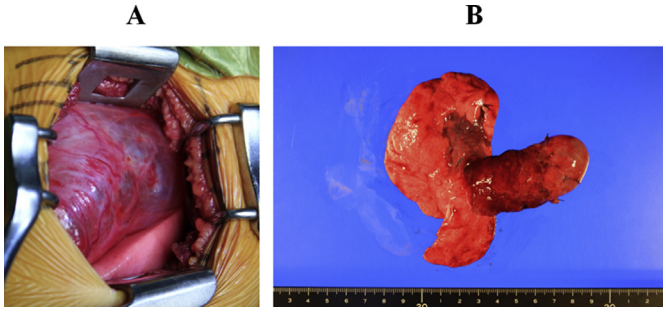

Fig. 3. Operative findings of the cyst and macroscopic findings of the specimen. (A) The cystic lesion was present in lingula of the left lung. A left upper lobectomy was performed. (B) The cystic lesion protruded from the pulmonary surface of the lingula.