

CASE REPORT

Pleuropulmonary blastoma – primary malignant lung tumor in children

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ABSTRACT

Pleuropulmonary blastoma (PPB) is a primary, malignant tumor in children up to 6 years of age. It is a rare tumor and may cause diagnostic difficulties. A 3-year-old girl was hospitalized due to pneumonia and dyspnea. Based on the symptoms, laboratory tests and computed tomography images, inflammatory changes were suspected to be caused by a congenital lung defect. There was no improvement after conservative treatment, so the decayed basal segments of the left lower lobe were removed by thoracotomy. Histopathological examination confirmed PPB type III with the DICER1 mutation. The girl underwent postoperative chemotherapy. There were no signs of progression after treatment. Pleuropulmonary blastoma is a malignant tumor and requires combined oncological treatment. The prognosis depends on the histological type and radical tumor resection. Testing for the DICER1 mutation is helpful in the diagnosis of solid-cystic lung lesions in children.

KEY WORDS:

lung malignancy, children, pleuropulmonary blastoma, DICER1 syndrome.

INTRODUCTION

Lung tumors in children are rare. They may originate from the tissue of the lung parenchyma and pleura, the tracheobronchial tree, or be a metastatic lesion of a malignant tumor with a different primary location. Primary tumors are benign or malignant and may be congenital (detected prenatally) or acquired. The most

common benign lung tumor in children is inflammatory myofibroblastic tumor. Among the malignant lesions, over 95% are metastatic lesions, mainly kidney tumors (Wilms' tumor) and bone tumors (osteosarcoma, Ewing's sarcoma). The most common primary malignant tumors are carcinoid tumor of the trachea and bronchi and pleuropulmonary blastoma (PPB) [1–3] (Table 1).

TABLE 1. Lung tumors in children

Primary		Metastatic (80%)
Benign (25%)	Malignant (75%)	
Inflammatory myofibroblastic tumors (50%) Hamartoma Primary pulmonary paraganglioma	Carcinoid tumors (30%) Pleuropulmonary blastoma PPB (22%) Mucoepidermoid carcinoma Adenocarcinoma Neuroendocrine tumors	Wilms tumor Osteosarcoma Sarcoma ewinga Rhabdomyosarcoma Lymphoma Leukemia Langerhans cells histiocytosis

PPB – pleuropulmonary blastoma

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Pleuropulmonary blastoma is a primary malignant tumor originating from embryonic mesenchymal tissue, detected mainly in infants and young children or even prenatally. Due to its solid-cystic nature, it may imitate a congenital lung defect. According to the latest studies, PPB includes four main subtypes. Pleuropulmonary blastoma type I is a cystic entity with the best prognosis and outcomes despite microscopic malignant features. Metastatic disease has never been found with type I PPB. Purely cystic tumor without a primitive malignant component is classified as type Ir PPB (regression type). Type Ir is thought to have a lower risk for malignant progression. In the newborn or infant cystic type I PPB may imitate the most common cystic lung defect, congenital cystic adenomatoid malformation type IV and occur as a peripheral air cyst up to 10 cm [4]. The clinical course may be asymptomatic or complicated by infection or pneumothorax. There is a possibility of transformation into a solid-cystic form (type II) or a solid form (type III) with high malignancy. Such changes in the lung parenchyma are initially diagnosed as pneumonia with cavities or abscesses. Pleuropulmonary blastoma type II and type III have a high tendency to recur, spread within the lungs and develop distant metastases (especially the brain and bones). Therefore, these histological types require, in addition to surgical treatment, chemotherapy as for high-grade sarcomas, and potentially radiotherapy in cases of incomplete tumor resection. The combined oncological treatment leads to 5-year survival in the range 45–75% for type II and 35–67% for type III, with the worst outcomes in metastatic disease [5].

In most patients with PPB, a DICER1 mutation is detected. Although it has not been shown to be a prognostic factor in treatment, this mutation determines a genetic predisposition to the development of other neoplastic or dysplastic diseases in childhood (DICER1-related tumors). Further oncological supervision is necessary for early detection of cancer and genetic diagnosis of close family members. The detection of this mutation is also helpful in differentiating PPB type I from benign cystic lung lesions, which implies the rapid initiation of oncological treatment [6]. In PPB type I/Ir, with incomplete resection or an unresectable cyst, chemotherapy is recommended to prevent regrowth or progression to type II/III. In the case of R0 (i.e., microscopically complete resection), chemotherapy might be discussed to avoid relapse and should be individualized [7, 8].

CASE REPORT

A 3-year-old girl was referred to the Pediatric Surgery Department with a suspected congenital lung defect in the form of intralobar sequestration of the left lung. Family history was unbiased and neonatal history was unremarkable. Her development had been normal thus far. She had been hospitalized once due to a urinary tract infection. Her medical history included fever and

shortness of breath with symptoms of a generalized inflammatory reaction for several days. Laboratory tests revealed elevated inflammatory markers, and the child required oxygen therapy. A computed tomography (CT) scan of the chest revealed solid-cystic lesions in the lower lobe and atelectatic-inflammatory lesions in the upper lobe of the left lung. Due to the lack of improvement after broad-spectrum antibiotic therapy, the girl was scheduled for emergency surgery. The decayed basal segments of the lower lobe of the left lung were removed by thoracotomy. After the procedure, due to cardiorespiratory failure, the girl required intensified treatment at the Intensive Care Unit for several days. Histopathological examination revealed PPB type III. The surgical incision line in the lung parenchyma was free of tumor infiltration, and no lymph node metastases were found. According to the description of the surgical procedure and histopathological diagnosis, the tumor resection was considered complete. Magnetic resonance imaging of the head and CT scan of the abdominal cavity did not reveal any metastases. Bone scintigraphy showed no foci of pathological uptake of the metastatic type, and local postoperative changes in the ribs were described. The girl was started on postoperative chemotherapy including 9 cycles of VAI (vincristine, actinomycin, ifosfamide), which, due to the malignant nature of the tumor, was initiated before histopathological verification. The diagnosis was confirmed abroad (Bonn, Germany) as PPB type III, along with a positive next-generation sequencing genetic test result for the presence of DICER1 gene mutations in the tumor tissue. Genetic diagnostics were extended to confirm somatic and germline mutations. A pathogenic variant was detected in one allele of the DICER1 gene, different from that in the tumor tissue, which is correlated with a syndrome of predisposition to carcinogenesis with autosomal dominant inheritance with incomplete penetrance. The girl completed the planned oncological treatment in full doses, without any serious complications or significant delays. Studies confirming disease remission showed no local progression or dissemination during treatment. The patient remains in remission one year after the diagnosis of malignant tumor, including five months of follow-up after the cessation of chemotherapy (Fig. 1).

DISCUSSION

The clinical course of lung tumors in children may vary, depending on the localization and histological type. Small peripheral tumors may be asymptomatic and detected accidentally during radiological imaging. Some tumors may cause symptoms imitating bronchial asthma, while others may present with pneumonia and pleurisy, and emergency symptoms may include pneumothorax and hemoptysis. Attention should be paid to specific symptoms for focal lesions, such as wheezing limited to one area or recurrent or untreatable unilateral pneumonia. The possibility of lung

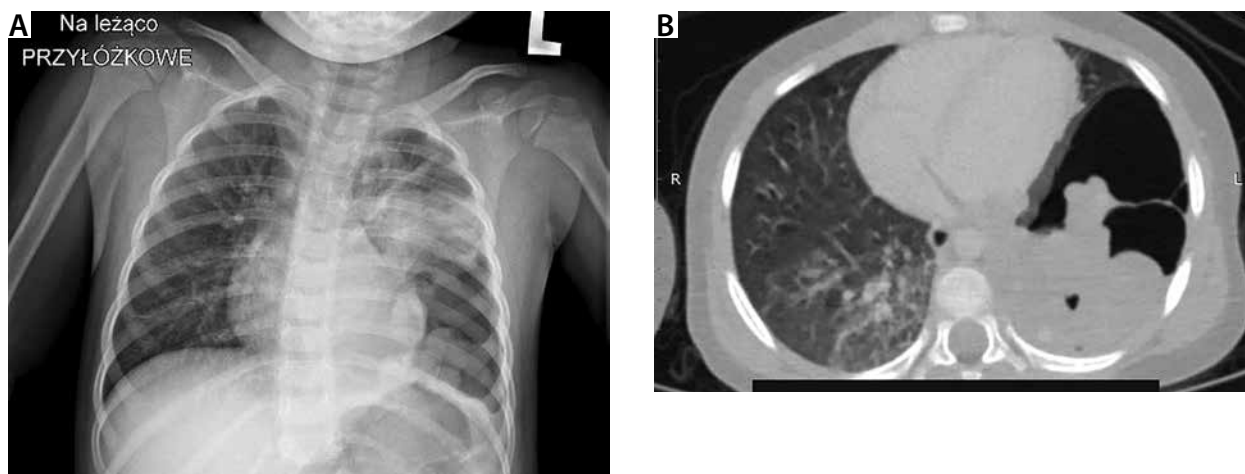


FIGURE 1. A) Chest X-ray showed cystic and solid changes on the lower lobe of the left lung and inflammatory consolidations in the upper lobe. B) A computed tomography imaging of the chest revealed a solid-cystic lesions in the lower lobe of the left lung and atelectatic-inflammatory changes in the right lung

cancer in children must be taken into account when suspecting a lung defect and determining the optimal period for surgery. This applies especially to defects with cystic changes suggesting a benign nature. Imaging tests do not allow for a certain differentiation of inflammatory changes, developmental disorders and the proliferative process. The final diagnosis requires surgery and histopathological examination. In inoperable cases, genetic testing should be performed for the DICER1 gene mutation, which in most cases coexists with PPB [9].

CONCLUSIONS

Pleuropulmonary blastoma is a primary, malignant lung tumor in young children, which may imitate or co-exist with a congenital defect in the form of solid-cystic changes in the lung parenchyma. The most important prognostic factors in the treatment of PPB are the histological type (type I gives the best prognosis, while types II and III are associated with worse treatment results) and radical surgery to remove the tumor. Pediatric patients with cystic lesions in the lungs should undergo genetic testing for the presence of DICER-1 mutations. Early detection of type I PPB is important due to the risk of histological progression to type II/III, with a much worse prognosis.

DISCLOSURES

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