# Pleuropulmonary Blastoma in a 3-year-old Girl: A Report of a Rare Case and Review of the Literature

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## Abstract

Pleuropulmonary blastoma (PPB) is a rare, pediatric soft-tissue sarcoma that mainly occurs in the pleural cavity or lungs. Patients with PPB present with nonspecific symptoms mimicking pneumonia or respiratory distress syndrome. Herein, we report a 3-year-old, female case of PPB presenting with fever, cough, chest pain, and progressive shortness of breath. Chest X-ray demonstrated near complete opacification of the right hemithorax with a mild shift of mediastinum to the left, which could be due to large, right-sided pleural effusion. However, any underlying pneumonic consolidation or mass could not be excluded. On ultrasound, small right-sided pleural effusion was confirmed. However, complex cystic mass with fine septation within the pleural cavity was also identified. A recommendation was made to place a chest tube to decrease the compressive effect on the cardiovascular system and contralateral lung and help the patient with his worsening respiratory compromise. Two days after, initial insertion of the chest tube, tissue fragments were draining out from the tube, which was sent for pathologic evaluation. Histopathologic examination revealed a tumoral lesion composed of spindle cells admixed with islands of cartilage and primitive dark cells, which showed a positive reaction to S-100, vimentin, and desmin in immunohistochemical staining. The findings were consistent with a diagnosis of PPB. The patient received neoadjuvant therapy and then underwent surgical resection. The main interesting feature of the case was tissue collection from the chest tube with no need for biopsy or any other invasive procedure to obtain the tissue samples required for histopathologic analysis.

**Keywords:** *Immunohistochemistry, pathological diagnosis, pediatric, pleuropulmonary blastoma, pulmonary mass, thoracic neoplasms*

## Introduction

Pleuropulmonary blastoma (PPB) is a rare malignancy of childhood that mainly originates from the pleura and lungs.[1] Although it is a rare soft-tissue sarcoma, PPB is a common thoracic malignancy of childhood.[2,3] There is no gender predilection with this malignancy. PPB is mainly seen after the 2nd year of life but in children younger than 7–8 years old.[2,4] Based on the gross morphology of the lesion, PPB is categorized into three subtypes: pure cystic (Type I), solid and cystic (Type II), and pure solid (Type III). Types II and III tumors have a more aggressive behavior with potential for local recurrence and distant metastasis. Genetic factors play an important role in the pathogenesis of this cancer.[4,5] Although few case reports on PPB have been previously published,[3-10] this neoplastic entity still represents a clinical diagnostic dilemma. Herein, we describe PPB in a three-year-old girl who presented with respiratory distress and lung symptoms simulating acute pneumonia.

## Case Report

A 3-year-old female was admitted to the pediatric emergency department with a 3-week history of worsening fever, cough, chest pain, and progressive shortness of breath. The family history was unremarkable. Physical examination revealed signs of respiratory distress, including tachypnea, increased work of breathing, and use of accessory muscles of respiration as well as facial edema and clubbing of her fingers. Decreased respiratory sounds on the right and dullness on the right hemithorax on percussion were also noted. Complete blood cell count revealed neutrophilia and thrombocytosis. She had a high erythrocyte sedimentation rate and increased C-reactive protein level [Table 1]. A posterior-anterior chest radiograph demonstrated near complete opacification



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of the right hemithorax with a mild shift of mediastinum to the left, which could be due to large right-sided pleural effusion. However, any underlying pneumonic consolidation or mass could not be excluded [Figure 1]. On ultrasound, small right-sided pleural effusion was confirmed. However, complex cystic mass with fine septation within the pleural cavity was also identified. A spiral computed tomography scan of the thorax with intravenous contrast was performed, which revealed a large right-sided complex solid and cystic mass occupying almost the entire right hemithorax, as well as right-sided pleural effusion and collapse of the right middle and lower lobes, due to compressive effect of the mass [Figure 2]. Differential consideration included infected sequestration or bronchogenic cyst. The recommendation was made to place a chest tube to decrease the compressive effect on the cardiovascular system and contralateral lung and help the patient with her worsening respiratory compromise. Insertion of a chest tube at the bedside resulted in draining serosanguinous pleural fluid, laboratory analysis of which revealed exudative effusion by LIGHT's traditional criteria (pleural fluid protein/serum protein ratio of 1 and pleural fluid lactate dehydrogenase (LDH)/serum LDH ratio of 3.6). Two days later, the chest tube started draining fragments of cream-grayish colored tissue. A specimen received in the pathology department showed multiple pieces of grayish-colored tissues, altogether measuring 1 cm × 0.5 cm. The hematoxylin and eosin stain revealed a tumoral lesion composed of neoplastic spindle cells admixed with primitive round-to-oval neoplastic cells that arranged themselves in a nested pattern. Islands of cartilage were also visible [Figure 3a and b]. Mitotic figures were conspicuous. A preliminary diagnosis of PPB was made. Immunohistochemistry was performed to rule out other sarcomas and to confirm the diagnosis. Neoplastic cells stained strongly for vimentin and desmin, and a negative reaction pattern was seen for CK7, alpha smooth muscle actin, epithelial membrane antigen, and myogenin.

**Table 1: Laboratory parameters showed first and second admission of the patient**

| Parameter | First admission | Second Admission | Normal range |
|---|---|---|---|
| WBC | 13700 | 9600 | 3500-10000 |
| Hemoglobin | 12.4 | 9 | 11.5-18.8 |
| Platelet | 681000 | 310000 | 165-415 |
| ESR | 35 | 30 | up to 22 |
| MCV | 79.58 | 78.82 | 80-96 |
| Urea | 22 | 17 | 17-42 |
| Cr | 0.6 | 0.6 | 0.6-1.3 |
| Na | 137 | 136 | 134-145 |
| K | 4.8 | 4.2 | 3.5-5.5 |
| Ca | 9.1 | 8.8 | 8.6-10.3 |
| Serum Albumin | 4 | 3.5 | 3.5-5.2 |
| Total Protein | 5.6 | 5.6 | new born: 4.2-6.7<br>Up to 18: 5.7-8 |

Islands of cartilaginous cells stained with S-100 antibody, and the Ki67 rate was 70% [Figure 4a and b]. Finally, PPB was confirmed, and the patient received neoadjuvant chemotherapy and underwent surgery for resection of the mass. Gross examination of the resected mass demonstrated gray-yellowish colored tissue with a bosselated surface altogether measuring 13 cm × 9 cm × 5.5 cm. On the cut section, a cystic space was seen with solid, yellowish-colored areas [Figure 5]. Histopathological examination showed a high-grade neoplasm composed of neoplastic spindle cells, which had large, hyperchromatic nuclei, and numerous islands of neoplastic cartilaginous cells with large, bizarre nuclei, and conspicuous mitotic figures. Blastemal round cells were admixed with other components. Cystic spaces were also present, lined by multiple layers of tall columnar epithelial cells with papillary projections [Figure 6a and b]. PPB Type II was confirmed. The patient was admitted to the pediatric intensive care unit and is now under special care and chemotherapy.

## Discussion

PPB is a rare primary intrathoracic pediatric malignant tumor, first described by Manivel *et al*. in 1988.[7] The

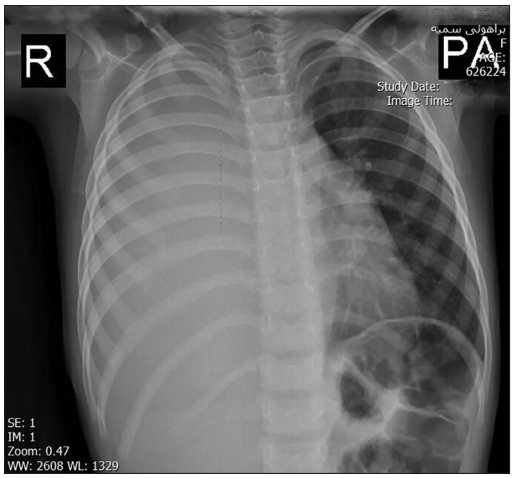


**Figure 1: Posterior-anterior chest radiograph shows complete opacification of the right hemithorax with a mild shift of mediastinum to the left**

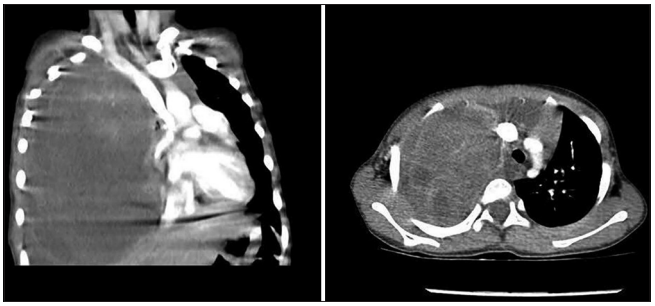

**Figure 2: A spiral computed tomography scan of the thorax with intravenous contrast reveals a large right-sided complex solid and cystic mass occupying almost the entire right hemithorax, as well as right-sided pleural effusion and collapse of the right middle and lower lobes, due to compressive effect of the mass**

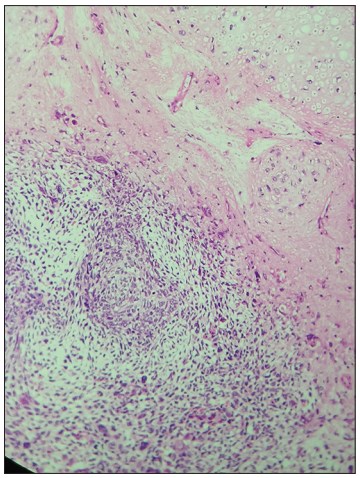

**Figure 3: Tumoral lesion composed of neoplastic spindle cells admixed with a primitive round to oval cells that arranged in nests pattern with islands of cartilage (H&E, ×20)**

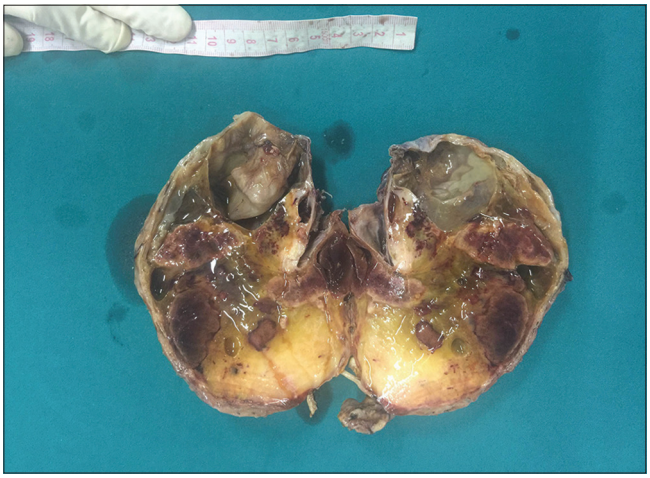

**Figure 5: Tumoral lesion composed of cystic space with solid yellowish-colored solid areas**

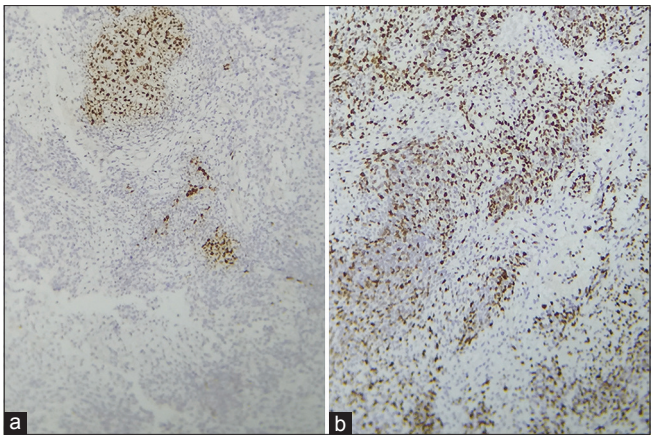


**Figure 4: (a) The positive reaction of neoplastic cartilaginous cells for S-100. (b) Positive reaction pattern of neoplastic cells for Ki67 (IHC, ×20)**

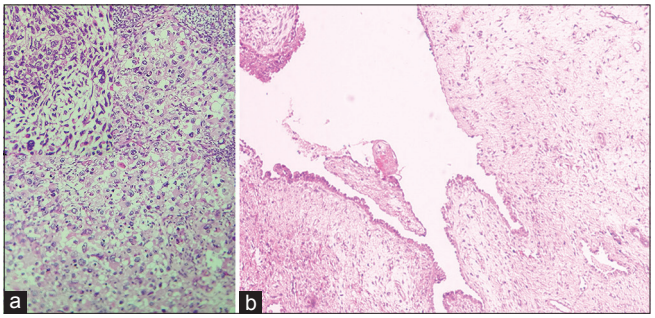


**Figure 6: (a) Neoplastic spindle cells have large hyperchromatic nuclei admixed with islands of neoplastic cartilaginous cells have large bizarre nuclei and conspicuous mitotic figures and also blastemal round cells nests, (b) Cystic spaces are lined by multilayered of tall columnar epithelial cells with papillary projections (H&E, ×20)**

familial type of the tumor is seen in familial tumor predisposition syndrome, also known as DICER1-PPB or DICER1 tumor predisposition syndrome.[1] Germline mutation in the *DICER1* gene has been considered a major etiologic factor of this malignant sarcoma.[2,3] Based on previously published literature, PPB has been categorized into three types, with Type I (purely cystic lesion) mainly affecting infants from the prenatal period to 10 months old, Type II (solid and cystic lesion) mostly involving children with a mean age of 34 months old, and Type III (pure solid lesion) showing the most aggressive behavior with the highest potential for distant metastasis, mainly seen in pediatric patients with a mean age of 44 months old.[7-10] Respiratory distress syndrome, progressive shortness of breath, or pneumonia-like symptoms, such as fever, cough, fatigue, loss of energy, and weight loss, are the most frequent symptoms at presentation as in our case, which presented with pneumonia-like symptoms.[6,7] Imaging findings are nonspecific; however, unilateral focal pulmonary consolidation/mass or hemithorax opacification reported as a major imaging findings.[4,7]

Large tumors may cause a contralateral shift of the mediastinum and a compressive effect on the adjacent structures, or they could manifest as tension pneumothorax, as reported in a case by Addanki *et al*.[8,9] Ultrasound features of PPB may consist of a complex cystic mass with fine septation, a mixed solid-cystic lesion, or a purely solid mass involving the pleuropulmonary cavity.[10]

Histologically, the tumor is composed of neoplastic oval to spindle cells admixed with cartilaginous tissue and blastemal cells that demonstrate dark hyperchromatic nuclei and scanty cytoplasm. In Type II and III of PPB, the sarcomatous component is predominant with some of the neoplastic cells showing high-grade nuclear features.[7-10]

This was true, in our case, where both cartilaginous and stromal neoplastic cells showed large, pleomorphic, bizarre-shaped nuclei with conspicuous mitotic figures. Sarcomatous components resembled rhabdomyosarcoma, chondrosarcoma, fibrosarcoma, or monophasic synovial sarcoma.[1,3] Previously published literature showed that immunohistochemical studies provide limited diagnostic

information for differentiation of PPB from other sarcomas.[8-10] Blastematous areas also may resemble Wilm's tumor, which is why historically, the disease was called pulmonary Wilm's tumor.[3-6]

Various treatment options have been suggested, depending on the stage of the disease.[6,8] For Type I (purely cystic) disease, surgery and watchful waiting seem to be the best treatment options. Types II and III are more aggressive than Type I, with poorer outcome and worse prognosis, due to earlier local recurrence and distant metastasis.[5-10] Accordingly, for Type II and III diseases, neoadjuvant therapy before surgical resection has been recommended.[5,7] Unlike the reported case of PPB by Hashemi *et al*.,[10] in which a 42-year-old male patient first underwent resection of a lung mass and then was given neoadjuvant chemotherapy because the mass was incompletely resected, our case was first given chemotherapy, and then, the mass was completely resected.

## Conclusion

PPB is a rare, highly malignant pediatric lung cancer with nonspecific clinical symptoms, such as pneumonia. Neoplastic primitive cells admixed with spindle cells produce a diagnostic dilemma, which could result in PPB being misdiagnosed as fibrosarcoma, rhabdomyosarcoma, or monophasic synovial sarcoma. The most accurate method for diagnosis of PPB is a biopsy or surgical resection, but in rare cases, part or parts of the tumor could be spontaneously detached from the pleural or lung parenchyma and exit through the chest tube. Immunohistochemical studies are nonspecific and would be conducted to exclude other round cell neoplasms. Neoadjuvant therapy before total surgical resection is a treatment of choice to reduce the size of the tumor.

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### Conflicts of interest

There are no conflicts of interest.

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