ACCSCIENCE PUBLISHING

Tumor Discovery

CASE REPORT

Pleuropulmonary blastoma in a child masquerading as massive pleural effusion: A case report

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Abstract

Pleuropulmonary blastoma (PPB) is a rare dysembryonic lung neoplasm of childhood. Its aggressive nature is demonstrated by its large size and metastasis at the time of diagnosis. Here, we present a case of a 5-year-old male with a history of sudden dyspnea who was initially referred to the primary health-care center for emergency medical services. His initial chest radiography showed massive hydropneumothorax in the right pleural cavity, with gross mediastinal displacement. These clinical findings and rapidly decreasing peripheral saturation prompted the emergency team to insert a right-sided intercostal drainage tube. Initially, this step was able to stabilize the condition, but a subsequent computed tomography scan revealed a vast cystic-solid mass in the right hemithorax. After establishing the diagnosis of PPB by means of histopathology and immunohistochemistry, he was operated on urgently for cytoreductive purposes. Despite the initial macroscopic clearance, the mass recurrence occurred after 3 months, contributing to the ultimate fatal outcome for the patient. Due to the cystic-solid nature of type II/III PPB, it could be masquerading as hydropneumothorax in the initial chest X-ray, a misleading yet the sole initial presentation of this rare entity.

Keywords: Pleuropulmonary blastoma; Lung neoplasm; Pediatric oncology; Thoracic surgery

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1. Background

Pleuropulmonary blastoma (PPB) is a rare dysembryonic thoracic tumor of mesenchymal origin in the childhood age group. It was first recognized by Manivel *et al.* in a study of 11 patients in 1988[1]. So far, four types of PBB have been described in the medical literature. Type I PPBs are virtuously cystic tumors that occur in young children of less than 2 years with a median age of 10 months. Type I tumor may progress to type II or III or regress to another type Ir, where "r" stands for regressing (no malignant cells are present). Type II PPBs are a mix of cystic and solid tumors usually occurring at a median

age of 35 months. Type III PPBs are solid tumors usually arising at a median age of 41 months. Type II and type III tumors are very aggressive and tend to recur or metastasize early. The common sites of metastasis are the brain, liver, lymph nodes, pancreas, kidney, and adrenal glands. Type I/Ir PPB has the best prognosis and type III has the least[2].

The clinical presentations of PPB are non-specific; hence, the chances of misdiagnosis are very high, with a poor prognosis. Surgery has been cited as the standard treatment, supplemented with chemotherapy for better curative effect. Surgical resection is usually challenging for various reasons, such as the extent and large size of the tumor, its relation with large vessels and neighboring vital structures in the thorax, and neighboring invasion. In this age group, choosing an incision for proper exposure with maximum lung preservation is also problematic. It is presumed that surveillance of *DICER1* genetic mutation may permit the earlier discovery of PPB, abrogate possible advancement to other types, and improve final outcomes[2,3].

2. Case presentation

A 5-year-old male with severe respiratory distress coupled with peripheral desaturation was referred to the emergency department, and he was initially managed with right-sided intercostal tube drain insertion as an emergency measure based on X-ray findings. After temporary stabilization, he was then referred to our institute. Contrast-enhanced computed tomography (CT) scan showed a sizeable neoplastic cystic-solid mass lesion with necrotic areas occupying the right hemithorax, compressing pericardium and great vessels, and causing the right upper and middle lobe bronchus cut-off with the pleural invasion with severe tracheal and mediastinal shift toward the left side (Figure 1). Based on CT scan findings of cystic-solid nature of the mass, PPB with extraskeletal Ewing's sarcoma, synovial sarcoma, and embryonal rhabdomyosarcoma were suggested as possible differential diagnosis. CT-guided biopsy and immunohistochemistry established the diagnosis as type II/III PPB. Microscopy indicated primitive blastema-like small cells with a high nucleocytoplasmic ratio and a poorly differentiated tumor. On immunohistochemistry, immunoreactivity for vimentin in blastemal areas with focal desmin positivity for rhabdomyoblastic cells was positive but immunonegative for epithelial membrane antigen, S100, and others. A CT scan of the brain was conducted to rule out metastasis. Screening by abdominal ultrasonography did not yield any unusual findings. The patient went into severe hypoxia and shock on the 3rd day after admission while undergoing further investigations, and urgent intubation was performed to revive him.

Due to rapid deterioration, surgical intervention was implemented for the patient after proper consents of his parents were obtained. Under general anesthesia, a clamshell incision with bilateral thoracotomy was made. The cystic-solid tumor resulted in the complete collapse of the right lung due to compression. The tumor abutted the pericardium and large vessels (both vena cavae and azygos vein), and anteriorly crossed the retrosternal space to the opposite side. There was no invasion of the pericardial or left pleural cavity. The left lung was normal. We could dissect the tumor almost to its entire extent after gentle dissection and freeing it from large vessels and the anterior surface of the pericardium. After tumor removal with right lower lobe excision, the upper and middle lobes of the right lung were preserved with complete macroscopic clearance of the thoracic cavity (Figure 2). The excised tumor was around 650 g in weight and approximately 15 × 10 × 9 cm in dimensions (Figure 3). The incision was closed in layers with bilateral intercostal drainage tubes. The excised tumor mass was again sent for detailed histopathological examination using immunohistochemical approach. The histopathology images showed that tumor has primitive blastema-like small cells with hyperchromatic nuclei, high nuclear to cytoplasmic ratio, spindled and ovoid cells, rhabdomyoblastic cells, and nodules of immature chondroid elements along with clusters of large anaplastic cells with pleomorphic nuclei. Areas of necrosis were seen in the myxoid and fibrous stroma in the tumor (Figure 4). The patient was extubated the 2nd day after operation. The

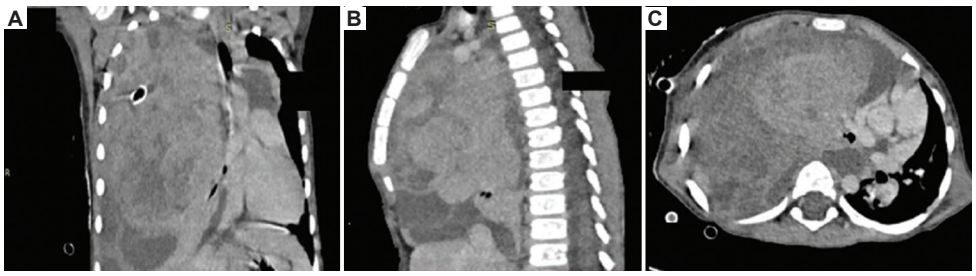


Figure 1. Computed tomography scan of the chest. (A) Coronal view showing right-sided intercostal tube in tumor mass with gross mediastinal shift. (B) Sagittal view showing the right hemithorax cystic-solid tumor. (C) Axial view showing right hemithorax cystic-solid tumor, mediastinal shift with compressed left lung.

left-sided chest tube was removed on the 4th post-operative day, while the right-sided chest tube was removed on the 6th day after expansion of the right lung, and no drainage was performed. Post-operative chest X-ray showed complete expansion of a previously collapsed right lung. A repeat chest CT scan showed clear bilateral lung zones with no evidence of recurrence or metastasis (Figure 4A). The clamshell incision wound was well healed, and the patient was healthy at discharge on the 9th post-operative day. He had been planned for doxorubicin-based chemotherapy treatment and genetic testing of *DICER1*, but his parents and family members were unwilling to send the patient for further testing, intervention, and treatment. After 87 days of surgery, he was sent back to the hospital due to severe respiratory distress with a recurrence of gross mediastinal mass (Figure 4B). In the hospital, we worked with the medical oncology team to stabilize the patient's condition at the time, but to no avail, he succumbed within 2 days of admission.

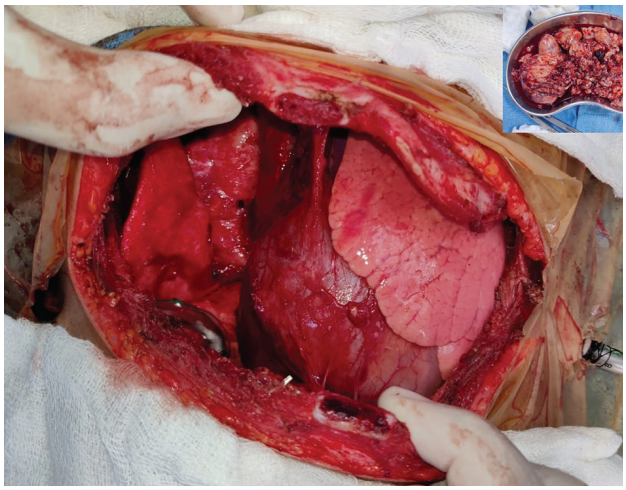


Figure 2. Intraoperative picture showing a healthy left lung, intact pericardium, and compressed right-sided lung upper and middle lobes after tumor removal. The inset shows the resected tumor mass.

3. Discussion

PPB is a rare embryonal thoracic tumor. It is highly aggressive by nature, arising from both lung and pleura, and accounting for 0.5% of all primary malignant lung tumors in the pediatric population. Three types of PBBs have been described in the literature. Type I PBB is purely cystic; type II comprises cystic and solid elements; and type III is exclusively solid. It is solely confined to the pediatric age group, specifically restricted to children under 7 years of age according to most reports[2]. In 2009, a heterozygous germline mutation in *DICER1* was identified as the first identified genetic cause in the majority of documented PPB cases. The *DICER1* gene located on human chromosome 14 instructs cells to make a protein called DICER1, which processes molecules to make microRNA. This germline mutation in *DICER1* can lead to a unique hereditary cancer predisposition syndrome, which is accompanied by PPB, cystic nephroma, ovarian Sertoli-Leydig cell tumors, ciliary body medulloepithelioma, nodular hyperplasia, pituitary blastoma, pineoblastoma, nasal chondromesenchymal hamartoma, and differentiated carcinoma of the thyroid gland. However, a review of 350 confirmed PPB cases by Messinger *et al.* confirmed that there were no clinical differences in terms of germline *DICER1* mutation and thus no distinct prognostic value[3].

Type I tumors (median age at diagnosis: 8 months) have minimal malignant components and are mostly benign. They may change to type II or type III tumors.

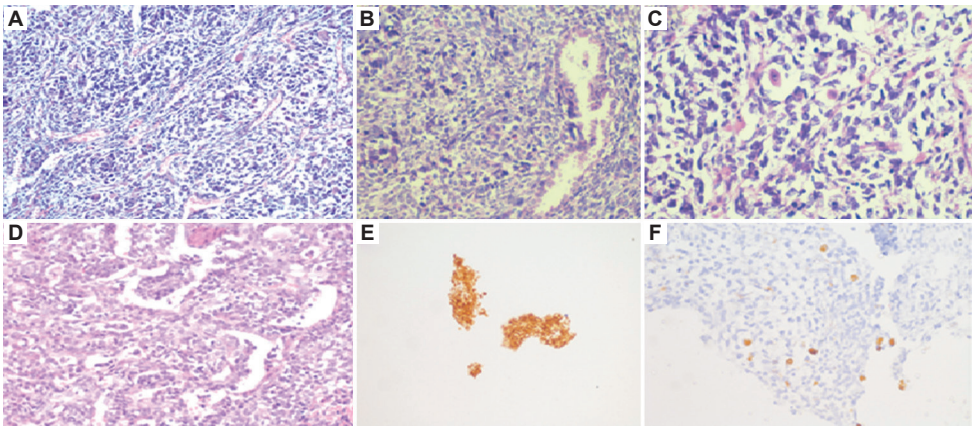


Figure 3. Histopathological findings. (A) Blastemal and sarcomatous cells (hematoxylin-eosin staining, ×400 magnification). (B) Pleomorphic anaplastic cells in sarcomatous areas (hematoxylin-eosin staining, ×400). (C) Rhabdomyoblasts in the blastemal areas (hematoxylin-eosin staining, ×400). (D) Low-grade fetal adenocarcinoma component (hematoxylin-eosin staining, ×400). (E) Tumor cells showing cytoplasmic immunoreactivity for vimentin in blastemal areas (vimentin staining, ×400). (F) Rhabdomyoblasts in tumor cells showing desmin immunoreactivity (desmin staining, ×400).

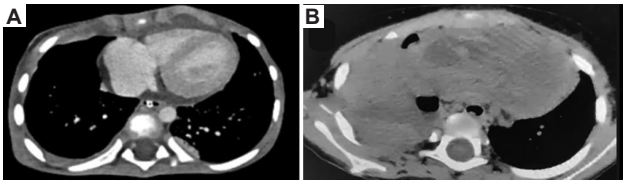


Figure 4. (A) Immediate post-operative computed tomography scan of the chest shows clear bilateral lung fields without residual macroscopic lesion. (B) A computed tomography scan of the chest shows gross local recurrence of mass in the right hemithorax with mediastinal shift at the time of readmission.

Type I (median age at diagnosis 46.5 months) is a subtype that lacks primitive cell components. In the documented registry, most cases of type I and Ir cysts are unilateral (74%), with only 55% larger than 5 cm in size. Type II tumors have cystic and solid areas of blastomatous or sarcomatous components with anaplasia in up to 60% of these cases, with the median age during diagnosis at 35 months, and distant metastases happen in 7% of patients at the time of diagnosis. Type III tumors consist of purely solid components (blastomatous and sarcomatous), with anaplasia occurring in 70% of these cases. The median age at diagnosis of type III tumor is 41 months, and distant metastases reportedly happen in 10% of patients at the time of diagnosis[3,4]. Type II and type III tumors are more metastasizable at early stage and can metastasize to the brain, lungs, and bone, with the brain being the most common site of metastasis[5]. Therefore, pre-operative staging using magnetic resonance imaging or CT scan of the brain, chest, abdomen, and sometimes, a bone scan, is strongly recommended[6]. A study by Priest *et al.* documented an overall survival rate of 45% at 5 years with an event-free survival rate of 49% at 2 years among PBB patients[7]. Type II and type III PPBs manifest aggressive behavior, with 2-year and 5-year overall survival rates of 62% and 42%, respectively, despite multimodal therapy.

Due to gross enlargement, these masses usually cause compression of vital structures in the mediastinum. In some patients with severe respiratory distress, a needle decompression can be performed or a chest tube can be inserted as a lifesaving procedure. However, chest tube placement is not favored due to possible contamination of the pleura, which might result in tumor upstaging and increase the risk for *en bloc* resection[8]. Although three treatment modalities (surgery, chemotherapy, and radiotherapy) have been tested for their efficacy in treating PBB, no clear consensus can be drawn due to the rarity, peculiarity and late presentation of the tumor.

Complete surgical resection is cited as the standard management strategy for type I tumors because it delivers good patient outcomes. For type II and type III, surgery is favored for debulking and macroscopic clearance. This technique is usually narrowed down to non-anatomical or wedge resection, lobectomy or pneumonectomy, and removal of infiltrated structures such as pericardium, diaphragm, or parietal pleura. In general speaking, gross surgical resection of the tumors may improve survival of the patients. Aggressive mediastinal dissection should be weighed against surgical morbidity and mortality[9,10]. In type II and type III PPBs, chemotherapy is mandatory for maximizing the chance of curing the patients. If metastatic disease is present, neoadjuvant chemotherapy should always be included in the treatment regimen, and doxorubicin is an important agent for type II and type III PPB. Multidrug regimens for rhabdomyosarcoma, such as ifosfamide-vincristine, actinomycin D (IVA), and IVA with doxorubicin (IVADo) or cyclophosphamide for replacing ifosfamide, can been considered for treatment, but curative evidence and optimal duration of chemotherapy have not been established. Radiotherapy has a minimal impact on this tumor. The significant international effort promoted by the EXPeRT/PARTNER group proposed possible overall strategies to treat patients with PBB. However, more corroborative evidence is needed to answer some open questions.

Prognosis is determined mainly based on the type of tumor, resection margin, metastasis, and post-operative adjuvant chemotherapy[11]. A recent report by Duc *et al.* showed that despite tumoral resection and chemotherapy, local recurrence and spinal metastasis still occurred in a 2-year-old girl with type III PPB after 5 months of treatment[12], indicating the challenges in the treatment and control of PBB. It is recommended that treatment plan should be personalized according to the specific conditions of each patient after multidisciplinary tumor board discussion since the standard consensus and guidelines surrounding the treatment of PBB are evolving[13].

4. Conclusion

The initial chest X-ray findings may misconstrue type II and type III PPB as hydropneumothorax due to the cystic-solid nature of these subtypes, and this may be the sole initial presentation of this rare entity as in our case. Further, after establishing the diagnosis, cytoreductive surgery was performed with the primary goal of complete removal of all macroscopic disease, but the patient succumbed to death due to the rapid local recurrence within a short duration, possibly caused by the lack of chemotherapy not administered in this case. Hence, multimodality treatment should always be considered for more prolonged survival in advanced cases of PPB.

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Conflict of interest

The authors declare that they have no conflict of interest and no competing interests.

Author contributions

Conceptualization: Anshuman Darbari, Ishan Jhalani, Meenu Singh
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Writing – review & editing: Anshuman Darbari, Ajay Kumar, Prashant Durgapal,

Ethics approval and consent to participate

This case report study has been approved by the institute Ethical Committee (IEC) of All India Institute of Medical Sciences, Rishikesh, India (DHR Regn no.-EC/NEW/Inst./2022/UA/0180, Letter no.: AIIMS/IEC/23/251).

Consent for publication

Written informed consent was obtained from the patient's guardian (father) for this report publication.

Availability of data

Data can be obtained from the corresponding author upon reasonable request.

References

1. Manivel JC, Priest JR, Watterson J, *et al*., 1988, Pleuropulmonary blastoma. The socalled pulmonary blastoma of childhood. *Cancer*, 62: 1516–1526.

   https://doi.org/10.1002/1097-0142(19881015)62:8<1516::AID-CNCR2820620812>3.0.CO;2-3

2. PDQ Pediatric Treatment Editorial Board, 2002, Childhood pleuropulmonary blastoma treatment (PDQ®): Health professional version. In: PDQ Cancer Information Summaries. Bethesda, MD: National Cancer Institute US.

3. Messinger YH, Stewart DR, Priest JR, *et al*., 2015, Pleuropulmonary blastoma: A report on 350 central pathology-confirmed pleuropulmonary blastoma cases by the international pleuropulmonary blastoma registry. *Cancer*, 121: 276–285.

   https://doi.org/10.1002/cncr.29032

4. Zhang N, Zeng Q, Ma X, *et al*., 2020, Diagnosis and treatment of pleuropulmonary blastoma in children: A single-center report of 41 cases. *J Pediatr Surg*, 55: 1351–1355.

   https://doi.org/10.1016/j.jpedsurg.2019.06.009

5. Nakano Y, Gatell SP, Schultz KA, *et al*., 2019, Successful treatment of metastatic cerebral recurrence of pleuropulmonary blastoma. *Pediatr Blood Cancer*, 66: e27628.

   https://doi.org/10.1002/pbc.27628

6. Gbande P, Abukeshek T, Bensari F, *et al*., 2021, Pleuropulmonary blastoma, a rare entity in childhood. *BJR Case Rep*, 7: 20200206.

   https://doi.org/10.1259/bjrcr.20200206

7. Priest JR, McDermott MB, Bhatia S, *et al*., 1997, Pleuropulmonary blastoma: A clinicopathologic study of 50 cases. *Cancer*, 80: 147–161.

8. Zamora AK, Zobel MJ, Ourshalimian S, *et al*., 2020, The effect of gross total resection on patients with pleuropulmonary blastoma. *J Surg Res*, 253: 115–120.

   https://doi.org/10.1016/j.jss.2020.03.019

9. Wang F, Zhuang L, Liang J, *et al*., 2022, Treatment and prognosis of pleuropulmonary blastoma: A single-center report of 31 cases. *Pediatr Pulmonol*, 57: 2237–2243.

   https://doi.org/10.1002/ppul.25930

10. Grigoletto V, Tagarelli A, Sparber-Sauer M, *et al*., 2020, Inequalities in diagnosis and registration of pediatric very rare tumors: A European study on pleuropulmonary blastoma. *Eur J Pediatr*, 179: 749–756.

    https://doi.org/10.1007/s00431-019-03566-7

11. Bisogno G, Sarnacki S, Stachowicz-Stencel T, *et al*., 2021, Pleuropulmonary blastoma in children and adolescents: The expert/partner diagnostic and therapeutic recommendations. *Pediatr Blood Cancer*, 68(Suppl 4): e29045.

    https://doi.org/10.1002/pbc.29045

12. Duc LA, Vu LT, Ngoc DV, T, *et al*., 2021, Pleuropulmonary blastoma (type III) in a two-year-old: A case report. *Radiol Case Rep*, 16: 2978–2980.

    https://doi.org/10.1016/j.radcr.2021.07.024

13. Mlika M, Anjum F, El Mezni F, 2023, Pleuropulmonary blastoma. In: StatPearls. Treasure Island, FL: StatPearls Publishing. Available from: https://www.ncbi.nlm.nih.gov/books/nbk534211 [Last accessed on 2023 Apr 27].