Bilateral pleuropulmonary blastoma (PPB) in a 2-year-old girl: A case report with review of literature

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Abstract
Pleuropulmonary blastoma (PPB) is a rare aggressive malignant tumor of infancy and early childhood accounting for 0.25-0.5% of primary lung tumors. PPB is a dysontogenic tumor composed of immature malignant epithelial and/or mesenchymal tissues whose features may resemble early embryological lung tissues. It is the pulmonary analog of other tumors of childhood including Wilms' tumor, neuroblastoma, hepatoblastoma, pancreatoblastoma and retinoblastoma. Morphologically, PPB has three types (I, II, and III). A fourth type (Ir) was added in 2006 by PPB registry. Type II and III are very aggressive malignancies with metastatic potential. Bilateral PPB is very rare. To the best of our knowledge, only two cases of bilateral PPB have been reported. No cases of bilateral PPB have been reported from India. Herein, we are reporting a case of bilateral PPB (type II) in a 2-year-old girl who presented with cough, dyspnea and mild fever for past 4 months. She died few days after admission.

Key words: Bilateral pleuropulmonary blastoma, Bronchogenic cyst, Congenital pulmonary airway malformations, Dysontogenic tumor, PPB registry, Primitive neuroectodermal tumors

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Case report
A 2-year-old girl presented with the complaint of right sided chest pain, mild fever and shortness of...
breath for 4 months. She was diagnosed as pneumonia based on chest X-ray findings and started on antibiotics in an outside hospital. But, there was no improvement in patient’s condition. At admission to our hospital, she was dyspneic with respiratory rate of 60/min, BP: 120/70mm Hg, pulse rate: 120/min and oxygen saturation of 91% on room air. Subcostal, intercostal retractions and nasal flaring were present. There was no cyanosis or clubbing. She had no significant medical or surgical history. She had no significant family history. Chest examination revealed bilateral dullness on percussion, more on right side. Examination of other systems was unremarkable. Routine blood examination was normal. Chest radiograph showed opacity of the right hemithorax (Fig 1). Thoracic ultrasound (USG) showed a large homogenous mass in right hemithorax without calcification (Fig 2). Computed tomography (CT) of thorax revealed a large, hypodense homogeneous round tumor with cystic components occupying almost whole of the right hemithorax. Solid components showed moderate enhancement. Similar lesion of smaller size was noted in left hemithorax. The mass lesion abuts chest wall and pericardium. Mild right pleural effusion noted. There was no evidence of chest wall invasion, rib erosion or calcification within mass (Fig 3). She underwent USG-guided fine-needle aspiration cytology (FNAC) which was suggestive of PPB (Fig 4). She was shifted to pediatric intensive care unit. Unfortunately, she died few days after admission possibly due to respiratory compromise. Based on radiological and cytological findings, diagnosis of bilateral PPB type II was made.

**Discussion**

PPB present as parenchymal and/or pleural based mass lesion and divided into three types (I, II, and III) based on morphological characteristics by Dehner et al. A fourth type (Ir) was added in 2006 by PPB registry. Type Ir (type I-regressed) tumors are cystic containing few spindle shaped cells in the cyst wall with few foci of dystrophic calcification but without subepithelial malignant cell condensation. It might represent a regressed or a genetically destined but abortive type I tumor.

Certain genetic mutations are associated with pleuropulmonary blastomas including germ line DICER1 mutation (loss of function) in familial cases, gains of chromosome 8 (most consistent chromosomal abnormality), trisomy 2, unbalanced translocation between chromosomes 1 and X, and p53 mutations or deletions.

Type I (14%) tumors are less aggressive ‘Purely Cystic’ tumors which presents at earlier age with median age of diagnosis 10 months and 5-year survival rate of 83%. They account for 15 to 20% of all PPB. The cyst wall is lined by cuboidal or columnar ciliated respiratory epithelium. Under the epithelium there is cambium-like areas with proliferation of primitive mesenchymal cells with foci of blastematosus cells.

Type II (48%) tumors are ‘Solid and Cystic’ tumors where cystic lesion shows features of type I PPB and solid lesions shows feature of type III PPB and median age of diagnosis 34 months. Type III (38%) tumors are ‘Purely solid’ with the median age of diagnosis of 44 months. Both type II and type III tu-
Tumors are more aggressive with 5-year survival rate of 42% despite chemotherapy and radiotherapy. The solid component seen in type II and III tumors are similar and show blastematous and sarcomatous characteristics. The pathogenetic linkage among the cystic, cystic and solid, and solid PPB is supported by the recurrence of a type I PPB as type II PPB, with both epithelial-lined cysts and complex blastematous and sarcomatous features in the solid component. These three tumor types form a continuum with progression over time from type I to type III tumor. At times type II and III tumors show hemorrhagic and necrotic areas may be seen. The histologic components of type III PPB generally include blastematous islands, cartilaginous nodules, rhabdomyoblasts, and anaplastic cells.

Clinically, the patient presents with chest or upper abdominal pain, fever, dyspnea, cough, hemoptysis, anorexia, malaise, or neurological symptoms resulting from brain metastasis. Metastasis to other areas may lead to signs and symptoms associated with abnormalities in the affected organs and systems of the body. A detailed family history is needed to rule out familial association. Radiological features show varied appearance depending upon tumor type. Chest X-ray shows partial or complete opacification of hemithorax with mediastinal shift to contralateral side. Transectional imaging shows unilocular cysts, a multicystic structure, a cyst containing a polypoid mass, and solid-cystic or entirely solid masses of variable sizes located peripherally in the lung with or without involvement of the pleura or chest wall and may fill the entire hemithorax.

The diagnosis of PPB is often missed at first, because the clinical and radiographic findings are thought to indicate other respiratory disorders such as pneumonia or a benign congenital cyst, particularly a congenital cystic adenomatoid malformation.

**Fig 3.** (a) Axial Non-contrast computed tomography (CT) mediastinal and lung window showing bilateral homogenous hypodense mass in both hemithoraces, almost occupying whole of the right hemithorax. No evidence of calcification, chest wall invasion, rib erosion was noted. (b) Axial contrast enhanced CT showing few cystic areas within the mass. There is moderate enhancement of the mass. (c) Minimal right pleural effusion noted.
Specific imaging findings to favor PPB are rightsided, pleural-based, peripherally located mass without chest wall invasion that causes almost complete opacification of the hemithorax and mass effect, shows heterogeneously low attenuation with no calcification. It may be associated with pleural effusion and pneumothorax.

USG could be preferred before CT or magnetic resonance imaging (MRI) scan because of its low cost, lack of radiation, contrast injection or sedation. When both pulmonary and pleural lesions are present, distinction between these two lesions is not always easy at chest radiographs, USG enables differentiation of pleural pathologies from pulmonary parenchymal lesions. Large consolidation without sonographic air bronchogram finding could also be a clue for PPB cases.

FNAC may not give conclusive diagnosis always but it has been used for diagnosis before histologic evaluation of the excised mass. Biopsy of multiple areas of cystic and solid areas is required for accurate diagnosis. A metastatic workup with type II and type III PPB may include CT scans or MRI of the brain as well as CT scans of the abdomen and pelvis and whole-body bone scan. Because solid PPB tumors can extend into the thoracic great vessels, preoperative echocardiography may be indicated.

Due to the presence of the malignant spindle cell component, the differential diagnosis for type II and type III tumors includes primary or secondary rhabdomyosarcoma, malignant teratoma, synovial sarcoma, other spindle cell/undifferentiated sarcomas, or pulmonary blastoma, whereas due to the presence of primitive blastema, the differential diagnosis includes metastatic Wilm’s tumor. Location, morphology, imaging studies, and immunohistochemistry are helpful in making this differentiation. Desmin and muscle specific actin are usually positive in the obvious rhabdomyoblasts. Immunohistochemical staining mirrors a range of differentiation with vimentin, histiocytic markers or myoid antigens being common.

General imaging differential considerations include: intrathoracic soft tissue sarcoma, primitive neuroectodermal tumours (PNET) of thorax, large bronchogenic cyst/lung cyst (for type I), fetal lung interstitial tumor (FLIT), types 1 and 4 congenital pulmonary airway malformations (CPAM’s) for type 1 PPB.

The recommended treatment for type I tumors consists of surgical excision and adjuvant chemotherapy followed by follow up to look for recurrence. For the usual type II and type III tumors, the treatment consists of aggressive surgery and chemotherapy.
For large type II and type III tumors, after initial confirmation by multiple needle core biopsies, 2 to 4 courses of neoadjuvant chemotherapy are instituted reducing the tumor size usually by more than 90%, followed by surgical resection. 

In the largest series of PPB published, 5-year survival rates were 83% for type I PPB and 42% for type II and type III PPB. It has also been suggested that “extrapulmonary” involvement in PPB, defined as involvement of “the pleura, diaphragm or mediastinum,” indicates a less favorable prognosis. Metastasis to brain, bone, lymph nodes, liver, pancreas, kidney and adrenal glands is also seen, commonest to brain which occurs in aggressive forms of PPB: Types II and III PPB. Cerebral metastases occur in 11% of type II and 54% of type III patients and may appear when thoracic disease is under control.

Conclusion

Pleuropulmonary blastoma is a rare aggressive malignant tumor of infancy and early childhood with poor prognosis. A high index of suspicion is needed to diagnose PPB because clinical and radiographic findings may mimic other respiratory disorders such as pneumonia or a type I PPB because clinical and radiographic findings may mimic other respiratory disorders such as pneumonia or a type I PPB because clinical and radiographic findings may mimic other respiratory disorders such as pneumonia or a type II PPB because clinical and radiographic findings may mimic other respiratory disorders such as pneumonia or a type II PPB because clinical and radiographic findings may mimic other respiratory disorders such as pneumonia or a type III PPB. Cerebral metastases occur in 11% of type II and 54% of type III patients and may appear when thoracic disease is under control.

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References