

Case Report

# Primary Pulmonary Primitive Neuroectodermal Tumor of Lung in a Child

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## Abstract

**Introduction:** Peripheral primitive neuroectodermal tumor (pPNET) arising from lung without involvement of chest wall is very rare. Peripheral primitive neuroectodermal tumor are poorly differentiated, highly aggressive tumor of undetermined histogenesis with a tendency toward early metastasis. Diagnosis needs to be established conclusively by histopathology, immunohistochemistry and molecular studies.

**Presentation of the cases:** A 2 year 10-month old child was investigated for fever, cough and cold and was detected to have right intrathoracic cystic mass on imaging. The mass was excised with possibility of pleuropulmonary blastoma. After excision child was referred to our center for decision on further management. Histopathological examination, immunohistochemistry and molecular study for EWSR gene rearrangement proved the diagnosis of Ewing sarcoma. Metastatic work up for our case was negative. Child is currently undergoing chemotherapy and is asymptomatic.

**Conclusion:** Primitive neuroectodermal tumor (PNET) of lung without chest wall involvement in pediatric age group is a rare occurrence. Available literature suggests highly aggressive nature of such tumor. This case report summarizes the differential diagnosis of such rare pulmonary neoplasm in children and role of immunohistochemistry and molecular studies to establish the diagnosis conclusively.

**Keywords:** Primitive Neuroectodermal tumor, EWSR gene rearrangement, Pediatric solid tumors, PNET Lung, Chemotherapy

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**Consent:** Consent was taken from the patient for publication of this case report.

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## Introduction

Ewing sarcoma (ES) is the second most common primary malignant bone tumor in children and young adults. Classical Ewing sarcoma (ES) of bone, extra skeletal ES, Askin tumor of the thoracic wall, and peripheral primitive neuroectodermal tumor are poorly differentiated, highly aggressive tumor of undetermined histogenesis with a tendency toward early metastasis. The world health organization (WHO) classification uses Ewing's sarcoma/PNET as unifying term for this group [1]. Ewing's sarcoma originates most commonly in bone and soft tissue of children and young adults. First description of ES was also in the form of diffuse endothelioma of bone by James Ewing [2]. The histogenesis of ES has been a matter of controversy and has been ascribed to endothelium, mesenchymal and hematopoietic stem cell based on ultrastructural findings. Bony lesions generally arise from the long bones like femur, humerus or pelvic bone. Soft tissue lesions arise from deep tissues in paravertebral, thoracic, pelvic or lower extremity region. PNET arising from other organs like kidney [3], ovary [4], urinary bladder [5], myocardium [6] and pancreas [7] are infrequently reported. We report a case of primary pulmonary PNET in a child who was initially operated for a pulmonary mass suspected to be pleuropulmonary blastoma and later the diagnosis could be established by histopathology, immunohistochemistry and confirmed with molecular studies.

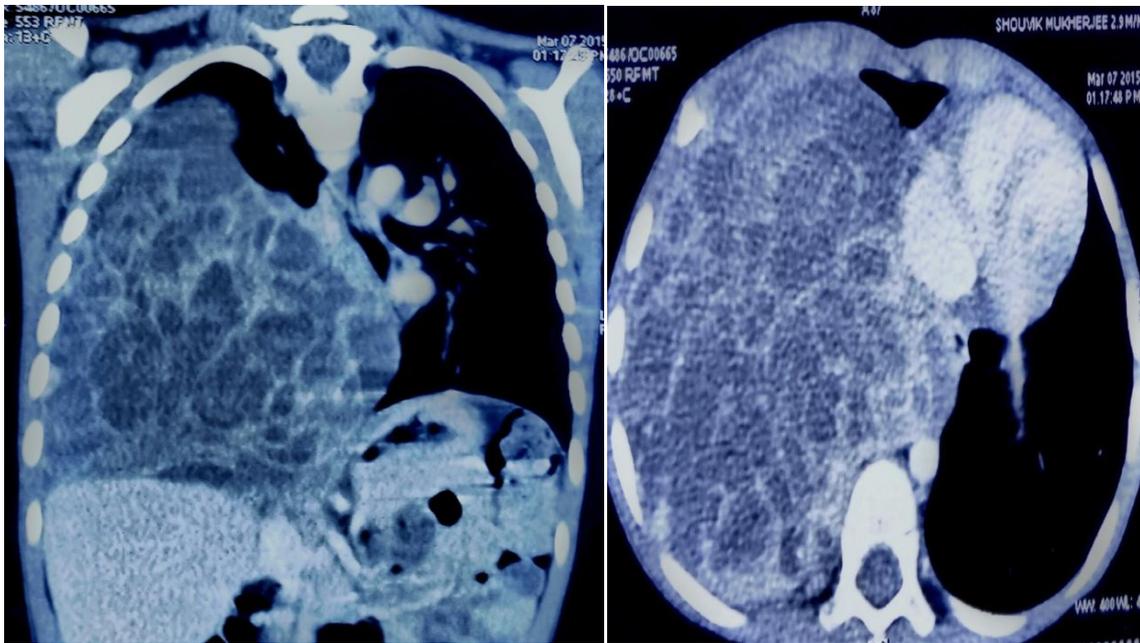
## Case Presentation

A 2 year 10 month old male premonitory asymptomatic, well thriving child was seen initially with complaints of fever, cough and fast breathing. A diagnosis of lower respiratory tract infection was considered; a chest x-ray was ordered and treated with oral antibiotics. He improved partially with resolution of fever but had persistent tachypnea and chest x-ray was reported as right sided pleural effusion. Further evaluation with contrast enhanced CT scan of the chest revealed a heterogeneously enhancing intrathoracic, pleural based mass lesion involving almost whole of the right hemi thorax with cystic and solid areas but there was no involvement of chest wall (Figure 1a and 1b). A diagnosis of pleuropulmonary blastoma type 2 was considered based on radiological features and the child underwent exploratory thoracotomy with excision of the mass. Surgery was uneventful and he remained asymptomatic post-surgery. The child was then referred to our centre for further management.

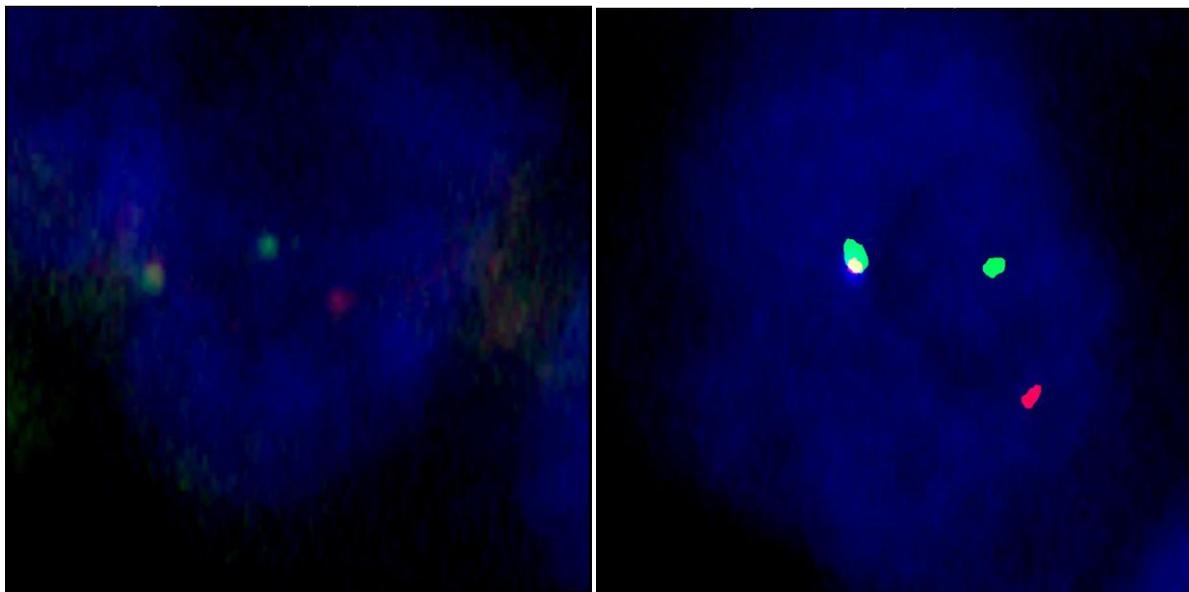
At presentation to our centre the child was asymptomatic with only positive finding being decreased air entry over right lower lung fields. The child's history, preoperative radiograph and histopathology slides were reviewed at our centre.

Histopathological examination of the tissue section from mass revealed small round cell tumor arranged in sheets with interspersed cystic spaces and foci of hemorrhage. Tumor cells were positive for Vimentin, MIC-2 (strong, membranous) while negative for cytokeratin, chromogranin, synaptophysin, desmin, myogenin, EMA, S100. With these findings a possibility of Ewing's sarcoma was kept and molecular study for EWS translocation done. EWSR1 gene rearrangement assay using FISH showed 90 % of the sample positive for EWSR1 translocation (Figure 2a and 2b). A diagnosis of PNET of pulmonary origin was made and metastatic work up was undertaken for same. Bone marrow examination was normal. Post-operative CECT chest showed only subsegmental collapse of right lower lobe with no bony lesion (Figure 3a and 3b). PET CT examination didn't show any evidence of metastatic disease. The differential diagnosis for such lesions includes neuroblastoma, lymphoma, rhabdomyosarcoma, monophasic synovial sarcoma, small-cell carcinoma and desmoplastic small round cell tumor; all of these are indistinguishable by light microscopy. Immunohistochemistry helps

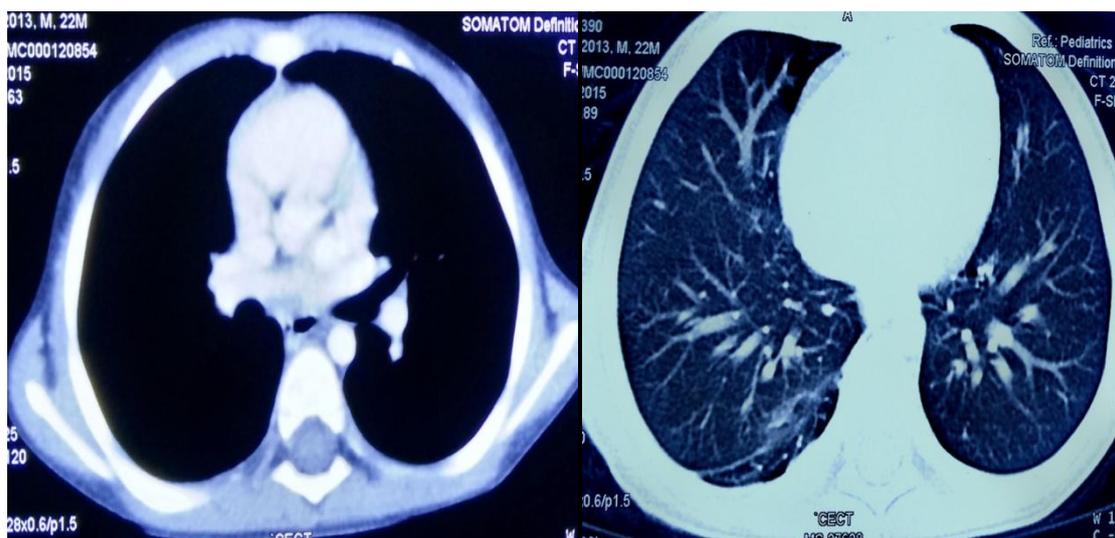
in distinguishing some of these differentials with cytokeratin, epithelial membrane antigen, CD99, and BCL2 are positivity in synovial sarcoma. True Rhabdomyosarcoma of lung often manifests as endobronchial mass.



**Figure 1a (left) and 1b (right)** Pleural based mass with solid and cystic components in the right hemi thorax.



**Figure 2a (left) and 2b (right)** Positive EWSR1 gene rearrangement on interphase nucleus using FISH



**Figure 3a (left) and 3b (right)** Post-operative CECT chest showed only sub segmental collapse of right lower lobe with no bony lesion

Pleuropulmonary blastoma (PPB) which was preoperative radiological diagnosis in our case is a poly phenotypic mesenchymal malignancy. PPB is classified on basis of gross morphology with purely cystic type 1, solid and cystic lesion as type 2 and purely solid lesions as type 3. They are diagnosed mainly in infants and toddler. A cytogenetic abnormality unique to PPB is not identified.

Child initially underwent exploratory thoracotomy and excision of the mass. Once the diagnosis of PNET was confirmed, child was started on standard chemotherapy with Ifosfamide and Etoposide. Currently he has completed three cycle of chemotherapy and is asymptomatic.

## Discussion

Primitive neuroectodermal tumors belong to the family of “small round cell tumors”, originating from the neural crest with varying degrees of neuroectodermal differentiation [1]. Tumor cells in PNET stain positive with Vimentin, mic 2, neural markers, such as NSE and occasionally Cytokeratin [1]. The molecular characterization of PNET, Ewing’s sarcoma (ES) and Askin’s tumor has unified this group into a single pathological and diagnostic entity. The hallmark of these tumors is a chimeric gene that represents fusion of the N- terminal domain of EWS (for ES) gene on 22q12 to the C-terminal domain of ETS (Erythroblastosis-virus transforming sequence) family genes translocated from 11q24 [8].

Peripheral primitive neuroectodermal tumor (pPNET) arising from lung without involvement of chest wall is very rare and is being restricted to only few case reports, that too mostly in adults [9-29] (Table 1). Our case in only the second such case reported below 10 years of age and first below 5 years.

On review of literature the commonest age of presentation seems to be early adulthood (average age 30 years with a range of 8-67 years) with a slight male preponderance (1.5:1). The presenting complaint included cough, shortness of breath, chest pain and hemoptysis. Our child was also male

and had cough with fast breathing as the main presenting complaint.

Pleuropulmonary blastoma, which was the preoperative provisional diagnosis, is an important radiological differential diagnosis for intrathoracic neoplasm in this age group though the management approach and prognosis differ considerably [30]. Lung is a common site of involvement by the other conditions listed in the group of “small round cell tumor” family; on the other hand, primary pulmonary PNET is a very rare entity. Therefore, molecular diagnosis remains one of the invaluable means of diagnosis in such cases. The molecular characterization of ES group of tumor can be done by detection of expression of chimeric gene between EWS and ETS by RT PCR [31]. Cytogenetic analysis can also demonstrate the translocations which lead to formation of these chimeric genes [32]. Interphase Fluorescence in situ hybridization (FISH) can be used to show different chromosomal translocation associated with ES/PNET, it has the advantage of being performed on formalin fixed, and paraffin embedded sections [33], which helped us confirm the diagnosis from tissues sections.

The treatment modality for these tumors includes combinations of radical surgical resection, neoadjuvant and adjuvant chemotherapy and irradiation [34]. Even with aggressive and multimodality approach to therapy the reported mortality remains high [25]. Even though in our case there was no evidence of metastasis and child is currently doing well on chemotherapy, long term follow up is required as recurrence is well known.

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