

## Case Report

# Askin tumor in a child: an interesting case report

Dhrithiman Shetty, Prijo Philip\*

Department of Pediatrics, K.S. Hegde Medical Academy, Mangalore, Karnataka, India

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**\*Correspondence:**

Dr. Prijo Philip,

E-mail: [prijophilipkk@gmail.com](mailto:prijophilipkk@gmail.com)

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### ABSTRACT

Primary neuroectodermal tumors (PNET) have been known to have associations with Ewing Sarcoma family. Tumors that originate from lung parenchyma are a rarity and fatal as well. While the presenting symptoms are non-specific, diagnosis requires histological examination, utilizing immunohistochemical markers such as O13, HBA-71, and 12E7. Treatment is centred around surgical resection and chemotherapy. The authors present one such case, where early diagnosis and appropriate treatment have resulted in tumor regression and symptomatic-free period since last three years.

**Keywords:** Askin tumor, Ewing sarcoma, Primary neuroectodermal tumor

## INTRODUCTION

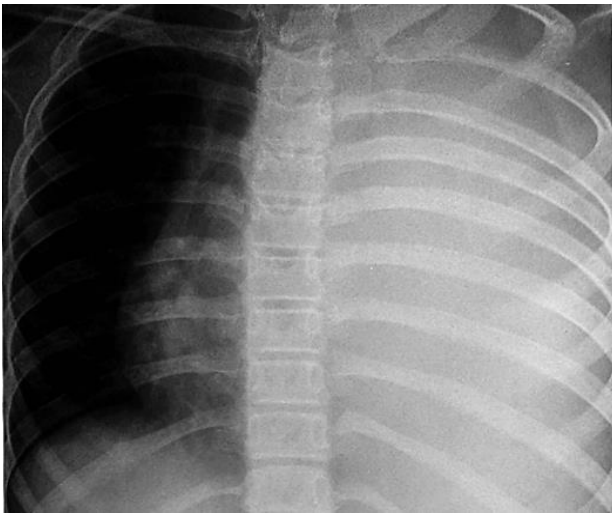
Primitive neuroectodermal tumors (PNETs) are a specific entity that have been postulated to be associated with the Ewing sarcoma family. Literature reports a more frequent presence in adolescents or younger adults (usually younger than 35 years), albeit with a minor male preponderance.<sup>1</sup> The PNET is essentially a very malignant neoplasm that is composed of small, undifferentiated neuroectodermal cells; the more frequent sites of origin being the long bones, such as the femur and humerus, and sometimes, the pelvic bones as well. Various literature reports have also established the presence of PNET in the liver, kidneys, and adrenal glands.<sup>2</sup> When the thorax is involved, PNET commonly arises from the chest wall and this special entity has been called an Askin tumor.<sup>3</sup> However, reports of PNETs arising from the lung parenchyma devoid of pleural or chest wall involvement are extremely rare, and few if any have been reported.<sup>2</sup> The authors would like to present one such case of PNET, of primary thoracic origin, that afflicted an adolescent female.

## CASE REPORT

A thirteen year old female presented in the pediatric out-patient department with primary complaints of pain in the left infraclavicular area since the preceding three months. The pain was found to be radiating along the shoulder and was associated with intermittent fever for one month with cough, breathlessness and hoarseness of voice of 15 days duration. Probing of history also revealed significant weight loss and loss of appetite, but negative with respect to significant past respiratory illnesses or contact with tuberculosis. Upon presentation, child was sick looking and in respiratory distress. Vitals revealed tachycardia and tachypnea although blood pressure was low normal, for age. General examination revealed the child to have pallor, but no cyanosis, clubbing, edema or lymphadenopathy. Further observations revealed the presence of a diffuse, poorly defined but firm swelling over the left chest, involving the supraclavicular and infraclavicular areas and associated with tenderness. Respiratory system examination revealed trachea and apex beat to be shifted to the right side and presence of suprasternal and intercostal retractions. Percussion of

respiratory zones revealed stony dullness in all areas on the left side with absent breath sounds being the prominent findings on auscultation. Gastrointestinal and central nervous system exam was normal. A provisional diagnosis of massive left sided pleural effusion, probably tubercular origin (Progressive pulmonary tuberculosis) was made, with the differentials being mediastinal malignancy and empyema thoracis.

Blood reports were normal except for anaemia (Hb: 9g/dl). Mantoux test was negative and erythrocyte sedimentation rate was 32 mm/hour. Renal and liver functions were normal. Chest X-ray revealed tracheal shift and mediastinal shift to right and scoliosis, Left side revealed a homogenous opacity of left hemithorax, crowding of ribs, obliteration of the costophrenic angle and erosion of the second rib (Figure 1).



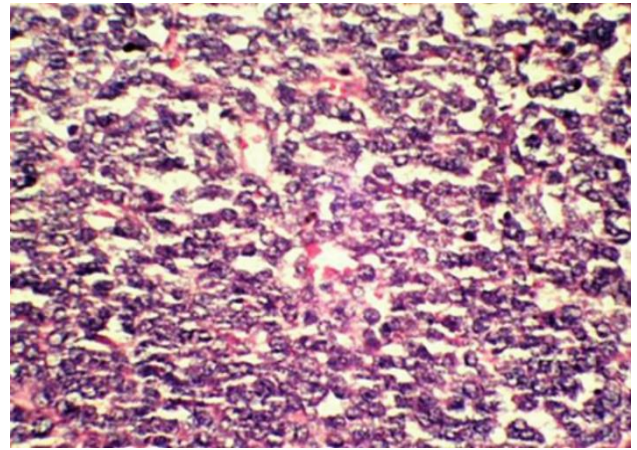
**Figure 1: Chest X-Ray depicting a left hemithorax homogenous opacity, crowding of ribs and mediastinal shift to right.**



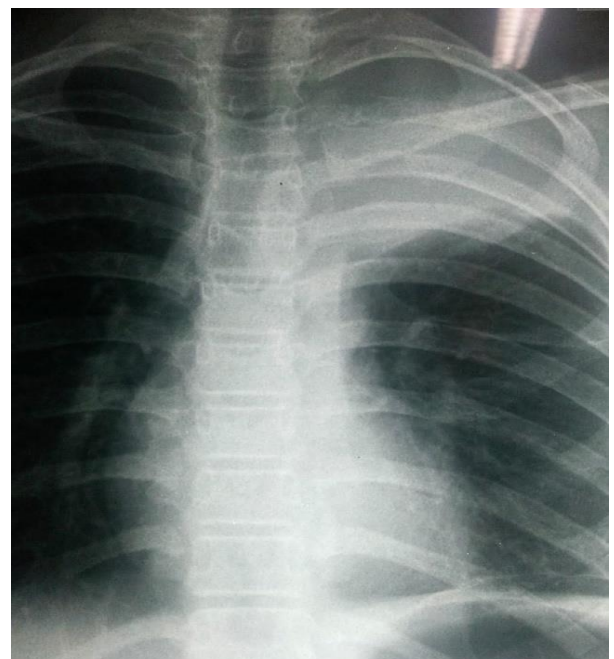
**Figure 2: Computerized tomography depicting (A) heterogenous mass lesion; (B) pleural effusion, (C) drop metastasis of tumor.**

Pleural tap revealed hemorrhagic fluid (150 ml was tapped). Cytology showed numerous RBCs, lymphocytes, atypical cells and few mesothelial cells, elevated protein and reduced glucose levels. Gram stain, Acid Fast Bacilli staining and culture were negative. Computerized Tomography (CT) was done which confirmed the findings of left sided heterogenous mass lesion and pleural effusion (Figure 2).

Histopathology showed sheets of small round tumour cells arranged in lobules with areas of necrosis, high Neutrophil: Cytoplasm ratio, scanty eosinophilic cytoplasm and finely dispersed chromatin (Figure 3).



**Figure 3: Histopathology depicting sheets of small round tumour cells arranged in lobules with areas of necrosis, high Neutrophil: cytoplasm ratio, scanty eosinophilic cytoplasm and finely dispersed chromatin.**



**Figure 4: Chest X-Ray depicting near regression of tumor after 2 radiotherapy cycles.**

Immunohistochemistry was confirmative and was observed to be MIC 2 positive. From these observations, a confirmatory diagnosis of Askins tumor was made and the patient was initiated on initial induction chemotherapy with vincristine and doxorubicin. This was followed by 15 cycles of treatment with etoposide and ifosamide.

After the completion of a year of treatment, she was also initiated on radiotherapy, that involved 28-day cycles, following which near total regression of tumor was observed (Figure 4 and Figure 5). The patient has been on regular follow-up since and has been asymptomatic since last three years.



**Figure 5: Image depicting regression of tumor following radiotherapy.**

## DISCUSSION

PNETs and Ewing sarcoma (ES) have been previously widely observed to be clinically and histologically identical tumors. Incidentally, both were seen to consist of small round cells. However, they are both unusual entities and comprise only about 5% of all cases of small round cell tumors.<sup>4</sup> While they can occur in the kidneys, adrenals, pancreas and other sites, in the thoracic region, they have been noted to have origins from the chest wall (“Askin tumor”). Askin et al, had initially reported 20 cases of a malignant small cell tumor of the thoracopulmonary region (Askin tumor) in the year 1976.<sup>5</sup> Newer research have postulated that while the degree of neuronal differentiation was a factor that was earlier used to distinguish between classical ES and PNET, molecular biology studies have now been successful in showing that all these said tumors do share a common gene rearrangement pattern involving the *EWS*

gene on chromosome 22. Hence, this particular distinction is now considered an obsolete entity. Moreover, PNETs can be further classified into central and peripheral tumors.<sup>2</sup> Peripheral primitive neuroectodermal tumors (pPNETs) are those that occur external to the central nervous system and places its foci of origin from neuroectodermal differentiation disorders.<sup>6</sup>

As stated previously, adolescents and young adults are commonly afflicted. Previous review of available literature have depicted a male preponderance (M:F = 1.8 : 1) with the mean age of involvement being 28.2 (8-56) years.<sup>7</sup> Other studies have described the average age of these patients to be 30.6 (8-75) years, again with a male predilection (M:F=1.5:1).<sup>2</sup> However, the common recurring theme is that only about 15-20 cases of primary lung PNETs have been reported in literature so far.<sup>2,8</sup>

The main presenting symptoms were largely unspecific and misleading; cough, fever, dyspnea, hemoptysis, and chest pain being the major symptoms.<sup>9</sup> The diagnosis of this entity is centered on hematoxylin and eosin staining. The discerning features are the monomorphic small round tumor cells along with results of immune-histochemical (IHC) staining and cytogenetic analysis. Imaging investigations such as computerized tomography depict various heterogeneous masses, that are frequently seen to invade the surrounding tissues, including bones. However, it must be noted that the images are not helpful in differentiating the mass from other lung tumors.<sup>2</sup> The investigative entity that aids diagnosis though, is histological examination, utilizing various IHC markers and antibodies, some of them being O13, HBA-71, and 12E7 (the MIC2 gene product). These are of assistance in recognition of the cell surface antigen, expressed by the cluster of CD99.<sup>9</sup> Even though there are no specific markers identified for PNETs, CD99 has been widely noted to be positive in all scenarios.<sup>2</sup>

The treatment of PNET should include the utilization of a combination of early surgical resection, where feasible, along with adjuvant chemotherapy and radiation therapy.<sup>10</sup> PNET are comparable to Ewing sarcomas, in that it is an extremely malignant tumor with poor prognosis. After diagnosis is established, multiple modalities of treatments including systemic chemotherapy (neoadjuvant and adjuvant), surgery, as well as radiation, may all be thought of as alternatives, depending, of course, on disease progression.<sup>2</sup> The first-line drugs that have had proven success for Ewing sarcoma include vincristine, doxorubicin, cyclophosphamide, etoposide, and ifosfamide.<sup>11</sup> Second-line regimens such as cyclophosphamide/topotecan, irinotecan/temozolomide, and high-dose ifosfamide, are reserved for metastatic scenarios.<sup>12,13</sup> Targeted therapy has now opened the doors for higher avenues of therapy. As such, bevacizumab (Avastin) and sunitinib have been postulated to be prime candidates for consideration of targeted therapy for Ewing sarcoma.<sup>2</sup>

The differential diagnosis of PNET of the lung comprises small cell carcinoma and various small round-cell tumors, such as malignant lymphoma, Langerhans' cell histiocytosis, granulocytic sarcoma, rhabdomyosarcoma, classical neuroblastoma, and synovial sarcoma.<sup>14</sup> Histochemical and immune-histochemical studies are of utility to rule out the differentials.

The authors wish to utilize this case report to help enlighten clinicians about PNET, its rarity and its presentations. It stands to reason that in patients with a mediastinal mass, primary PNET of the mediastinum must be considered as a possible differential diagnosis of the mediastinal mass of primary lung carcinoma. Effective early diagnosis and treatment would help in improving survival rates. However, PNET is indefinitely associated with a poor prognosis and outcome. Previously, the 5-year survival rate has been postulated to be very poor, to the tune of less than 25 percent.<sup>2</sup> In our scenario, the patient has been asymptomatic for three years and tumor has regressed considerably, which the authors consider to be quite remarkable and worthy of mention.

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