Peripheral Primary Neuroectodermal Tumor (PPNET) of chest wall (Askin tumor) – Rare case report with review of literature

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ABSTRACT

Ewing’s sarcoma (EWS)/ Peripheral primitive neuroectodermal tumors (pPNETs) are rare malignant small round cell tumors primarily occurring in bone and soft tissues. They are believed to arise from the cells of the primitive neural crest. They typically affect children and young adults. In the thoracic region, these tumors (also called as Askin tumors) most commonly arise from the chest wall and may involve the lung secondarily. Peripheral PNETs are uncommon in comparison to central PNET which involve the central nervous system. It is well documented that chest wall pPNET belongs to Ewing’s sarcoma family due to genotypic and phenotypic similarities. In contrast to the more common central PNETs (cPNETs) which affects the central nervous system, (pPNETs) commonly affect the chest wall, head and neck, retroperitonium, pelvis and extremities. We report a case of pPNET of chest wall in a 19-year old male who presented with left-sided hemothorax following trauma. Left postero-lateral thoracotomy was performed and resected specimen of pleura showed features of PNET; which was confirmed on IHC.

Keywords: PNET, Askin tumor, malignant small round cell tumor, Ewing’s sarcoma

INTRODUCTION

Ewing sarcoma(ES) is a highly malignant bone tumor. It was first described by James Ewing in 1921 as a tumor of the long bone of children and young adults. Later, other malignant soft tissue tumors morphologically indistinguishable from ES were reported in soft tissues and were termed as extraskeletal ES. Therefore, a single entity, termed as ‘the ES family of tumors’ was coined including ES, extra skeletal ES and Primitive neuroectodermal tumors (PNET). Askin originally described PNETs of chest wall(so called Askin tumors) in 1978, which are peripheral PNETs of chest wall, ribs and thoracic cavity.1

Though most of these tumors involve the central nervous system, it can affect any peripheral nerve. Peripheral PNET(pPNET) of the chest wall belongs to the Ewing’s sarcoma family due to their genotypic and phenotypic appearance.2

PNET is the second most common sarcoma in children and young adults. 2 Literature search has revealed less than 20 cases of pPNET of chest-wall.3 We are reporting this case due to its unique presentation and rarity which was misdiagnosed clinically.

CASE HISTORY

A 19 year old man was admitted with complaints of fever, chest pain and breathlessness since 10 days. Fever was high grade, associated with rigors and sweating. History of trauma to chest 15 days back followed by pain and breathlessness. Physical examination revealed signs of hemothorax. Hematological and biochemical workup of the patient were within normal limits. Ultrasoundography and radiography of chest revealed gross left pleural effusion. CT thorax revealed lobulated lesion of 12x11x10cm, suggestive of neoplastic activity with hemothorax and rib destruction.

Left Postero-Lateral Thoracotomy was performed and specimen received werefibrosed lung tissue with clots and biopsy taken from the mass attached to rib.

Gross examination showed multiple bits and pieces- 20x8x5cm, grey-brown, soft and fleshy with hemorrhagic and fibrotic areas.[Figure-1] Microscopyof fibrosed lung with blood clots showed a malignant tumor composed of cells arranged in sheets and nests separated by...
fibrovascular tissue. [Figure-2] Individual tumor cells were small, round with hyperchromatic nuclei, coarse chromatin and moderate eosinophilic cytoplasm. Cells showed moderate pleomorphism with mitotic activity of 4-5/hpf. [Figure-3]

**Figure 1:** Gross showing multiple, grey-brown, hemorrhagic and fibrotic masses

Vascular emboli and pseudo rosettes were seen with large areas of necrosis and haemorrhage. However no lung tissue or bone identified. Based on the above findings, features were suggestive of high grade malignant small round cell tumor plausibly pPNET. The differential diagnoses were non-Hodgkin’s lymphoma and rhabdomyosarcoma.

Immunohistochemistry was negative for synaptophysin, desmin, CK (cytokeratin), LCA (leucocyte common antigen) and positive for MIC-2 (CD-99). Therefore, final diagnosis was given as pPNET (Askin tumor).

**Figure 3:** H and E, 40x, tumor cells showing pleomorphism and mitotic activity

**DISCUSSION**

Peripheral Primitive neuro-ectodermal tumor is a rare aggressive malignant tumor originating from embryonic migrating cells from the neural crest. It is proved that classic ES and pPNET represent a spectrum of a single neoplastic entity.

Peripheral PNET of the chest wall is rare typically seen in children and young adults. Overall, 27% of cases are said to occur in first decade, 64% in second decade and 9% in the third decade of life, with equal distribution in both sexes. In our case, the patient was 19 year old male.

The common clinical presentations include chest pain, respiratory distress syndrome and a chest wall mass. PNET lesions are painful because of its capacity to invade the chest wall, lung or mediastinum. However, in our case, there was no involvement of lung and mediastinum. The haemorrhagic pleural effusion in our case as the chief presentation has also been described. However, history of trauma as a cause for pleural effusion was misleading in our case.

The family of Ewing’s sarcoma(ES) tumor is said to include: classical ES(osseous origin), atypical ES(extra osseous), PNET and Askin tumors. Askin tumors are small round cell tumours found in the thoracopulmonary region which were first described by Askin et al in 1979. It has now been accepted that the original tumor described by Askin et al is similar to PNET found elsewhere in the body. In our
case, tumor involved chest wall, involving pleura and rib-bone.
Ewings sarcoma/PNET primarily occurs in bone and soft tissues, both characterised as a group by the presence of the typical translocation t (11:22) (q24; q12). Grossly, PNET presents as soft and fleshy mass with hemorrhage and necrosis.

Microscopically, tumors at the poorly differentiated (Ewing’s) end of spectrum have scanty cytoplasm and round to ovoid open nuclei with finely distributed chromatin pattern. At the opposite end of the spectrum cells have eosinophilic cytoplasm and coarse chromatin pattern with frequent nucleoli. Mitotic figures are said to be common in PNET, as are necrosis and endothelial hyperplasia. A further aid in the differential diagnosis is provided by the presence of Homer-Wright rosettes in PNET.

On light microscopy, PNETs typically show undifferentiated small, round malignant cells with uniform inconspicuous nuclei with scant cytoplasm arranged in lobules, rosettes or pseudo-rosettes with areas of necrosis with little stroma. Differential diagnosis includes, Non-Hodgkin’s lymphoma, rhabdomyosarcoma, neuroblastoma (NBT), malignant melanoma, synovial sarcoma and desmoplastic small round cell tumor.

To diagnose a tumor as PNET, the criterion is small round cells forming rosettes or pseudorosettes with positivity for at least two of the tumor markers.

Immunohistochemical positivity for CD99, NSE, synaptophysin and chromogranineA are said to be useful in differential diagnosis. Presence of Homer-Wright rosettes is typical for neuroblastomas. LCA positivity supports the diagnosis of Lymphoma. Small cell carcinoma of lung shows positivity for cytokeratine, while rhabdomyosarcoma is positive for desmin, actin, myoglobin. The desmoplastic round cell tumor is positive for cytokeratine and desmin but is negative for CD99.

In our case positive expression was seen for CD99 and Fli-1 and negative for expression of cytokeratin, MyoD1, Tdt, CD3, desmin, and LCA. This was suggestive of pPNET.

The prognosis of ES/PNET is said to be determined by the metastatic spread than local control of tumor. Favourable prognostic factors reported are age less than 10 years, distal extremity, volume of the tumor less than 100ml and chemotherapy treatment prior to resection. The unfavourable factors are tumor in the pelvis, tumor size more than 8cm, elevated WBC count and ESR. Over-expression of tumor suppressor gene p53, cell proliferation nuclear antigen, Ki67 and Her 2 neu are also said to be associated with poor prognosis.

CONCLUSION

Even though rare, EWS/ pPNET should be considered in the differential diagnosis of malignant tumors of chest wall presenting as hemothorax especially in young individuals.

REFERENCES