Peripheral Primitive Neuroectodermal Tumor of the Chest Wall in Childhood: Clinico-Pathological Significance, Management and Literature Review

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Peripheral primitive neuroectodermal tumor of the chest wall is a rare malignant tumor usually occurring in children. The tumor shares a similar histology, immunohistology and cytogenetics to Ewing's sarcoma. The location of the tumor in the chest wall poses a major challenge with respect to the diagnostic workup and treatment which involves multidisciplinary management. Neoadjuvant chemotherapy is given initially and is followed by complete surgical resectioning of the mass followed by repeat chemotherapy with or without radiotherapy. We report a case of peripheral primitive neuroectodermal tumor of the chest wall in a 5-year-old boy and review the literature regarding its diagnosis and management. *(Chang Gung Med J 2011;34:213-7)*

Key words: askin tumor, Ewing's sarcoma, primitive neuroectodermal tumor, small round cell tumor

Primitive neuroectodermal tumor (PNET) is the second most common sarcoma in children and young adults. Though most of these tumors commonly involve the central nervous system, it can affect any peripheral nerve including branches of the cranial nerves. Peripheral primitive neuroectodermal tumor (pPNET) of the chest wall belongs to the Ewing's sarcoma family due to their genotypic and phenotypic appearance. We report a case of pPNET of the chest wall in a 5-year-old child and discuss the diagnostic, clinico-pathological significance of the lesion with a concise literature review of its management.

CASE REPORT

A 5-year-old boy presented with history of respiratory distress and fever for 20 days. He had no history of chest pain or chest mass. His chest x-ray revealed homogenous opacity in the right hemithorax (Fig. 1A), since it appeared like pleural effusion, a chest drain was inserted in the right hemithorax, which drained hemorrhagic fluid. The fluid cytology did not reveal the presence of any malignant cells. The mountex test was negative and none of his family members had tuberculosis. A post chest drain insertion chest x-ray showed persistence of the homogenous opacity on the right side (Fig. 1B). He was further investigated with contrast enhanced computerized tomography (CECT) of the chest (Fig. 2A) which showed a heterogenous lobulated mass in the right hemithorax with heterogenous enhancement and hypodense areas suggestive of necrosis. The right 10th rib was eroded and there was associated

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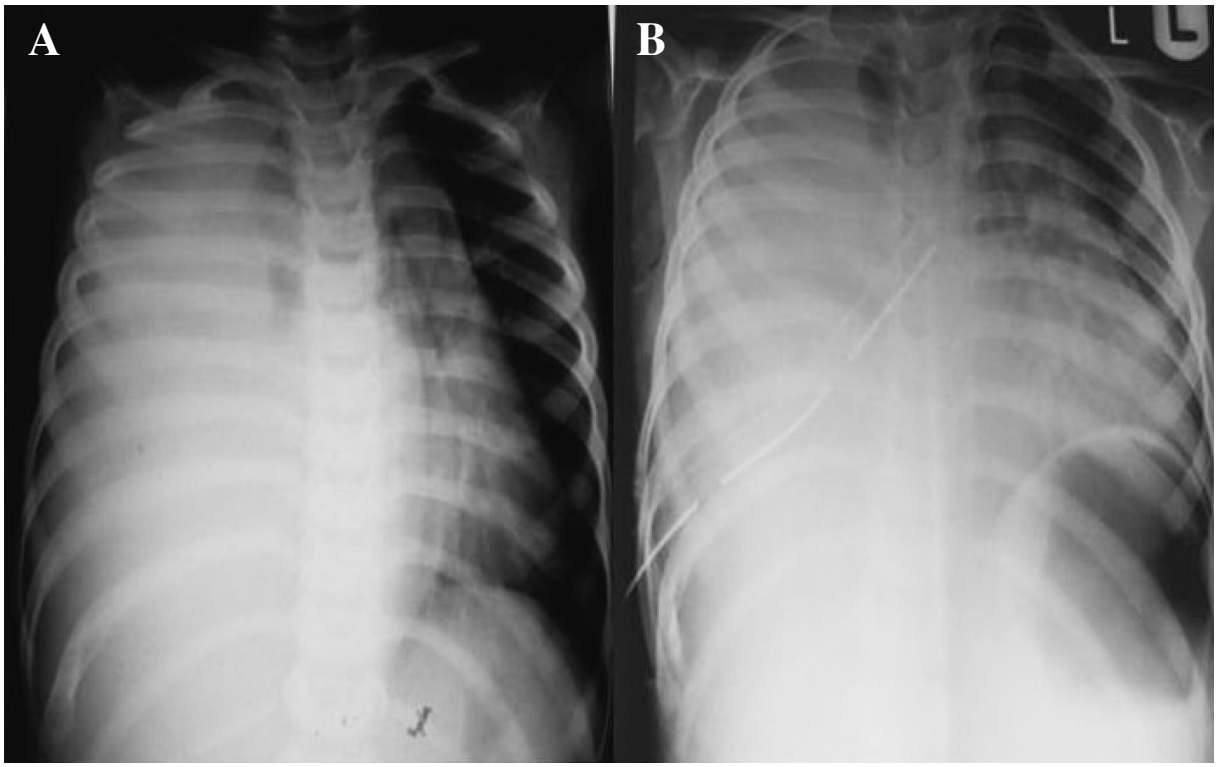

Fig. 1 Pre and post intercostal drainage chest X-ray showing persistence of right sided chest homogenic appearance due to tumor, which was previously thought to be due to effusion.

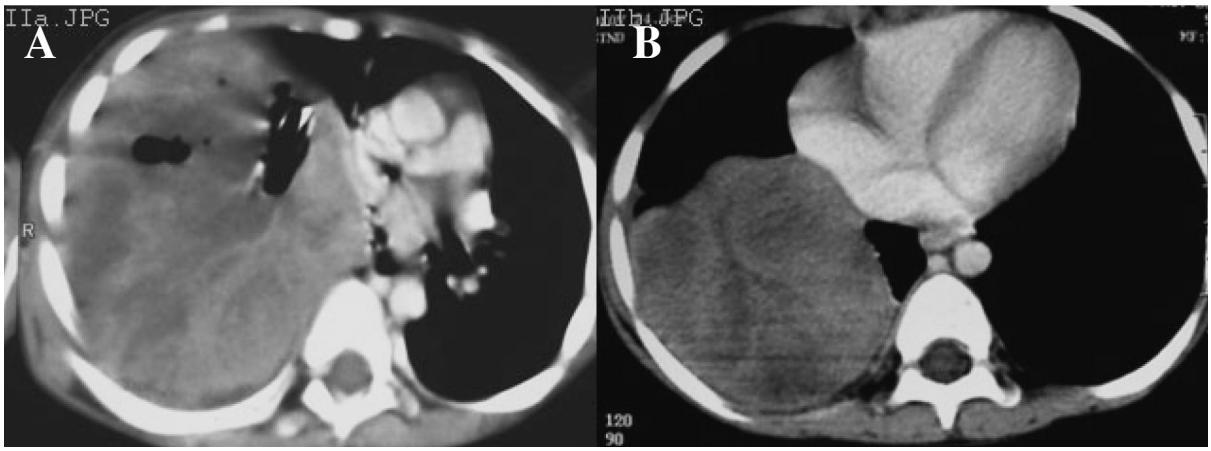

Fig. 2 Computed tomogram of chest showing prechemotherapy (A) and post chemotherapy (B) tumor.

right pleural effusion. The ipsilateral lung was completely collapsed due to compression. Ultrasound guided fine needle aspiration cytology (FNAC) of the mass was performed, which showed a malignant small round cell tumor. The immunohistochemistry study of the FNAC specimen was strongly positive for MIC2 (CD99) and Vimentin but was negative for cytokeratin (CK), neuron specific enolase (NSE) and desmin. Based on these immunohistochemistry findings, the diagnosis of PNET of the chest wall was

confirmed. The child was administered four cycles of chemotherapy with Vincristine, Cyclophosphamide, Doxorubicin and Actinomycin-D. A repeat CECT 4 months later showed significant regression of the mass (Fig. 2B). Following this, surgical excision of the tumor was performed via a right posterolateral thoracotomy. Intraoperatively, the mass was well encapsulated with the lower part adherent to the diaphragm. The ipsilateral lung was compressed but was free from tumor invasion. The entire tumor with a part of the tenth rib and a part of the adhered diaphragm was completely excised. Post operative recovery was uneventful. The histological examination of the mass showed tumor with sheets of small round cells and frequent Homer-Wright rosettes. The diagnosis of PNET of the chest wall was established (Fig. 3). Margins including the pleura were negative for the tumor. The child received a further course of chemotherapy using the same agents, but no radiotherapy was given as margins were free from tumor. After 8 months of follow up the child is well and has no evidence of recurrence or distant metastasis.

DISCUSSION

Chest wall tumors in children can be caused by a wide range of benign and malignant diseases. About 1/5th of the thoracic tumors occurring in childhood originate from the chest wall.[1] In children, Ewing's sarcoma is the most common chest wall tumor; while in adults chondrosarcoma predominates.[1] In a series of 73 malignant chest wall tumors reported by Shamberger and Gries, 56% were Ewing's sarcoma, 23% were rhabdomyosarcoma, 15% were lymphoma, 5% were fibrosarcoma, 3% were osteosarcoma and 3% were chondroma.[2] Peripheral primitive neuroectodermal tumor of the chest wall is a rare malignant tumor seen in children and young adults.[1,2]

Before discussing the tumor, as surgeons we need to understand the various confusing terminologies involved which are used interchangeably in literature. This may not be a problem for the pathologist but is confusing for the surgeon. Ewing's sarcoma describes a family of tumors of neuroectodermal origin that occurs in both bone and soft tissue. The family of Ewing's sarcoma (ES) tumor includes classical ES (osseous origin), atypical ES (extraosseous), PNET and Askin tumor.[1] Askin tumors are small round cell malignant tumors found in the thoracopulmonary region and were first described by Askin in 1979.[3,4] Askin tumor is now considered the same as PNET as no histological difference has been noted between Askin and non-thoracopulmonary PNET.[1] The common locations of PNET originating from the peripheral nerve are the chest wall, head and neck, retroperitoneum, pelvis and extremities.[3]

The common presentation in patients with PNET of the chest wall is chest pain, respiratory distress or a chest wall mass.[1,2,4] The presentation with hemorrhagic pleural effusion as in the index case has also been described.[3-5] The diagnostic radiological

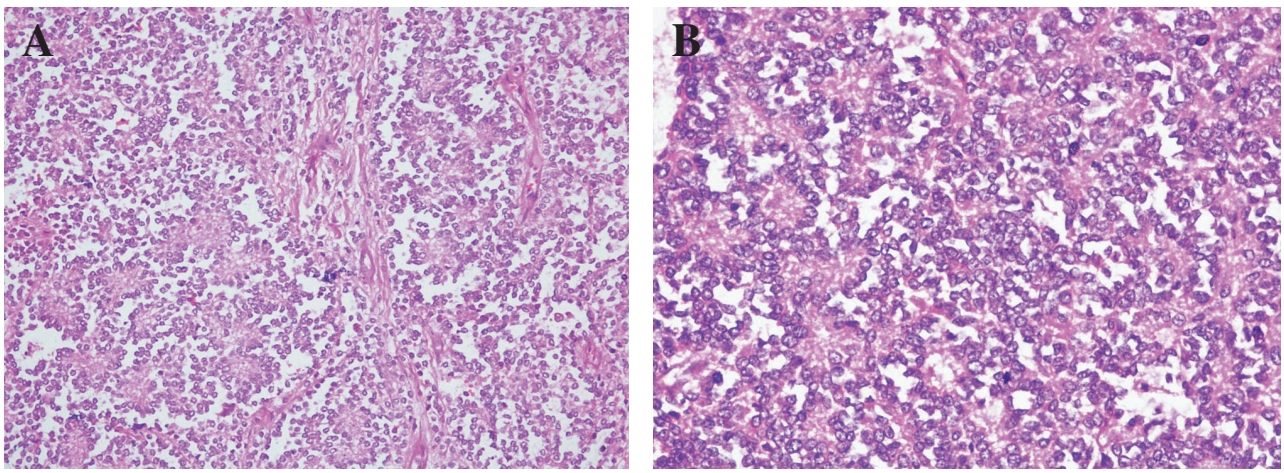

Fig. 3 Histopathological examination of the mass showing a tumor with sheets of small round cells and frequent Homer-Wright rosettes. (H & E staining, magnification x200 and x500)

workup requires CT scan or MRI. The characteristic CT picture in the patient with Askin tumor/pPNET is that of a heterogenous mass of chest wall origin with areas of necrosis and hemorrhage with or without an intrathoracic component.[6] Calcification is rarely seen in these tumors. Expansion of the tumor may cause compression of the underlying lung or may directly invade it. Winer-Muram et al. in their series of 8 patients with Askin tumor could not differentiate lung compression from invasion using both CT and MRI.[6] Tumor extension to pleura, as found in the index case, is known to occur and is associated with effusion. Distant metastasis spreads to lungs, bones, bone marrow, liver and brain, but is a rare or late event with pPNET.[4,5]

Malignant PNET forms a distinct entity and is differentiated from other small round cell tumors such as neuroblastoma, rhabdomyosarcoma, and lymphoma by their light and electron microscopic features.[3,4] Light microscopic criteria included: fairly uniform, poorly differentiated round cells arranged in cords, nests, or clusters, plus occasional pseudorosettes without dendritic cytoplasmic projections; absent periodic acid-Schiff staining or, if present, sparse and diastase resistant and no ganglionic or Schwannian differentiation. Ultrastructurally, a tumor shows neuro-secretory like granules, which differentiates it from Ewing's sarcoma.[3-5,7] Their neuroectodermal origin is confirmed by various immunohistochemical markers. Most tumors show strong positivity for NSE and MIC2 proteins.[3-5,7] Cytogenetic studies have demonstrated a similar type of genetic abnormality in pPNET tumors and ES tumors, which is translocation of the long arms of chromosomes 11 and 22 [t (11; 22) (q24; q12)], giving rise to the EWS/FLI-1 (Ewing's sacroma gene/ Friend Leukemia Virus Integration 1 gene) fusion gene.[4,5,7]

The prognosis of the tumor is more related to its anatomical spread to the adjacent structures. Involvement of bone, pleura and epidural space is considered a bad prognostic factor for survival especially in younger patients.[3]

The accepted protocol for the management of this tumor is neoadjuvant chemotherapy followed by surgical excision of the tumor followed by post operative chemotherapy with or without radiotherapy.[1-4,8,9] The neo-adjuvant chemotherapy leads to better local control of the disease, less extensive surgery and treats the distant microscopic metastasis. The intergroup studies in Ewing's sarcoma patients showed that delayed resectioning following chemotherapy results in a negative margin in 71% of the cases as compared to only 37% cases operated primarily.[9] Chemotherapy formerly consisted of a combination of Vincristine, Actinomycin-D, and Cyclophosphamide. Nowadays Doxorubicin is added in most protocols. Other drugs used in the majority of patients are Ifosfamide and Etoposide.[1-4,8,9] Surgery with wide margins is ideal, but infrequently possible in patients with chest wall tumor. These are the patients who require post operative radiation. Due to the late effects of radiotherapy like lung damage, increased cardiac toxicity with the use of anthracyclines, chest wall deformities, and secondary malignancies, the treatment should be aimed at avoiding these issues.[1,2,4,8,9] As in the index case, margins were negative for the tumor; post operative radiotherapy was not given. The reported 2 and 6 year survival of the tumor is 37% and 14% respectively.

With this case report we wish to highlight the importance of keeping the possibility of pPNET tumors in mind while dealing with cases of chest wall tumor. The diagnosis requires immunohistochemical workup supported by imaging investigations. The role of pre-op chemotherapy is to be carefully considered as it will result in better surgical tumor clearance and avoidance of post operative radiation which itself adds to morbidity due to side effects.

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