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Primary peripheral neuroectodermal tumor of the chest wall in a boy presenting with massive pleural effusion : A case report

Suwannee Phumeethum*
Suchada Sritippayawan* Nuanchan Prapphal*
Jitladda Deerojanawong* Rujipat Samransamruajkit*

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We report a case of a 9-year-old boy who had a massive left pleural effusion with masses on the left pleura and left anterior chest wall. Histopathological and immunocytochemical studies of the pleural mass were compatible with primary peripheral neuroectodermal tumor (PPNET) of the chest wall. The child responded well to chemotherapy and local irradiation, despite having pleural and distant bone metastases. PPNET of the chest wall should be considered as another possible cause of massive, non-specific profile, pleural effusion in children. Early diagnosis and treatment can ensure a good outcome in these patients.

Key words : *Pleural effusion, Peripheral primary neuroectodermal tumor of chest wall.*

Reprint request: Sritippayawan S. Division of Pulmonology and Critical Care, Department of Pediatrics, Faculty of Medicine, Chulalongkorn University.

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*Department of Pediatrics, Faculty of Medicine, Chulalongkorn University

สุวรรณี ผู้มีธรรม, สุชาดา ศรีทิพยวรรณ, นวลจันทร์ ปราบพาล, จิตลัดดา ดีโรจนวงศ์, รุจิภัตต์ สำราญสำรวจกิจ. โรค Peripheral neuroectodermal tumor ปฐมภูมิของผนังทรวงอกในผู้ป่วยเด็ก ซึ่งมาด้วยอาการแสดงของน้ำคั่งจำนวนมากในช่องเยื่อหุ้มปอด : รายงานผู้ป่วย. จุฬาลงกรณ์เวชสาร 2548 ธ.ค; 49(12): 709 – 15

รายงานผู้ป่วยเด็กชายอายุ 9 ปีมาด้วยเรื่องมีน้ำคั่งจำนวนมากในช่องเยื่อหุ้มปอดข้างซ้ายร่วมกับมีก้อนที่เยื่อหุ้มปอดและผนังทรวงอกด้านซ้าย ผลการตรวจทางพยาธิวิทยาและการย้อมพิเศษของก้อนที่เยื่อหุ้มปอดเข้าได้กับเนื้องอกของผนังทรวงอกปฐมภูมิชนิด peripheral neuroectodermal tumor (PPNET) ผู้ป่วยได้รับการรักษาด้วยยาเคมีบำบัดร่วมกับการฉายแสงที่เนื้องอกบริเวณผนังทรวงอก ผู้ป่วยตอบสนองต่อการรักษาเป็นอย่างดีแม้ว่าจะมีการแพร่กระจายของเนื้องอกไปยังเยื่อหุ้มปอดและกระดูกแล้วก็ตาม เนื้องอกของผนังทรวงอกชนิด PPNET เป็นสาเหตุของการเกิดภาวะน้ำคั่งจำนวนมากในช่องเยื่อหุ้มปอดที่พบได้ในเด็กและควรได้รับการนึกถึงไว้ด้วยในผู้ป่วยเด็กที่มาด้วยภาวะดังกล่าว แม้ว่าผลการตรวจทางห้องปฏิบัติการเบื้องต้นของน้ำในช่องเยื่อหุ้มปอดจะไม่บ่งบอกถึงโรคใดโรคหนึ่งโดยเฉพาะ การให้การวินิจฉัยและรักษาเนื้องอกชนิดนี้อย่างรวดเร็วมีส่วนช่วยให้ผลการรักษาในผู้ป่วยเหล่านี้ดีขึ้น

คำสำคัญ : *น้ำคั่งในช่องเยื่อหุ้มปอด, โรคเนื้องอกของผนังทรวงอกชนิดหนึ่ง*

Tumors of the chest wall are rare in children, but a high proportion of them are malignant. [1] We report a case of primary peripheral neuroectodermal tumor (PPNET) of the chest wall that occurred in a school-aged boy who presented with massive pleural effusion.

Case Report

A 9-year-old Thai boy was admitted to King Chulalongkorn Memorial Hospital with a history of facial swelling, mild cough and dyspnea for three days. Physical examination revealed: body temperature 37.2°C, pulse rate 80 beats/min, respiratory rate 40 breaths/min and blood pressure 115/60 mmHg. Arterial oxygen saturation recorded by pulse oximetry (SpO_2) in room air was 100 %. He looked dyspneic and had a swollen face. Chest examination showed swelling of the left anterior chest wall. The trachea was deviated to the right. Decreased breath sound/ vocal resonance and percussion dullness were noted over the left hemithorax. Others findings were unremarkable.

Laboratory investigations showed hemoglobin 12.5 gm/dl, hematocrit 38 %, white blood cell count 16,180/mm^3 (91 % neutrophils, 8 % lymphocytes, 1 % eosinophils) platelet count 370,000 /mm^3. Urinalysis, serum electrolytes and BUN/Cr were normal. Chest roentgenogram demonstrated haziness over the left hemithorax with a right shift of the mediastinum (Figure 1A). The ultrasonography of the chest revealed a massive left pleural effusion with multiple left pleural masses. Thoracentesis revealed straw-colored pleural fluid with protein 3.2 gm/dL (pleural fluid/serum protein ratio 0.9), lactic acid dehydrogenase (LDH) 989 U/L (pleural fluid/serum LDH ratio 2.1), and leukocyte count 5 cells/mm^3 (100 % mononuclear cells). Cytological examination showed no malignant cells. Microbiological studies including bacterial culture and acid-fast bacilli stain of pleural fluid were negative. Tuberculin test was 0 mm. Computed tomography (CT) of the chest revealed a massive left pleural effusion with multiple masses on the left pleura, adjacent to the left anterior chest wall. (Figure 1B) Edematous subcutaneous tissue of the left hemithorax was also

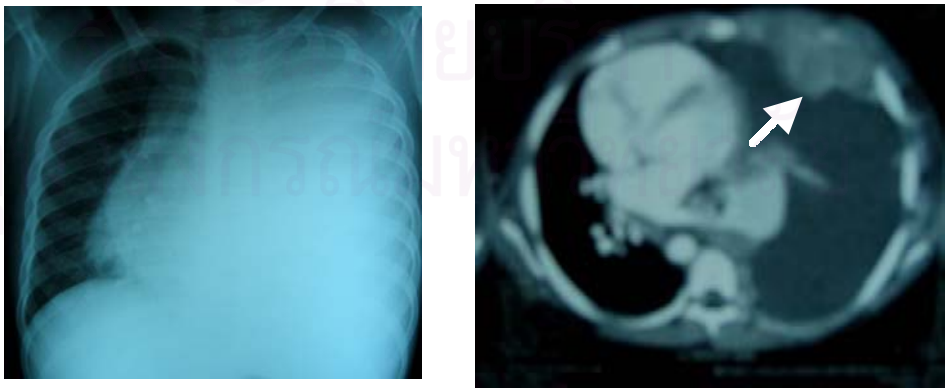

Figure 1A, 1B. Chest roentgenogram (1A) showed a haziness over left hemithorax with mediastinal shift to the right. Computed tomography of the chest (1B) revealed massive left pleural effusion with multiple masses over left pleura and adjacent anterior chest wall (Arrow).

noted. Fine needle, CT-guided, aspiration of the pleural mass was performed. The histopathologic study showed small round tumor cells with hyperchromatic nuclei and scanty cytoplasm (Figure 2). The immunocytochemical study of the cells showed positive staining for CD99, compatible with PPNET. Bone marrow aspiration showed no evidence of tumor metastasis. However, bone scan revealed increased uptakes at the right scapula and sacroiliac joints, indicating distant bony metastases.

The patient was diagnosed with PPNET of the chest wall. He was treated with combined chemotherapy (vincristine 1.5 mg/m^2, cyclophosphamide 1200 mg/m^2 and doxorubicin 75 mg/m^2) and local irradiation. Chest roentgenogram performed at one week after the treatment showed a dramatic decrease of the left pleural effusion (Figure 3A). CT of the chest performed three months later revealed disappearance of pleural effusion but some residual pleural nodules (Figure 3B). No evidence of recurrent tumor at the 7^{th} month of treatment.

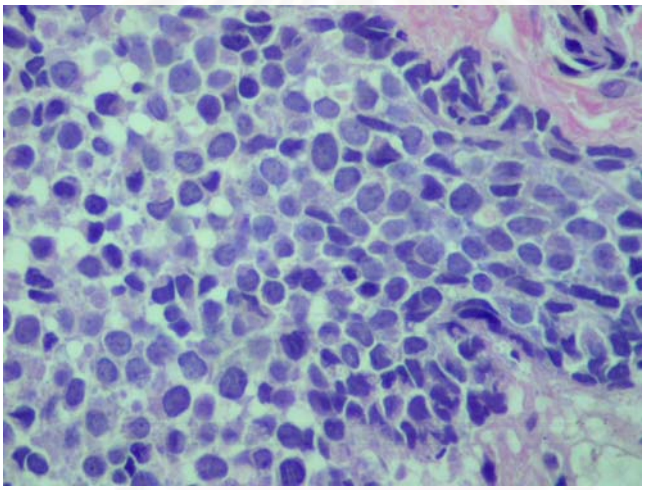

Figure 2. Histologic study of fine needle aspiration demonstrated uniform small round tumor cells with scant cytoplasm, round homogenous and uncertain nuclei.

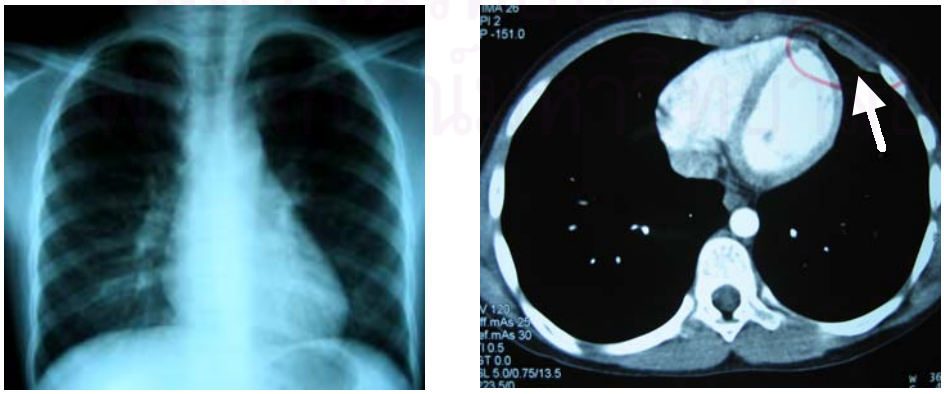

Figure 3A, 3B. Chest roentgenogram (3A) performed at one week after treatment showed dramatic decrease of left pleural effusion. Computed tomography of the chest (3B) performed at 3 months after treatment showed marked decrease of left pleural effusion with residual pleural masses (Arrow).

Discussion

Massive pleural effusion is not common in children. The major causes reported in adults are parapneumonic effusion, tuberculous pleurisy and malignancy.[2, 3] Our patient presented with a massive left pleural effusion. Thoracentesis revealed a non-specific, exudative profile of pleural fluid without evidence of malignancy or infection. Microbiological studies and tuberculin test were not suggestive for either parapneumonic or tuberculous effusion. However, CT of the chest showed multiple masses over the left pleura and adjacent anterior chest wall. Nevertheless, it could not be determined from the CT whether these pleural masses were metastatic tumors from the chest wall or vice versa.

Most of the pleural masses are metastatic tumors arising from adjacent chest wall, lymph node, lung and breast.[4, 5] Primary tumors of the pleura are very rare in children. The most common one is malignant mesothelioma which is related to inhalation of organic and inorganic materials and rarely reported in children.[4-6]

Primary tumors of the chest wall are also rare in children. Most of them are malignant.[1] The most frequent tumors are malignant small round cell tumors (Ewing's sarcoma/PNET family) followed by rhabdomyosarcoma, osteosarcoma, chondrosarcoma and other sarcomas.[1]

In our patient, it was difficult to conclude from the CT whether the primary site of the tumor was at the pleura or the chest wall. However, a fine needle aspiration of the pleural mass revealed small round tumor cells. The differential diagnosis of small round tumor cells in childhood include Ewing's sarcoma, neuroblastoma, lymphoma, rhabdomyosarcoma and PPNET. In our case, the immunocytochemical study of the tumor cells revealed the positive stainings for CD99, compatible with PPNET or peripheral neuroepithelioma which is a more differentiated form of Ewing's sarcoma family of tumors (ESFT) occurring as a primary tumor of bone and soft tissue.[7] This suggested that these pleural masses were metastatic tumors from PPNET of the adjacent chest wall.

PPNET of the chest wall or Askin tumor is a highly malignant PNET infrequently reported in children and young adults.[8] The reported annual incidence is 2.1 cases per million children.[7] It is commonly found during the second decade of life. The tumor can be primarily located at periphery (such as the extremities) or the central axis (such as the chest wall) which is the more common site.[7] Presenting symptoms and signs depend on the sites of the diseases. Pain and swelling (or both) at the affected sites are common presenting symptoms.[7] Our patient presented with swelling of the face and left anterior chest wall without local tenderness. The swelling of the face and the chest wall might be related to the obstruction of the lymphatic drainage caused by the tumors.

Metastasis of PPNET can occur either by local invasion or hematogenous spreading. The common sites of metastases are pleura, lung, bone and bone marrow.[7] Massive pleural effusion secondary to pleural metastasis is common in PPNET of the chest wall.[9] The pleural fluid profile is non-specific, as that found in our patient. However, increased LDH and neuron-specific enolase (NSE) in pleural fluid has been reported.[9]

Patients who present with metastatic diseases, especially to bone and bone marrow have unfavorable prognosis with less than 30 % survival

despite having surgical treatment combined with radiation and chemotherapy.[10] Early diagnosis and treatment are crucial for improving survival outcome of the patients.[11]

The National Cancer Institute (NCI) of the United States of America reported 17 patients with PPNET who were treated with intensive VDC regimen (vincristine, doxorubicin and cyclophosphamide), local and total body irradiations. One-half of the patients presented with localized diseases demonstrated continuous complete remission, whereas more than 90 % of those presented with metastatic diseases had recurrence.[11]

In our patient, there were evidences of pleural and distant bony metastases. However, he demonstrated a dramatic response to the treatment with combined intensive VDC regimen and local irradiation. CT of the chest performed at the 3rd month of treatment showed minimal residuals of pleural nodules.

In conclusion, we report a rare case of PPNET of the chest wall in a school-aged boy who presented with pleural masses and massive pleural effusion. The pleural fluid profile was non-specific. However, immunocytochemical study of the pleural mass obtained by a fine needle aspiration confirmed the diagnosis of PPNET. PPNET of the chest wall should be considered as another possible cause of massive, non-specific profile, pleural effusion in children. Early diagnosis and treatment can provide a good outcome in these patients.

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