Peripheral primitive neuroectodermal tumour of the chest wall invading
lung with regional lymph node metastasis

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Abstract

Here we present the case of a 26-year-old man in whom peripheral primitive neuroectodermal tumour of chest wall origin invaded the left lung with regional lymph node metastasis. He underwent initial resection of the left chest wall tumour with combined left lower lobectomy, left S5 segmentectomy, and lymph node dissection in order to facilitate a definitive diagnosis and also to obviate the risk of fatal bleeding due to tumour invasion of the pulmonary artery. Histological examination of the resected sample revealed small round cell proliferation with neural differentiation, and confirmed lymph node involvement within the left lower lobe. EWS/FLI-1 fusion gene transcripts were detected by the reverse-transcription polymerase-chain reaction. Diagnosis of peripheral primitive neuroectodermal tumour was confirmed. After surgery, combination chemotherapy with cyclophosphamide, vincristine, doxorubicin, ifosphamide, and etoposide was given. Five years after resection, the patient remains alive and well, with no signs of recurrence.

Keywords: Primitive neuroectodermal tumour; Chest wall; Lymph node metastasis; Surgery; Chemotherapy

1. Introduction

Peripheral primitive neuroectodermal tumour (pPNET) of chest wall origin is a rare malignant tumour in children and young adults [1]. Because pPNET has the same type of genetic abnormality as many Ewing’s sarcomas (ES), namely a translocation of the long arms of chromosomes 11 and 22, giving rise to the EWS/FLI-1 fusion gene [2], it is included in the pPNET/ES family. Therefore, pPNET should principally be treated in the same manner as ES. In the treatment of pPNET of chest wall origin, surgery after combination chemotherapy is preferred for a successful complete resection and avoidance of irradiation to chest wall, lung, and occasionally heart [3,4].

However, in some cases, initial resection of pPNET of chest wall origin is required for a definite diagnosis or prevention of tumour invasion to vital organs in the thoracic cavity. We describe a case of pPNET of the chest wall successfully treated with initial resection in order to prevent invasion of the pulmonary artery that could have been fatal, followed by combination chemotherapy.

2. Case report

A 26-year-old otherwise healthy man visited a local hospital because of left chest pain persisting for 1 week. Chest X-ray (Fig. 1A) revealed abnormal shadow on his left chest wall. Small round malignant tumour cells were identified following needle biopsy but a definite diagnosis could not be made because of the small sample size. The patient was referred to our hospital for treatment. Computed tomography revealed a tumour of 9 cm maximum diameter arising from the left chest wall, and invading the left lower lobe adjacent to the pulmonary artery (Fig. 1B), but no other lesions. From clinical presentation and cytologic features, we suspected pPNET. With regard to treatment, orthopaedic oncological consultation indicated initial resection followed by chemotherapy, to arrive at a definite diagnosis and to avoid the risk for lethal haemorrhage from pulmonary artery invasion, should initial combination chemotherapy not have been effective. Therefore, we performed en bloc resection of 15 cm × 12 cm of the chest wall from the left sixth intercostal muscle to ninth rib including the tumour, combined left lower lobectomy and segmentectomy of left S5 invaded by the tumour, and upper and lower mediastinal, and hilar lymph node dissection. The chest wall was reconstructed using expanded polytetrafluoroethylene sheeting.

Histopathologically, small round cell proliferation (Fig. 2A), directly invading the left lower lobe, was observed. Metastasis to lymph node adjacent to the left lower bronchus...
was detected, but no tumour cells were identified in the resected margins. The tumour cells were positive for MIC-2 and neuron-specific enolase (Fig. 2B and C), indicating neural differentiation. Prior to testing for EWS/FLI-1 chimeric mRNA in the tumour, written informed consent was obtained from the patient under the approval of the local ethics committee. According to Tokudome et al. [5], the EWS/FLI-1 fusion transcript was found to be expressed in the tumour (Fig. 2D). On the basis of all these findings, the tumour was diagnosed as pPNET.

Thirty-three days after resection, the patient received postoperative combination chemotherapy consisting of vincristine (2 mg/body), cyclophosphamide (2000 mg/m² × 2 days), and doxorubicin (20 mg/m² × 3 days) in cycles 1, 3, 5, and 7, and ifosfamide (2200 mg/m² × 5 days) and etoposide (100 mg/m² × 5 days) in cycles 2, 4, and 6. Five years after resection, the patient is well doing and has no signs of recurrence.

3. Discussion

For non-metastatic pPNET/ES, chemotherapy consisting of doxorubicin-containing regimens and ifosfamide/etoposide regimen with resection or radiotherapy is the strategy of choice [6]. However, this approach is accompanied by a considerable treatment-related death rate and development of secondary cancers [6,7]. Therefore, making a definite diagnosis of pPNET/ES is mandatory before initiating chemotherapy.

Diagnosis of pPNET/ES is based on the presence of small round cells with neural differentiation [1,2]. Although these characteristics can be established in most cases using the small samples obtained by needle biopsy, diagnosis may be difficult in others because of many differential diagnostic possibilities [5]. Detection of EWS/FLI-1 fusion gene transcripts has recently become a useful tool for the diagnosis of pPNET/ES [1,2].

In our case, initial resection of the tumour was performed for making a definite diagnosis of pPNET and for preventing invasion to the pulmonary artery that could have been fatal. Definitive diagnosis of pPNET was made histopathologically, immunohistochemically, and genetically. Thereafter, the patient received combination chemotherapy and has experienced no recurrence for 5 years. Complete resection with intensive chemotherapy thus achieved a cure of this aggressive tumour with accompanying lymph node metastasis.

The significance of regional lymph node metastases for pPNET prognosis seems unknown because regional lymph node involvement is reported to be atypical in imaging studies [8–10]. However, pPNET is an aggressive tumour and, in cases directly invading the lung, metastases to lymph nodes within the bronchial tree should be considered. Therefore, for complete resection, lymph node dissection as in primary lung cancer surgery is justified in pPNET with direct lung invasion.

In our case, we will need to continue to monitor the adequacy of this treatment strategy of initial resection followed by chemotherapy. For patients receiving combination chemotherapy, the 5-year event-free survival of patients with primary resection followed by chemotherapy and patients with post-chemotherapy resection was the same [4]. Resection after chemotherapy may be more beneficial due to the likelihood of complete resection with negative margins. Additionally, eliminating the necessity for chest radiation therapy for residual tumour after resection may avoid the pulmonary fibrosis, myocardial damage, or secondary cancer to which irradiation may contribute [3,4]. Therefore, when successful resection with negative tumour margins is anticipated, initial resection followed by chemotherapy for pPNET of chest wall origin may be a treatment strategy of choice, both for confirming the diagnosis and/or avoiding lethal tumour invasion to vital organs.
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References


Fig. 2. (A) Histopathological examination of the resected specimen showing small round cell proliferation (HE staining, ×100). (B and C) Immunohistochemical staining of tumour cells with MIC-2 (B, ×100) and neuron-specific enolase (C, ×100). (D) Expression of the EWS/FLI-1 fusion transcript (arrowhead) in the tumour using the reverse-transcription polymerase-chain reaction.