Primary Ewing's sarcoma of the lung parenchyma – A case report

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Abstract

Ewing's sarcoma (ES) family of tumors (EFT) is a group of neoplastic diseases including ES, peripheral primitive neuroectodermal tumors, malignant small-cell tumor of the chest wall (Askins tumor) and atypical ES. Primitive neuroectodermal tumours and extraskeletal ES have a similar neural phenotype and can be considered as the same entity. EFT can develop in any bone or soft tissue, but primary appearance in the lung parenchyma is rare presentation. We report a case of young male with primary ES arising in the left lung. Patient referred with history of dry cough and hemoptysis. Computed tomography scan revealed a mass lesion of the left upper lobe and lingula, without verified distal metastasis. Repeated bronchoscopy failed to resolve diagnostic dilemma so minimal thoracotomy was performed. Cytologic diagnosis on the intraoperative samples was malignant neoplasm, possibly epithelial. Based on histology and immunohistochemistry final diagnosis was ES, which was further proved by RT-PCR analysis demonstrating EWS/ERG translocation. Due to difficulties in diagnosing and agressiveness of tumor itself the diagnosis was set at the time when tumor was inoperable with metastatic spread. Although primary Ewing's sarcoma of the lung parenchyma is an extremely rare condition, it should be considered as a part of differential diagnostic algorithm for lung masses.

Keywords: Ewing, lung, neuroectodermal tumor, sarcoma.

Introduction

Ewing's sarcoma (ES) and peripheral primitive neuroectodermal tumor (PNET) were originally described as distinct clinicopathologic entities. Over the last decades, it has become clear that these entities include the same spectrum of neoplastic diseases known as the Ewing sarcoma family of the tumors (EFT). EFT is a group of neoplastic diseases which includes Ewing's sarcoma (ES), peripheral primitive neuroectodermal tumors, malignant small-cell tumor of the chest wall (Askins tumor) and atypical ES (1-3). EFT can develop in any bone or soft tissue but primary appearance in the lung parenchyma is extremely rare presentation.

Case report

We report a case of a 32-year-old male with primary Ewing's sarcoma arising in the left lung. Patient referred to the emergency unit with a history of dry cough and hemoptysis. Computed tomography scan revealed a mass lesion of the left upper lobe and lingula, but without verified distal metastasis. First, cytological bronchoscopic samples were imprinted smear of bronchial mucosa biopsy and fine needle aspiration (FNA) of bronchial lesions during bronchoscopy. Imprint smear of bronchial mucosa biopsy was negative, containing only bronchial cells and blood. Positive finding was in fine needle aspirations (FNA) of bronchial lesions. There was a mixture of blood and necrosis in the background, as well as bronchial cells and lymphocytes. Malignant cells were scattered, mostly single or in small aggregates, medium sized to large with large, excentric, round to cuboid nuclei. Chromatin was fine, with inconspicuous nucleoli and basophilic, scanty cytoplasm (Figure 1. A).

Cells morphology resembled mostly to lymphoma, but differential diagnosis because of necrotic background and localisation was also small cell lung carcinoma. Immunocytochemistry was performed in the limited setting (four slides only and small amount of cells) and malignant cells were vimentin positive, some of the larger cells were leucocyte common antigen (LCA) positive, as well as small lymphocytes and pancytokeratin and TTF-1 negative (Figures 1. B, C). Cytologic diagnosis was malignant neoplasm, possible lymphoma.

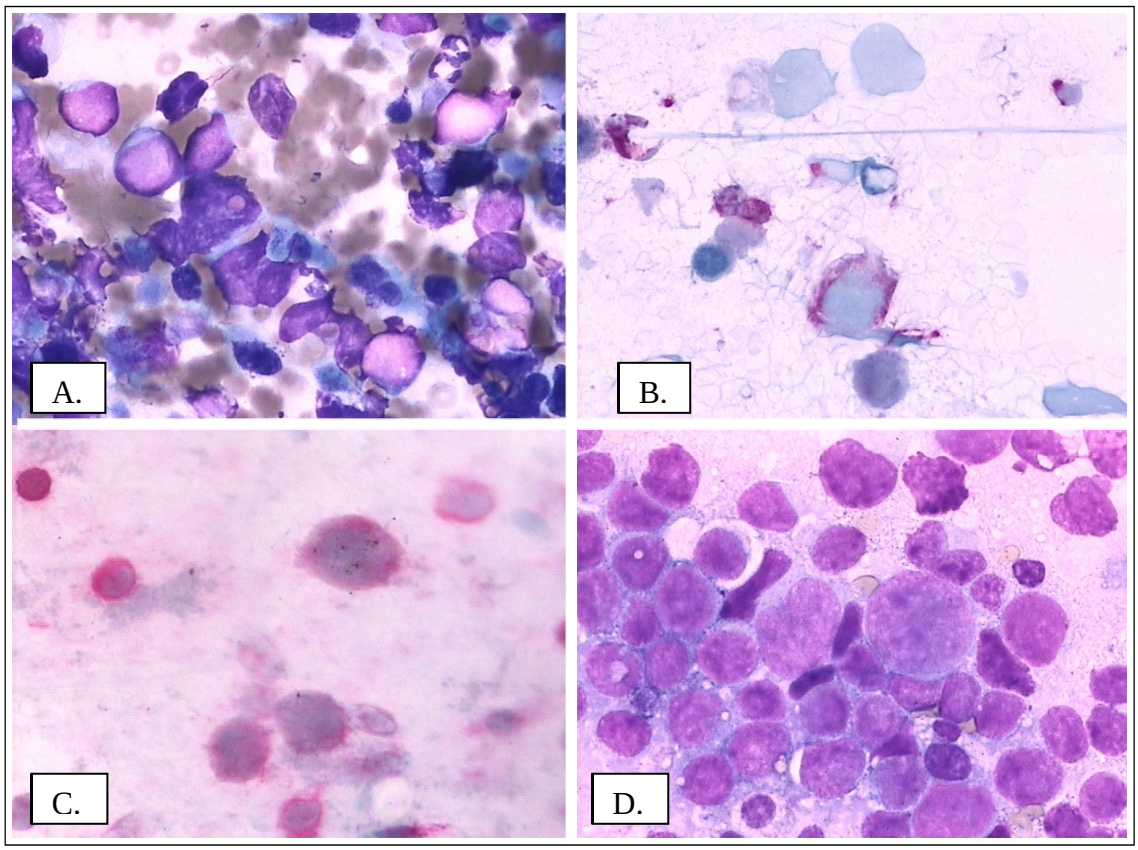
Second bronchoscopy was performed and imprint smear of bronchial mucosa biopsy was inconclusive again – only small and medium sized lymphocytes, bronchial cells with some atypia.

Although two transbronchial biopsies were performed samples contained only bronchial wall, granulation tissue and oedema. Even bone biopsy was done because of suspicion for lymphoma, but bone marrow was without any infiltration.

Repeated bronchoscopy failed to resolve diagnostic dilemma so thoracotomy was performed.

Intraoperative cytological samples included imprint smear of lung tumour and pleural fluid smears. In all samples malignant cells were prominent and numerous. Cells distribution was in large clusters and aggregates, with obvious anisocytosis and polymorphism. Some areas resembled to picture from brochoscopic samples with scattered, single cells resembling lymphoma cells. Surprisingly, there were areas of large cells with epithelial characteristics, but larger then small cell lung carcinoma cells, with oval and irregular nuclei, coarse chromatin, obvious nucleoli and moderate amount of cytoplasm (Figure 1. D). Necrosis was prominent. Cytologic diagnosis on the intraoperative samples was malignant neoplasm, possibly epithelial. Due to tumour size, tumour was inoperable and only biopsy was performed.

Figure 1. A. Scatterd single malignant cells resembling lymphoma cells, eritrocytes and necrosis in the background (MGG, FNA, original magnification 400x).
B. Malignant cells positive for vimentin (immunocytochemistry, FNA, original magnification 400x.
C. Malignant cells and small lymphocytes positive for LCA (immunocytochemistry, FNA, original magnification 400x.
D. Area with larger, polymorphic cells (MGG, imprint smear of lung tumour, original magnification 400x)



Pathologic examination of the specimen demonstrated lung parenchyma infiltrated with tumor tissue composed of atypical cells with hyperchromatic nuclei, scarce cytoplasm, numerous mitoses and positive for CD56 (NCAM), synaptophysin, CD99, and negative for CK, TTF-1, CD3, CD20, TdT, CD10 and PAX5 (Figure 2, Figure 3). Based on histology and immunohistochemistry our final diagnosis was Ewing's sarcoma, which was further proved by RT-PCR analysis demonstrating EWS/ERG translocation (Figure 3).
After diagnosing Ewing's sarcoma the patient was reffered to Oncology Clinc for further treatment.

Disscussion

ES/PNET family is uncommon malignant neoplasm, and shares common histological features of closely packed small primitive round cells. Differential diagnoses of PNET of the lung include other round cell tumors, such as lymphoma, small cell carcinoma, rhabdomyosarcoma, granulocytic sarcoma, synovial sarcoma, Langerhan's cell histiocitosis and classical neuroblastoma.

Tumor identification is fundamental between these tumours as treatment modalities vary. The morphological features of intrapulmonary tumours are similar to those of the ES/PNET in variety of other locations (4-7).
Although not specific for PNET or ES, CD99 expression is almost always present in these tumors. A characteristic reciprocal cytogenetic translocation,

Figure 2. Lung parenchyma infiltrated with tumor composed of small blue cells with scant cytoplasm. Lower part of the figure demonstrates alveolar space with reactive pneumocytes (hemalaun-eosin, objective x40)

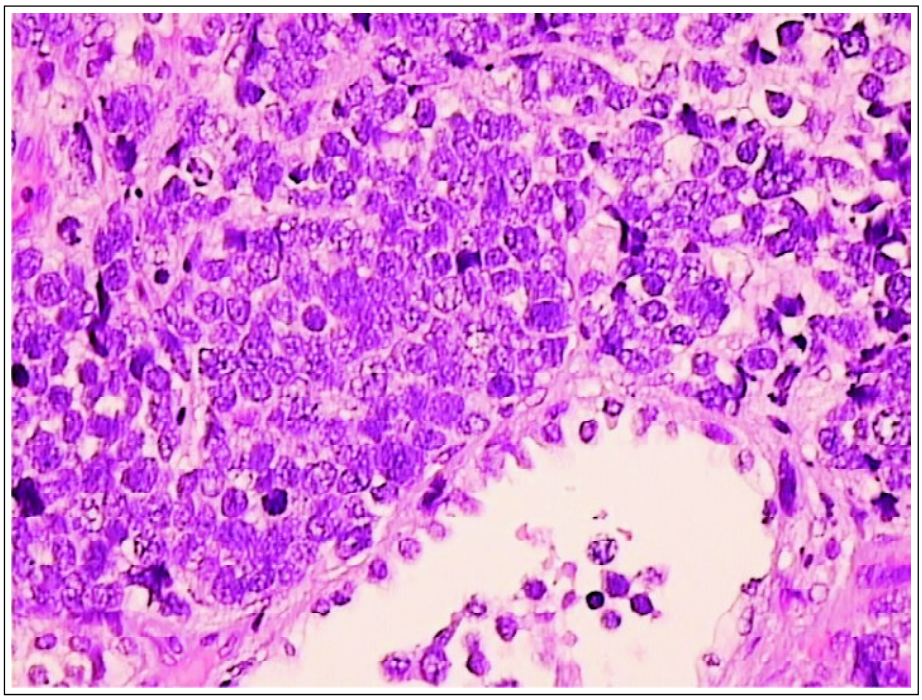


Figure 3. Tumor cells were positive for CD99 antibody, characterisitic for Ewing sarcoma/ PNET (immunohistochemistry, objective x40)

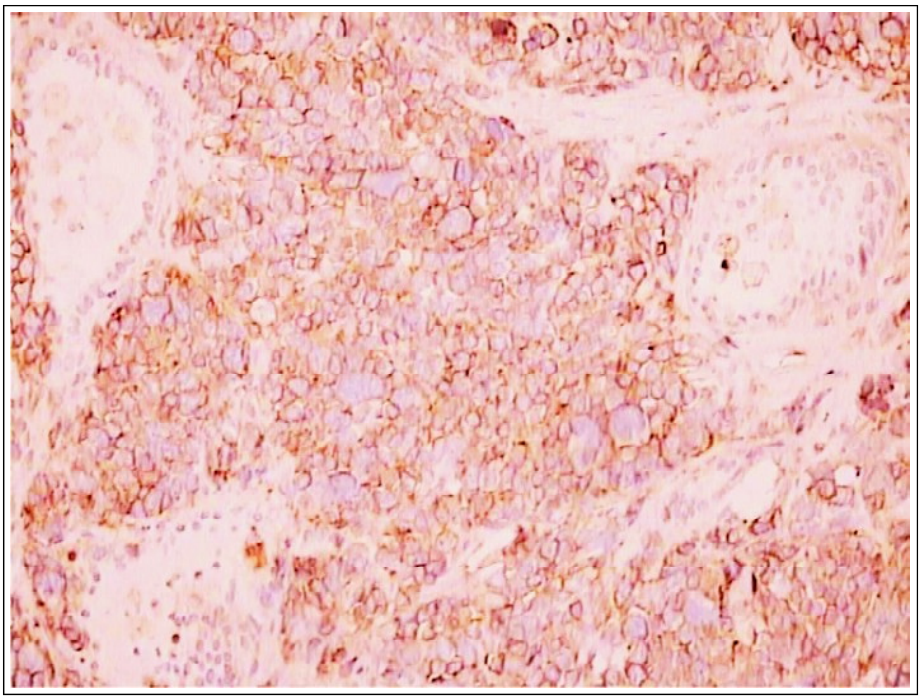
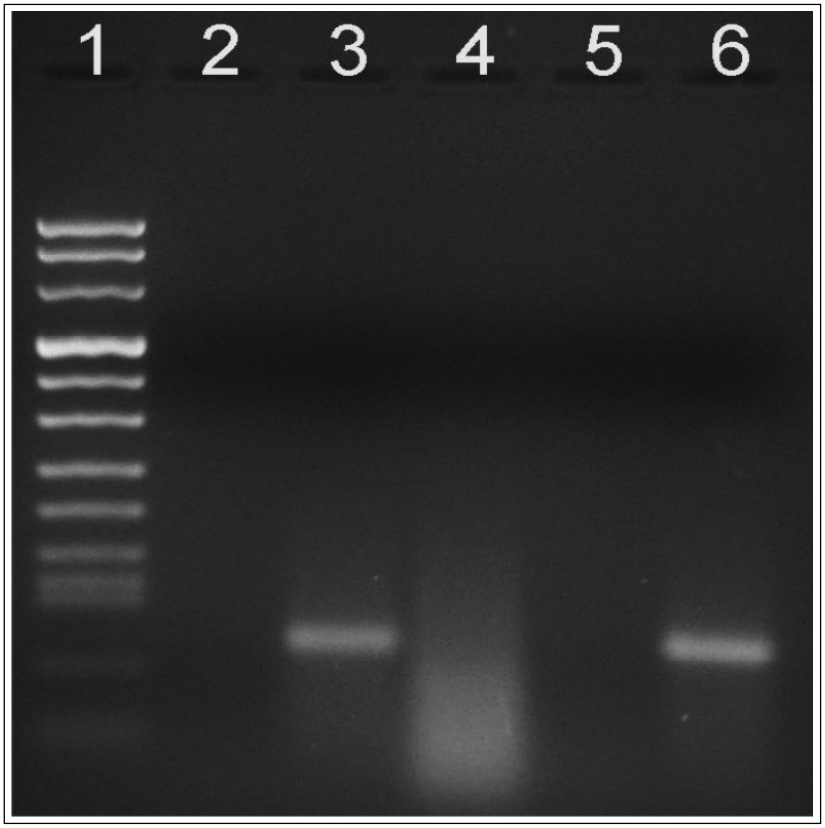


Figure 4. RT-PCR analysis proved EWS/ERG translocation [t(21;22)(q22;q12)] in our patient



1. DNA Molecular Weight Marker VIII (Roche)
2. EWS/ERG negative control
3. EWS/ERG positive control
4. Patient without EWS/ERG mutation
5. Patient with EWS/ERG mutation
6. Our patient, with positive EWS/ERG mutation

t(11;22)(q24;q12), is also shared with members of the ES/PNET family.

Careful histological evaluation, use of several immunohistocemical markers and, if necessary, molecular or citogentic analysis can lead to a correct diagnosis. Because primary pulmonary ES/PNET is very rare, we tested several markers for small cell carcinomas such as cytokeratin, chromogranin, TTF-1, wich were all negative. Thus, a phenotype such as it was found in our case, wich was CD99, vimentin positive, and CK i TTF-1 negative, is highly suggestive of PNET. Ultimately, FISH revealed an EWSR 1 22q12 rearrangement, which confirmed the diagnosis genetically.

Ewing's sarcoma family of the tumors (ESFT) of the lung is an aggressive malignant tumour, overall five-year survival rate is 61% (8).

The most significant prognostic factor in ESFT is considered to be whether the disease has spread (9). At diagnosis of Ewing's sarcoma approximately 25% of patients have metastatic spread (4) a 5-year survival rate in this group of 20-30% has been noted (10). Factors such as tumour size, however, are not thought to show prognostic value (5). A younger age at time of diagnosis is associated with improved survival (5). In this case, at the time of admission to

hospital no metastatic spread was diagnosed, but at the time of final diagnosis patient had metastatic spread in bones, lymph nodes and contralateral lung. ESFT is recognised as a systemic disease and therefore, indications for systemic treatment are predictable. In this case, due to tumour size, only surgical byopsis was performed and chemotherapy was subsequently administered.

Due to the infrequent presentation of ESFT optimal tretment modalities remain an area of debate. Combinations of aggressive therapy including surgery with chemotherapy and high-dose radiotherapy are used. Current knowledge would favour early surgical resection with additional chemotherapy (5,7). Ewing's sarcoma is radiosensitive so there may be a role for additional therapy. No dramatic differences have been noted in treatment modalities of these tumours during last three decades (8) and optimum treatment needs to be established.

In conclusion, we experienced difficulties in diagnosing a primary pulmonary ES/PNET. Due to difficulties in diagnosing and agressiveness of tumour itself, the diagnosis was set at the time when tumour was inoperable with metastatic spread and only chemotherapy treatment could be performed. Patient was referred to Oncology clinic, treated with chemotreapy, but died 6 months after diagnosing. Although different kinds of pulmonary metastasis from Ewing's sarcoma are common, the primary pulmonary ES/PNET is an extremely rare tumour, it shoud be considered in the differential diagnosis of a primary pulmonary mass.

This case report has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Parents of patient gave their consent prior to be shown as a case report.

All figures are original, made by authors listed above.

Conflicts of interest: None declared.

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