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LATE ONSET OF PRIMARY PULMONARY PRIMITIVE NEUROECTODERMAL TUMOR: A CASE REPORT

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Abstract

Lungs are one of most metastatic areas for primitive neuroectodermal tumor (PNET), however primary pulmonary PNET is extremely rare. Here we present a case of a 58-year-old male patient with a tumor in the right lung that originated from the lung but not from chest wall. Patient was diagnosed with PNET following histological and immunohistochemical examination of CT-guided percutaneous tru-cut needle biopsy and no distant metastasis were detected in PET-CT scan. As advised recently in published literature, surgical resection following neoadjuvant chemotherapy protocol is preferred in the treatment of our patient as it has better success of complete resection leading to higher 5-year survival rates. Although primary pulmonary PNET is uncommon, it should be taken into account and complete surgical resection should be aimed as treatment to achieve higher survival rates.

Keywords: neuroectodermal tumor, primitive, lung, neoadjuvant therapy

Introduction

Primitive neuroectodermal tumor (PNET) is a member of Ewing's family of tumors with Ewing's sarcoma (ES), and almost 70% of all patients with Ewing's family of tumors are under the age of 20, with a slight male predominance [1]. However, it is very rare in liver, kidneys and adrenal glands [2,3]. The form observed in the thoracic region is often Askin tumor, which arises from the chest wall [4]. Although lungs are one of most metastatic areas for PNET, primary pulmonary PNET (pPNET) is very rare. There were only 15 cases reported in English-language special literature until a six patients' series was published by Weissferdt et al. in 2012 [5-15].

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Case Report

A 58-year-old male patient, with the diagnosis of hypertension and hyperlipidemia, was admitted to the Department of Internal Medicine of Gulhane Research and Training Hospital (Ankara, TURKEY) for an annual control without any complaints. No pathologic result, other than elevated sedimentation rate (66 mm/hr), was detected during laboratory examination. A radiopaque appearance associated with a mass lesion of 6 cm was detected in his right lung in chest X-ray (Figure 1). A contrast-enhanced computed tomography (CT) scan of chest revealed a paravertebral located, pleural-based mass with irregular margins in the lower lobe superior segment of right lung. The mass was 77 x 74 x 41 mm in size, constituting local pleural retraction and containing necrotic areas (Figure 2).

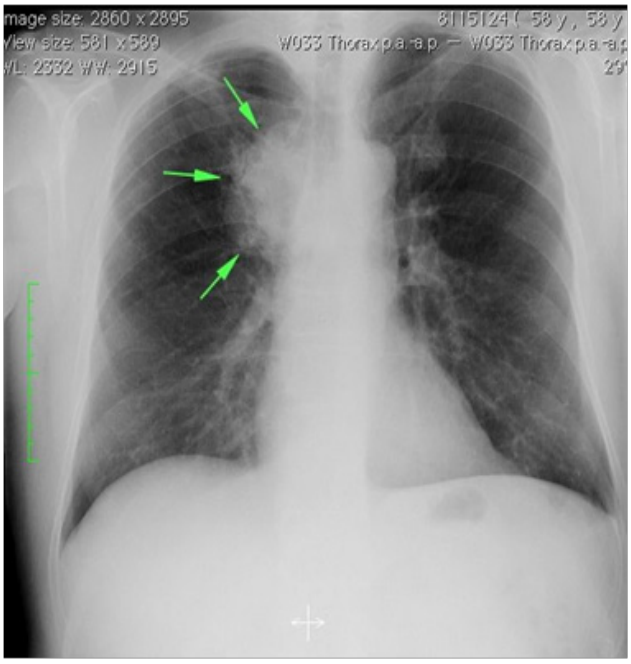

Figure 1. The mass image in the right lung (*Chest X-Ray*).

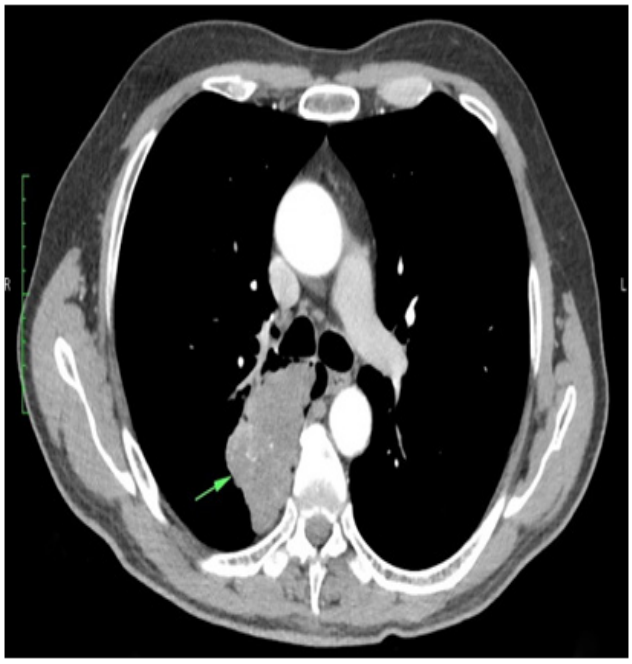

Figure 2. The mass image in the right lung *(horizontal cross-section view of thoracic CT scan).*

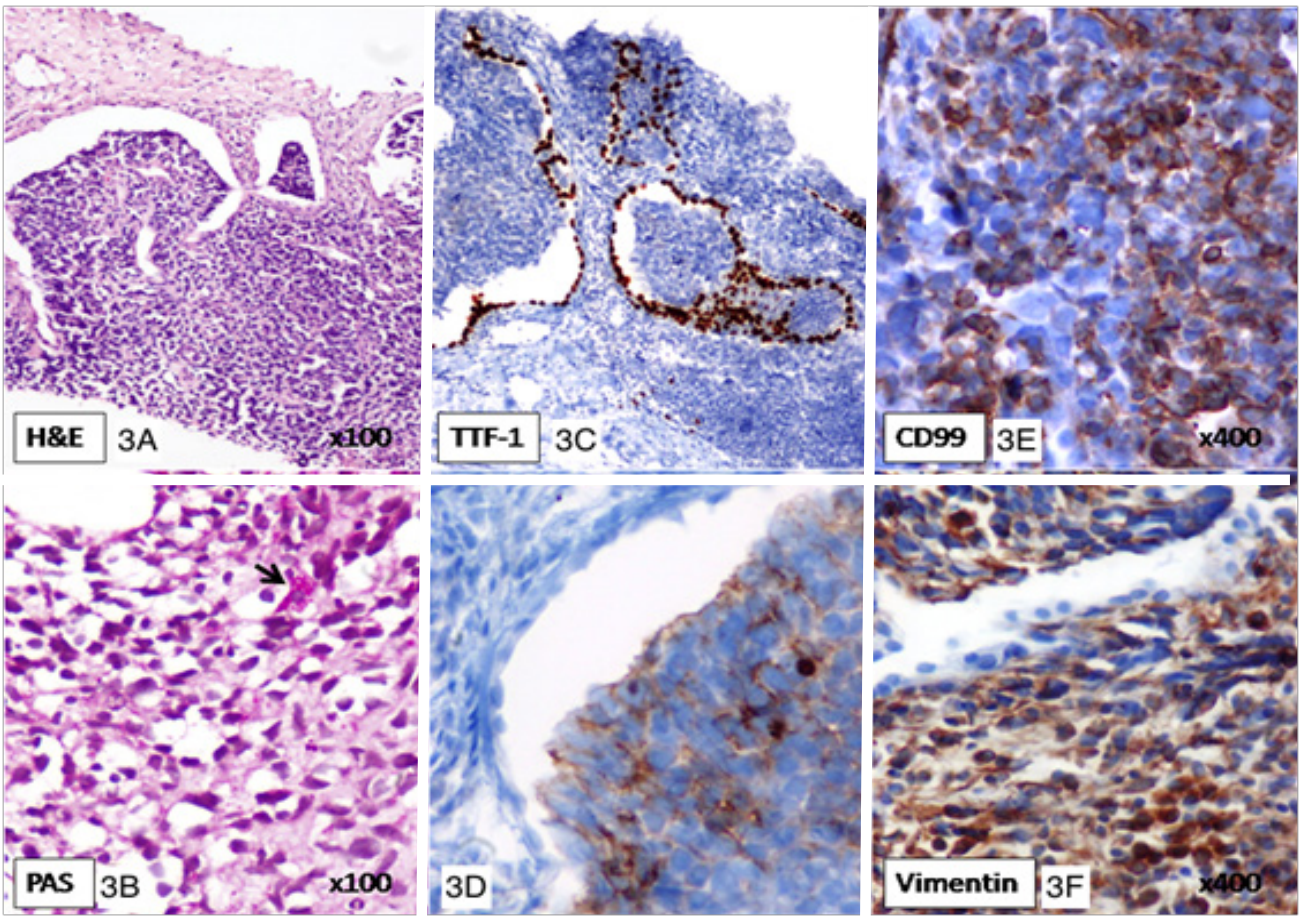

Figure 3A. Small round atypical cells with narrow cytoplasm and hyperchromatic nuclei. **Figure 3B.** PAS positive intracytoplasmic perinuclear eosinophilic globular accumulations. **Figure 3C.** Tumor cells filling alveolar cavities were negative for TTF-1, while pneumocytes were marked **Figure 3D.** Neoplastic cells show membranous and cytoplasmic immunoreactivity with CD56 **Figure 3E.** Cells showing membranous immunoreactivity with CD99 **Figure 3F.** Cells showing cytoplasmic immunoreactivity with vimentin.

CT-guided percutaneous tru-cut needle biopsy was performed. Histopathological examination of the biopsy specimen indicated small round atypical cells with narrow cytoplasm and hyperchromatic nuclei constituting solid layers (Figure 3a). Histochemical examination revealed Periodic Acid-Schiff (PAS) positive intracytoplasmic perinuclear eosinophilic globular accumulations (Figure 3b). Immunohistochemical analysis of 4-µm formalin-fixed, paraffin-embedded tissue sections demonstrated that the tumor cells filling alveolar cavities were negative for transcription termination factor, RNA polymerase I (TTF-1; mouse anti-TTF-1 monoclonal antibody; cat. no. MAB-0266), while pneumocytes were significantly marked (Figure 3c). On the other hand, tumor cells showed membranous and cytoplasmic immunoreactivity with cluster of differentiation (CD)56 (mouse anti-CD56 monoclonal antibody; cat. no. MAB-0256) (Figure 3d) and also membranous with CD 99 (mouse anti-CD99 monoclonal antibody; cat. no. MAB-0059) (Figure 3e) and cytoplasmic with vimentin (rabbit anti-vimentin monoclonal antibody; cat. no. RMA-0547) (Figure 3f), respectively. Based on all of these data, patient was considered as having a pPNET.

2- [18F] fluoro-2-deoxy-D-glucose (FDG)/ Positron emission tomography (PET) - CT was performed in order to assess the metabolic activity of the mass in the lung and the detection of possible metastatic foci. The maximum standardized uptake value (SUV) of the mass located in the superior segment of the lower lobe of the right lung as previously described in CT, was found to be 17.2 (Figure 4). Other than the lesion, no focus was detected indicating pathological uptake. Thus, the mass in the lung was considered as the primary focus and no distant metastasis was observed.

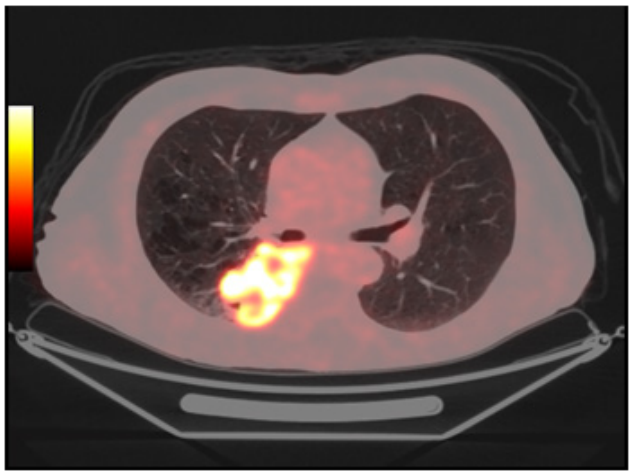

Figure 4. The mass showing significantly elevated intense metabolic activity (SUV max=17.2) in the superior segment of right lower lung lobe by FDG-PET / CT.

Following the diagnosis of pPNET, 3 cycles of neoadjuvant chemotherapy including vincristine, adriamycin, cyclophosphamide, ifosfamide and etoposide were administered. Following completion of neoadjuvant chemotherapy the patient was treated with complete surgical resection and 3 cycles of adjuvant chemotherapy was continued after the operation. Follow-ups were scheduled every 3 months, and the patient is currently in a good condition. Written informed consent was obtained from the patient for the publication of this study.

Discussion

ES / PNET family of tumors are rare malignant tumors in adults. Although it often arises from soft tissue and bone, it might be seen in rare focuses such as myocardium, lung, ovaries, testes, uterus, kidney, pancreas and palate [6,16-19].

While it is more common in adolescents and young adults, it can be seen in all age groups. The primary pPNET cases in the literature are in the range of 8-67 years of age and the incidence in men is about 1.5 times higher than in women [5-15]. Cough, fever, dyspnea, hemoptysis and chest pain might be observed at admission but also there may not be any symptoms such as in our case. Large tumors (3.6 - 9 cm) are usually originating from the peripheral lung parenchyma and rarely from bronchial system [5-15]. Age, gender predominance and tumor size of our patient is similar with current literature.

The diagnosis of PNET is based on morphological and immunohistochemical analyses of tissue specimen. Typical morphological appearance of the PNET consists of small, round, blue cells with faded cytoplasm. PNETs should be positive for CD99, neuron-specific enolase (NSE), CD56 and should be negative for markers for epithelial, lymphoid, smooth / skeletal muscle and melanoma [3]. PAS could be found positive in some cases. At least two of these markers should be positive in order to diagnose a tumor as a PNET [3]. In the histopathological examination of our patient small round blue cells were noted and the immunohistochemical examination specimen was positive for CD 99, CD 56 and PAS, while negative for TTF-1 and RNA polymerase I.

There are different treatment approaches available including neoadjuvant and adjuvant chemotherapy, radiotherapy and surgical resection. In a study carried out by Demir et al. the success of complete resection was found significantly higher (p=0.027) in patients receiving neoadjuvant chemotherapy prior to surgical resection, compared to patients who did not [13]. 5-year survival was found to be 56% in patients with complete surgical resection, and 25% in those in which complete surgical resection failed (P=0.13). Five-year survival was observed 77% and 37%, respectively, in those administered neoadjuvant chemotherapy as compared to untreated group (p=0.22) [13].

In a study conducted by Grier et al., 398 non-metastatic ES/PNET patients were randomly assigned to the standard-therapy group (doxorubicin, vincristine, cyclophosphamide, and dactinomycin) and to the experimental-therapy group (addition of ifosfamide and etoposide to a standard regimen). 5 year event free survival (69% and 54%, $p<0.005$) and overall survival (72% and 61%, $p<0.01$) are found significantly higher among patients in the experimental-therapy group. Same study was also conducted with randomly assigned 120 metastatic patients, but no significant difference was reported in 5 year event free survival between groups (P=0.81) [20].

In accordance with current information, neoadjuvant chemotherapy including ifosfamide and etoposide in addition to doxorubicin, vincristine, cyclophosphamide, and dactinomycin was administered to our patient prior to surgery and surgery was scheduled after the third cycle of chemotherapy.

Although PNET appears rarely in adults, it should be considered in the differential diagnosis of large tumors of the lungs. While immunohistochemical studies have major role in diagnosis, FDG PET / CT should be performed to investigate distant metastases prior to treatment. Surgical resection after neoadjuvant chemotherapy significantly increases 5-year survival rate compared to only surgical resection. Ifosfamide and etoposide should be added to a standard regimen for nonmetastatic patients.

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