Askin Tumor: Malignant Round Cell Tumor in the Thoracopulmonary Region

Özlem (Malas) Oruç, MD[1]; Arzu Hocaoğlu, MD[1]; Benan Çağlayan, MD[1]; E Sevda Özdoğan, MD[1]; Nusret Erdoğan, MD[2]

[1] Dr. Lütfi Kırdar Kartal Training and Research Hospital, Department of Chest Diseases, İstanbul, Turkey
[2] Taksim Training and Research Hospital, Department of Pathology, İstanbul, Turkey

Abstract

A 29-year-old male patient was admitted to our clinic with complaints of chest pain and dyspnea. Radiological examination showed a chest wall mass on the left side, which caused rib destruction and massive pleural effusion. The diagnosis was made by transthoracic needle aspiration biopsy, cytological examination of the pleural fluid and pleural biopsy which showed the presence of a malignant round cell tumor. Immunohistochemical assays together with the clinical and radiological findings led to the definite diagnosis of Askin tumor.

Turkish Respiratory Journal, 2002;3 (3):109-112

Key words: *Askin tumor, PNET, Ewing sarcoma*
Abbreviations: *PNET: Primitive neuroectodermal, HE: Hematoxylin-eosine, CT: Computerized tomography, LCA: Leukocyte common antigen, HHF 35: actin, smooth muscle Ab-4, PAS: Periodic acid schiff, PAN CK: PAN cytokeratin*

Introduction

Askin tumor has been defined by Askin and Rosai in 1979. This malignant round cell tumor, which originates from the soft tissue of the chest wall, is also called extraskeletal Ewing sarcoma or peripherical primitive neuroectodermal tumor (PNET) (1,2).

Ewing sarcoma and PNET tumors are composed of blue round cells and most of the cases show cytogenetic translocation and special immunohistochemical features. When compared with Ewing sarcoma; PNET shows more significant neuroectodermal differentiation. Although once accepted as distinct entities, today Ewing sarcoma, Askin tumor and PNET are all considered as members of the Ewing family of tumors and if localized in the thoracopulmonary region, they are defined as Askin tumor (3). Though the frequency of Ewing sarcoma and PNET amoung childhood tumors is 2%, the incidence of Askin tumor is not clear because of the rarity of the disease. Very few clinical studies performed after the report of Askin et al. in 1979 are available (1,4,5,6). In the treatment of the tumor the combination of surgery, radiotherapy and chemotherapy is used. Survival is associated with age and advanced age is the cause of poor prognosis and short survival.

Correspondence: *Dr. Özlem (Malas) Oruç,*
Batı Mah. Çamlık Sok. No: 19/4, 81480, Pendik,
İstanbul, Türkiye
Tel: (0-216) 4831304
Fax: (0-216) 4421884
E-mail: ozoruc@hotmail.com

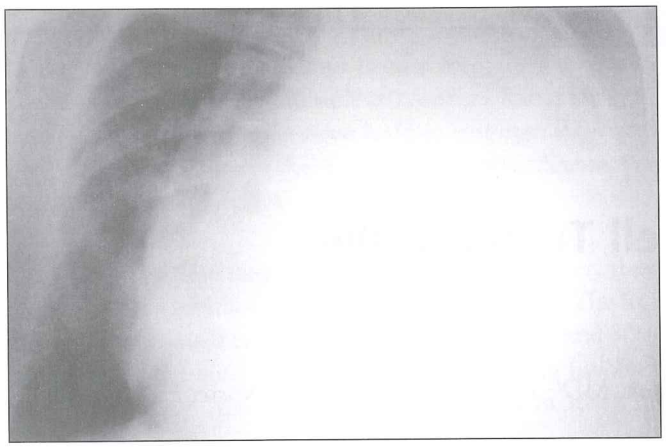

Figure 1. *Postero-anterior chest X-ray showing a homogenous opacity on the left hemithorax and deviation of the trachea and mediastinium to the right.*

Case Report

A 29-year-old male patient with a 9-month history of complaints of chest pain, dyspnea and a mass on the chest wall, was admitted to our clinic. He had no significant personal or family history. On physical examination vital findings were normal. On inspection and palpation, a hard, approximately 15x20 cm in size, fixed and painful mass was detected on the left anterolateral hemithorax. On auscultation, a bronchial sound was heard on the upper regions of the left hemithorax and breath sounds were diminshed in the bases. Other system examinations were normal. Blood tests were normal except for a high erythrocyte sedimentation rate (95 mm/h). Chest X-ray revealed a homogenous opacity on the left hemithorax with the deviation of the trachea and mediastinium to the right (Figure 1). Thoracic computerized tomography revealed a 50 mm diameter mass on the lateral wall of the left hemithorax with destruction of adjacent ribs. There was also a massive pleural effusion with compression atelectasia in the left lung (Figure 2-3).

Thoracentesis and needle aspiration biopsy were performed. The pleural fluid was hemorrhagic and exudative. The cytological examination of the pleural fluid (Figure 4) and of the needle aspiration biopsy specimen revealed a malignant small round cell tumor. The pathological examination of the pleural biopsy specimen revealed the same result (Figure 5). Immunohistochemical investigations were performed for the differential diagnosis of round cell malignant tumors such as nonhodgkin lymphoma, alveolar rhabdomyosarcoma, Merkel cell tumor, metastatic pulmonary small cell Ca, mesenchymal chondrosarcoma, extraskeletal Ewing and PNET. Vimentin was strongly positive, chromagranin was negative. Leukocyte common antigen (LCA), PAN cytokeratin (PAN CK), Actin, smooth muscle Ab-4 (HHF 35) (focal), periodic acid schiff (PAS) tests were positive Tissue MIC 2 was positive (Figure 6).

These results combined with the radiological features, led to a diagnosis of PNET or Askin Tumor.

Surgical approach was not considered as a treatment choice, due to the presence of massive malignant effusion and pleural invasion. Chemotheraphy was planned as a combination of cisplatin (100 mg/m^2) and epurubicine (100 mg/m^2). On the first day of therapy, the patient experienced a sudden deterioration with cardiopulmonary arrest. Bed side urgent electrocardiogram and echocardiogram findings were compatible with massive pulmonary embolism which caused sudden death. Scintigraphic examination or spiral CT could not be performed as the period of progression to death was too short.

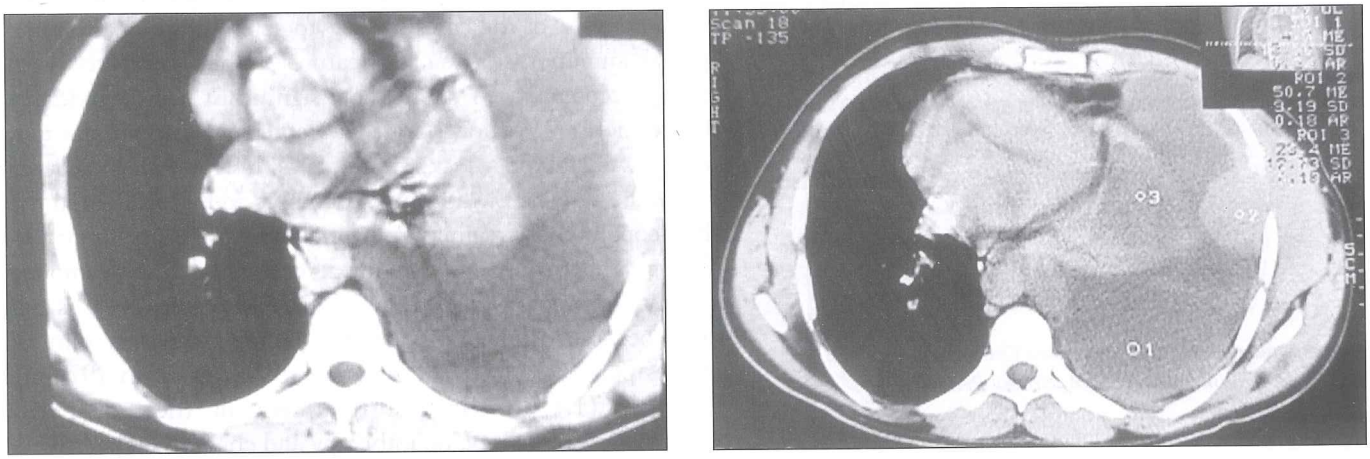

Figure 2-3. *Chest CT of the patient: Massive pleural effusion with atelectasia in the left lung and a mass 50 mm in diameter mass on the lateral wall of the left hemithorax, with destruction of adjacent ribs.*

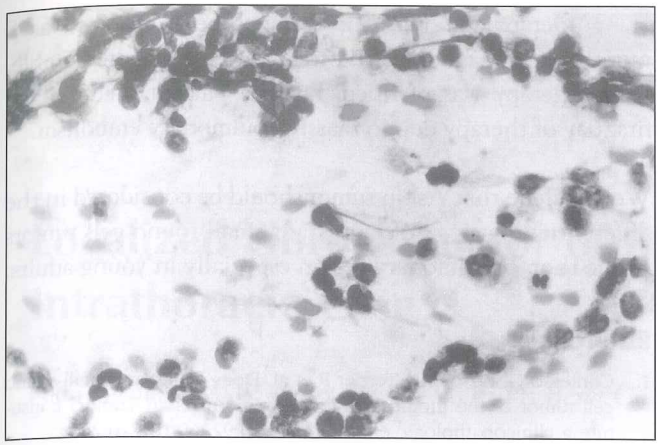

Figure 4. *Cytological examination of the pleural fluid: Malignant small round tumor cells (Hematoxylin-eosin (H.E.) stain X 40).*

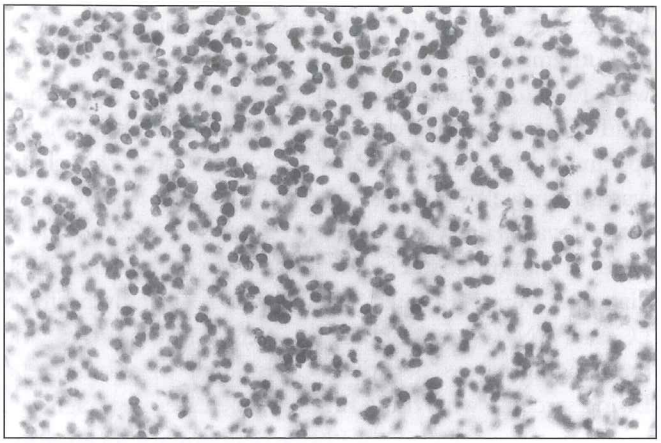

Figure 5. *Pleural biopsy material: Diffuse tumoral proliferation of the necrobiotic small round cells (H.E. stain X 10).*

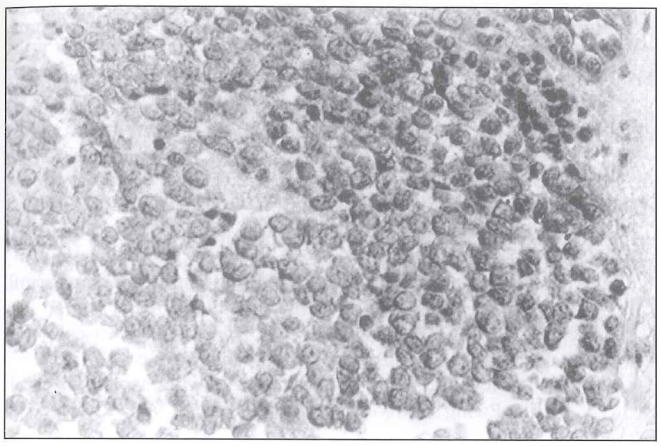

Figure 6. *Pleural biopsy material: MIC 2 diffuse expression in the malignant tumor cells (Immunohistochemical MIC 2 X 40).*

Discussion

Ewing sarcoma, PNET, rhabdomyosarcoma, neuroblastoma and lymphoma are small round cell tumors encountered in children and young adults. (5). Although Ewing sarcoma and PNET can easily be differentiated microscopically in this group, the differential diagnosis between these two entities is not possible.

Recently, a new type of tumor which caused confusion about histogenesis and terminology was reported. This type, named as 'extraskeletal Ewing sarcoma' or 'soft tissue Ewing sarcoma' shows a neural differentiation which can be demonstrated by immunohistochemical and ultrastructural methods. Similar to Ewing sarcoma and PNET, these tumors have positivity in some neural markers such as neuron specific enolase, 70 kd neuroflaments and also neuroendocrine marker positivity such as chromagranin. Also in some extraskeletal Ewing sarcoma cases, focal positivity of keratin and MIC 2 gene products are detected and such cases are classified as a separate clinicopathological group and referred to as Askin tumor. These tumors are generally localized in the thoracopulmonary region (2,7,8). Since this lesion has the clinical features of Ewing sarcoma or exhibits a primitive neuronal differentiation as in PNET, almost all research projects have focused on differentiating whether this tumor is a different kind of Ewing sarcoma or a thoracopulmonary localized variant of Ewing sarcoma and PNET. According to the current consensus, the so-called Askin tumor is a variant of Ewing sarcoma and PNET that involves the thoracopulmonary region (7).

Askin et al. reported that small round cell tumors of childhood and adolescence located in the thoracopulmonary region are more common in females and that the median age for these cases is 14.5 years (6). Radiological characteristics were a unilateral chest wall mass, pleural fluid and thickness, invasion to the adjacent lung parenchyma, pulmonary nodules and sometimes lymphadenopathy (9). Contesso et al. also investigated round cell malignant tumors (n=30) and reported invasion in regional ribs, destruction and tumoral infiltration in soft tissue. Seven of these 30 cases were presented with pleural effusion as the first finding. Our case presented with a unilateral chest wall mass, destruction in adjacent ribs and massive pleural effusion on the same side.

The diagnosis of Askin tumor rests on cytopathological investigations and immunohistochemical tests.

In a study of Sahu et al. on the diagnostic value of fine needle aspiration biopsy in tumors of Ewing sarcoma family, round tumor cells with narrow cytoplasm were seen in all except one of the needle aspiration biopsy specimens of 14 cases and PAS was found positive in all cases (10).

In our case, malignant cells with their marked nucleolus and unremarkable cytoplasm showing slight pleomorphism were found in the cytological examination of the pleural fluid and of the transthoracic needle aspiration biopsy specimen. In a pleural biopsy performed later, the pleura was infiltrated by a tumor showing the same features. The patient was diagnosed as round cell malignant tumor and a series of immunohistochemical analyses for the differential diagnosis were performed. Vimentin was strongly positive, LCA, PAN CK and HHF 35 were focal positive and chromagranin was negative. Considered as extraskeletal Ewing sarcoma with these findings, the case was diagnosed as Askin tumor due to the thoracopulmonary localization of the tumor.

As local recurrences and metastases are frequently seen in Askin tumor, it has a poor prognosis and a short survival (1). The best prognosis can be provided by surgical treatment with wide resection (4). Recurrences in the primary tumor site are important in differentiating these tumors from other tumors in children and adolescents (6). Another factor determining the prognosis is the age of the patient. Being older than 26 years, having metastatic disease and presence of a extraosseous primary tumor are factors for high risk of short survival (3). Our patient was 29 years old and it was not possible to make surgical resection, thus was at high risk for poor prognosis and short survival.

Treatment in Askin tumor consists of radical surgery, neoadjuvant or adjuvant chemotherapy and radiotherapy. Although a long survival is intended by multimodel therapy, prognosis is generally poor. Recently remission rate has improved from 26 % to 65% with aggressive chemotherapy (11-12). Survival has been reported as 8 months after diagnosis (6). Since our case was inoperable, chemotherapy was planned, but the patient died on the first day of therapy due to massive pulmonary embolism.

We conclude that Askin tumor should be considered in the differential diagnosis of malignant small round cell tumors in the thoracopulmonary region especially in young adults.

References

1. Contesso G, Bosch AL, Terrier P et al. Does malignant small round cell tumor of the thoracopulmonary region (Askin Tumor) constitute a clinicopathologic entity? Cancer 1992; 69:1012-1020.
2. Schmith D, Hermann C, Jürgens H et al. Malign peripheral neuroectodermal tumor and its necessary distinction from Ewing's sarcoma. Cancer 1991; 68:2251-2259.
3. Baldini EH, Demetri GP, Fletcher CD et al. Adults with ESE/PNET: adverse effect of older age and primary extraosseous disease on outcome. Ann Surg 1999; 230:79-86.
4. Ahmad R, Mayol BR, Davis et al. Extraskeletal Ewing sarcoma. Cancer 1999; 85:725-731.
5. Krams M, Peters J, Boeckel F et al. In situ reverse transcriptase polymerase chain reaction demonstration of the EWS/FLI-1 fusion transcript in Ewing and PNET. Virchows Arch 2000; 437:234-240.
6. Askin FB, Rosai J, Sibley RK et al. Malignant small cell tumor of the thoracopulmonary region in childhood. Cancer 1979; 43:2438-2451
7. Dorfman HD, Czerniak B. Bone tumors. 1st Ed. St. Louis. Mosby; 1998, p.649-653.
8. Aksoy F, Özsan H, Dervişoğlu S et al. Parietal kemik yerleşimli Ewing sarkomu. Türk Patoloji Dergisi 1994; 10:56-58.
9. Fraser RS, Pare PD, Colman N et al. Diagnosis of diseases of the chest, 4th ed.USA. W.B. Saunders Company; 1999,p.3028-3029.
10. Sahu K, Pai RR, Khalidkar UN et al. Fine needle aspiration cytology of the Ewing's sarcoma family of tumors. Acta Cytol 2000; 44:332-336.
11. Angervakk L, Enzinger FM. Extraskeletal neoplazm resembling Ewing sarcoma. Cancer 1975; 36:240-251.
12. Soule EH, Newton W, Moon TE et al. Extraskeletal Ewing sarcoma. Cancer 1978; 42:259-264.

İstanbul in winter. Photography by Turgay Çelikel, MD, PhD