A Rare Case of Epithelial Type Malignant Mesothelioma Associated with Axillary Lymph Node Metastasis and Tuberculous Lymphadenitis

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Abstract

We report a patient with pleural epithelial type mesothelioma who presented with metastasis to axillary lymph nodes. Pathology also revealed findings consistent with tuberculous lymphadenitis.

A 47-year-old man presented with chest pain, dyspnea and a history of asbestos exposure, and on physical examination a 2 cm lymph node in the right axilla and a 1 cm lymph node in the left supraclavicular area were detected. The lesions were hard in consistency, moveable and tender. Excisional biopsies were performed to both sets of lymph nodes and a transthoracic fine needle aspiration biopsy was performed to the extensive mass in the right hemitorax. Morphological, immunohistochemical, and ultrastructural findings of both biopsies revealed malignant mesothelioma. Histological examination of the left supraclavicular lymph node biopsy specimen showed a granulomatous lesion with caseation, a finding consistent with a tuberculous infection.

We believe this is the first reported case of pleural epithelial type mesothelioma with metastasis to axillary lymph nodes which is also associated with tuberculous lymphadenitis.

Turkish Respiratory Journal, 2003;4:(3):160-163

Key words: *mesothelioma, metastasis, tuberculous lymphadenitis.*

Introduction

The most common primary malignant tumor of the pleura is malignant mesothelioma, an insidious neoplasm with a dismal prognosis arising from the mesothelial surfaces of the pleura and peritoneal cavities as well as from the tunica vaginalis and pericardium. Eighty percent of all cases of mesothelioma are pleural in origin. Approximately 70 percent of cases of pleural mesothelioma are associated with documented asbestos exposure (1). Malignant mesothelioma may metastasize to lymph nodes outside thorax (2). However, distant metastases are rare, and it is exceptional for patients to present with lymphadenopathy prior to the discovery of the primary tumor (3).

Case Report

A 47 year-old male patient presented with progressive dyspnea, fatigue, chest pain, weight loss of 3 kg over a three month period and a painful right axillary mass. He has been smoking for 30 years and living in an asbestos area in central Anatolia

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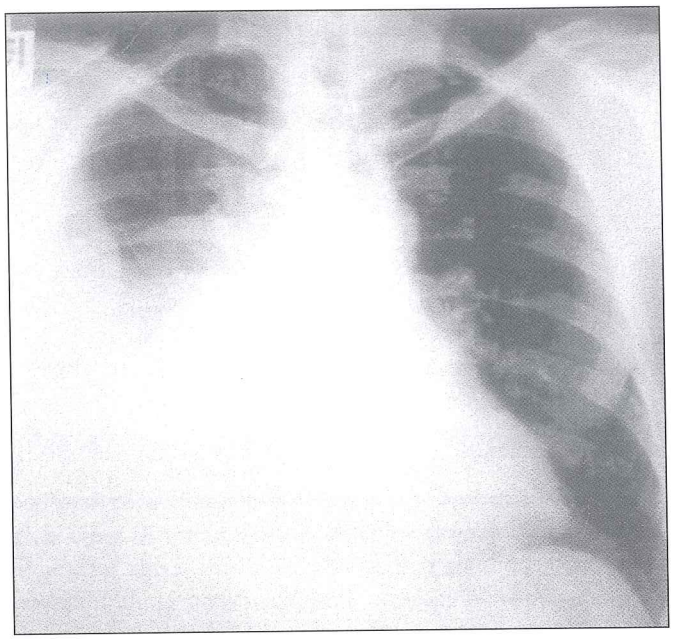

Figure 1. *Appearance of the lungs on the chest radiogram.*

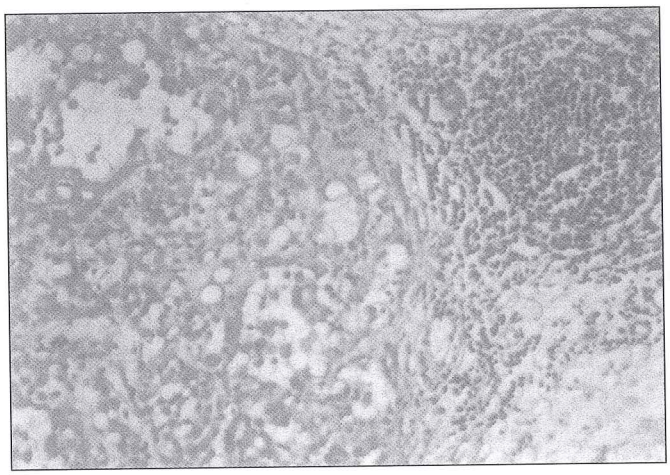

Figure 3. *Atypical mesothelial cells which infiltrated the lymph node as tubular and adenoid structures (HE X 200).*

since he was born. Physical examination revealed a 2 cm lymph node in the right axilla and a 1 cm lymph node in the left supraclavicular area; which were hard, moveable and tender. On percussion, the right lower lung field was dull and breath sounds were markedly decreased in the same area. The routine laboratory findings were normal except for a sedimentation rate of 60 mm/h (Westergreen). The chest radiography showed an area of increased homogenous density on the right side (Figure 1). Thorax ultrasonography showed a right sided extensive mass and ipsilateral minimal pleural effusion, but pleural fluid could not be obtained. Computed tomography (CT) of the chest showed that the right lung was encased with a lobulated, irregular and nonhomogenous pleural mass (Figure 2). Fiberoptic bronchoscopy revealed no pathological findings. Sputum smear for acid fast bacilli (AFB) was negative. Tuberculin

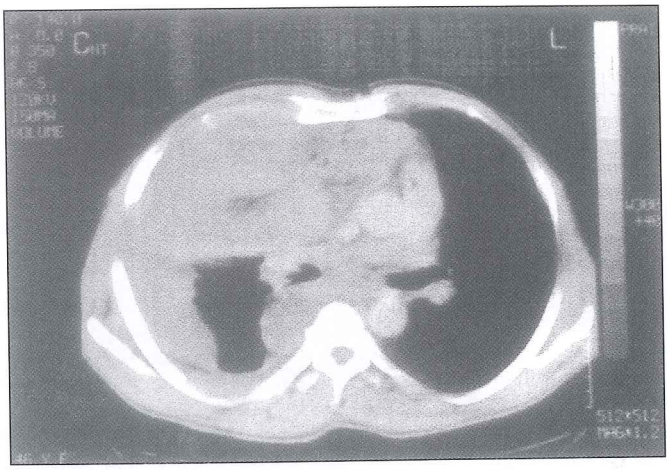

Figure 2. *Computed tomography of the chest.*

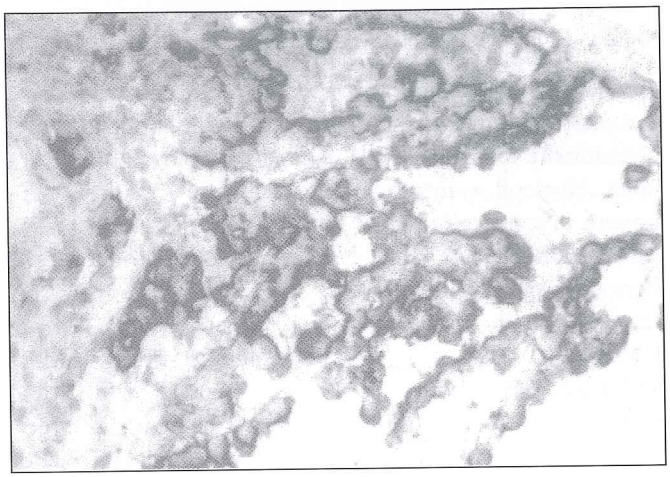

Figure 4. *HBME-1 positivity of tumor cells in çytoplasmic membrane (HBME–1X400).*

skin test (PPD) showed an induration 4 mm in diameter. Whole body bone scan, cranium CT, abdomen ultrasonography and echocardiography were all normal. Biopsy specimens were taken from the enlarged right axillary and left supraclavicular lymph nodes. A specimen was also taken from the extensive mass in the right hemithorax extensive mass at the right hemithorax by transthoracic fine needle aspiration biopsy.

Pathology

The axillary lymph node measured 2 cm in diameter. This node was described as firm and greyish yellow in colour. On microscopic examination, the nodal architecture was preserved partially and the subcapsular medullary sinuses were distended by malignant cells. The tumor cells were arranged as epithelial-like sheets, which were alveolar or tubular papillary in structure (Figure 3). The noncohesive tumor cells were scattered within a mucilagenous pool as a papillary projection. Most of the tumor cells were round, polygonal shape

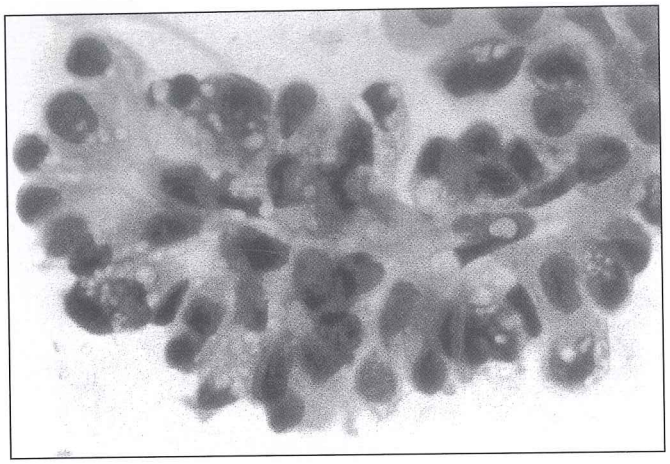

Figure 5. *Tumor cells with papillary structures and ruffled cytoplasmic borders (HE X 1000).*

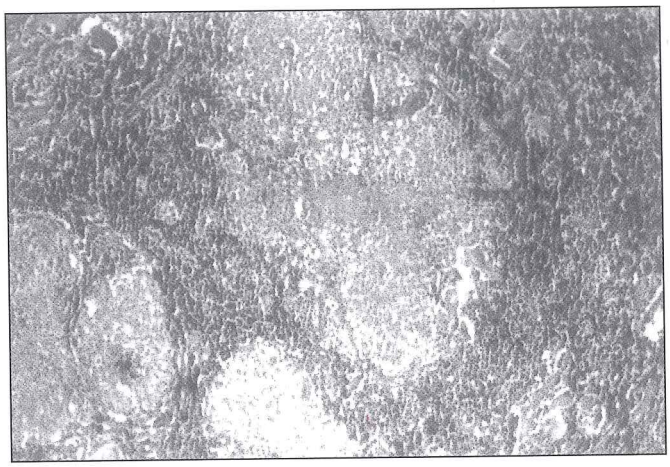

Figure 6. *Granuloma made up of epitheloid histiocytes which have infiltrated the lymph node and showing central caseation.*

and had a relatively uniform, light colored appearance. Their cytoplasm was abundant, eosinophilic and homogeneous, occasionally it was foamy or marked by variously sized vacuoles. Nucleoli were generally inconspicuous. Mitosis were present in some cells but was usually scanty.
Mucicarmine stains were negative. In most tumor cells Periodic Acid Shift (PAS) reaction was positive. Immunohistochemical stains showed positivity for HBME-1, low molecular keratin, epithelial membrane antigen (EMA) and negative reactivity for CEA and vimentin. HBME-1 was found to react with tumor cells in a characteristic "thick membrane" pattern. The diagnosis of malignant mesothelioma was confirmed (Figure 4).

The aspirate obtained from the pleural nodules was highly cellular. The smears showed cytologically atypical mesothelial cells. Some tumor cells formed clusters with papillary configurations and some were scattered individually. The cells had irregular cytoplasmic borders; the cytoplasm was abundant, pale and containes small, distinct vacuoles. The nuclei were eccentrically placed and had prominent nucleoli (Figure 5). The left suprascapular lymph node biopsy specimen contained granuloma with central caseation and giant cells. Tuberculous bacilli could not be detected in this lesion by the Ziehl-Neelson method (Figure 6).

The case was accepted as M1 in stage IV according to the International Mesothelioma Interest Group (IMIG) staging system, and in stage III according to the Butchard staging system (4,5) and was followed without any specific treatment. The patient died 6 months after the diagnosis.

Discussion

Pleural mesothelioma typically presents with chest pain and pleural effusion. These tumours often involve the lower half of the hemithorax but may spread to the entire pleural space. Both pleura, interlobular septa, pericardium, chest wall, diaphragm and even peritoneum may be involved. Distant metastatic disease is unusual in mesothelioma but may involve the liver, bone, brain, adrenals, kidney, pancreas, thyroid, spleen, skin and lymph nodes. The metastases are usually clinically silent and typically an end-stage manifestation of the disease. Hilar and mediastinal lymph node involvement occurs in less than 50 percent of patients. Extrathoracic lymph node involvement is very rare. Lymph node metastases at autopsy have been reported in cervical, supraclavicular, axillary, inguinal and abdominal sites (6–14).

Clinically documented distant lymph node metastases from pleural mesothelioma during life time are rare. They have been reported only in the brain, in the infraorbital region of the face and in lymph nodes (axillary, cervical, abdominal) (3,8,14-17). Most of these patients were symptomatic and had a previously established diagnosis of mesothelioma; the metastases occuring late in the course of the disease. Pleural mesothelioma presenting with peripheral lymphadenopathy is exceptionally rare. Sussman and Rosai reported six cases in which lymphadenopathy was the initial manifestation of malignant mesothelioma. The involved lymph nodes were cervical in four cases, mediastinal in one and inguinal in one (3). Ansari and Derias reported cervical lymph node metastases as the first manifestation of malignant mesothelioma (6). In patients with chest wall involvement, a higher frequency of axillary lymph node metastases is expected because of the pattern of lymphatic drainage (10).

Kim et al reported the first case of pleural mesothelioma which was diagnosed by axillary lymph node biopsy (8). Craig et al, reported malignant pericardial mesothelioma which had metastasized to axillary lymph nodes (2). In autopsy studies, Urschel et al reported one axillary lymph node metastasis, Whitwell et al, also reported one axillary lymph node metas-

tasis in malignant mesothelioma (9,10). Öksüzoğlu et al, reported a case who showed hematogenously disseminated metastases involving the brain and axillary lymph nodes (18).

Others have drawn attention to the fact that benign processes such as a hyperplastic lymph node and tuberculous lymphadenitis could simulate the metastatic lesions of malignant mesothelioma and should be considered in the differential diagnosis (19).

Our case had unusual features because, at the time of the diagnosis, the axillary lymph node findings were positive with an epithelial type malignant mesothelioma. All histological types of tumors give rise to blood-borne metastases, but while this is true for over half of sarcomatous tumors, less than a quarter of other types of tumours show this spread (10). What is also interesting about this particular case is that the pathology showed findings consistent with tuberculous lymphadenitis. The left supraclavicular lymph node showed a granulomatous caseating lesion, indicating that the patient was already infected with tuberculosis, which is a common illness in our country. According to a WHO report, the incidence of tuberculosis in Turkey in 2001 is 26/100 000 (20). According to the classification of Clancy (21), our country is a moderate risk region regarding tuberculosis. This patient may have developed tuberculosis lymphadenitis following regression in his immune system caused by the malignancy. Immune deficiency in patients with cancer may lead to an activation of former tuberculous foci and may facilitate the development of lesions due to exogenous superinfections (22).

In conclusion, although extrathoracic lymph node metastases in malignant mesothelioma are very rare, nevertheless, in suspected cases, lymph node biopsy needs to be performed for the diagnosis of the metastatic lesions. To our knowledge, our patient is the first malignant mesothelioma patient who presented with a metastatic axillary lymph node which was accompanied by tuberculosis lymphadenitis in the supraclavicular region.

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