Case Report

Nuran Katgi, Mehmet Unlu*, Pinar Cimen, Emre Oner, Bilkay Serez, Derya Giakoup

Pseudomesotheliomatous primary squamous cell lung carcinoma: The first case reported in Turkey and a review of the literature

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Abstract: In rare cases, pseudomesotheliomatous tumors spread diffusely within the pleura to form an encasing mass, which may be confused with diffuse malignant mesothelioma (DMM). A 73-year-old male presented with chest pain, dyspnea and a significant loss of weight and appetite. His radiological and clinical features suggested DMM. However, immunohistochemical studies revealed a primary squamous cell cancer of the lung. To the best of our knowledge, this is the first case report of pseudomesotheliomatous primary squamous cell lung cancer in Turkey, and also the seventh case worldwide. The present report aims to present this case, along with a review of the medical literature.

Keywords: Pseudomesotheliomatous carcinoma; Squamous cell lung cancer; Diffuse malignant mesothelioma

1 Introduction

Diffuse malignant mesothelioma (DMM) is now the most frequently detected pleural malignancy. It commonly presents with pleural thickening, pleural mass, increased pleural nodularity or pleural fluid [1]. However, these findings are not specific to DMM and may be present in other tumors in rare cases [2]. The term 'pseudomesotheliomatous' refers to rare tumors that mimic DMM radiologically but differ from DMM histopathologically. Primary squamous cell carcinoma of the lung constitutes an extremely rare subgroup of these already-rare tumors. The purpose of this article is to present the first case of pseudomesotheliomatous squamous cell lung cancer in Turkey along with an appropriate literature review.

2 Case report

A 73-year-old male patient was admitted to our hospital for loss of appetite and weight, chest pain and shortness of breath that had persisted for the last two months. The patient had worked as a farmer for about fifty years and was illiterate. He had a history of active smoking, specifically 75 pack-years. There was no known history of chronic disease or asbestos exposure.

Upon physical examination, the patient's blood pressure was 130/70 mmHg, and electrocardiography showed sinus tachycardia with a rate of about 110 beats/minute. No breath sounds were heard in the middle and lower zones of the left lung upon auscultation. An examination of the patient's blood samples revealed leukopenia (3800/mm^3), neutropenia (1120/mm^3), lymphopenia (460/mm^3) and anemia (hemoglobin: 10.6 g/dl). Blood biochemistry levels were within normal limits. The erythrocyte sedimentation rate was 70 mm/h, while the serum C-reactive protein level was measured as 1.5 mg/dl.

Posteroanterior chest radiography revealed a homogeneous density that blunted the left costophrenic and cardiophrenic sinuses, along with the formation of Damoiseau's line, which suggested pleural effusion (Fig. 1a). Computed-tomography (CT) scanning of the thorax demonstrated pleural fluid accumulation and pleural thickening areas, accompanied by pleural nodules in the

***Corresponding author: Mehmet Unlu,** Department of Pulmonology, Luleburgaz State Hospital, Kirklareli-Turkey, Lüleburgaz Devlet Hastanesi, Göğüs Hastalıkları Kliniği, Lüleburgaz-Kırklareli-TÜRKİYE, Mobile: +90 507 650 76 16 E-mail: lidokain21@hotmail.com
Nuran Katgi, Pinar Cimen, Department of Pulmonology, Izmir Training and Research Hospital for Thoracic Medicine and Surgery, Izmir-Turkey
Emre Oner, Department of Emergency Medicine, Adana State Hospital, Adana-Turkey
Bilkay Serez, Department of Pulmonology, Trakya University Medical Faculty, Edirne-Turkey
Derya Giakoup, Department of Pulmonology, Luleburgaz State Hospital, Kirklareli-Turkey

left hemithorax. The largest of these pleural nodules was found to be 2x1 cm in size and involved an invasion of the third rib from the posterolateral area (Fig. 2). Although positron emission tomography-computed tomography (PET-CT) did not reveal 18-fluorodeoxyglucose (18-FDG) uptake by the pleural fluid, intense 18-FDG uptake was determined via the presence of several thickened mediastinal and costal pleural areas, as well as the absence of a salient primary lesion in the lung parenchyma. In addition, PET-CT showed the destruction of the posterolateral area of the third rib secondary to tumoral invasion (Fig. 3).

An Abrams needle biopsy was performed following thoracentesis to clarify the etiology of the left pleural effusion, which was determined to be exudative based on Light's criteria. Histopathologically, the effusion was determined to have benign characteristics, and the pleural samples taken for the needle biopsy were determined to be in concordance with non-specific chronic pleuritis. Subsequently, using the guidance of CT, a tru-cut biopsy was performed on the pleural thickening areas to obtain a tissue diagnosis. Based on the results of the tru-cut biopsy, a histopathological diagnosis of squamous cell carcinoma of the lung was made. Immunohistochemical studies demonstrated the expression of only p63, while there was no expression of TTF-1. In addition, the tumor cells could not be stained with vimentin or calretinin stains (Fig. 4).

After establishing a diagnosis, the patient received systemic chemotherapy consisting of Cisplatin (75 mg/m^2, day 1) and Docetaxel (75 mg/m^2, day 1) once every three weeks for six cycles and showed a nearly complete response (Fig. 1b). However, serious problems were encountered in the clinical course after chemotherapy. Approximately four months after the last course of chemotherapy, sudden and severe pains developed in the fingers of the left hand and the upper femoral area. Because the patient's radiological findings were compatible with newly developed bone metastases in these areas, palliative radiotherapy was applied to the femoral region (20 Gy

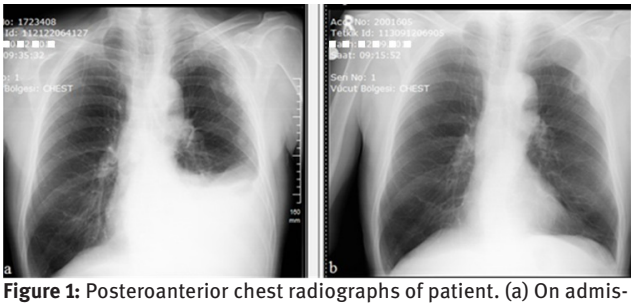

Figure 1: Posteroanterior chest radiographs of patient. (a) On admission. (b) After six cycles of chemotherapy.

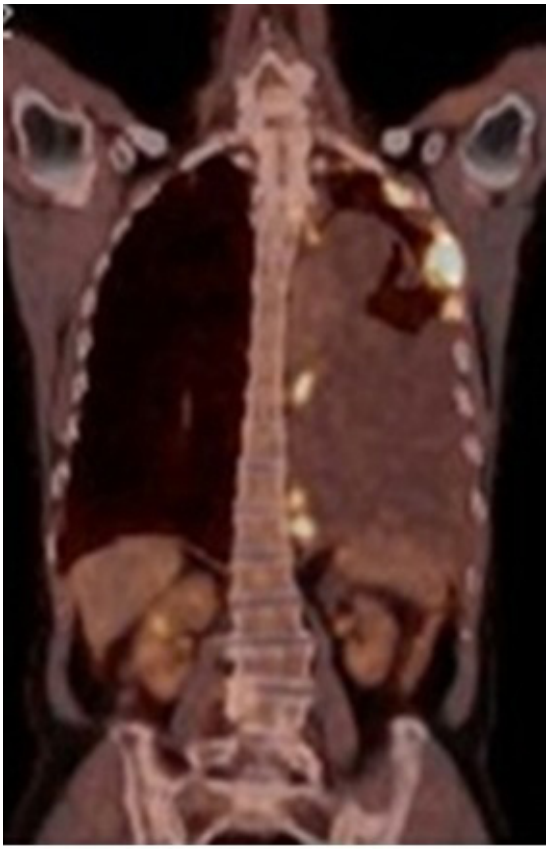

Figure 3: PET-CT demonstrating intense 18-FDG uptake by several thickened mediastinal and costal pleural areas, without the presence of a salient primary lesion in the lung parenchyma.

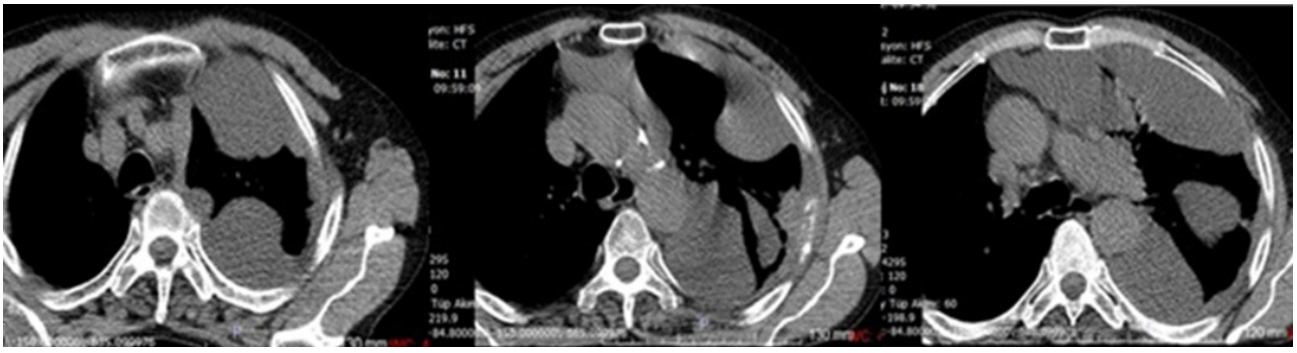

Figure 2: Thorax CT showing pleural fluid accumulation and pleural thickening areas, accompanied by pleural nodules in the left hemithorax.

in five fractions). Three weeks later, new brain metastases were determined, which caused sudden difficulties in speech (Fig. 5). Although antiedematous treatment with a combination of intravenous dexamethasone (4 mg every 6 hours) and a 20% mannitol solution (at a dosage of 1.0 g/kg in 30 minutes, then 50 g every 3 hours) was initiated immediately, the patient passed away approximately two days after the detection of the brain metastases. His clinical status did not allow the consideration of palliative brain radiotherapy.

Ethical approval: The research related to human use has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration, and has been approved by the authors' institutional review board or equivalent committee.

Informed consent: Informed consent has been obtained from all individuals included in this study.

3 Discussion

The term 'pseudomesotheliomatous' was used for the first time in 1976 by Harwood et al. to define six cases that mimicked DMM from a clinical and radiological perspective but were proven to be histopathologically compatible with primary lung adenocarcinoma [3].

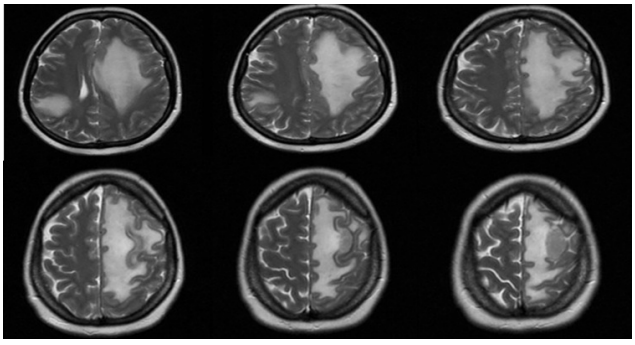

Figure 5: Brain magnetic resonance imaging revealing a metastatic lesion in the left frontoparietal lobe and peritumoral edema in the left frontopariteal and right parietal lobes.

To date, the most comprehensive study in the literature remains that performed by Attanoos et al., which states that pseudomesotheliomatous tumors constitute approximately 6% of all pleural malignancies [4]. In that study, 53 pseudomesotheliomatous tumor cases were evaluated. The researchers histopathologically divided these tumors into two main groups: primary lung tumors that spread into the pleura (47 cases) and the diffuse carcinomatous involvement of the pleura in a metastatic tumor (six cases). Lung adenocarcinoma was the most frequently detected subtype among primary lung cancers (34 of 47 cases), and squamous cell lung carcinoma was detected only in four cases [4].

As a result of the literature review we performed, it was determined that approximately 160 pseudomesotheliomatous tumor cases have been reported worldwide and that more than 100 of those were cases of primary lung adenocarcinoma, in accordance with the study mentioned above. Squamous cell lung carcinoma has only been reported in six cases worldwide, and no cases have been reported in Turkey. Therefore, the presented case is the seventh case worldwide and the first case in our country.

Pseudomesotheliomatous tumors are mostly found in men, especially between the fifth and seventh decades of life [4, 5]. The majority of patients are heavy smokers [4, 5]. As in DMM, asbestos exposure is a well-known etiological factor for pseudomesotheliomatous tumors, and it is present in 17%-76% of the patients [4, 6]. The characteristics of the six cases reported to date are summarized in Table 1. The study performed by Attanoos et al. is fundamentally concerned with the immunohistochemical markers used in the diagnosis of pseudomesotheliomatous tumors, and unfortunately, no information regarding demographic characteristics, clinical findings, treatment methods and survival states is provided. In the other two cases, it was observed that patients were male and that

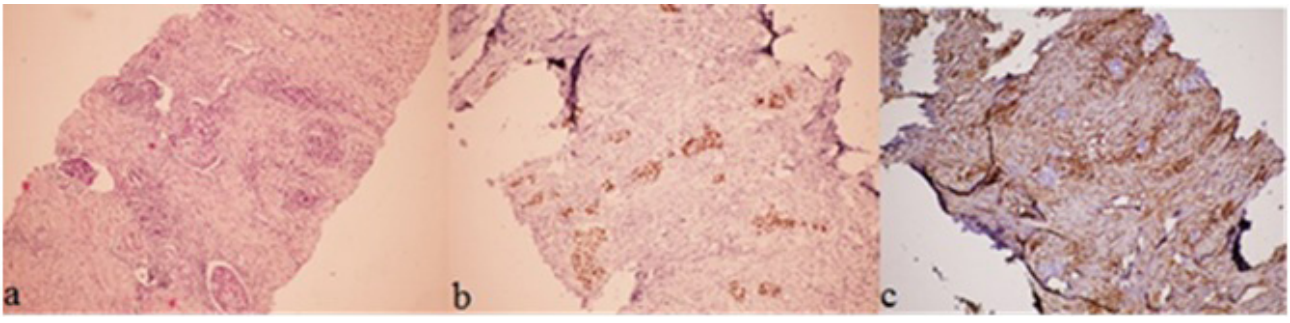

Figure 4: Pathological view of the tumor cells. (a) Hematoxylin and eosin staining showing island formation of tumor cells in the inflammatory stroma. (b) Nuclear staining with p63 antibodies (100x). (c) No staining with vimentin antibodies (100x).

Table 1: Characteristics of pseudomesotheliomatous primary squamous cell lung cancer cases reported in the literature.

	Reference			
	Dodson et al. [5]	**Nakomori et al. [7]**	**Attanoos et al. [4]**	**Case presented**
Number of patients	1	1	4	1
Age	77	80	Not reported	73
Gender	Male	Male	Not reported	Male
Occupation	Not reported	Not reported	Not reported	Farmer
History of smoking (pack-years)	Not reported	50	Not reported	75
Exposure to asbestos	None	None	Not reported	None
Survival (months)	Not reported	Not reported	Not reported	9
Treatment method	Not reported	Not reported	Not reported	CT+Palliative RT

CT: Chemotherapy RT: Radiotherapy

Table 2: Main immunohistochemical markers performed by Attanoos et al. in primary pulmonary carcinomas with diffuse pleurotropic growth and in the presented case.

		CEA n(%)	**Leu-M1 n(%)**	**Calretinin n(%)**	**Vimentin n(%)**	**CK 5/6 n(%)**	**TTF-1 n(%)**	**p63 n (%)**	**Thrombo-modulin n(%)**
Attanoos et al. (n=47)	Adenocarcinoma (n=34)	27(79)	25(74)	**0(0)**	ND	0(0)	**12/18 (67)**	ND	11(30)
	Pleomorphic carcinoma (n=5)	1(25)	2(40)	**0(0)**	ND	1(20)	ND	ND	1(20)
	Squamous carcinoma (n=4)	3(60)	1(25)	**0(0)**	ND	2(50)	ND	ND	0(0)
	Small-cell carcinoma (n=2)	1(50)	0(0)	**0(0)**	ND	0(0)	ND	ND	0(0)
	Basaloid carcinoma (n=1)	1(100)	1(100)	**0(0)**	ND	0(0)	ND	ND	0(0)
	Carcinosarcoma (n=1)	1(100)	1(100)	**0(0)**	ND	0(0)	ND	ND	0(0)
Presented case	**Squamous carcinoma (n=1)**	ND	ND	**0(0)**	**0(0)**	ND	**0(0)**	**1(100)**	ND

ND: Not Done

the disease had been detected in their seventies, as in our case [5, 7]. Although exposure to asbestos has been reported to be an important etiological factor for these tumors, no history of asbestos exposure was detected in the other two cases in the literature, just as there was no such exposure in our case [5, 7]. Our patient was a heavy smoker, as in the case reported by Nakomori et al., the only case which information regarding smoking history was provided [7].

In some cases, serious difficulties are encountered in the differential diagnosis of pseudomesotheliomatous tumors, particularly their differentiation from epithelial type DMM. Immunohistochemical methods are especially important in such situations. DMM tumor cells can be stained with vimentin and calretinin [8]. TTF-1 has been found to be particularly expressed in primary lung adenocarcinomas, whereas squamous cell lung cancers express p63 [8]. Attanoos et al. revealed no staining with calretinin in the four cases they reported, and they considered this method to be the most reliable way of distinguishing pseudomesotheliomatous tumors from DMM, as in our case [4]. In addition, although no studies were performed concerning p63, and TTF-1 was only studied in some cases (18 primary lung adenocarcinomas), the researchers had

no difficulty in the determination of diagnoses due to the typical morphological characteristics of the tumor cells [4]. Unfortunately, no information could be obtained from the other two published articles regarding which immunohistochemical staining method was used [5, 7]. In our case, the diagnosis of squamous cell carcinoma was established based on the tumor cells demonstrating only p63 positivity, while no staining was observed with TTF-1, vimentin or calretinin. The main immunohistochemical markers chosen by Attanoos et al. for primary pulmonary carcinomas with diffuse pleurotropic growth, as well as the markers found in the present case, are summarized in Table 2. Furthermore, because no significant 18-FDG uptake was observed apart from the lung lesions, our case was believed to be a primary squamous cell lung carcinoma.

The treatment method for pseudomesotheliomatous tumors depends on the origin of a given tumor. Although the three articles in the literature did not clearly indicate treatment methods, in our case, chemotherapy was administered, along with palliative radiotherapy, which was applied to the metastatic foci. Pleurodesis may be an option in cases with massive pleural effusion; however, the success rate is not very high [9]. As in cases of DMM, pseudomesotheliomatous tumors have poor prognoses, and the associated life expectancy is approximately about 6-8 months [4, 6, 10]. No distinct information about the survival of patients could be obtained from the articles we reviewed [4, 5, 7]. Our patient survived for approximately 9 months following the establishment of a diagnosis.

In conclusion, pseudomesotheliomatous tumors are very rare malignancies, and primary squamous cell lung carcinoma constitutes an extremely rare subtype of these already-rare tumors. The purpose of this article is to present the first such case in Turkey and thus contribute to the literature, as well as providing a literature review regarding these rare tumors. Moreover, this article aims to emphasise the necessity of using advanced immunohistochemical methods in the differential diagnosis of these rare tumors, which can mimic DMM in terms of their clinical and radiological findings.

Conflict of interest: The authors report no conflicts of interest.

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