Spontaneous hydropneumothorax: a rare presentation of pleural mesothelioma

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Abstract

Malignant mesothelioma is an invariable lethal neoplasia that arises from mesothelial cells from pleura, peritoneum, and pericardium or tunica vaginalis. It represents less than 1% of all tumors and its incidence is rising in the last years. The typical clinical presentation is thoracic pain, dyspnea and recurrent pleural effusion. The authors present a clinical case of an 80 year-old man with a hydropneumothorax, which etiologic investigation culminated with the diagnosis of malignant mesothelioma.

Key words: Hydropneumothorax, pleura, mesothelioma, asbestosis, asbestos.

CLINICAL CASE

The authors present a case of a male patient, aged 80 years, a retired construction worker, non-smoker, who was referred to the emergency department of our hospital by his GP due to changes in lung auscultation observed during a routine check up.

The patient had a history of high blood pressure, congestive heart failure (CHF) and mixed dyslipidaemias. He was referred to the Cardiology clinic, where he received two pleural taps for a right pleural effusion that was difficult to control, the first around 2 years prior to admission and the second around six months prior to admission, with no resulting complications, i.e. without the formation of iatrogenic pneumothorax, as demonstrated by normal control x-rays conducted after the interventions in the pleural space.

The patient was on a regular regimen of acetylsalicylic acid 150 mg daily, Spironolactone 25 mg daily, Simvastatin 20 mg daily, Carvedilol 12.5 mg daily and Valsartan 160 mg daily.

On the objective examination on admission, the patient was awake and oriented; eupnoeic, with skin and mucous membranes hydrated, and healthy coloring. Cardiac auscultation was normal and lung auscultation revealed decreased vesicular sounds in the lower 2/3 of the right lung. He had no peripheral edemas or lymphadenopathy in selected spots.

Analyses were carried out on admission and showed no significant changes *(Table I)*.

Electrocardiogram revealed a heart rhythm compatible with auricular fibrillation (again) and nonspecific alterations in the ST segment.

Chest X-ray revealed a massive anteroposterior hydropneumothorax on the right *(Fig 1)*. Arterial gasometry while breathing room air revealed pH of 7.45, pO2 of 64 mmHg, pCO2 of 38 mmHg, HCO3 of 26.7 mmol/L and SatO2 of 93%.

A chest tube was inserted, which resulted in clinical and radiological improvement. The patient was then hospitalized so that an etiological hydropneumothorax study could be conducted.

CT scan of the chest revealed multiple pleural nodules on the right, in the parietal or visceral pleura, with varying sizes of up to 2.8 cm in diameter, compatible with metastatic lesions. No changes were observed in the pulmonary parenchyma or mediastinum (*Fig. 2*).

Despite the clinical and radiological improvement, and the chest tube in active drainage, air leak continued. After discussing the patient's case, it was decided to refer him to surgical thoracoscopy and thoracic surgery for biopsy of the pleural nodules. Posterior lateral right minithoracotomy was conducted, with the introduction of video-assisted thoracoscopy, in which nodular lesions of the pleura and lungs were observed. Biopsy of the pleural nodules revealed morphological characteristics consistent with malignant large cell carcinoma, with abundant eosinophilic

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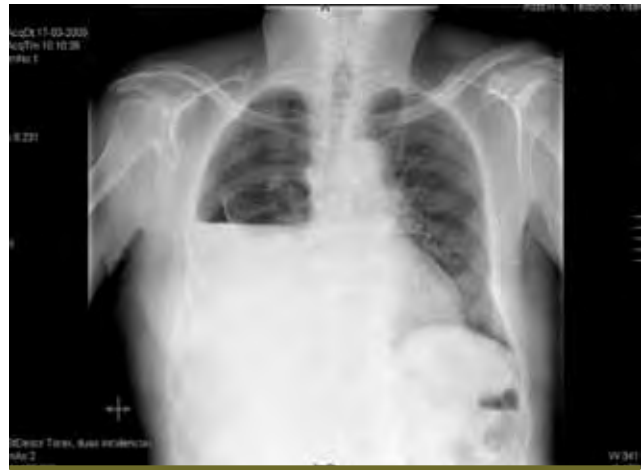
TABLE I

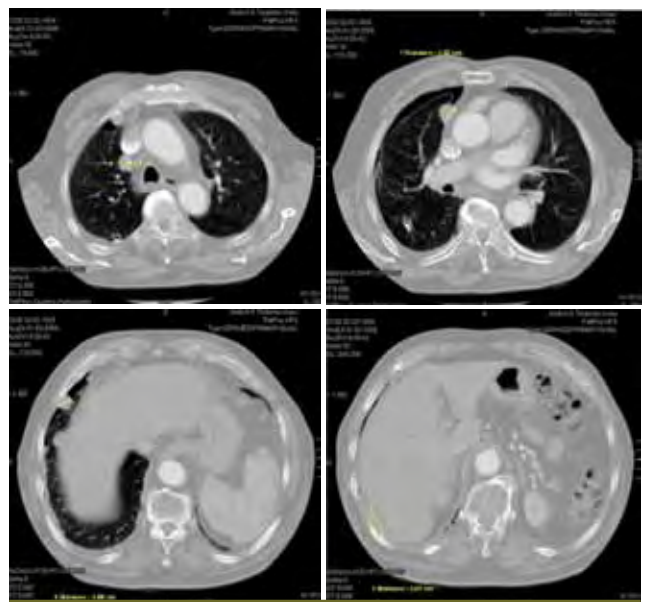
No relevant changes were observed in the analysis on admission

Leukocytes	10.7 x10^9 /L
Neutrophils	47,4 %
Lymphocytes	44,4 %
Monocytes	6,7 %
Eosinophils	1,1 %
Basophiles	0,4 %
Erythrocytes	3,88 x10^{12} /L
Hemoglobin	11,5 g/dL
Hematocrit	34,7 %
Mean Corpuscular Volume	89,2 fL
Mean Corpuscular Hemoglobin	29,7 pg
Prothrombin Time	12,4 seconds
Prothrombinemia	92 %
INR	1,05
Sodium	140 mmol/L
Potassium	4,8 mmol/L
Chlorine	102 mmol/L
Glucose	118 mg/dL
Urea	38 mg/dL
Creatinine	1,0 mg/dL
GGT	29,0 UI/L
GPT	35 UI/L
GOT	25 UI/L
LDH	251 UI/L
Ultra-sensitive C-Reactive Protein	4,65 mg/dL



Chest x-ray revealing a massive posteroanterior hydropneumothorax on the right.

FIG. 1



CT-scan of the chest revealed multiple pleural nodules on the right, the largest of which was 2.8 cm at its widest point.

FIG. 2

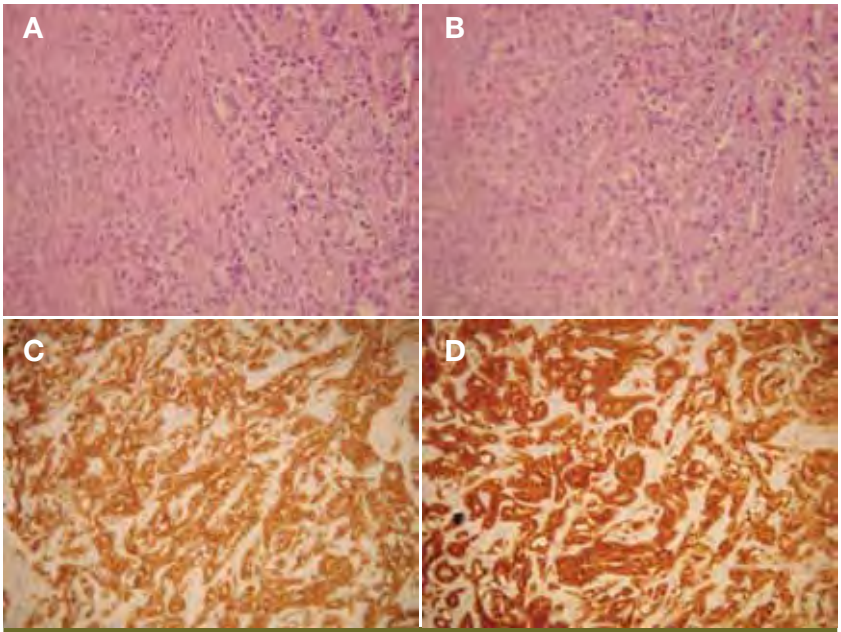
cytoplasm and vesicular nuclei with prominent nucleoli. Immunohistochemistry revealed intense and diffuse positivity for cytokeratin 7 and calretinin and negativity for cytokeratin 20, TTF-1 and lymphocyte markers *(Fig. 3)*.

Thus, the tumor morphology, analyzed in relation to the immunohistochemistry, resulted in a diagnosis of malignant pleural mesothelioma of epithelioid type.

The patient initiated chemotherapy with cisplatin and pemetrexed; so far, two cycles have been completed. The patient is now in follow-up by the Pulmonology and Oncology clinics and to date is in reasonable condition with no significant complaints.

DISCUSSION

Pleural mesothelioma is a rare neoplasm of insidious onset, which originates in the mesothelial surfaces of



Histological images. A - Morphological examination consistent with malignant large cell carcinoma, with abundant eosinophilic cytoplasm and vesicular nuclei with evident nucleoli. Hematoxylin & Eosin. 200x enlargement. B – Greater enlargement showing in detail the cells with eosinophilic cytoplasm, large nuclei and evident nucleoli. Hematoxylin & Eosin. 400x enlargement. C - Staining with cytokeratin 7, which positively marks the cytoplasm of the neoplastic cells. 200x enlargement. D - Staining with calretinin, which positively marks the cytoplasm and nucleus of the neoplastic cells. 200x enlargement.

FIG. 3

the pleura, peritoneum, tunica vaginalis or pericardium. Around 80% of all cases are of pleural origin and, in around 70% of cases, there is well-documented history of exposure to asbestos.

The incidence of pleural mesothelioma has increased by approximately 50% in the last decade[1,2] and is expected to continue rising until around 2015. Thereafter, it is forecast that the incidence of the disease will decrease as a result of the current legislation, which dramatically reduces exposure to asbestos by the population.[1,3]

Asbestos is the generic trade name for a group of minerals of the silicate group, which can be found in natural rock formations.[1,3] It is a material of great interest for industry, due to its physical-chemical properties of high heat resistance, and it has been widely used for thousands of years.[4]

Workers who are exposed to asbestos fibers on a daily basis have around a 50% higher chance of dying from a neoplastic disease (i.e. lung or pleural cancer) than other citizens, for whom the risk is 18%. There is a latency period of approximately 30 to 40 years between exposure to asbestos and the onset of pleural mesothelioma.[5] There seems to be a direct relationship between the intensity and duration of environmental exposure, and the development of the disease.[5] Also, there is an inverse relationship between heavier exposure and the latency period before the onset of the disease.[6]

Although less evident than for lung mesothelioma, environmental exposure to asbestos also appears to be responsible for a significant number of cases of peritoneal mesothelioma.[7]

Other possible causes for the onset of pleural mesothelioma are supradiaphragmatic radiotherapy[8,9] and viral oncogenes, namely, the virus SV-40 polyoma, which has oncogenic potential, due to the probable inactivation of the tumor suppressing genes[10,11,12]

Pleural mesotheliomas most commonly occur in the fifth to seventh decades of life. Usually, there is a history of dyspnea and nonpleuritic chest pain. In rarer cases, the patient is asymptomatic, and the diagnosis is only suspected after a unilateral pleural effusion is observed in the chest x-ray.[13,14] On objective examination, besides the elimination of vesicular sounds in the stroke area, it is common to find unilateral solidness on percussion, palpable masses in the chest wall, and scoliosis towards the side with the neoplasm.[13,14,15]

In the differential diagnosis, chronic inflammatory reactions should be considered, such as organized chronic empyema; metastatic pleural involvement of primary tumors in the lung, breast, stomach, kidney, ovary or prostate; fibrosarcoma, or malignant fibrous histiocytoma.[13]

A definitive diagnosis can occasionally be made through thoracentesis or pleural biopsy, but these often do not allow a sufficient sampling of tissue to enable a precise histological distinction between lung adenocarcinomas and mesotheliomas.[16] The complementary exam that provides better results for an accurate diagnosis is video-assisted thoracoscopic surgery (VATS), which has a diagnostic accuracy of

98%, compared with 26% and 39% for thoracentesis and pleural biopsy, respectively, as demonstrated in a 17-year retrospective trial involving 188 patients with mesothelioma.[17]

A flexible bronchofibroscopy is of little interest in cases of mesothelioma, as endobronchial lesions are rare in this entity. In certain cases, it might be interesting to differentiate mesothelioma from pulmonary adenocarcinoma.

The stages of a mesothelioma are identified through imaging and/or surgery. CT scan of the chest is very useful in detecting invasion of the chest wall, ribs and mediastinal structures;[18,19] magnetic resonance imaging presents no clear advantage over CT scan.[18]

In the direct morphologic examination, mesotheliomas are solid, gray tumors growing from a pleural (visceral or parietal) surface, forming nodules or plaques. Adjacent structures are involved in the early stages of the disease and hematogenous metastasis is more frequent, particularly in the liver, lung, bones and adrenal glands.[20]

Histologically, there are three distinct types of mesothelioma: epithelioid, sarcomatoid and biphasic.[20] The epithelioid type comprises around 50-60% of all mesotheliomas and has a more favorable prognosis. Sarcomatoid mesotheliomas can mimic malignant mesenchymal tumors, such as fibrosarcomas or leiomyosarcomas, having a more difficult prognosis. The biphasic or mixed type has characteristics of both of the above.[20]

Although there is no marker that in isolation, has sufficient sensitivity and specificity to diagnose a mesothelioma, immunohistochemical studies are useful for differentiating epithelioid mesotheliomas from primary lung neoplasms.[21,22] *Table II* summarizes some of the main immunohistochemical markers used in the differential diagnosis of mesotheliomas with lung adenocarcinomas.

In terms of clinical outcome, pleural mesotheliomas generally have a very poor prognosis. The average survival time ranges from 4 to 13 months for untreated patients,[23] and 6 to 18 months for patients undergoing any type of therapy.[24,25] There are several factors which are predictive of a poorer prognoses on admission; the presence of thrombocytosis, leukocytosis, anemia, fever, age over 65 years, male, and the presence of sarcomatoid or mixed mesothelioma.[26] The morbidity and ultimately, the mortality of mesothelioma patients are a consequence of the slow but inexorable local invasion of these tumors. Patients typically report dyspnea and chest pain as the tumor proliferates and the pleural space becomes obliterated. There is gradual lung encapsulation with shunt effect, which leads to fatigue, exertional dyspnea and chronic hypoxemia, often refractory to therapy with supplemental oxygen.[1]

Meanwhile, the intrathoracic growth and invasion often lead to compression of neighboring structures, and may result in dysphagia, hoarseness, Horner's syndrome, superior vena cava syndrome or compression of the brachial plexus.[1,2]

TABLE II

Main immunohistochemical markers used in the differential diagnosis of malignant pleural mesothelioma with pulmonary adenocarcinoma

Marker	Pulmonary adenocarcinoma (n=50)	Pleural Mesothelioma (n=60)
	Percentage positivity	Percentage positivity
Calretinin	8	100
Cytokeratin 5/6	2	100
WT1	0	93
Thrombomodulin	14	77
Mesotelin	38	100
TTF-1	74	0
CEA	88	0
Ber-EP4	100	18
B72.3	84	0
Leu-M1	72	0
EMA	100	93
Vimentin	38	55

key: WT1: Wilm's tumor 1 gene product; TTF-1: thyroid transcription factor 1; EMA: epithelial membrane antigen.

Table adapted from Ordonez, NG. The Immunohistochemical Diagnosis of Mesothelioma: A Comparative Study of Epithelioid Mesothelioma and Lung Adenocarcinoma. Am J Surg Pathol 2003; 27(8):1031-1051.

CONCLUSION

We present a clinical case of a rare neoplasm with unusual presentation in the patient in question, in

the form of hydropneumothorax. Only three cases of mesotheliomas with these initial characteristics have been described in current medical literature in English,[27] so doctors should be aware, and include malignant pleural mesothelioma in the differential diagnosis of hydropneumothorax. ■

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