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Squamous cell carcinoma as a primary pleural tumor – case report

Katarzyna Szklener[1,A-E], Agnieszka Kopystecka[2,A-F], Patrycja Hatala[2,A-D], Martyna Gruba[2,A-D], Mateusz Glaza[2,A-D], Sławomir Mańdziuk[1, E-F]

[1]Department of Clinical Oncology and Chemotherapy, Medical University, Lublin, Poland
[2]Faculty of Medicine, Student Research Group at the Department of Clinical Oncology and Chemotherapy, Medical University, Lublin, Poland

A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of the article

Abstract

The differential diagnosis of primary pleural tumors is a very difficult challenge. The clinical symptoms are insufficient to make a clear and definitive diagnosis. This report presents the case of a 63-year-old male patient who was admitted to Department of Pulmonology due to evidence of increasing respiratory failure due to COVID-19 infection. The X-ray showed massive infiltrate on the left pleural cavity. A bronchofiberoscopy was performed with material removal for histopathological examination. No tumor cells were found in the first pathomorphology report. A videothoracoscopy was performed, in which excerpts from the wall and pleura of the lungs were taken. Pathomorphologic findings excluded mesotheliomas and adenocarcinomas, and after additional reactions a low-differentiated squamous cell carcinoma with adenomatoid differentiation features. The final diagnosis was squamous cell carcinoma. This case highlights that the diagnosis of tumors of the pleura requires cooperation between pathomorphologists and clinicians. Further studies are needed to associate COVID-19 infection with the occurrence of rare pleural tumours.

MeSH Keywords: Neoplasms, Pleural, Carcinoma, Squamous Cell, COVID-19

Introduction

Malignant neoplasms of the pleura are quite rare lesions. The current (2021) World Health Organization [WHO] Classification of Lung Tumours centers primarily on the identification of mesothelioma (usually with a better prognosis, if complete resection of localized tumour applicable) and its differential diagnoses, including metastates (especially from the lung carcinoma) and mesenchymal tumours. There are three main histological subtypes of the given neoplasm: epitheliod, sarcomatoid and biphasic. While the histotypes play a crucial role in the assessment of possible therapeutic options, also specific pattern (architectural), cytological and stromal features may be important, so their recognition under the 2021 classification has been increased. [1] Primary pleural tumors are rare and diffuse or localized mesothelioma is the most common type. Primary squamous cell carcinoma of the pleura (PSCCP) is extremely rare. In the absence of adequate clinical experience, early primary pleural SCC can be easily misdiagnosed as localized mesothelioma, which may lead to delayed or inappropriate treatment. [2,3] Differential diagnosis of primary pleural neoplasms may appear to be a very difficult challenge. The definitive diagnosis should be based on a histopathological examination in combination with immunohistochemical staining, which is not always conclusive. Delays in obtaining a correct diagnosis significantly postpone the commencement of oncological therapy, and thus adversely affect the patient's prognosis.

Objective

The aim of this case report was to present the diagnostic process of a patient with squamous cell carcinoma, and to highlight the challenges that occur during the diagnostic process of pleural tumors.

Materials and method

The research material for this case report was collected on the basis of the medical records of Clinical Oncology and Chemotherapy of the Medical University of Lublin, obtaining the appropriate consent from the Director of the Hospital, and following the provisions of the Polish Act on Patient Rights and Patient’s Rights Ombudsman. The case report was fully anonymised, and none of the data presented in it make it possible to identify the patient. The presentation of this case does not require the consent of the Bioethics Committee in accordance with the requirements of Polish law.

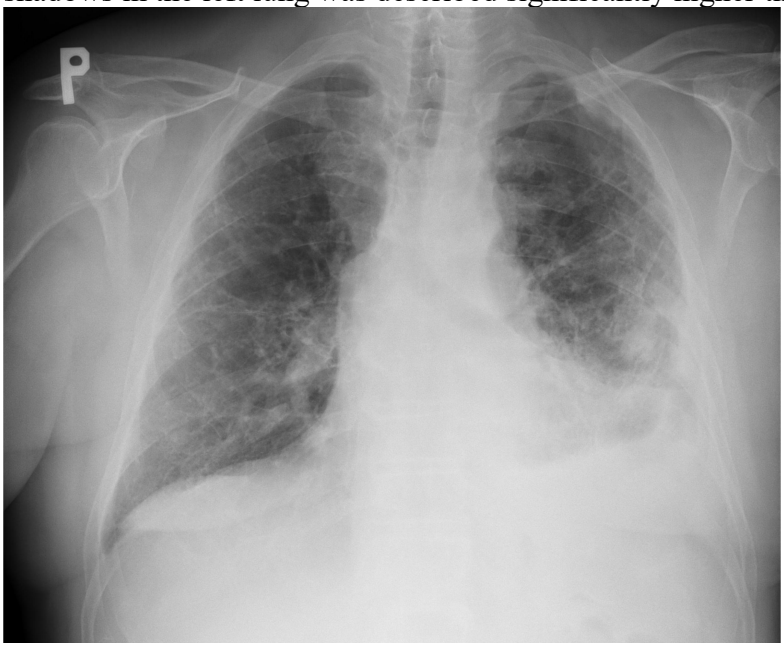
Case study

A 63-year-old male patient, a press operator by profession, with a history of long-term smoking, psoriasis, congestive heart failure, respiratory failure, hypertension and liver failure, came to the Pulmonology Department in Zamość (Poland) in November 2020 for COVID-19 treatment.

In August 2021, the patient was admitted as scheduled to the Department of Lung Diseases and Tuberculosis in Lublin (Poland) due to persistent shortness of breath due to the presence of fluid in the left pleural cavity. Bronchoscopy and EBUS needle biopsy were performed. The histopathological examination of the lymph nodes did not confirm the neoplastic process. Pleural puncture was performed and 1,800 ml of bloody fluid was obtained. The bronchoscopy performed at that time showed no abnormalities.

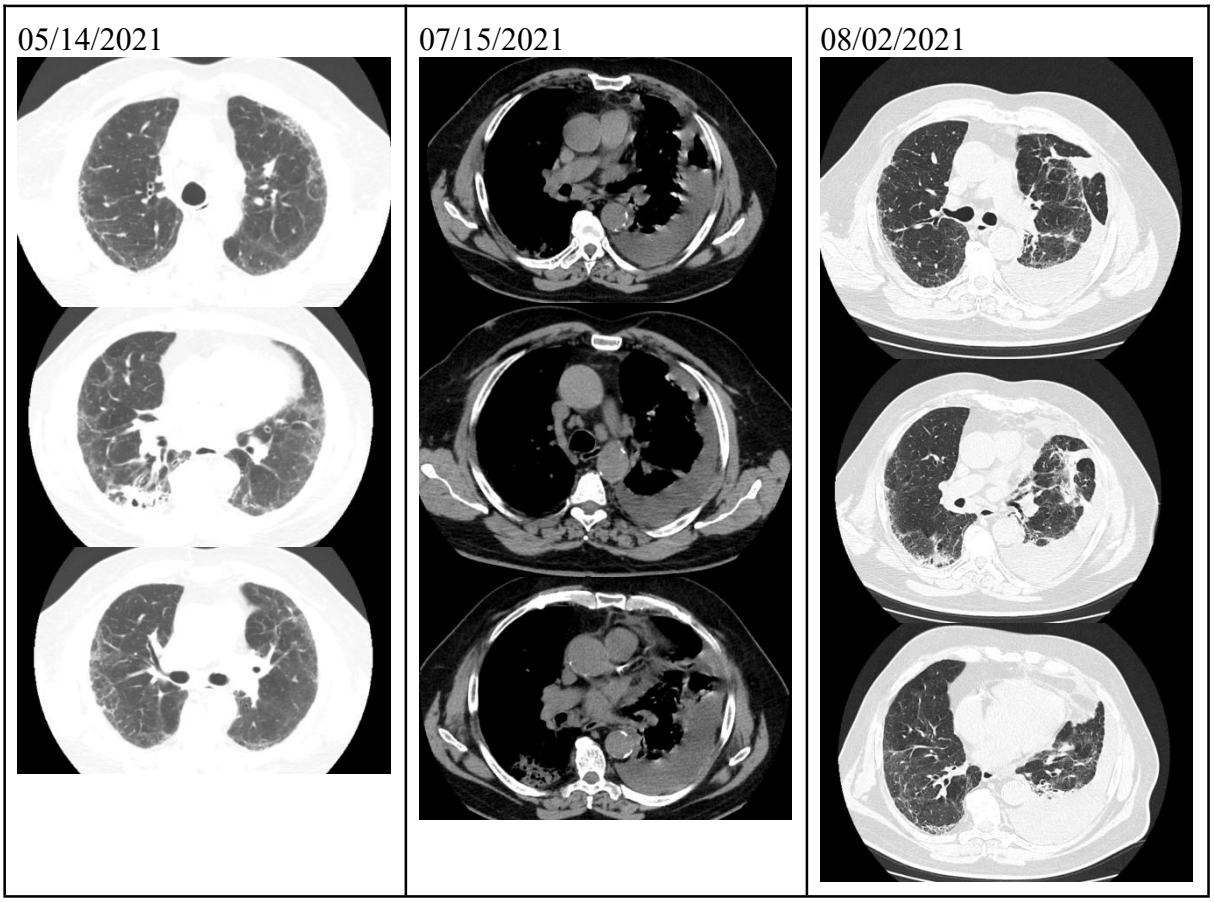
The patient was transferred to the Department of Thoracic Surgery due to persistent fluid in the left pleural cavity and exacerbation of chronic respiratory failure and an ambiguous radiological picture [pic.1] in the late August 2021, for the purpose of a possible surgery. The X-ray showed local honeycomb lesions (common in patients with a history of COVID-19) as well as heterogeneous shading imaged peripherally in the left lung, described as parenchymal and pleural lesion, possibly with the presence of fluid.

Left-sided videothoracoscopy was performed, and samples of the parietal pleura and the pulmonary pleura were taken.
On September 10, 2021, a pathomorphological examination of the parietal pleura and pleural fluid samples was performed. Based on the surgical material, a diagnosis of a non-small cell malignant tumor was rendered. The pleural lesion examination described a poorly differentiated infiltration of adenocarcinoma (BerEP4 +). The Immunohistochemical (IHC) staining for paraffine specimen were positive for Epithelial Membrane Antigen (EMA) and citokeratin 7 (Ck7), while negative for Napsin A , desmin, calretinin, Thyroid transcription factor 1 (TTF1) and citokeratin 20 (Ck20).
In the follow-up X-ray examination at the beginning of September 2021, the consolidation of shadows in the left lung was described significantly higher than in the previous one.



Pic. 1. The RTG picture, persistent fluid in the left pleural cavity.

At the end of September 2021, a computed tomography (CT) examination was performed, showing a diffuse nodular thickening of the visceral and parietal pleura of the left lung in the costal, mediastinal and posterior diaphragmatic parts, corresponding to extensive neoplastic infiltrates.
There was also a small amount of fluid in the pleural cavity leading to the formation of encysted cavities within the pleural cavity passing through the nodular thickening of the anterior pericardium. Pathological lymph nodes of the aorto-pulmonary window, subcutaneous, and also of the right and left lung hilum were demonstrated. The left adrenal gland had a nodule 10 mm in diameter (BWW 91%, WWW 63%). The CT examination also showed slight infiltrations of the left cortical layer of the VII, VIII, IX, X ribs at the site of the adjacent pleural nodules. [Pic. 2]



Pic. 2. The CT examination showed slight infiltrations of the left cortical layer of the VII, VIII, IX, X ribs at the site of the adjacent pleural nodules.

The results of positron transmission tomography (PET-CT) examination performed (2 months after CT) at the beginning of November 2021 showed an infiltration on the left side with increased fludeoxyglucose (FDG) accumulation, covering almost the entire pleura (Max. Standardized Uptake Value - SUVmax 30.5) with involvement of the chest wall structures (including the ribs with their destruction and the Th3 vertebrae), medial infiltration reaching the descending aorta, pericardium (involvement of the pericardium cannot be excluded). The abnormal tissue structures were partially confluent at the anterior chest wall on the left side (mainly in the lower part) and between the chest wall and the pericardium (SUVmax 17.9), contributing to the image of extensive neoplastic metastases. Left paraspinal lymph node abnormalities at Th1 (SUVmax 3.8), left clavicle and left subclavian (SUVmax 6.1), right pre-vascular (SUVmax 4.2), aorto-pulmonary window (SUVmax 3.2), subacute (SUVmax 10.9) and retrocrural (SUVmax 13.9) were also detected. In addition, during the examination, multiple foci of increased FDG accumulation (SUVmax 3.4) in the liver were described, suggesting the possible presence of neoplastic implants or focal lesion in the liver. Farther possible lesions were desribedsubcapsularly, at the bottom of the stomach and medially from the left kidney, both as meta lymph nodes and implants (SUVmax 4.4).
Moreover, the examination showed numerous foci of increased FDG in the muscles (SUVmax 13.6) in the multiple parts of the body, including left semispinalis capitis, left masseter, shoulder girdle, iliac girdle, paraspinal girdle muscles, proximal muscles of both arms and thighs, intercostal areas at the level of the right 5th intecostal space. However, the suspected image of the musculoskeletal system was most pronounced within the structures of left gluteal

great muscle and thoracic vertebrae, were uneven accumulation of FDG in the bone marrow was described, with foci of the highest accumulation in the vertebral bodies Th10 (SUVmax 5.7) and smaller Th6 and Th8 (metastasis cannot be excluded). Non-uniformly increased densivity with low accumulation of FDG was described in the distal body of the left femur with a metabolic dimension of 64mm (SUVmax 2.2).
In December 2021 the patient was admitted to the Department of Clinical Oncology and Chemotherapy in order to qualify for systemic treatment. On admission, the patient reported increased fatigue, dyspnoea and pain around the left side of the chest. The general examination revealed a muffled vesicular murmur above the lower lobes of left lung, edema of the lower limbs, obesity, abdominal pain on the left side, and trophic ulcers of the lower limbs. Therefore, skin and muscle biopsy was performed. The histopathological results described the fragments of the skin with the features of slight sub-epidermal elastosis as well as the fragments of subcutaneous tissue, but skeletal muscles without significant deviations from the norm. Despite the symptomatic treatment, we introduced immediately, the patient died at the end of December 2021.

Discussion

Primary squamous cell carcinomas of the pleura are extremely rare and constitute a significant diagnostic problem. Due to a lack of clinical experience, early primary pleural SCC is often misdiagnosed as localized mesothelioma, leading to delayed or inappropriate treatment. A set of tumor markers may be helpful in identifying the type of pleural tumor. The transformation-related protein 63 (P63) is always negative in mesothelioma and almost always positive in SCC [3]. Calretinin is considered to be one of the best markers of differentiation between mesothelioma and other types of thoracic neoplasms because it is highly diffuse and positive in all types of mesothelioma, and generally negative or only focally positive in other types of tumors [3]. Multiple studies have found that the fragment of cytokeratin 19 (CYFRA 21-1) is the most sensitive biomarker of SCC [3]. Although the SCC antigen (SCCA) has a lower sensitivity than CYFRA 21–1, it has a higher specificity for the SCC [3].
The available literature does not privide much more than a dozen of case reports with a similar pathomorphological features diagnosed as PSCC.
Lin XM et al. [3] in 2013 described the case of a patient who, 2 years after removal of an asymptomatic tumor, was diagnosed as pleural mesothelioma. Imaging tests led to the diagnosis of recurrent pleural mesothelioma. The CT examination showed changes indicating the presence of neoplastic infiltrates. Preoperative tumor antigen testing of this patient showed an elevated level of squamous cell carcinoma (SCCA) antigen. A thoracotomy was performed, and the diagnosis of primary pleural SCC was rendered on the surgical specimen.
In 2017 Z Chen et al. [4] described the case of a 49-year-old woman with primary squamous cell carcinoma of the pleura, in whom the results of IHC tests were positive for p63, protein 40 (p40), cytokeratin 5 (CK5), CK 6, EMA, and negative for calretinin. It should be noted that IHC results coincided with the results of the examinations of our patient. Moreover, also the PET-CT, showed an increased metabolism of FDG in the vertebral bodies, exudate and pleural lesions in both the cases.
The 2017 case report by A Ronchi [5] reports the case of a 56-year-old man in whom CT showed numerous nodular thickenings of the right visceral and parietal pleura. IHC markers were positive for P63 and P40, and negative for TTF1, and Wilms Tumor 1 (WT1) protein, which confirmed the diagnosis of primary pleural squamous cell carcinoma (also being consistent with our case). The authors pointed the possible inflammatory basis of the tumor.
In 2020 I Sigala et al. [2] described the case of a 48-year-old patient with a pleural tumor and interpleural effusion. The IHC profile was positive for p63, p40, CK5, CK5, p40 and negative

for TTF-1. Therefore the IHC tests results were consistent with the results of the case presented in our report. Patient's long history of smoking was also a common feature.
In 2021 Wang Y et al. [6] described a case of primary pleural squamous cell carcinoma (PPSCC) in a 71-year-old man. IHC staining was positive for p63, and p40, while negative for cluster differentiation protein 20 (CD20), being consistent with our case. In addition, our patient, as well as the patient described by Wang Y et al. had no history of exposure to asbestos.
The symptoms revealed in the literature review were significantly similar to symptoms of in patient. The most common PCSS manifestations reported are: chest pain, cough, dyspnoea and sputum production. Several studies dealt with the aspect of the possible influence of inflammatory factors on the development of PSCC [5]. Although the etiopathogenesis has not yet been known, previous reports have associated it with, inter alia, history of thoracosurgical treatment or chronic inflammation [2] caused by tuberculosis, bronchopleural fistula or empyema.

Conclusion:
Pleural neoplasms other than mesothelioma are very rare and constitute a significant diagnostic problem. In this case, the immunohistochemical staining, necessary for an appropriate diagnosis, ruled out the most common pleural neoplasms. In the available literature, a number of similar cases (including common pathomorphological features) are reported as eventually diagnosed as primary PSCC. In our case, the patient was hospitalized for the first time in the course of Covid-19 infection. The influence of SARS-CoV2 on the development of neoplasms has not been known so far, therefore the assessment of the influence of SARS-CoV2 infection as a cancer risk factor may require a further research.

Ethics approval
According to the "Rules of operation of the Bioethical Committee at the Medical University in Lublin" the Bioethical Committee approval is not applicable to this type of study.
Consent of participants
Not applicable.
Competing interests
The authors declare that they have no competing interests.
Data Availability Statement
Not applicable.
Funding
The research has no external founding.

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