CASE REPORT

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Pseudomesotheliomatous carcinoma of the lung

Pseudomezoteliomatozni karcinom pluća

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Abstract

Introduction. Pseudomesotheliomatous lung carcinoma is a special, rare entity characterized by large pleural growth and minor invasion of lung tissue. Clinically, radiologically, macroscopically and even histologically this tumor can be misdiagnosed as malignant pleural carcinoma. **Case report.** We represent a 64-year-old male patient, former smoker. Due to difficulties in the form of dry cough, feeling of discomfort and pain in the right hemithorax, fatigue, heavy breathing, sweating, fever up to 39.6°C the patient was treated as with combined antibiotic therapy (macrolides, cephalosporins and penicillin), but without improving of his condition. Chest radiography showed a shadow of pleural effusion by the height of the front end of the third right rib. Chest MSCT showed the extremely thickened pleura apically and to the posterior along the upper right lobe in addition to existence of massive pleural effusion. Subpleural condensation of parenchyma ranging about 30 mm was described in the upper right lobe. Cytological analysis of the pleural effusion showed the presence of malignant cells impossible to differentiate whether they were metastasis of adenocarcinoma or malignant pleural mesothelioma. By histochemical and immunohistohemical analyses of a pleural sample, pseudomesotheliomataus lung adenocarcinoma was diagnosed. **Conclusion.** Pseudomesotheliomataus carcinoma of the lungs can be a diagnostic problem. Its diagnosis is based on recognition of histopathological characteristics which enable its discernment from the epithelial variant of malignant pleural mesothelioma.

Key words:
lung neoplasms; adenocarcinoma; diagnosis; diagnosis differential; mesothelioma, malignant; prognosis; treatment outcome.

Apstrakt

Uvod. Pseudomezoteliomatozni karcinom pluća je poseban, redak entitet koji se karakteriše obimnim pleuralnim rastom i manjim zahvatanjem plućnog parenhima. Klinički, radiološki, makroskopski, pa i histološki ovaj tumor može biti pogrešno dijagnostikovan kao maligni mezoteliom pleure. **Prikaz bolesnika.** U radu je prikazan bolesnik, star 64 godine, bivši pušač. Zbog tegoba u vidu suvog kašlja, osećaja nelagodnosti i bolova u desnoj polovini grudnog koša, malaksalosti, otežanog disanja, pojačanog znojenja, povišene telesne temperature i do 39,6°C lečen je kombinovanom antibiotskom terapijom (makrolidima, cefalosporinima i penicilinom) bez poboljšanja. Na radiografiji grudnog koša uočena je senka pleuralnog izliva do visine prednjeg okrajka trećeg rebra sa desne strane. Multislajsni skener (MSCT) grudnog koša pokazao je izrazito zadebljalu pleuru apikalno i posteriorno uz gornji desni režanj, uz postojanje masivnog pleuralnog izliva. U gornjem desnom režnju opisana je subpleuralna kondenzacija parenhima promera oko 30 mm. Citološkom analizom pleuralnog izliva viđene su maligne ćelije za koje nije bilo moguće odrediti da li se radi o metastazi adenokarcinoma ili malignom mezoteliomu pleure. Histohemijskom i imunohistohemijskom analizom uzorka plućne maramice utvrđeno je postojanje pseudomezoteliomatoznog adenokarcinoma pluća. **Zaključak.** Pseudomezoteliomatozni karcinom pluća može da predstavlja dijagnostički problem. Njegova dijagnoza bazira se na prepoznavanju patohistoloških karakteristika koje omogućavaju njegovo razlikovanje od epitelne varijante malignog mezotelioma pleure.

Ključne reči:
pluća, neoplazme; adenokarcinom; dijagnoza; dijagnoza, diferencijalna; mesoteliom, maligni; prognoza; lečenje, ishod.

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Introduction

Pseudomesotheliomatous carcinoma (PMC) of the lungs is a special variant of peripheral lung cancer characterized by extensive pleural growth and minimal invasion of lung parenchyma. Clinically, radiologically and macroscopically it cannot be discerned from malignant epithelial pleural mesothelioma [1–7]. The diagnose is made with immunohistochemical staining (IHC). The term, pseudomesotheliomatous lung cancer, was first introduced by Harwood et al. [1] in 1976 showing that it was a special variant of lung cancer. The frequency of this carcinoma is not known due to limited number of case reports in the literature.

Case report

A 64-year-old male patient, former smoker, had difficulties in the form of dry cough, feeling of discomfort in the right hemithorax that had appeared one year before coming to specialist examination. Due to intensifying of difficulties along with appearing of malaise, fatigue, heavy breathing, sweating, fever up to 39.6°C, pain in the right hemithorax that lasted a month, the patient was treated as an outpatient with a combined antibiotic therapy of macrolides, cephalosporins and penicillin, but without improving of his condition.

In his personal anamnesis the patient reported diabetes and hypertension because of which he had been taking oral hypoglycemic drugs and antihypertensives.

In clinical findings upon admission he was eupneic, acyanotic, hemodinamically compensated. On auscultation, over the bottom half of the right lung there was a weakened to silent breathing sound, with a shortened percussion sound.

Laboratory analysis showed upon admission increased sedimentation of erythrocytes [98 mm/h (normal < 15 mm/h)], increased number of white blood cells (Leu), 11.49×10^9/L (normal range – NR 4–11×10^9/L), decreased number of erythrocytes (Er) 3.81×10^{12} (NR 4.5–6.5 × 10^{12}/L), hemoglobin (Hgb) 103 g/L (NR 130–180 g/L), hematocrit (Hct) 0.32 L/L (NR 0.40–0.54 L/L), glycemia 7.6 mmol/L (NR 4.1–5.9 mmol/L), urea 9.5 mmol/L (NR 2.5–7.7 mmol/L), lactate dehydrogenase (LDH) 783 U/L (NR 208–378 U/L), alkaline phosphatase (ALP) 36 U/L (NR 90–360 U/L). Other parameters of biochemical analyses and transaminases were inside the normal values. Spirogram and flow/volume curves were normal. Chest radiography showed a shadow of pleural effusion by the height of the front end of the third right rib (Figure 1). Chest multislice computed tomography (MSCT) showed the extremely thickened pleura apically and to the posterior along the upper right lobe in addition to the existence of massive pleural effusion. Subpleural condensation of parenchyma ranging about 30 mm was described in the upper right lobe. Precarinal lymph nodes were ranging up to 15 mm (Figure 2) Abdominal ultrasound examination was normal.

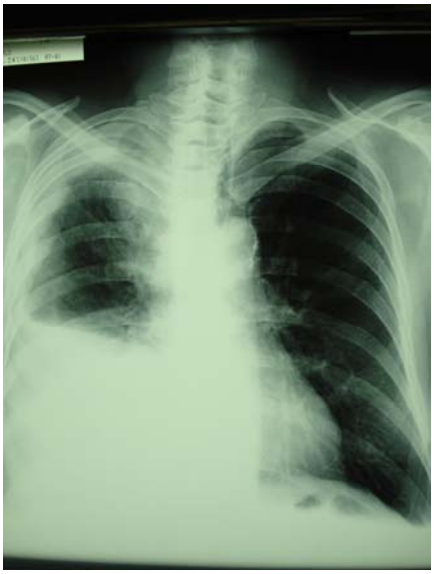
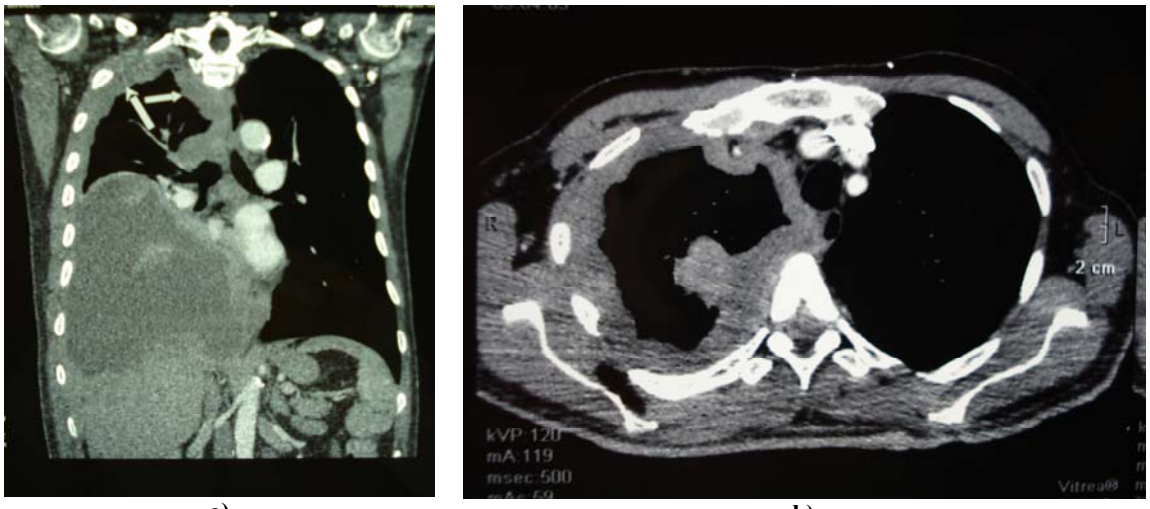


Fig. 1 – Chest X-ray showing pleural effusion shadow up to the height of the front end of the third right rib.



a) **b)**

Fig. 2 – a) Axial and b) Coronal section of computed tomography scan showing the thickened pleura apically and to the posterior along the upper right lobe in addition to the existance of massive pleural effusion. In the upper right lobe there is a subpleural condensation about 30 mm in diameter. Precarinal lymph nodes with 15 mm of size.

Bronchoscopically, hyperemia of the mucosa of the end portion of the right main bronchus was detected as well as in the apical segment of the upper lobe with mild extramural compression.

Right sided diagnostic thoracocentesis showed effusion with biochemical characteristics of exudate. Cytological analysis of the pleural effusion showed the presence of malignant cells impossible to differentiate whether they were metastasis of adenocarcinoma or malignant pleural mesothelioma (Figures 3–5).

Histopathological examination of pleural sample from blind biopsy presented the tissue made of large groups of neoplastic glands of medium size surrounded by thick cellular stroma lined in fascicular order (Figure 6).

The presence of intracellular neutral mucine and the periodic acid-Schiff (PAS+) consistence was histochemically proven within tumor cells alongside with intracytoplasmatic intensive PAS diastase (PAS-D) positivity (Figure 7).

The immunophenotype of the analyzed tumor indicated the profile of adenocarcinoma – pan CK (cytokeratin), CK 5/6, CK 7 (Figure 8), which were positive in more than 50% of the tumor cells, thyroid transcription factor (TTF) in around 30% of cells, CD 15 in around 15% of cells, with extreme positivity of carcinoembryonic antigen (CEA) (Figure 9). Calretinin reactions (Figure 10), thrombomoduline and anti-mesothelioma antibody (HBME) gave non-specific reaction in cytoplasm of few cells where pan cytokeratin antibody (panCK) was detected in the same time.

This microscopic image alongside with data of tumor localization, histochemical and immunohistochemical analysis confirmed that the tumor was pseudomesotheliomatous adenocarcinoma of the lung.

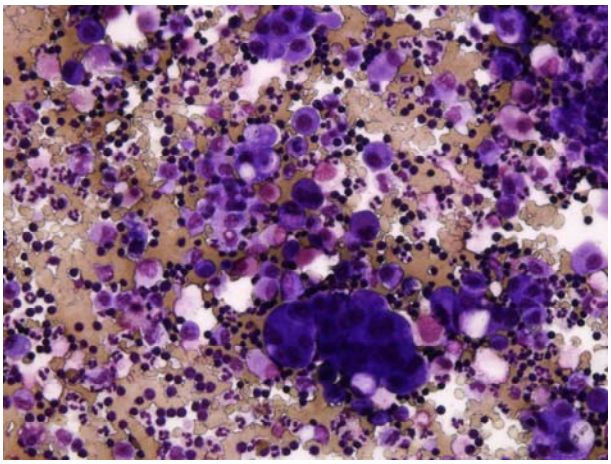


Fig. 3 – Cytospin specimen of pleural fluid showing admixture of dominating lymphocytes, neutrophils, eosinophils, macrophages, mesothelial cells, and clusters of reactive mesothelial cells in the background of erithrocytes. Clusters of cells similar to mestothelial ones by morfology are also seen, but their chromatine is coarse, with visible nucleolus, and cytoplasmic vacuoles [May-Grunwald Giemsa (GMM), ×20].

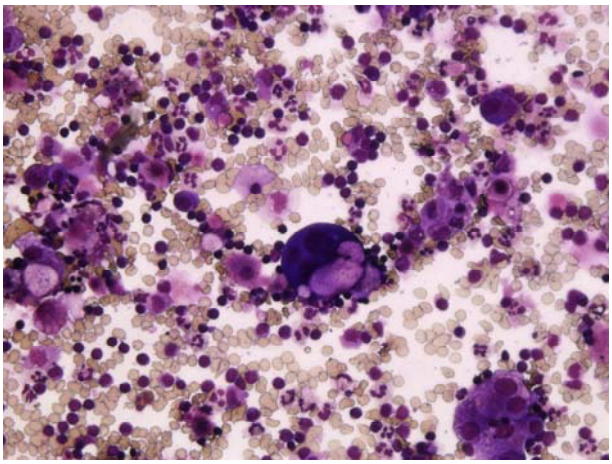


Fig. 4 – Cytospin of the same specimen of pleural fluid that emphises one of the numerous single cells that have irregular, often multiple nuclei, prominent nucleoili, and abundant cytoplasmic vacuoles [May-Grunwald Giemsa (GMM), ×20].

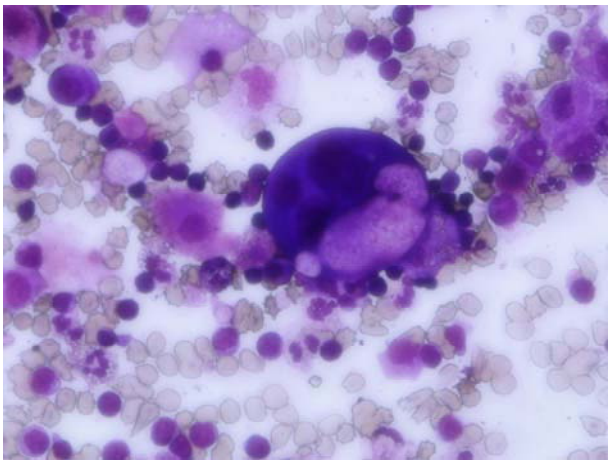


Fig. 5 – Single cell with cytomorfology of malignant cell [May-Grunwald Giemsa (GMM), ×100].

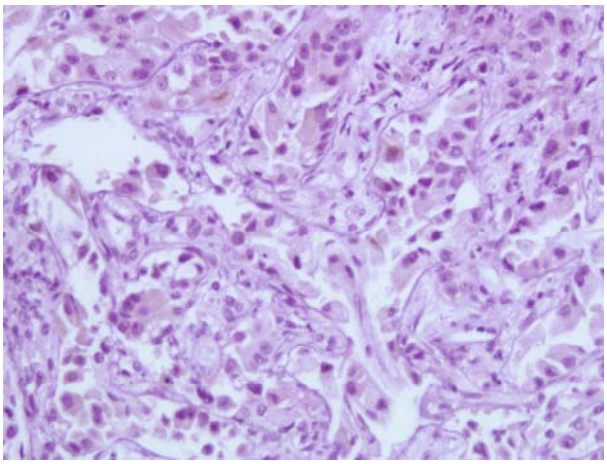


Fig. 6 – Infiltrated parietal pleura with acinar and tubular formations of epitheloid cells with abundant cytoplasm [hematoxillin and eosin (HE), ×200].

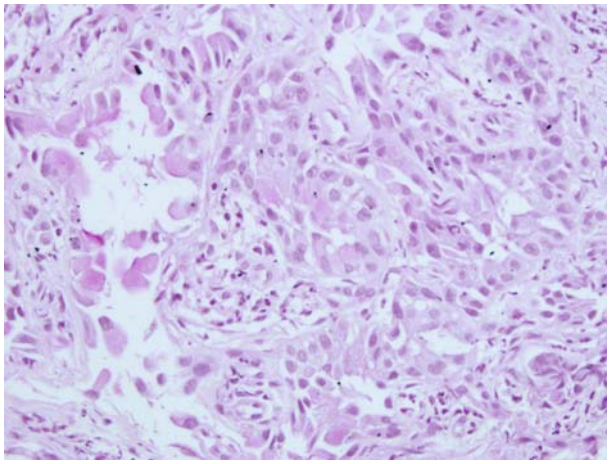


Fig. 7 – Anti-mesothelium antibody (PAS-D) resistant content in tumor cells (×200).

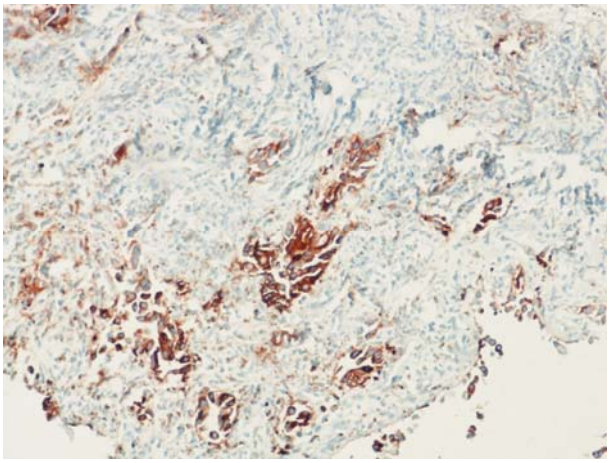


Fig. 8 – Intensive immunohistochemical reaction with carcioembrionic antigen (CEA, ×100).

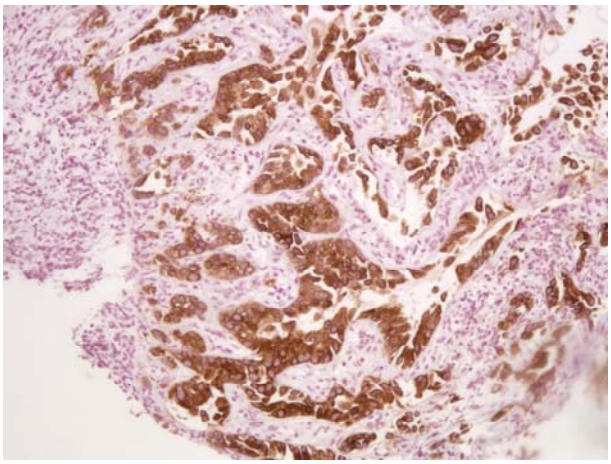


Fig. 9 – Malignant glandular forms with acinar pattern of tumor cells (cytokeratin 7 – CK7, ×100).

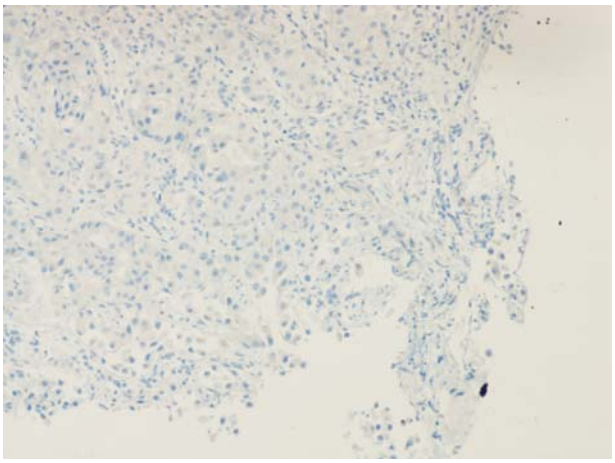


Fig. 10 – Negative immunohistochemical reaction of tumor cells (Calretinin, ×100).

According to the decision of the Oncological Consilium the treatment was thoracal drainage with pleurodesis and chemotherapy by the protocol with gemcitabine and cisplatin. After two cycles of chemotherapy by previously given protocol progression of disease was determined. Because of a poor performance status Eeastern Cooperative Oncology Group 3 (ECOG 3) the treatment was continued by application of only symptomatic therapy.

Discussion

Pseudomesotheliomatous tumors are a heterogenous group of tumors. Most often these are adenocarcinomas [8], but there are reports on pleomorph carcinomas, small-cell carcinomas, basaloid carcinomas, carcinosarcomas [8], neuroendocrine carcinoma [9], large cell carcinoma [10]. Also, there are reports on squamous carcinoma, paget carcinoma [11] and atypical carcinoid [12].

According to former knowledge, unlike mesothelioma, pseudomesotheliomatous cancer cannot be clearly connected to the exposition to asbestos or other environment carcinogens [1]. Newer researches show the connection between increased asbestos concentration in the lung tissue and the appearance of PMC [13].

The commonest histopathological diagnostic problem in pleural biopsy is the distinction between mesothelioma and adenocarcinoma, mostly pulmonary adenocarcinoma. There are different histological patterns of epitheloid mesothelioma, including acinar pattern, the commonest subtype of pulmonary adenocarcinoma.

Different histochemical and immunohistochemical methods were suggested to aid a differencial diagnosis of pleural mesothelial cancer and pleural metastasis of adenocarcinoma [1–7, 14–17].

The presence of neutral mucins, PAS-D, CEA, CK7 and thyroid transcription factor-1 (TTF-1) positive reaction with "carcinoma markers" and negative with "mesothelioma markers" (trombomodulin, calretinin, CK5/6 and HBME) lead to the diagnosis of adenocarcinoma.

Extremely positive reactions to Lu-M1 and B, 72.3, are useful in discerning pseudomesotheliomatous lung cancer and malignant mesothelioma of the pleura. Also, the results of some studies suggest that immunohistochemical demonstration of surfactant apoprotein inside tumor cells [18] invading the pleura, may be helpful to differentiate between metastasis of lung cancer and metastasis of extrapulmonary malignant tumors.

Despite similarities with type II and Clara cells, one cannot conclude that tumor derives from these cells. During the development of cancer, repressed genes can be activated, ones that regulate differentiation, which in the end leads to transformation of epithelial cells to highly specialized cells as type II and Clara cells are. Because of its significant desmoplastic reaction, the recommended approach is like to that in scar adenocarcinoma.

Despite its resemblance to invasive adenocarcinoma [World Health Organization (WHO) classification 2015] [19–21] and other peripheral lung cancers constituted of type II and Clara cells, pseudomesotheliomatous carcinoma has a distinctly different biological behaviour. Because of its extensive invasion of the pleura, patients have bad prognosis. Average period of survival is 8 months, similar to IV stadium non-small cell lung cancer (NSCLC) [8, 22] which is the consequence of tumor aggessiveness and characteristic localisation of tumor – near the rich lymphatic pleural network.

Conclusion

Pseudomesotheliomatous carcinoma of the lungs is a rare entity that can represent a diagnostic problem. The diagnosis of pseudomesotheliomatous lung cancer is based on recognition of the specific histopathological characteristics, that enable its discerning from epithelial variant of pleural malignant mesothelioma.

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