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Malignant pleural mesothelioma: a case report

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Abstract

Background. Malignant pleural mesothelioma – is a rare malignant tumor of the pleura. The most common risk factor is asbestos exposure. It is prognosed that the incidence of the mesothelioma will increase due to intensive use of asbestos in 20th century. This disease has a very poor prognosis. The average survival time after diagnosis is about 1 year. The biggest diagnostic dilemma is - the mesothelioma and benign pleural diseases have the same clinical features. However, our aim is to prove that by using radiological and histological testing it is possible differentiate these diseases and diagnose a mesothelioma earlier. The patient survival time could be prolonged.

Case report. A 74-year-old man with suspected malignancy in the right lung was sent to an oncology institute. After repeated a chest x-ray and the first computer tomography scan a possible pleural mesothelioma with metastases to the right adrenal gland was suspected. A surgeon performed a video-assisted thoracoscopic surgery for diagnostic and treatment purposes. In biopsy of the tumour, loss of BAP-1 expression was found. The pathologist diagnosed an epithelioid malignant pleural mesothelioma. The patient was treated with combination of carboplatin and pemetrexed. After 2 cycles of chemotherapy a computer tomography was repeated. Images showed partial response to the treatment, but overall prognosis was poor.

Conclusion. The patient's radiological images showed typical signs of the mesothelioma: pleural mass, pleural effusion, thickening of the pleura, involvement of intralobular fissures, ipsilateral volume loss of the lung. Recognizing these features could help differentiate malignant and benign lesions. Loss of BAP1 marker's expression is the most important indicator for a mesothelioma in histology.

Keywords: malignant, pleural, mesothelioma, diagnosis.

Introduction

Malignant pleural mesothelioma (MPM) – is a rare malignant tumour of the pleura, originating from the mesothelium (1,2). Previous use of radiotherapy, gene mutations, chronic pleural inflammations - all can cause the MPM. However, the most common risk factor is asbestos exposure. Clinical signs of a mesothelioma can occur even 50 years after previous contact (1–3). In Lithuania, asbestos have been used from 1956 until 2003 for industrial purposes. In 2001 it was officially stated that asbestos is harmful in working condition (4). According to the data on the incidence of cancer in Lithuania, in 2020 mesotheliomas accounted for 0,08% of all the cancer cases (5). Epidemiological data suggest that there is still no declining in prevalence of the mesotheliomas. In addition to this, it is prognosed that the incidence of the mesotheliomas may increase due to intensive use of asbestos in industry during the last decades of the 20th century, even in areas where there is no known cases at this time (6). It is expected that in Lithuania the incidence of the MPM will be rising as well (7).

The MPM prognosis is poor. The chance of surviving for 3 years is only 7%. There are 4 histopathological types: epithelioid, sarcomatoid, mixed and desmoplastic. Sarcomatoid type has the worst prognosis with median survival of 4 months, while epithelioid type has the best survival time of 13 months (1). If the mesothelioma is diagnosed at late stages there is no effective treatment (8). However, diagnosing mesothelioma at an early stage could help prolong survival time (2). But there are diagnostic problems: mesothelioma and benign pleural diseases have the same clinical features

(1). That is why, radiological findings can be helpful for differential diagnosis. By using computer tomography (CT), positron emission tomography (PET-CT), ultrasound (US) and magnetic resonance imaging (MRI) the radiologists could evaluate tumour features, dissemination, the treatment options. By knowing radiological features radiologists could diagnose mesotheliomas at early stages and improve outcomes of the disease (2).

In this paper we present a clinical case report of a malignant pleural mesothelioma.

Case report

A 74-year-old man was sent to the outpatient clinic for a consultation after suspicious findings in the lungs in a chest x-ray. Patient complained of weakness, shortness of breath and said that he lost about 20 kg during the last 2 years. At the time of presentation his weight was 56 kg, height 166 cm. During physical examination there were no breath sounds in the bottom of the right lung. He smoked about 20 cigarettes per day for 50 years. No family history of oncology was stated.

In the chest x-ray the radiologist found fluid in the right pleura and atelectasis in the right lung with possible metastases and infiltration. In oncology department linear and right lateral digital chest x-rays, digital tomosynthesis of the thorax were performed. There were no specific lesions seen in the lungs. In the right paracostal, diagonal and horizontal pleura the radiologist observed many focal pleural masses up to 54 mm in size. Pleural effusion was seen in the right pleura up to VI rib (as shown in Figure 1). Typical pleural lesions led the doctor to think that it might be the right

pleural mesothelioma or secondary neoplasm with metastasis in pleural cavity.

A few days later, the doctors punctured the pleural cavity. During this procedure, a hydrothorax was seen on the right, and 1150 ml of clear yellowish fluid was drained. The pathologist examined the fluid and diagnosed a high grade non-small-cell carcinoma.

In this case it was essential to use the CT. Scanned views showed pleural effusion in the right pleural cavity and focal pleural masses in intralobular pleura (as shown in Figure 2). The biggest masses were seen above the diaphragm in the right pleura (~75x56 mm and ~47x40 mm in size). In the right pleura the radiologist noticed pleural thickening, a decrease in ipsilateral lung volume. The right hilar lymph node was 8 mm in diameter. Other lymph nodes were unremarkable. Radiological images showed tumour prolaboration to intercostal muscles (XI-XII) on the right side. It was noted that the right pleural lesions do not contradict the diagnosis of the mesothelioma with possible spread to the intercostal muscles. In addition, the radiologist found metastases in the right adrenal gland (as shown in Figure 3).

After diagnostic tests the doctors had a preliminary diagnosis, but they needed to confirm it with pathological tests. So, the patient was sent for a consultation with a thoracic surgeon. He decided to perform video-assisted thoracoscopic surgery (VATS) and resect the right parietal pleura for the biopsy. During the procedure the pleural cavity was examined with the video thoracoscope: right lung was seen in sparse adhesions; small and large nodules were visible in the parietal pleura as well as fibrin plaques. Small nodules were seen in the visceral pleura, the diaphragm, the mediastinum, and the

pericardium. The surgeon found and aspirated 1600 ml of fluid from the pleural cavity. For the recurrent pleural effusion and pneumothorax treatment, chemo pleurodesis with 8 g of talc was used. There were no complications after surgery.

The biopsy was sent to the pathologists, who diagnosed an epithelioid pleural mesothelioma. The pathologist found that the BAP1 marker was lost in the tumour. Immunohistochemistry results: Calretinin+++100%, BAP1-, CK7+/+++80%, TTF1-.

After a few days, the patient went home. Final clinical diagnosis: *Mesothelioma pleurae dex. penetrans ad parietalis thoracis dex. Mts ad gl. suprarenalis dex.* (St.IV cT3NxM1). After a multidisciplinary discussion, a systemic treatment (combination of carboplatin and pemetrexed) was given. Doses were reduced by 25% because of the patients older age and comorbidities.

After 2 cycles of treatment and VATS, a repeated CT was assigned to evaluate the dynamics of the oncological process. The radiologist noted a decrease in the fluid, with a small amount of fluid remaining above the diaphragm. The pleura in the lower parts was calcified. The pleural masses decreased in size significantly, for example, the mass in the mediastinal pleura decreased from 26x19 mm to 18x11 mm. The right hilar lymph node remained the same (8 mm) (as shown in Figure 4) as well as the metastatic mass in the adrenal gland (~30x20 mm in size) (as shown in Figure 5). The radiologist concluded that in the right pleura he saw decreased lesions, a smaller hydrothorax, but the tumour in the right adrenal gland remained almost the same.



Figure 1. Linear and right lateral digital chest X-rays, digital tomosynthesis. Hydrothorax up to VI rib, many focal masses up to 54 mm seen in the pleura.

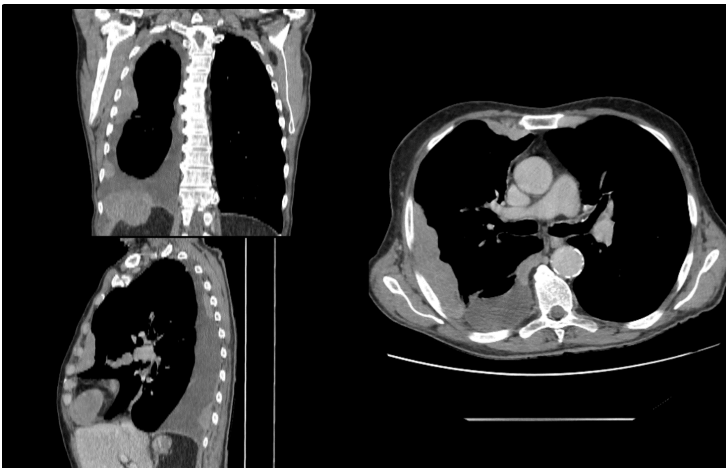


Figure 2. Coronal, sagittal and axial plains in the chest CT before VATS: pleural effusion and focal pleural masses seen in the right pleura.

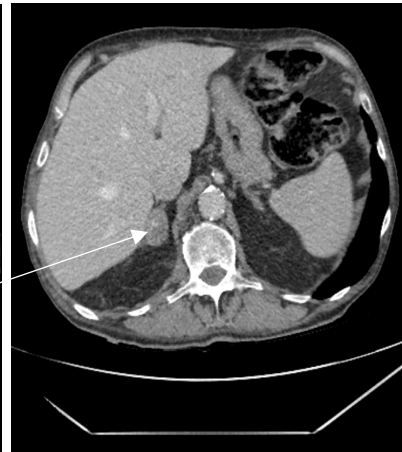


Figure 3. CT of the abdomen. The axial view shows metastases in the right adrenal gland (arrow).

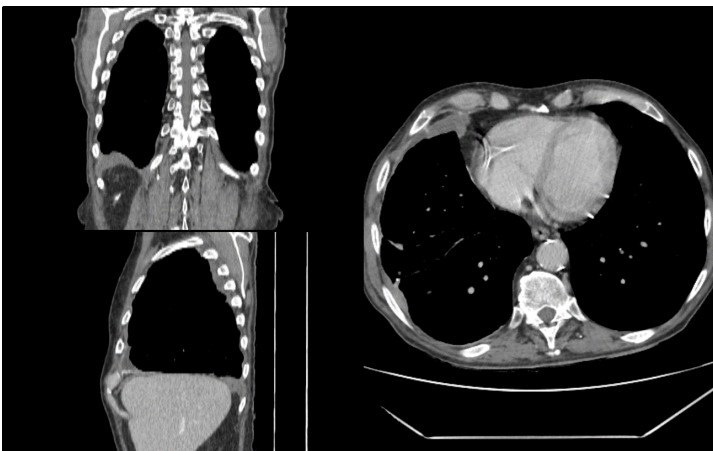


Figure 4. Coronal, sagittal and axial plains in chest CT after the treatment: decreased changes in the right pleura, good response to the treatment.

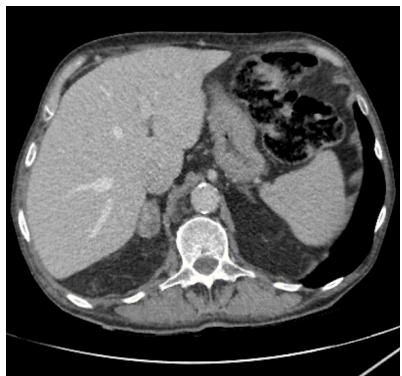


Figure 5. CT of the abdomen. The axial view shows that after the treatment, the metastasis in the right adrenal gland remained almost the same size.

Discussion

We presented the clinical case of a 74-year-old man. It is known that the mesothelioma is more common in men and is often diagnosed around at 70-84 years old (1,3). In 70% of the cases the MPM is associated with asbestos exposure (1). In our case, the patient did not recall any prior exposure to asbestos, but he worked in a factory, so it is possible that he was exposed, but he was not informed about it. As we know now, asbestos has been used in Lithuanian industry since 1956 and until 2003 (4). Moreover, the mesothelioma has a latency of 20-50 years (1,3). Knowing that, we cannot rule out possible exposure in the described case. In addition, the patient was a smoker for 50 years (~20 cigarettes per day), but, in literature, smoking is not associated with an increased risk of the MPM (9).

There are no specific clinical signs in the mesothelioma. As in our case, the patients feel weakness, shortness of breath and they lose a lot of weight. During auscultation, no audible breath sounds in one of the lungs is also a characteristic feature (3). In the presented case, breathing was inaudible in the lower part of the right lung. It is difficult to differentiate the mesothelioma from benign pleural diseases using just clinical signs. This is one of the reasons why the diagnosis of mesotheliomas is often delayed (1).

Radiological diagnostic methods can help differentiate malignant and benign pleural diseases. During prophylactic examination by using chest x-ray, fluid was observed in the right pleura. If fluid is found in the pleura, and especially if there are additional irregularities or foci, a mesothelioma should be suspected, because in the MPM pleural effusion is seen in

30-94% of the cases (1,2,10). A decrease in ipsilateral lung volume was found in the middle and lower lobes of the right lung as fluid accumulation and derivatives compressed the healthy lung tissue (10). Multiple pleural masses up to 54 mm were observed in the right pleura during digital tomosynthesis. Pleural mass is found in up to 60% of the patients with a mesothelioma (2,10). No other signs of malignancy were seen. The radiologist suspected an oncologic ailment in the right pleura, because two characteristic signs for the MPM were found. In that case, it is recommended to perform a CT scan (1,2,10).

In CT images derivatives of mesothelioma were found in the basal and interlobular pleura. This site is known as the second most common localization of the MPM. In up to 77% of the cases, lesions are found in the mediastinal pleura. Pleural lesions in these three parts of the pleura are found in 82% of the patients. Therefore, it is emphasized that a greater radiologist's attention in these areas could lead to a better sensitivity of the CT scan and an earlier diagnosis of the MPM (11). Pleural thickening in patient images is found in up to 92% of the cases. It is the most common radiological feature in the CT images (2,10). The second most common one is pleural effusion with 89% occurrence (2). Our patient had fluid accumulation in the right pleura as well. The radiologist distinguished focal pleural masses, involvement of intralobular fissures. Focal masses are usually noticed in 8-32% of MPM images, while involvement of intralobular fissures – in 73-86% (10). These factors had influence on unilateral decrease in the volume of the right lung in the patient's images. Thickening of the parietal pleura is a less

common feature (only 20% of the MPM) and in our case it was not observed. There were no radiologically significant changes described in the diameter of the lymph nodes. The biggest lymph node was the hilar (8 mm), but the dimension must be greater than 10 mm to be considered indicative (2). Changes in the interstitial structures (the heart, the oesophagus, the trachea, the blood vessels) are assessed in order to evaluate the spread of the tumour (2,10). In the given case, the tumour spread was noted in the intercostal muscles of the right side. It is difficult to accurately assess the spread to this location in CT images as the tissue attenuation is very similar between the MPM and the chest wall musculature, the diaphragm, or the pericardium. This limits the ability to diagnose the early invasion in the chest wall (2). Pleural thickness, a pathological mass in the pleura, the hydrothorax, typical localization of lesions, involvement of intralobular fissures, possible spread to the intercostal spaces – all are signs of an MPM in CT images.

A PET-CT is considered to be a more accurate method for assessing the spread of the MPM to organs and lymph nodes (1,10), it is known to be the most sensitive radiological test (2). However, it was not used in our case as well as the MRI and US. The MRI is used in order to assess the spread of the tumour to the soft tissues (1,2,10). While an US is chosen when the patient has pleural effusion (10).

The MPM is a primary neoplasm, and it usually spreads to the local areas: the pleura and the peritoneum. Distant metastases can be seen in the later stages of the disease (12), commonly in the liver, the spleen, the thyroid (13). In the presented case, metastases were found in the right adrenal gland, which is rare

(14). These findings led the doctors to think that it is a late stage MPM.

However, the diagnosis of a mesothelioma cannot be confirmed by radiological imaging alone, a pathological examination is required to make an accurate diagnosis (15). VATS is one of the best methods to take a biopsy. It has the sensitivity of 94-100% (1). During VATS the surgeon can take a biopsy, aspirate fluids, assess the spread and treatment options, as well as perform pleurodesis (16). In our clinical case, VATS was performed, parietal pleural was resected for the biopsy, 1600 ml of fluid was aspirated, the surgeon evaluated the MPM spread and found nodules in the parietal and visceral pleura, the diaphragm, the mediastinum, the pericardium. The surgeon performed a pleurodesis with talc in order to eliminate the pleural cavity between the visceral and the parietal pleura and thus prevented the recurrence of pleural effusion or spontaneous pneumothorax (17).

After VATS the biopsy tissue was sent for pathology review and immunohistochemistry of the tumour was: Calretinin+++100%, BAP1-, CK7+/+++80%, TTF1-. BAP1 marker plays an important role in the MPM diagnostic algorithm. Loss of BAP1 expression is associated with mesothelial malignancy, especially epithelioid type. It is broadly used to differentiate benign and malignant lesions, because a benign tumour does not show loss of BAP1 expression (18). Other markers did not oppose to the diagnosis of the mesothelioma. So, the pathologist diagnosed an epithelioid malignant pleural mesothelioma.

Our patient got the systemic treatment (combination of carboplatin and pemetrexed), which is commonly chosen for the patient's

survival time prolongation (8). Usually the doctors prescribe combination of cisplatin and pemetrexed, but carboplatin can be chosen because of a simpler application and a lower toxicity (3,19). In the given case, the patient was classified as inoperable, because elderly patients with advanced MPM are not surgically treated (3). In the future, the mesothelioma is expected to be treated with immunotherapy and target therapy. It is predicted that better clinical outcomes will be achieved (8).

After 2 cycles of the treatment and VATS a repeated CT was assigned to evaluate the dynamics of the oncological process. No decrease in the adrenal metastasis size was observed, but relatively significant decrease was seen in amount of pleural fluid, the pleural tumour mass decreased by more than 30%. According to the mRECIST (Modified Response Evaluation Criteria In Solid Tumours) criteria, a tumour mass reduction of more than 30% is considered as a partial response to the treatment (20). After 4 or more weeks when another treatment cycle ends, the patient should have another CT scan for a more accurate evaluation.

The patient was diagnosed with a stage IV epithelioid malignant pleural mesothelioma with metastases in the right adrenal gland. The epithelioid type of the MPM has the best prognosis with about 1 year survival time (3), but in this case the patient was diagnosed with a stage IV tumour. The projected life expectancy of that condition is 3-4,6 months (11). Additionally, a worse prognosis is also associated with the male gender and a poorer physical condition of the patient (2). Taking all of these factors into account, the patient's

prognosis is considered very poor, despite a relatively good response to chemotherapy.

In conclusion, the patient's radiological images showed the typical signs of the MPM: a pleural mass, pleural effusion, thickening of the pleura, involvement of intralobular fissures, ipsilateral volume loss of the lung. Recognizing these features could be helpful in differentiating the malignant and benign lesions. While in histology, the loss of the BAP1 marker's expression is the most important indicator of the MPM.

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