CASE REPORTS

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A rare case of primary pleural synovial sarcoma

Redak slučaj primarnog sinovijalnog sarkoma pleure

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Abstract

Introduction. Pleural synovial sarcoma (SS) is a rare type of mesenchymal tumor, that can easily be misdiagnosed. **Case report.** We presented a case of primary monophasic SS of the pleura in a middle-aged woman who initially presented with dyspnoea and a large pleural effusion. Computed tomography (CT) scans showed a large, well-demarcated right lung tumor mass. After a blind closed biopsy of the pleura, the tumor was misdiagnosed as adenocarcinoma and treated with chemotherapy but without response. The correct diagnosis was established after surgery and histological and immunohistochemical analyses. The diagnosis was fulfilled with cytogenetic analysis showing the typical translocation t (X,18). The tumor was completely extirpated during surgery. CT of the chest done four, and positron emission tomography done six months after surgery showed encapsulated reactive pleural effusion without tumor rest or relapse. In contrast, a CT scan done nine months after surgery showed an extrapulmonary soft-tissue mass in contact with the lower right lobe highly suspicious of tumor relapse. Surgery was performed, and the described mass was extirpated, but histological analysis showed no presence of malignant tissue. CT scan performed three months later showed no signs of the disease relapse. **Conclusion.** Considering that pleural SS can easily be misdiagnosed, immunohistochemical as well as cytogenetic analysis should always be performed in order to reach the proper diagnosis.

Key words:
cytogenetics; diagnosis; immunohistochemistry; pleural neoplasms; sarcoma, synovial; thoracic surgical procedures; treatment outcome.

Apstrakt

Uvod. Sinovijalni sarkom (SS) pleure je redak oblik mezenhimalnih tumora čija dijagnoza lako može biti propuštena. **Prikaz bolesnika.** Prikazali smo slučaj primarnog monofaznog SS kod sredovečne žene koji se ispoljio u vidu otežanog disanja uz veliki pleuralni izliv. Kompjuterizovanom tomografijom (KT) viđena je velika, jasno ograničena tumorska masa u desnom plućnom krilu. Slepom biopsijom pleure postavljena je pogrešna dijagnoza adenokarcinoma na osnovu čega je sprovedena hemioterapija, ali bez terapijskog odgovora. Ispravna dijagnoza postavljena je posle hirurške intervencije i histoloških i imunohistohemijskih analiza uklonjenog tumora. Dijagnoza je upotpunjena citogenetskom analizom kojom je pokazano prisustvo tipične translokacije t (X,18). Tumor je kompletno uklonjen tokom operacije. Urađeni su KT grudnog koša posle 4 meseca i pozitronska emisiona tomografija posle 6 meseci od operacije i nađen je reaktivni inkapsuliranog pleuralni izliv bez recidiva tumora. Nasuprot tome, KT grudnog koša, urađena 9 meseci posle operacije, pokazala je ekstrapulmonalnu mekotkivnu masu u kontaktu sa donjim desnim režnjem pluća koja je bila sumnjiva na recidiv tumora. Hirurškom intervencijom je uklonjena opisana masa, a histološkom analizom isključeno je postojanje malignog tumorskog tkiva. Primenom KT grudnog koša tri meseca kasnije nisu nađeni znaci recidiva bolesti. **Zaključak.** Dijagnoza pleuralnog SS lako se može propustiti, pa je, u cilju postavljanja ispravne dijagnoze, uvek potrebno sprovesti imunohistohemijske i citogenetske analize tumorskog tkiva.

Ključne reči:
citogenetika; dijagnoza; imunohistohemija; pleura, neoplazme; sarkom, sinovijalni; hirurgija, torakalna, procedure; lečenje, ishod.

Introduction

Synovial sarcoma (SS) is a rare form of mesenchymal neoplasm and represents around 10% of all soft tissue tumors [1–3]. Pulmonary SS is uncommon as well as SS of the pleura, which is more often the consequence of metastatic disease from another primary soft tissue tumor [4]. Primary SS of the pleura is infrequent and represents less than 1% of all

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primary pulmonary malignancies [1]. To the best of our knowledge, no cases of primary pleural SS in Serbia have been published so far.

Case report

A 56-year old woman presented with dyspnea which initially appeared three months earlier but at that period was insignificant, and the patient did not seek medical help. The patient had no previous chronic diseases and was never a smoker. There were no malignant diseases in her family history.

At presentation, besides dyspnea, she had absent breath sounds in the right lung field. The rest of her physical exam was unremarkable. Chest radiography revealed large right-sided pleural effusion and computed tomography (CT) of the chest also visualized a well-demarcated tumor in the posterior part of right hemithorax, 116 × 87 × 106 mm in size, more probably of pleural than of pulmonary origin, with compressive atelectasis and without mediastinal lymphadenopathy (Figure 1, A and B). Thoracentesis was performed, and 1,400 mL of serous fluid was evacuated. Cytological analysis of the fluid showed a lymphocytic type of pleural effusion and microbiological analysis demonstrated that the evacuated fluid was sterile. No malignant cells were identified. No pathological findings were revealed during bronchoscopy. The patient subsequently underwent blind closed biopsy of the pleura and histological analysis of the sample discovered non-microcellular adenocarcinoma, epidermal growth factor re-

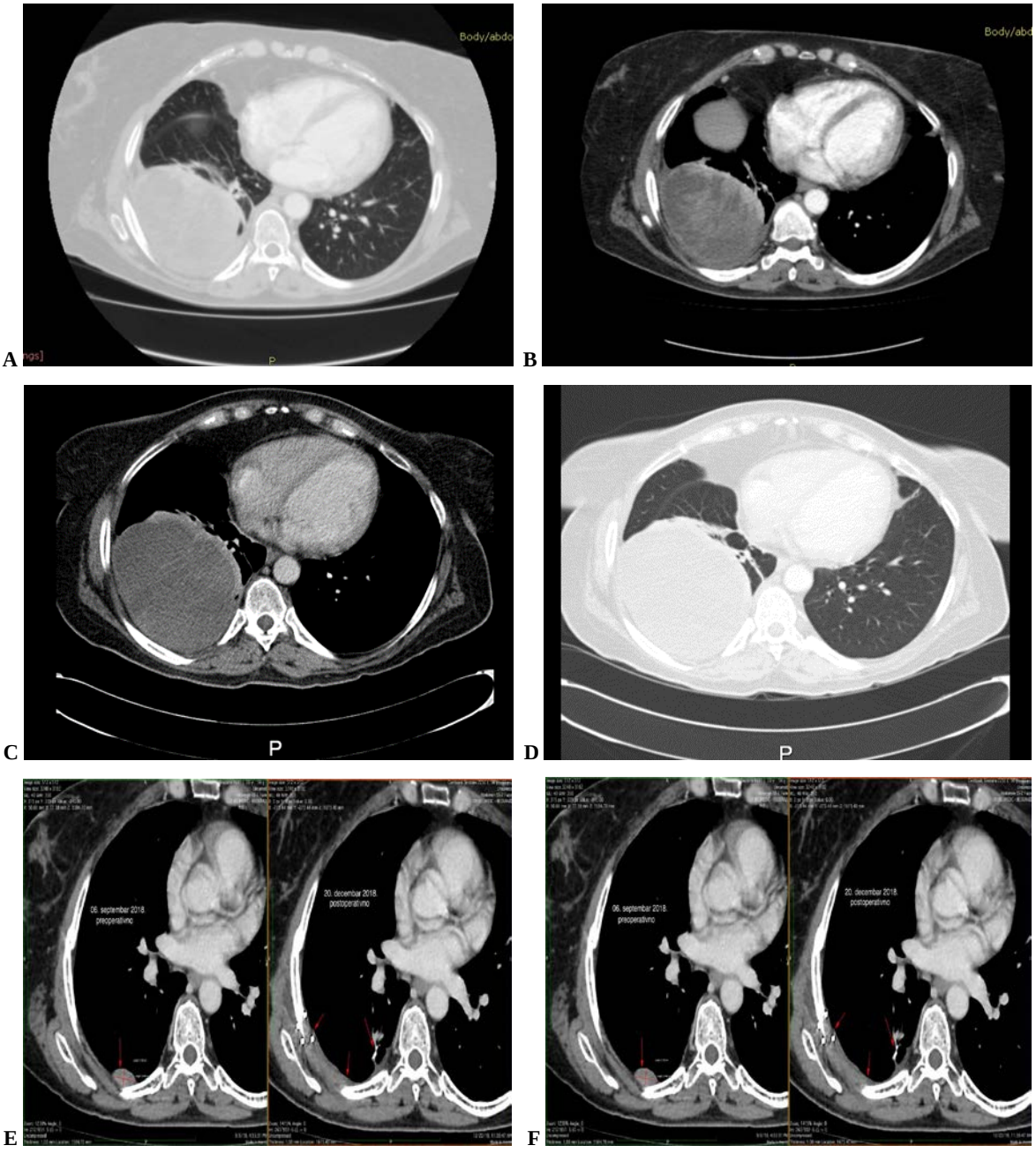

Fig. 1 – Chest computed tomography: A, B) At presentation; C, D) After initial chemotherapy; E) Nine months after first surgery; F) After second surgery.

ceptor (EGFR) wild type, anaplastic lymphoma kinase negative, programmed cell death-ligand 1 negative.

According to all of the aforementioned, the disease was considered to be in the IV stage, and three cycles of paclitaxel/carboplatin (Taxol-CBDCA) chemotherapy protocol were indicated. The CT scan, which was performed after chemotherapy, showed the progression of the disease. A non-homogenous, partially necrotic tumor in the lower right lobe, measuring 120 × 120 × 140 mm, was visualized. It infiltrated the pleura and was followed by compressive atelectasis and right pleural effusion, without mediastinal lymphadenopathy (Figure 1, C and D). The change of the chemotherapy protocol was indicated, and the patient underwent three cycles of cisplatin (Gemzar®-CDDP) protocol. The following thoracic CT scan showed no difference compared to the previous one.

After a studious reevaluation of the case, it was decided to perform a surgical intervention.

Namely, although the diagnosis was established by blind biopsy of the pleura, the minute insight of the CT scans suggested that the diagnosis might have been made by biopsying the tumor itself. This, in combination with no mediastinal lymphadenopathy, led to the conclusion that the patient is most probably in the IIIA (T4 No Mx) stage of the disease when surgery is indicated. Furthermore, since the tumor showed no response to chemotherapy, we considered the possibility of some other form of malignancy which was another reason to perform surgery.

The explorative right anterolateral thoracotomy was performed. Intraoperatively, a large tumor originating from the pleura was seen, localized posteriorly and above the diaphragm, measuring 120 × 120 × 140 mm (Figure 2). It was well-demarcated, partially solid and partially cystic, adherent to the lower right lobe, diaphragm, and posterior thoracic wall but without infiltration of these structures from which it was easily detached during resection. Tumor was completely extirpated. The postoperative course was uneventful.

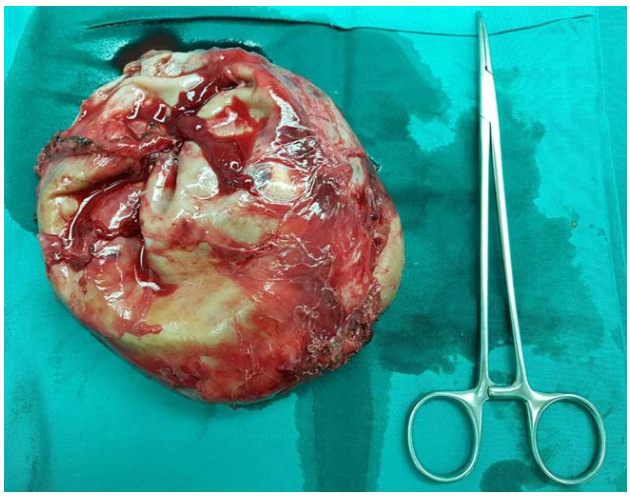

Fig. 2 – The extirpated tumor.

The histological analysis showed a poorly differentiated/undifferentiated malignant mesenchymal neoplastic proliferation sarcoma. Since in the sample obtained preoperatively during blind closed biopsy acinar structures of adenocarcinoma were seen, carcinosarcoma was considered as a potential differential diagnosis. Histology was reevaluated, and immunohistochemical analyses were performed. According to the immunohistochemical analysis [positive for vimentin, TLE-1, B cell lymphoma 2 (Bcl2) and CD99 and negative for cytokeratin 7, 8, 19, 20, epithelial membrane antigen (EMA), LCA, desmin, FLI-1, STAT 6, S100, CD 34, p53], the final diagnosis of high grade malignant mesenchymal monophasic SS of pleura was established. Genetic fluorescent *in situ* hybridization analysis identified t (X,18) translocation.

The CT scan of the chest done four months after surgery and positron emission tomography done 6 months after surgery showed reactive encapsulated pleural effusion without tumor rest or relapse. In contrast, a chest CT scan performed nine months after surgery visualized an extrapulmonary soft-tissue mass by the posterior part of the seventh right rib, which was highly suspicious of tumor relapse (Figure 1E). Thoracotomy was performed and atypical resection of the lower right lobe with the extirpation of the described mass was made. Histological analysis showed no malignant tissue but revealed the presence of well-demarcated organized pleural effusion. Therefore, there was no tumor relapse. Three months later, another CT scan was performed, and no signs of relapse were observed, meaning that one year after the first surgery, the patient was disease-free (Figure 1F).

Discussion

SS usually presents in younger people in soft tissues near large joints, but cases of primary SS localized in other atypical regions have also been reported [1]. SS of the pleura is extremely rare, and according to our knowledge, less than 40 cases have been described in the literature so far.

SS is histologically classified into four types: biphasic, monophasic fibrous, monophasic epithelial, and poorly differentiated [1]. In this report, the patient had a poorly differentiated monophasic primary SS of the pleura. Monophasic SS most often occurs in people between 33 and 69 years old, which is in accordance with the age of our patient [4].

SS of the pleura usually presents with dyspnoea, which was the case in our patient but can also present with thoracic pain, cough, and haemoptysis. Chest radiography and CT most frequently reveal pleural effusion or well-demarcated, sometimes large, soft tissue mass.

The diagnosis of SS is verified by histological and immunohistochemical analysis [1]. In order to confirm the diagnosis of primary pleural SS, primary extrathoracic localization must be excluded with CT and physical exam [1, 4].

Pleural SS can be easily misdiagnosed as malignant mesothelioma, adenocarcinoma, or carcinosarcoma [1]. In this report, the tumor was initially misdiagnosed as adenocarcinoma according to the result of histology of the sample gained by preoperative blind closed biopsy of the pleura. Misdiagnosis led to inadequate treatment and disease progression. At that point, the decision to perform surgery was made, and subsequently, the histology of the tumor taken intraoperatively enabled reaching the correct diagnosis. Having in mind the struc-

tures of adenocarcinoma seen in the preoperative sample, the initial diagnostic consideration after postoperative histological analysis, which revealed the presence of sarcoma, was that the intraoperative material was the sarcoma component of carcinosarcoma. Further immunohistochemistry used to differentiate SS from other pleural neoplasms established the diagnosis of poorly differentiated monophasic SS of the pleura. Immunohistochemically, in the majority of cases, SS are positive for cytokeratin, EMA, bcl-2, and vimentin and negative for S-100, desmin, smooth muscle actin, and vascular tumor markers [3]. The presence of bcl-2 differentiates SS from pleural mesothelioma. In the reported case, although the majority of the typical immunohistochemical findings were present, it was unusual that the tumor was EMA and cytokeratin negative. Dennison et al. [1] also reported a case of primary pulmonary SS negative for cytokeratin and EMA.

Nowadays, cytogenetic analyses are used to help confirm the diagnosis of SS. Translocation t (X,18) characteristic for SS and found in around 90% of cases was also confirmed in our patient [4, 5].

The optimal treatment regimen of SS is still not defined. It requires a multidisciplinary approach combining surgery, chemotherapy, and radiotherapy, with surgery being the treatment of choice [6, 7]. Adjuvant radiotherapy is usually advised after incomplete resection or extensive resection of large tumors [5, 6]. Neoadjuvant chemotherapy can be used preoperatively in order to reduce the size of large tumors [8]. SS are chemosensitive to ifosfamide and doxorubicin [9]. Radiotherapy, chemotherapy, and radiofrequency thermal ablation may be alternative treatment options for inoperable cases [10]. Furthermore, other options, like combined hyperthermia and chemoradiotherapy in patients with advanced inoperable primary pleural SS, have also been described [11].

Pulmonary SS is an aggressive tumor, and the prognosis of the disease is poor, with a 5-year survival rate of around 50% [1]. The main prognostic factor is the possibility for complete surgical resection [1]. Recurrences are frequent, and patients often require repeated surgical interventions. According to the literature data, the disease-free period was 2 to 14 months after surgical resection of primary pleural SS [12]. In the presented case, the tumor was completely extirpated and easily detached from the surrounding tissue, which might be of good prognostic value. One year after surgery, no recurrence of the tumor was discovered.

Conclusion

Primary pleural SS is a very rare tumor that can easily be misdiagnosed. Immunohistochemistry should always be performed as well as cytogenetic analysis whenever possible, in order to reach the proper diagnosis. Due to a small number of cases presented in the literature, there is no gold standard therapy for SS, but complete surgical resection should be performed whenever possible.

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