Case Report

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Primary Intrathoracic Biphasic Synovial Sarcoma – a Case Report*

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The authors present a rare case of a synovial sarcoma involving both pleural cavities in a 66-year old woman, confirmed by the t(X;18) translocation detected using the FISH method.

Introduction

Synovial sarcoma is a rare neoplasm of the soft tissues, most commonly involving the extremities in the vicinity of major joints. It accounts for approximately 14% of soft tissue tumors [1, 9]. It is very infrequently encountered as a primary tumor of the pleura, lungs and mediastinum; in these locations, it is more commonly a metastatic lesion. The initial reports describing primary synovial sarcomas were published in the eighties of the last century [10]. In recent articles, investigators describe larger series of patients from France and the United States [1, 8]. Cytogenetic studies, which were not available previously, suggest that numerous tumors formerly observed in this location were most likely misdiagnosed, and the incidence of these tumors situated in the chest is much higher, the thorax constituting the second after the extremities most common location of synovial sarcoma [1].

A significant diagnostic problem when synovial sarcoma is situated in the chest is posed by differential diagnosis, especially when we deal with a monophasic or poorly differentiated type, which account for the majority of cases in the investigated series [1, 8]. Recently, we have observed such a tumor, the diagnosis of which was confirmed by the t(X,18) translocation.

A Case Description

In October 2003, a 66-year old woman complained of effort dyspnea and pain at the left side, persisting for several weeks. Her past medical history indicated surgical treatment of varicose veins in the lower limbs in 1980 and a cholecystectomy due to cholelithiasis in 2001. Ultrasonography revealed a small volume of fluid in the left pleural cavity, while a chest radiogram demonstrated a solid opacity above the left phrenic dome, involving the entire inferior and a part of the central field, with the mediastinal shadow being shifted to the right (Fig. 1). Spirometry showed the following results – VC: 1.72 (70%), FEV: 1% VC 81.75 (106%), FEV1: 1.40 (71%). Bronchoscopy showed the compression of the uvular and inferior lobe bronchi, with the bronchus of the 6th segment being less affected. Histological examinations of sections from the bronchus demonstrated solely a small, non-specific inflammatory infiltration in the mucosa. Cytology of the pleural effusion fluid failed to demonstrate the presence of neoplastic cells. A left-side thoracotomy performed in the Zakopane Pulmonary Hospital showed a tumor in the pleural cavity measuring 30 × 20 × 15 cm, which was connected with the chest wall *via* a narrow vascularized pedicle; in addition, the tumor was connected to the parenchyma of the left inferior pulmonary lobe *via* a narrow band. A total tumorectomy was performed, and the postoperative course was uneventful.

The material was fixed in formalin, paraffin blocks were prepared and the resultant preparations were sent for a histological consultation to the Chair of Pathomorphology, Collegium Medicum, Jagiellonian University in Kraków.

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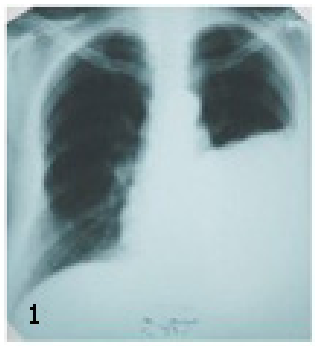
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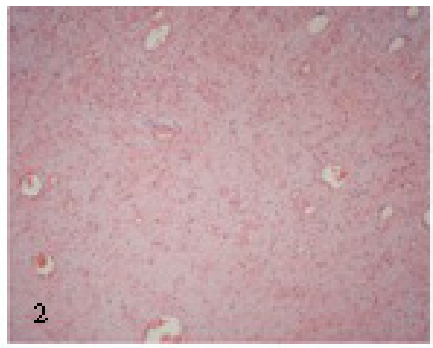
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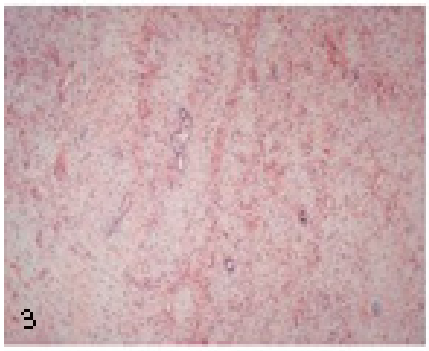
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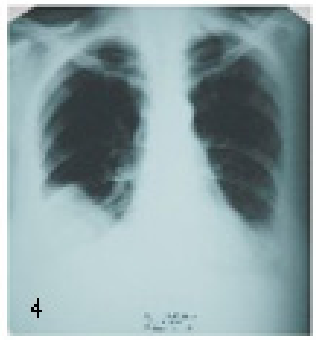
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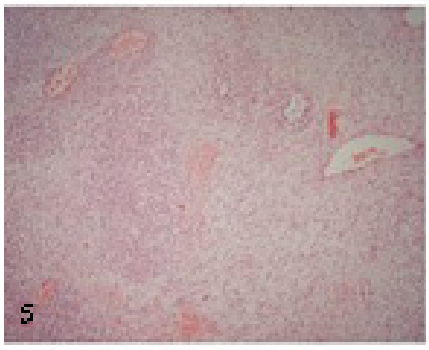
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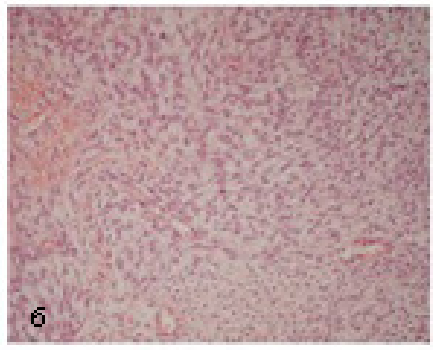
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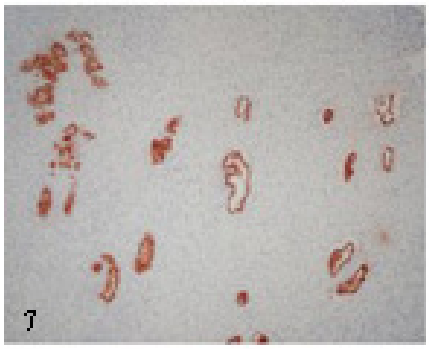
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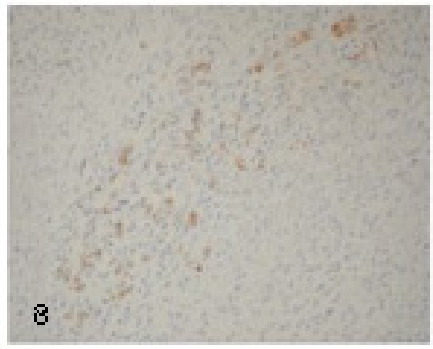
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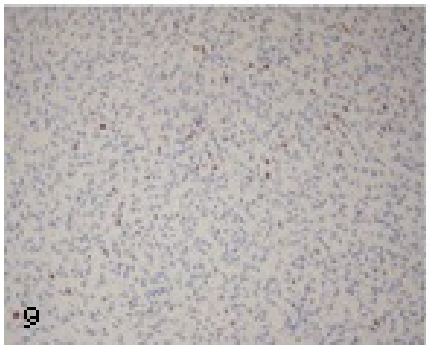
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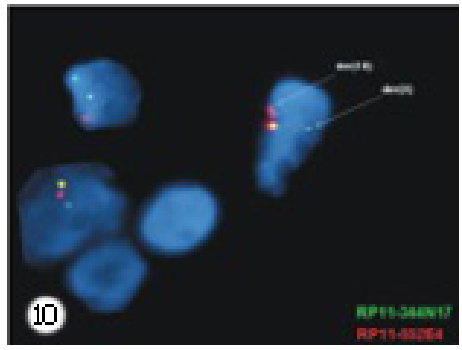
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Histological examination No. 1525717-7849/03 revealed a tumor with a solid structure, composed of mildly abundant spindle cells with elongated, uniform nuclei without mitotic figures, the cells being situated in the hyaline stroma with abundant thin-walled vessels, whose lumen was at times distended (Fig. 2). One of the numerous preparations demonstrated additionally several small cystic structures lined with a cuboid cell layer, which were interpreted as mesothelium covered fissures (Fig. 3). The tumor was encircled with the cuboid mesothelium. Fresh hemorrhages were noted within the tumor. Immunohistochemical reactions: EMA(-), CD99(-), S-100(-), bcl-2(-), desmin(-), Ki67(-). Smooth muscle actin and CD34 were present in the vascular walls. Tumor cells were strongly vimentin-positive.

The tumor was diagnosed as a pleural solitary fibrous tumor. The subsequent FISH test failed to confirm the presence of synovial translocation in the tumor cells (see below).

The patient reported for follow-up examinations every three months for one year. In December 2004, chest X-ray showed a solid tumor in the right pleural cavity, which was also seen in CT in the right pleural segment. The tumor measured 8.16 x 6.54 x 5.78 cm, was adjacent to the left phrenic segment in its central part and was characterized by marked progression (Fig. 4). Spirometric results were normal. Additionally detected lesions in the popliteal fossae might correspond to Baker's cysts. The patient was operated on again in February 2005, and the tumor was resected. HE slides and two paraffin blocks were sent for consultation to the Chair of Pathomorphology, Collegium Medicum, Jagiellonian University in Kraków (No. 1558643/225/05).

Histologically, the tumor was characterized by increased cellularity as compared to the previous lesion, as well as a higher degree of atypia and relatively numerous mitotic figures (Fig. 5). The neoplasm showed numerous small cysts, with a scattering of larger cyst-like spaces lined with cuboid cells (Fig. 6), some of the latter containing mucicarmin-positive substance (mucus). Immunohistochemical reactions demonstrated that the cells lining the cysts were strongly EMA and cytokeratin 19-positive (Fig. 7), while a strong reaction to vimentin was observed in all the spindle cells. Some cells, mostly of the spindle type, manifested a positive reaction to bcl-2 (Fig. 8). Reactions to S-100, CD99 and calretinin were negative. SMA and CD34 were positive only in the walls of fairly numerous thin-walled blood vessels. Reaction to Ki67 marked fairly numerous nuclei of tumor cells (Fig. 9). Certain similarities of the cells and structure of the tumor favored the concept that it is the same lesion that had been examined three months earlier, but which underwent malignant transformation.

Paraffin blocks from the present tumor material and from the previous lesion situated in the pleura were sent to the Chair of Biology and Genetics in Gdańsk for FISH examinations for synovial sarcoma.

FISH was carried out as described elsewhere. The following BAC clones were used as probes in the FISH experiments: RP11-552E4 (Accession No. AL683817; 47096261–47173328) and RP11-344N17 (AL606490; 47173329–47311004) as a pool for the whole cluster of the SSX1 gene. The clones belonged to the RPCI library (http://www.chori.org/bacpac/). The Ensemble database (http://www.ensembl.org/Homo sapiens/) was queried for the location of the clones. Probe RP11-552E4 was labeled with digoxygenin-dUTP, and RP11-344N17 with biotin-dUTP. The labeling of all the clones was performed by the use of the Nick translation Kit (Roche Applied Science). The hybridizations were performed on interphase cells from paraffin sections (1558643/225/05), and were analyzed using the Cytovision System (Applied Imaging, Newcastle, UK).

In the paraffin section originating from the investigated case, the split signal from the RP11-552E4 probe was found (Fig. 10). Such observation suggests the involvement of the SSX1 gene in the fusion, which is the consequence of the specific synovial sarcoma t(X;18) translocation in the second tumor [6, 7]. A specimen from the first tumor did not show this translocation.

Presently (June 2005), the patient manifests a recurrent tumor in the pleural cavity and thus is on chemotherapy.

Fig. 1. An anterior-posterior chest roentgenogram. Note a large tumor situated in the left pleura.
Fig. 2. Tumor structure composed of mildly abundant loosely scattered spindle cells. HE.
Fig. 3. Isolated fissure-like spaces layered with cuboid cells.
Fig. 4. An anterior-posterior chest roentgenogram of the patients with the recurrent lesion. The second tumor is situated in the right pleural cavity.
Fig. 5. Tumor situated in the right pleura. Note the increased cellularity and a greater number of glandular structures.
Fig. 6. Large magnification of the tumor demonstrates a high degree of cellularity, atypia and mitotic figures. Gland-like structures are also present.
Fig. 7. The EMA antigen shows a very strong reaction in the cells that for the lining of the gland-like structures.
Fig. 8. The bcl-2 antigen is present in some tumor cells.
Fig. 9. Numerous Ki67-positive tumor cell nuclei indicate an intensified tumor proliferation.
Fig. 10. The split signal from the RP11-552E4 probe suggests the involvement of the SSX1 gene in the fusion.

Discussion

Primary synovial sarcomas situated in the chest are detected in patients in all age groups, although they are more common in elderly individuals. As reported by Begueret et al. [1], the mean age at the onset of the disease is 47 years of life. A slight preponderance of males over female patients is also observed [1, 4, 8]. At times, the tumors are large, up to 20 cm, and they are usually diagnosed late.

The diagnosis of a primary synovial sarcoma in such an atypical site as the pleural cavity is very difficult, especially in the case of monophasic tumors. In differential diagnosis, one should consider mesotheliomas, peripheral nerve sheath tumors, solitary fibrous tumors, leiomyomas, fibrosarcomas, sarcomatoid carcinomas, pulmonary blastomas, or hemangiopericytomas. Histologically, similarly as in the case of other locations, synovial sarcomas situated in the chest appear as monophasic, biphasic and poorly differentiated tumors.

Differential diagnosis is aided by immunohistochemical tests, especially a positive reaction to bcl-2, a focally positive reaction to cytokeratin, EMA, vimentin and CD99 [1, 5, 8]. Suster et al. [8] emphasize a negative reaction to calretinin, but Miettinen et al. [3] noted a common occurrence of calretinin positivity in synovial sarcomas – in 52% of monophasic, 56% of poorly differentiated, and 71% of biphasic tumors. Also Begueret et al. [1] noted sporadic cases of calretinin presence in these cancers. In our case, the reaction was negative.

In doubtful cases, determinations of the t(X,18) (SYT-SSX) translocation using the FISH method is a decisive measure, since the translocation is characteristic for synovial sarcoma and is encountered in more than 90% of the tumors [1]. The translocations involve the SYT gene located on the chromosome 18, as well the SSX1 or SSX2 gene, and in rare instances – the SSX4 genes of the X chromosome [1]. The SSX2 translocation is believed to be associated mainly with monophasic synovial sarcomas. Some authors are of the opinion that the SSX2 translocation allows for longer metastases-free survival, but the issue has not been ultimately proven [1]. On the other hand, the SYT-SSX1 translocation is associated with intensified proliferation, what is manifested as an increased mitotic index and a more extensive Ki67 reaction [9]. Sections from the second tumor originating from the present patient demonstrate such a picture.

The absence of characteristic immunohistochemical reactions and translocation in *in situ* hybridization of the material originating from the first tumor sample is most likely the result of the said material being damaged in the course of fixing and processing procedures, or else it may be associated with the subsequent malignant transformation of the lesion, which was originally diagnosed as a pleural solitary fibrous tumor.

The prognosis in synovial sarcomas of the chest is poor. The mean survival in 33 patients from the group investigated by Begueret et al. [1] was 50 months, while 5-year survival was noted in 31.6% of the patients. Similar poor results are reported by other investigators [2].

References

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