胸膜原発滑膜肉腫の1例

A Case Report of Primary Pleuropulmonary Synovial Sarcoma

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ABSTRACT

A 35-year-old man was admitted to our hospital because of the abnormal opacity in the right lung. A malignant pleuropulmonary tumor was suspected and a video-assisted thoracoscopy biopsy was performed. Histologically, the tumor showed a dense proliferation of spindle cells with high mitosis. Though immunohistochemical study was performed, the diagnosis was unresolved. Because this disease was unresectable and the progression of tumor was very rapidly, we started the combined chemotherapy of cisplatin and gemcitabine. He did not respond to this treatment and died 2 months after presentation because of respiratory failure. *SYT-SSX 2* fusion gene transcript was detected by the cytogenetic analysis using RNA extracted from formalin-fixed, paraffin-embedded tissues. The final diagnosis was primary pleuropulmonary synovial sarcoma.

KEY WORDS

pleuropulmonary synovial sarcoma, SYT-SSX

INTRODUCTION

Primary pleuropulmonary synovial sarcoma is extremely rare. Synovial is characterized cytogenetically by a t(X;18)(p11.2;q11.2) translocation that results in fusion on the *SYT* gene on chromosome 18 with the *SSX 1* or *SSX 2* gene on chromosome. This distinctive chromosomal translocation is present in most of synovial sarcomas and it appears to be specific (1) (2).

We describe a case of primary pleuropulmonary synovial sarcoma of 35-year-old man diagnosed by the detection of *SYT-SSX 2* fusion gene transcript.

CASE REPORT

A 35-year-old man without smoking history was admitted to another hospital in January, 2007 because of fever, right chest pain and cough of 2 days duration. Chest X-ray showed a massive pleural effusion on the right side. He was diagnosed as pleurisy and received pleural drainage. He was also received Carbapenem and Lincomycin antibiotics. These therapies improved his symptoms and inflammatory changes. But the abnormal opacity in the right lung field extracted. He was referred to our hospital on March 2, 2007.

On physical examination, blood pressure was 104/60 mmHg, pulse 92 min^{-1}, temperature 36.8°C, respiration 14 min^{-1}. On examination of the respiratory system, there was dullness to percussion, and absent breath sounds over the right lung. The patient had a history of diabetes

mellitus and obstructive sleep apnea syndrome. No family history of cancer was reported.

Arterial blood gas analysis under room air showed pH 7.475, PaO_2 61.6 Torr, $PaCO_2$ 34.1 Torr, and HCO_3^- 24.5 mmol/l. The hemoglobin concentration was 11.3 g/dl (normal range: 13.2-17.2), lactate dehydrogenase was 300 IU/l (normal range: 119-228) and gamma-glutamyltransferase was 50 IU/l (normal range: 10-47). The results of tumor markers in the serum were normal.

Chest X-ray showed a mass in the right upper field and a hypolucent area in the right lower field (Figure 1A). Contrast-enhanced computed tomography scan revealed heterogeneous pleural based masses in the right lung (Figure 1B, 1C). We could not find the presence of abnormal shadow outside the thorax.

Video-assisted thoracoscopy was performed on March 5, 2007. The right thoracic cavity was filled up by a fragile tumor. The histological study of the tumor showed monophasic pattern with sarcomatous element. Sarcomatous area was composed of a proliferation of spindle cells arranged in sheets and fascicles with several mitotic figures (up to 10 mitoses/10 high-power fields) and areas of necrosis and bleeding (Figure 2A). The necrosis was present less than 50% of all tumor cells. On the immunohistochemical studies, tumor cells were negative for CEA, CAM5.2 (Figure 2B), keratin-wide (Figure 2C), anti-melanoma monoclonal antibody (HMB45), desmin, S-100 protein, calretinin, bcl-2, c-kit, CD34 and focally positive for alpha-smooth muscle actin (Figure 2D). Our initial diagnosis was spindle cell sarcoma of the right thoracic

cavity, such as synovial sarcoma, sarcomatoid carcinoma and pleuropulmonary blastoma. Because this disease was unresectable and the progression of tumor was very rapidly, we started the combined chemotherapy of cisplatin and gemcitabine before immunohistochemical studies of mentioned as above. He died on May 6, 2007 because of respiratory failure due to rapid progression of tumor.

At autopsy, tumor nearly filled the right thoracic cavity, and shifted the mediastinum and diaphragm to left and downward respectively. It also diffusely involved the chest wall, diaphragm and mediastinum, partially involved the right lung. The right lung was compressed and collapsed by the tumor. The left thoracic cavity and abdominal cavity were uninvolved. The tumor was solid with gray-white in color and soft in consistency. The histological study of the tumor at autopsy showed monophasic growth pattern. The tumor was focally positive for epithelial membrane antigen (EMA) (Figure 2E). *SYT-SSX 2* fusion gene transcript was detected by the cytogenetic analysis using RNA extracted from formalin-fixed, paraffin-embedded tissues. The final diagnosis was primary pleuropulmonary synovial sarcoma of monophasic fibrous type, after he had died.

DISCUSSION

Pleuropulmonary sarcomas constitute only 0.1-0.5% of all primary lung malignancies. The most

frequently reported subtypes of sarcomas in the lung are leiomyosarcoma, malignant fibrous histiocytoma, and fibrosarcoma (3). Synovial sarcoma accounts for up to 14% of all soft-tissue sarcomas (4). The most common sites of origin are the extremities. Although primary pleuropulmonary synovial sarcoma is very rare, this tumor is increasingly being reported as a result of growing awareness and diagnostic capabilities. The generally accepted histological subtypes of synovial sarcoma are (1) biphasic, (2) monophasic fibrous, (3) monophasic epithelial, (4) and poorly differentiated (5). The monophasic epithelial subtype is very rare. Previously reported cases of pleuropulmonary synovial sarcoma have identified mainly monophasic fibrous type (5) (6) (7) (8). Our case reported here showed this type. The monophasic type is difficult to diagnose, because it has a uniform spindle cell pattern and thus may be confused with other spindle cell neoplasms. The biphasic type is easily diagnosed based on the presence of both epithelial and spindle cell components.

Immunohistochemical study plays an important role in the diagnosis of pleuropulmonary synovial sarcoma. Typical pleuropulmonary synovial sarcomas show immunoreactivity for epithelial markers, such as cytokeratins and epithelial membrane antigen (EMA) (5) (8) (7). But these markers are not universally present in all cases (6) (9). In our case, tumor was negative for cytokeratins in surgically resected specimens, but focally positive for EMA in autopsy specimen.

Cytogenetic studies are helpful to confirm diagnosis. In our case, the diagnosis of pleuropulmonary synovial sarcoma was made by the observation of the translocation t(X; 18) (p11.2;q11.2) resulting in a fusion on the *SYT* gene on chromosome 18 with *SSX 2* gene on chromosome X. Both epithelial and spindle cells carry the translocation (10). The *SYT-SSX 1* fusion is present in the majority of biphasic tumors, while *SYT-SSX 1* and *SYT-SSX 2* fusions are seen with equal frequency in tumors of the monophasic subtype (11). This distinctive chromosomal translocation is present in >90% of synovial sarcomas and it appears to be specific (12) (13) (14) (15).

Factors predicting a poorer prognosis for patients with synovial sarcoma include tumor size (16) (17) (18) (19) (20), tumor histological grade (17) (19), tumor stage (17) (19) and incomplete resection. The main prognostic factor is the ability to archive a complete resection (21). Essay et al found that primary pleuropulmonary synovial sarcoma was locally more aggressive than soft tissue synovial sarcoma, and they suggested that this was in all likelihood related to the difficulties in obtaining tumor-free margins (7). Begueret et al showed that the prognosis of the intrathoracic synovial sarcomas is almost half compared with that of soft tissue synovial sarcoma (8). Hartel et al showed that 46 % of primary and mediastinal synovial sarcoma died of disease within 5 years after diagnosis, and that their prognosis was poorer than that of soft tissue synovial sarcoma of 35 % (6). The relationship between fusion type and prognosis is

controversy. While several studies of soft tissue synovial sarcoma have suggested a tendency for *SYT-SSX1* lesions to behave more aggressively than *SYT-SSX 2* tumors (22) (15) (23), more recent analysis has found no prognostic difference between fusion types (17) (18) (19).

There is no standardized therapy for patients with primary pleuropulmonary synovial sarcoma. Most patients are treated with extensive surgical resection, which occasionally was accompanied by radiation or chemotherapy. Several studies have suggested that synovial sarcoma is more chemosensitive than other soft tissue sarcoma subtypes (24) (25) (26) (27). However, the role of therapeutic (28), neo-adjuvant (29) or adjuvant (16) (29) (30) chemotherapy for synovial sarcoma has been controversial in the evidence of overall survival advantage.

In conclusion, we reported a rare case of primary pleuropulmonary synovial sarcoma, the diagnosis of which was confirmed by genetic analysis disclosing the existence of *SYT-SSX 2* fusion gene transcript.

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FIGURE LEDENDS

Figure 1A

Chest X-ray on admission to our hospital showing a mass in the right upper field and a hypolucent area in the right lower field

Figure 1B, 1C

Contrast-enhanced computed tomography scan showing heterogeneous pleural based masses in the right lung

Figure 2A

Microscopic findings showing a proliferation of spindle cells arranged in sheets and fascicles with several mitotic figures (up to 10 mitoses/10 high-power fields) and areas of necrosis and bleeding (hematoxylin and eosin x100)

Figure 2B

CAM5.2 was negative in the tumor (x400).

Figure 2C

Immunohistochemically, the tumor cells were negative for keratin-wide (x400).

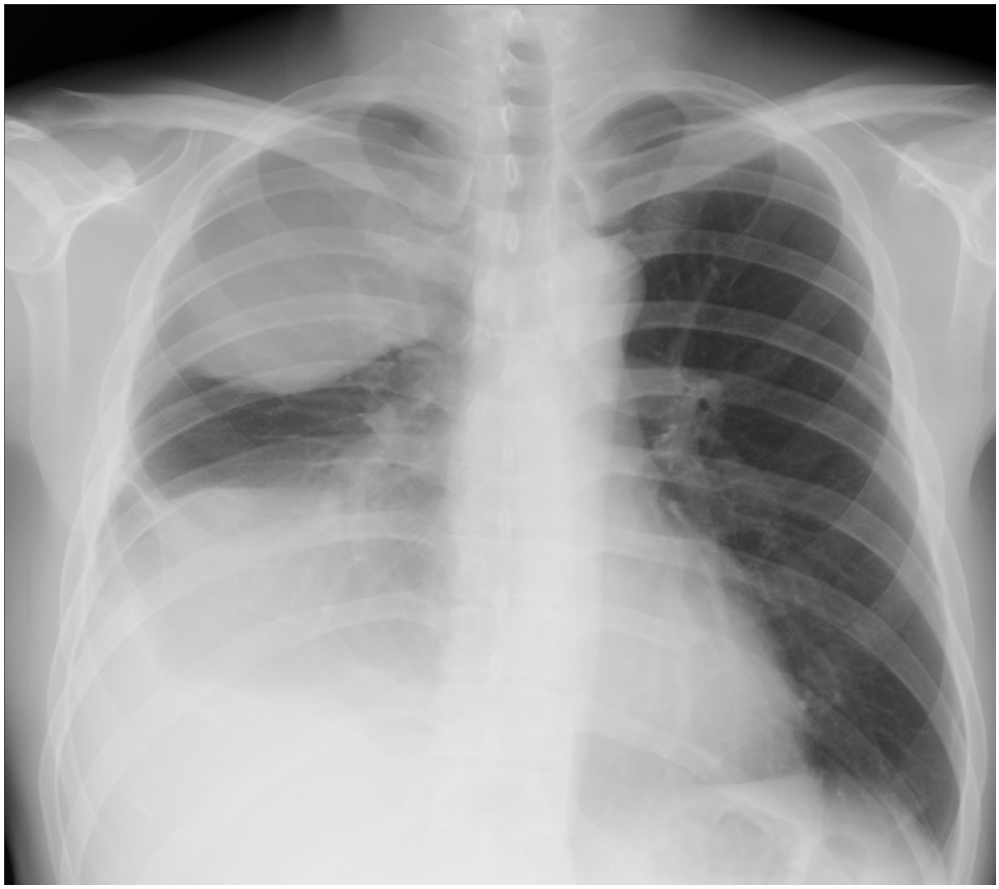
Figure 2D

Alpha-smooth muscle actin was focally positive in the tumor (x400).

Figure 2E

The tumor was focally positive for epithelial membrane antigen (EMA) (x400).

Figure 1A



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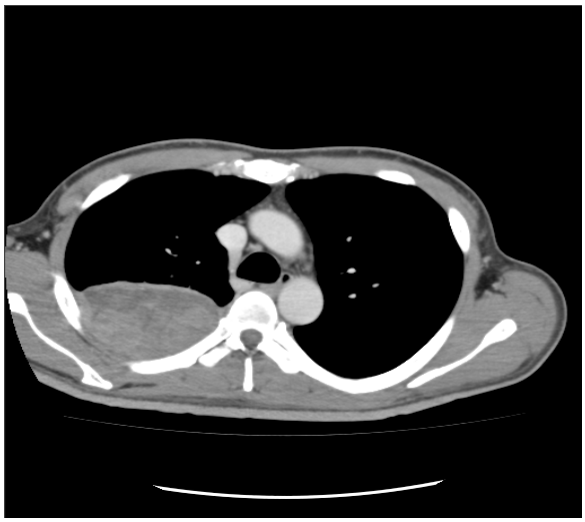


Figure 1C

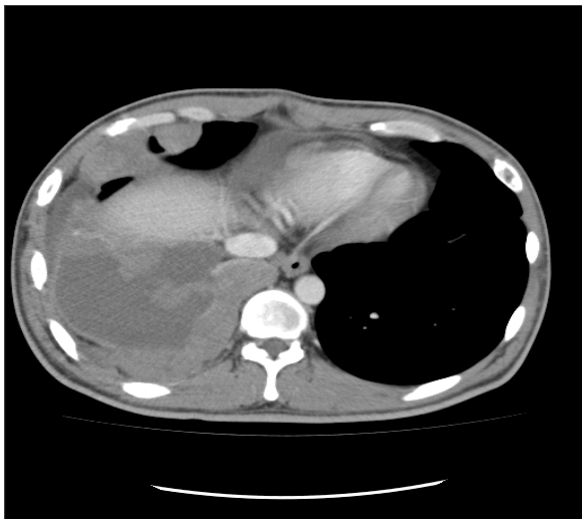
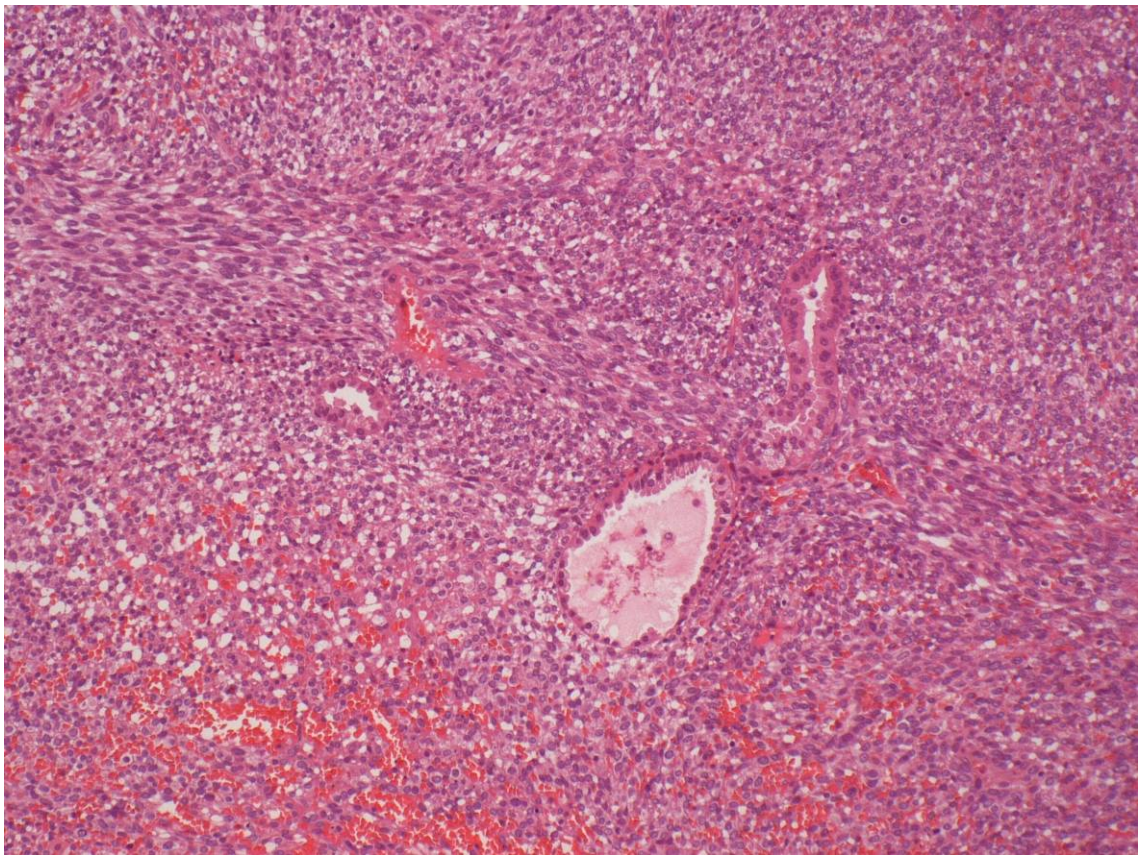


Figure 2A



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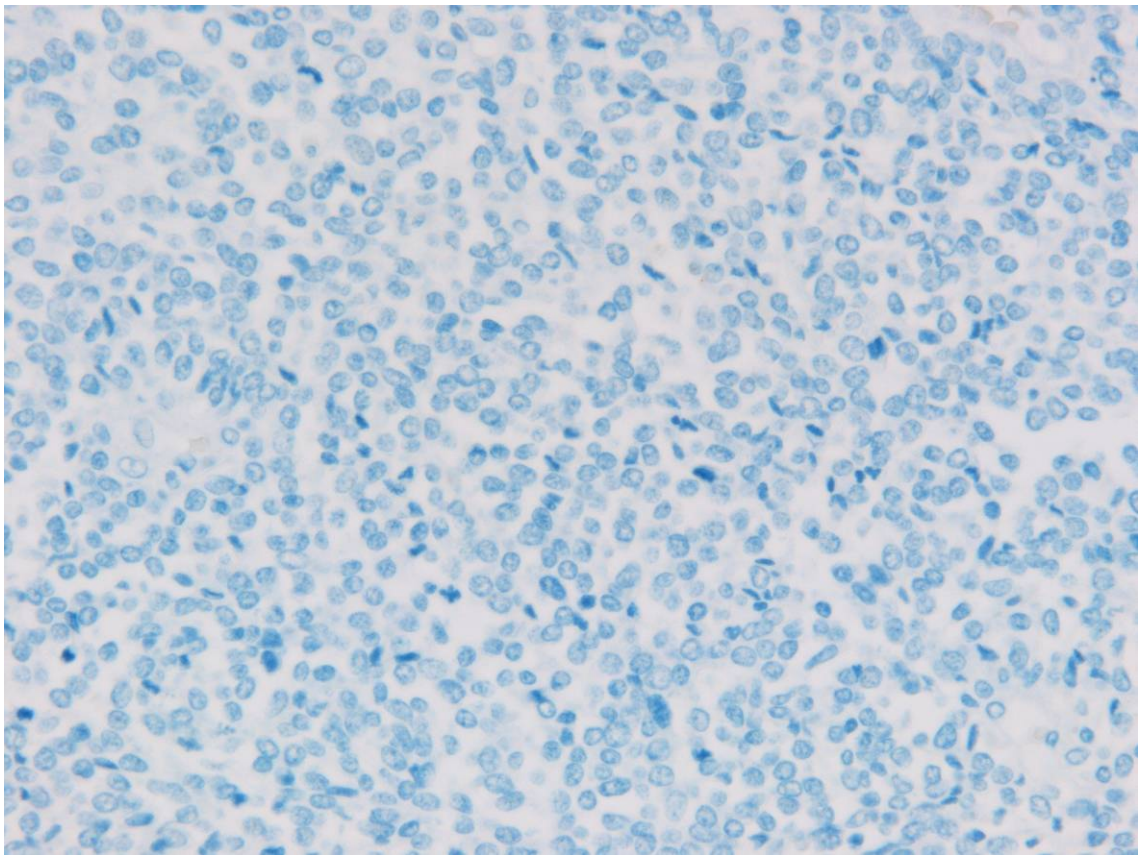

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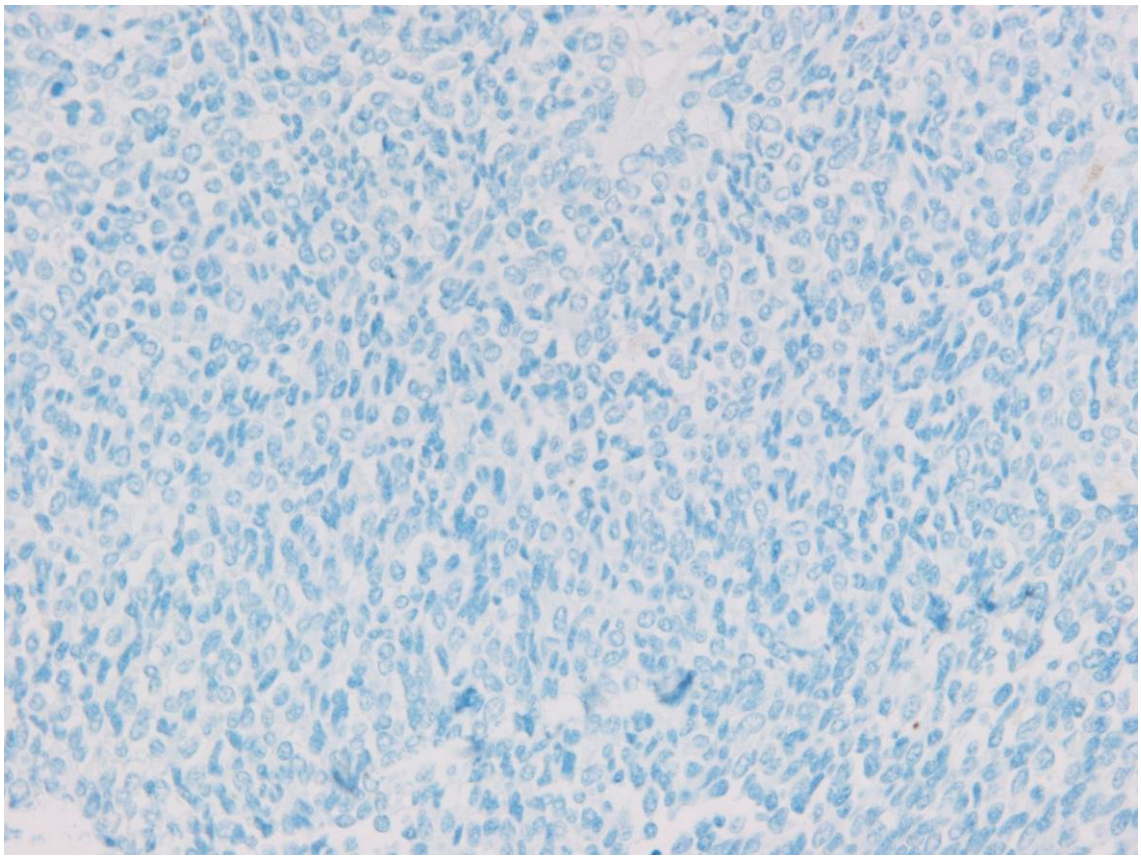

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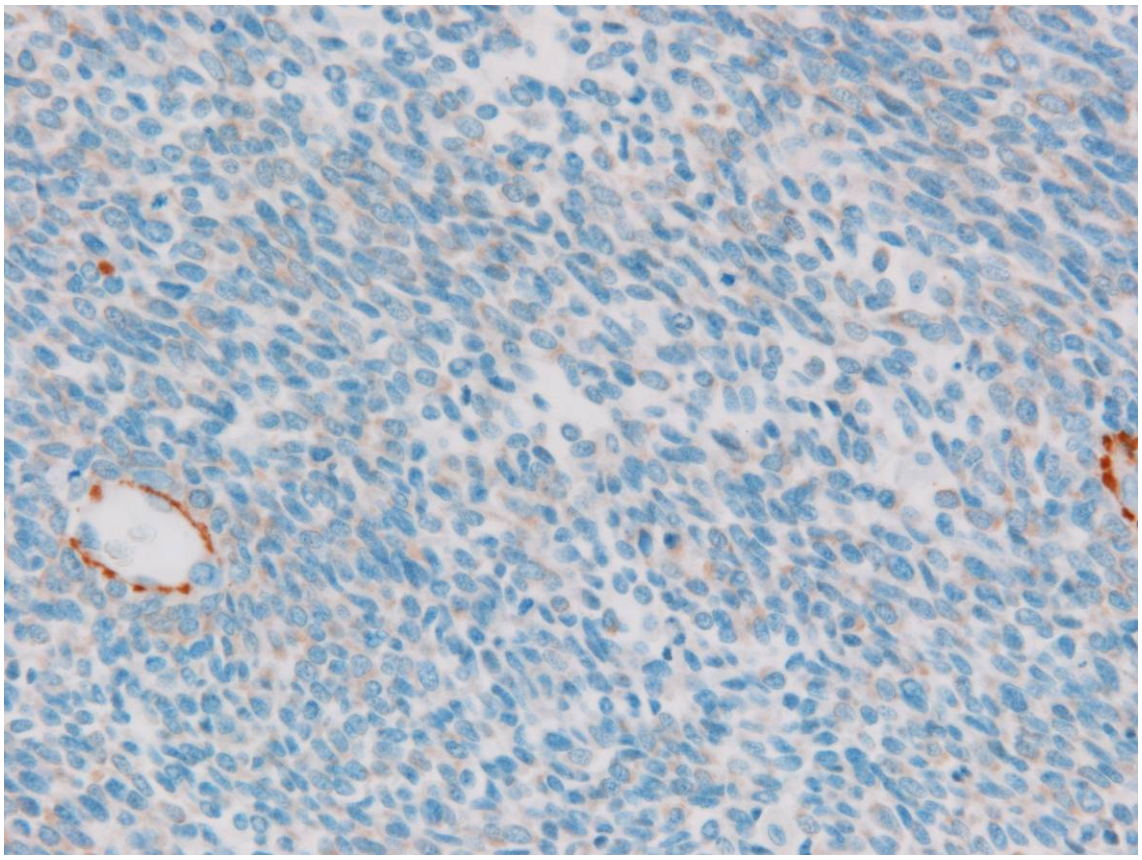

Figure 2E