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**Case Report**

# A 37-Year-Old Man with Myofibroblast Sarcoma Combined with Pleural Maculopathy: Case Report

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**Keywords**
Myofibroblastic sarcoma · Myofibroblastic tumor · Sarcoma · Pleural macula · Case report

**Abstract**
Myofibroblastic sarcoma (MS) is a malignant tumor of soft tissue or bone that can occur in children or adults, with a high rate of recurrence and metastasis. We report a case of low-grade malignant MS of the left shoulder, diagnosed based on pathological examination and immunohistochemical staining. However, the patient had unexplained pleural maculopathy. The patient passed away 6 months after the diagnosis of myofibroblast sarcoma due to multiple metastases throughout the sarcoma. Combined with the patient's history, ancillary findings, and after MDT discussion, the patient was ultimately considered to have a high probability of myofibroblast sarcoma combined with pleural maculopathy. In conclusion, when a patient is diagnosed with myofibroblast sarcoma in combination with pleural macula, in the absence of other causative factors, a deep tissue biopsy of the pleura should be actively performed to confirm the diagnosis.



## Introduction

Myofibroblastic sarcoma (MS) is a rare spindle cell sarcoma most commonly found in the head and neck, limbs, and trunk [1, 2]. However, MS is rarely combined with pleural lesions. We report a rare case of low-grade malignant myofibroblast sarcoma combined with pleural maculopathy.

Di-Wei Tu and Ting-Wei Zhang contributed equally to this work.

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## Case Presentation

On February 24, 2021, a 37-year-old male was admitted to the hospital with "chest tightness for 4 days." He had a history of "Hodgkin's lymphoma" for more than 20 years, which was cured at the time of diagnosis. He had a history of "hypothyroidism" for 6 years and had been on oral treatment with Euthyrox (50 μg bid) for a long time.

Physical examination: mild shortness of breath, low breath sounds in the left lung, and dry and wet rales in the right lung. The left shoulder mass (which had been found for 3 months), was approximately 3 cm × 3 cm in size, tough, with a dark red color around it, and the skin temperature was not high. The rest of the physical examination was unremarkable.

On February 23, 2021, chest CT was performed and showed multiple lamellar hyperdense shadows with blurred margins in both lungs, nodular foci in the right lung, and bilateral pleural effusions (Fig. 1a–c). Laboratory tests were on admission, which included the following: blood routine examination: leucocyte: 13.4 × $10^9$/L, neutrophil percentage: 83.1%; C-reactive protein (CRP): 44.3 mg/L; pro-brain natriuretic peptide: 666.9 pg/mL; blood gas analysis (arterial blood, 21% oxygen concentration): PH: 7.45, $PO_2$: 61 mm Hg, $PCO_2$: 36 mm Hg, $SO_2$: 92%, $HCO_3$−: 25 mmol/L, BE: 1.4 mmol/L; calcitonin normal; cryptococcus gonococcal polysaccharide antigen test, *G* test (fungal detection test), GM test (invasive *Aspergillus* detection test), antinuclear antibody, and anti-neutrophil cytoplasmic antibody test were all negative. Pulmonary function: severe obstructive ventilation dysfunction (FEV1/FVC: 67.4%, FEV1 predicted: 32.5%); negative bronchodilation test. Cardiac ultrasound: EF: 60%; pericardial effusion (small to moderate); aortic and mitral regurgitation (mild). Pleural ultrasound showed bilateral pleural effusion. Pleural fluid routine: orange-red color, cloudy with clots, total cell count 4,000 × $10^6$ cells/L, nucleated cells 430 × $10^6$ cells/L, monocytes 80%, multinucleated cells 20%, weakly positive for Levantine (±). Pleural fluid biochemistry: total protein of 36.5 g/L, glucose of 6.35 mmol/L, lactate dehydrogenase of 192.4 U/L. Pleural fluid culture and pleural fluid smear were negative for antacid bacilli; pleural fluid tumor markers (carcinoembryonic antigen, neuron-specific enolase) were negative; pleural fluid pathology: mesothelial cells, neutrophils, and lymphocytes were detected in the smear and sediment, and no malignant tumor cells were detected.

On February 26, 2021, a thoracoscopic pleural biopsy was performed because of the orange-red color of the pleural fluid, and yellowish tissue of varying sizes was seen in the wall pleura (Fig. 2a, b). Pathology of the left mural pleura: granulomatous hyperplasia and mesothelial hyperplasia are seen (Fig. 2c). Pathology of the mural pleura was sent to Peking Union Medical College Hospital, and the pathological diagnosis was consistent with ours. On March 5, 2021, we performed bronchoscopy, and pathology showed fibroblast proliferation with increased alveolar septa visible in the alveolar lumen and lesions consistent with organizing pneumonia (Fig. 3a). The patient had a history of Hodgkin's lymphoma, and organizing pneumonia was not considered to be associated with lymphoma after the hematology consultation.

Surgical resection was performed for the left shoulder mass and pathology showed a spindle cell tumor (Fig. 3b). Immunohistochemistry: vimentin: +, SMA foci: +; desmin: +, D68: +, Ki-67: 40% +, CK: −, Bcl-2: −, CD34: −, CD99: −, S-100: −. Combined with the pathological and immunohistochemical findings, this patient's left shoulder mass was diagnosed as a low-grade malignant myofibroblast sarcoma.

The patient was initially thought to have pneumonia, but the etiology was unknown, so symptomatic treatment with antibiotics against infection, bronchodilation, and diuresis was initiated. After 2 weeks of treatment, the patient's symptoms were relieved, the blood test was lower than before, and chest CT showed flaky high-density shadows in the right lungs, some of

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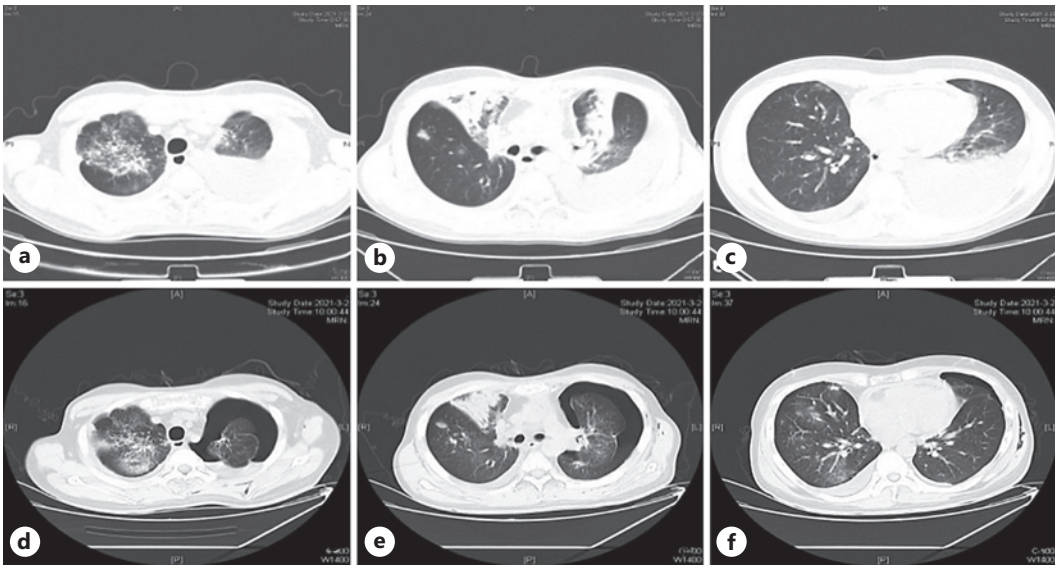


**Fig. 1. a–c** Chest CT showing multiple lamellar hyperintensities with blurred margins in both lungs, nodular foci in the right lung, bronchial inflation signs in some of the lesions, bilateral pleural effusions. **d–f** Right lung lamellar hyperintensity shadow, a nodular shadow is more than before, partly with ground-glass change, left pleural effusion is reduced, and with artificial pneumothorax.

which showed ground-glass changes, and the pleural effusion on the left side was reduced, and with artificial pneumothorax (Fig. 1d, e), suggesting that the patient's lung lesions are in remission from before. We adjusted the treatment plan to anti-infective combined with anti-inflammatory (methylprednisolone 40 mg) and other symptomatic supportive treatments according to the patient's progress. The patient's symptoms improved. However, the cause of the yellowish tissue in the pleura was unknown and the patient was advised to undergo another thoracoscopic biopsy, but the patient refused to receive further treatment. After 6 months of telephone follow-up, the patient's family members complained that the patient passed away due to the deterioration of the patient's condition caused by the spread of the sarcoma in many places throughout the body, the details of which were not clear.

## Discussion

Sarcoma is a malignant tumor originating from mesenchymal tissue, which can occur anywhere in the body [3, 4]. Sarcomas are divided into two main categories, skeletal sarcomas and soft tissue sarcomas, depending on their anatomical location. The treatment of first choice for osteosarcoma and STS is surgical resection of the primary tumor, usually accompanied by adjuvant chemotherapy (AC) and/or radiotherapy and/or neoadjuvant [5–9].

A retrospective meta-analysis identified 545 uterine leiomyosarcoma (uLMS) patients (AC: 252, observation: 293). Compared with observation, AC (with or without radiotherapy) did not decrease locoregional recurrence, distant recurrence, and overall recurrence in early-stage uLMS [10]. In addition, Rizzo et al. [11] summarized the US regarding adjuvant therapy, including chemotherapy, radiotherapy, and hormone therapy, having no definite survival benefit after surgery for uterine sarcoma. In recent years, immunotherapy has provided a new treatment option for cancer patients. A systematic review identified 49,425

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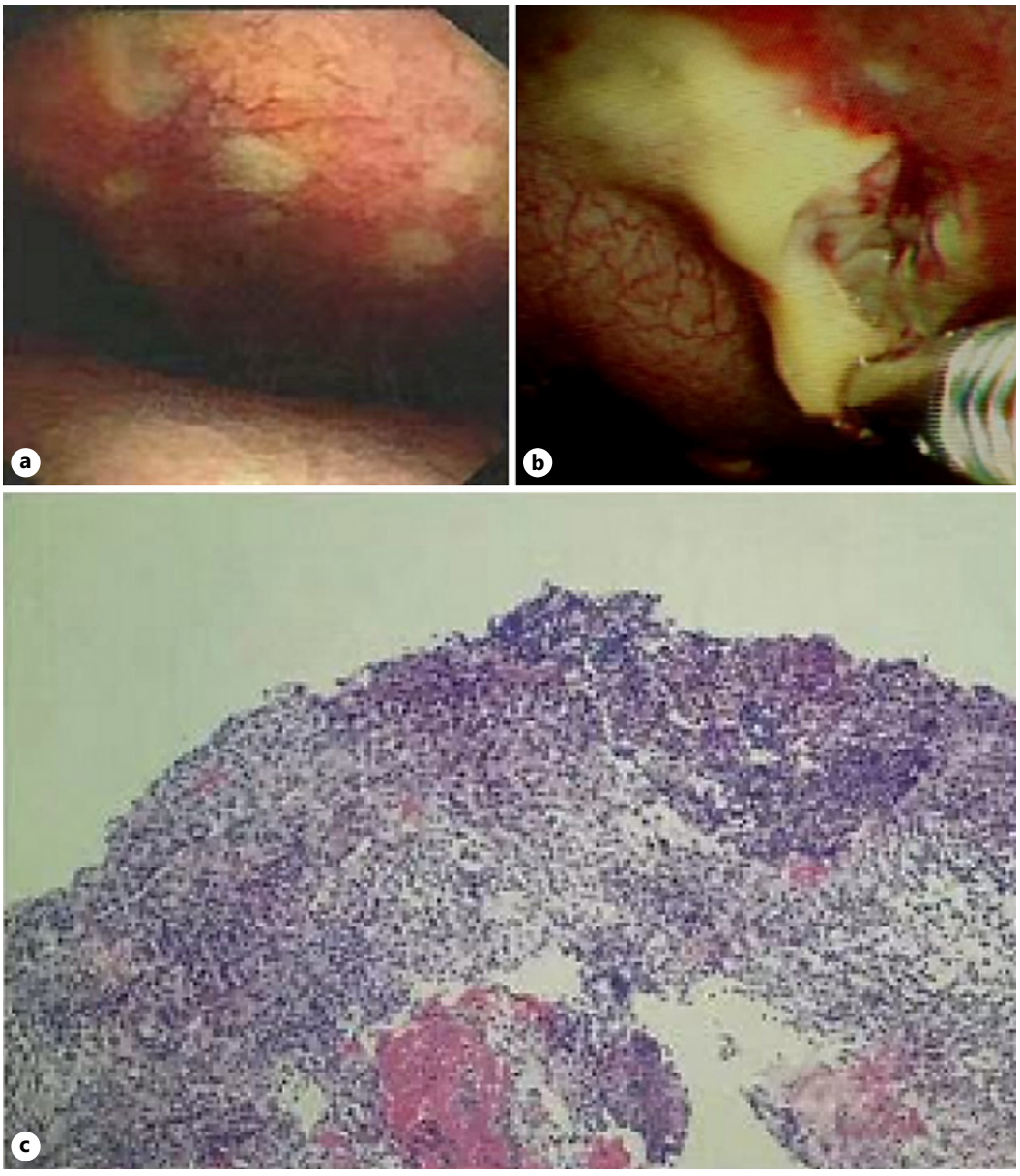


**Fig. 2. a** Thoracoscopic pleural biopsy: yellowish tissue of variable size is visible in the mural pleura. **b** Pathology of the wall pleura biopsy. **c** Pathology of the left mural pleura: granulomatous tissue hyperplasia and mesothelial hyperplasia are seen.

cancer patients from 85 clinical trials and assessed the complete remissions rate in cancer patients receiving immunotherapy versus control treatment by meta-analysis [12]. Higher complete remission rate was reported in cancer patients treated with immunotherapy or chemo-immunotherapy compared with control treatments. The discovery of immune infiltration in sarcoma is a new source of therapeutic targets. Immunocheckpoint inhibitors have provided new options for the treatment of sarcomas and accelerated the revolution in immunotherapy for sarcomas.

The biomarkers for immunotherapy of sarcoma include lymphocyte infiltration, PD-L1 expression within the tumor, and mutation load of sarcoma [13]. However, it has also been suggested that potential predictive biomarkers for sarcoma immunotherapy are B-cell-rich

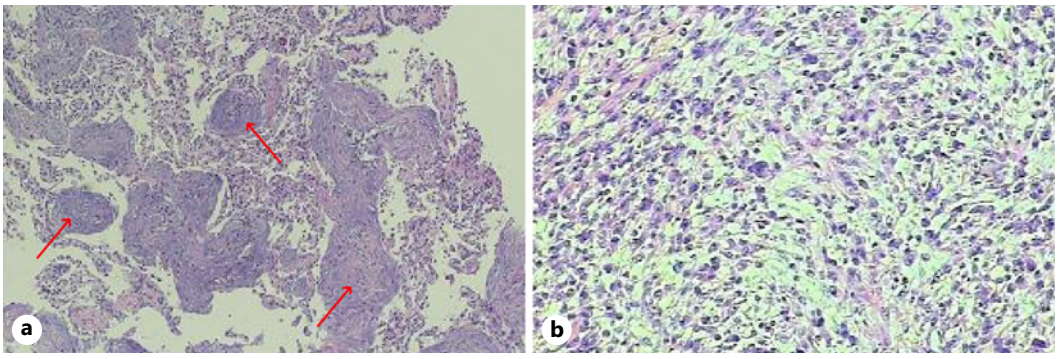


**Fig. 3. a** Pathology of the middle lobe of the right lung: alveolar structures are present, with Masson vesicle formation (red arrow) and partial widening of the alveolar septa visible in the alveolar lumen, with no obvious inflammatory cell infiltration. **b** Pathology of the left shoulder mass: spindle cell tumor, combined with immunohistochemistry, the lesion is consistent with a low-grade malignant myofibroblast sarcoma.

tumor-infiltrating lymphocytes, TMB, and IDO1 activity [14]. Furthermore, even though the high heterogeneity of PD-1/PD-L1 in sarcoma, it is not considered a suitable biomarker [13, 14]. In a recent study analyzing a database of 216 patients with uLMS from the cBioPortal and AACR-GENIE databases for mutational profiles [15], 81% of patients carried at least one interfering mutation in one of the four recurrently mutated genes, TP53, RB1, ATRX, and PTEN, with the most commonly mutated gene being TP53, followed by RB1. TP53, ATRX, and RB1 mutations were seen in both primary and metastatic foci, whereas PTEN mutations tended to be acquired in the late stages of the disease. Tumor mutations play a very important role in the metastasis and recurrence of sarcomas. In the future, further in-depth studies targeting the pathways of tumor mutations may provide an effective and targeted treatment for sarcoma patients.

MS is a type of soft tissue sarcoma, often with painless masses as the first symptom, that usually occurs deep in soft tissue, and can metastasize distantly [2, 16, 17]. The diagnosis of myofibroblast sarcoma is based on pathological analysis and myogenic markers. The most effective treatment method for MS is surgical resection, with a high postoperative recurrence and metastasis rate.

Reviewing the course of disease progression in this patient, the initial presentation of this patient was free of predisposing factors such as infectious agents, drugs, and connective tissue disorders, and he passed away at a later stage due to the recurrence and metastasis of the sarcoma that led to the deterioration of his condition. Combined with the patient's clinical manifestations, laboratory tests, and pathological findings, and after discussion at the MDT, the diagnosis of this patient was considered to be a low-grade malignant MS combined with pleural xanthomatosis and organized pneumonia, but other pleural tumors could not be excluded. Therefore, we would like to draw clinicians' attention to the fact that pleural macula is also one of the alert factors for malignant tumors. This case report is novel due to its clinical presentation as well as laboratory and image findings, which can guide us in making clinical decisions through algorithms when faced with similar clinical cases. We have summarized the main laboratory results and immunohistochemical findings in Table 1.

The diagnosis of the swelling on the left shoulder was clear in this case, but the diagnosis of the yellowish tissue on the pleura was not definite in this patient, and the pathology was reported as a fibrinous exudate, which was considered to be since only the superficial tissue was taken and the lesion was not taken. Also, this patient's pneumonia was considered to be secondary pneumonia, which led to a poor outcome because the primary focus was not taken

**Table 1.** Mainly laboratory studies and immunohistochemical findings

| Items | Results |
|---|---|
| Blood routine examination | Leukocyte: 13.4 × $10^9$/L; neutrophil percentage: 83.1% |
| CRP | 44.3 mg/L |
| pro-BNP | 666.9 pg/mL |
| Blood gas analysis (oxygen uptake: 21%) | PH: 7.45, $PO_2$: 61 mm Hg, $PCO_2$: 36 mm Hg, $SO_2$: 92%, $HCO_3$−: 25 mmol/L, BE: 1.4 mmol/L |
| Routine examination of pleural fluid | The pleural fluid was orange-red, turbid with clots; total cell count: 4,000 × $10^6$ cells/L; nucleated cells: 430 × $10^6$ cells/L; monocytes: 80%; multinucleated cells: 20%; Levantine (±) |
| Biochemical examination of pleural fluid | Total protein: 36.5 g/L, glucose: 6.35 mmol/L, LDH: 192.4 U/L |
| Pulmonary function tests | Severe obstructive ventilatory dysfunction; bronchodilation test (−) |
| Cardiac ultrasound | EF: 60%; small to moderate amount of pericardial effusion; mild aortic and mitral valve regurgitation |
| Immunohistochemistry (left shoulder mass) | Vimentin: +, SMA foci: +; desmin: +, D68: +, Ki-67: 40% +, CK: −, Bcl-2: −, CD34: −, CD99: −, S-100: − |

CRP, C-reactive protein; pro-BNP, pro-brain natriuretic peptide; LDH, lactate dehydrogenase.

for the aforementioned reasons. Ultimately, this patient died of multiple metastases throughout the body from sarcoma, considering that the tumor had invaded the pleura at that time. In the case of an unexplained pleural macula, the possibility of malignancy should be fully considered in the treatment process, and deep tissue should be retrieved for pathology.

Kuhnen et al. [18] describe a case of low-grade MS of the chest wall with multiple recurrences over years. Zhao et al. [19] reported a case of high-grade myofibroblast sarcoma of pleural origin who was treated with chemotherapy (epirubicin and ifosfamide in eight cycles) and radiotherapy and was followed up for 6 months with no tumor progression. An inflammatory myofibroblastic tumor is a rare lung tumor that presents clinically as a cough, with no abnormalities on physical examination or routine blood biochemistry, and a nodular lesion on chest CT [20]. The study found that pleural adhesion, pleural plaques, and pleural nodularity are among the prognostic factors of malignant pleural mesothelioma and suggest a poor prognosis [21]. In this patient's pleural lesion, we need to make a differential diagnosis for the abovementioned diseases.

## Conclusion

Myofibrosarcoma usually occurs deep in soft tissue [2]. If myofibrosarcoma occurs in the pleura, and it is difficult to take diseased tissue from the abnormal superficial pleural tissue, to avoid such a situation, deep tissue biopsies are performed as often as the patient's physical condition permits and in the absence of any other side effects. Pathological and immunological tests support the diagnosis. After resection of the primary lesion of MS, however, due to the high rate of recurrence and metastasis, regular review and systemic screening are required to reduce the harm caused by recurrence. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000533554).

## Statement of Ethics

Ethical approval is not required for this study in accordance with local or national guidelines. Written informed consent was obtained from the patient's next of kin for publication of the details of their medical case and any accompanying images.

## Conflict of Interest Statement

All authors declare no conflict of interest.

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## Author Contributions

D.-W.T. and T.-W.Z. drafted the first manuscript. Y.-Y.W., D.K., and H.-B.L. supervised the manuscript revision. All authors read and approved the final manuscript.

## Data Availability Statement

The data that support the findings of this study are publicly available. All data generated or analyzed during this study are included in this article and its online supplementary material files. Further inquiries can be directed to the corresponding author.

## References

1 Montgomery E, Goldblum JR, Fisher C. Myofibrosarcoma: a clinicopathologic study. Am J Surg Pathol. 2001;25(2):219–28.
2 Fisher C. Myofibrosarcoma. Virchows Arch. 2004;445(3):215–23.
3 Skubitz KM, D'Adamo DR. Sarcoma. Mayo Clin Proc. 2007;82(11):1409–32.
4 Grünewald TG, Alonso M, Avnet S, Banito A, Burdach S, Cidre-Aranaz F, et al. Sarcoma treatment in the era of molecular medicine. EMBO Mol Med. 2020;12(11):e11131.
5 Gamboa AC, Gronchi A, Cardona K. Soft-tissue sarcoma in adults: an update on the current state of histiotype-specific management in an era of personalized medicine. CA Cancer J Clin. 2020;70(3):200–29.
6 Strauss SJ, Frezza AM, Abecassis N, Bajpai J, Bauer S, Biagini R, et al. Bone sarcomas: ESMO-EURACAN-GENTURIS-ERN PaedCan clinical practice guideline for diagnosis, treatment and follow-up. Ann Oncol. 2021;32(12):1520–36.
7 Gronchi A, Miah AB, Dei Tos AP, Abecassis N, Bajpai J, Bauer S, et al. Soft tissue and visceral sarcomas: ESMO-EURACAN-GENTURIS Clinical Practice Guidelines for diagnosis, treatment and follow-up(☆). Ann Oncol. 2021;32(11):1348–65.
8 Bourcier K, Le Cesne A, Tselikas L, Adam J, Mir O, Honore C, et al. Basic knowledge in soft tissue sarcoma. Cardiovasc Intervent Radiol. 2019;42(9):1255–61.
9 Moreno Tellez C, Leyfman Y, D'Angelo SP, Wilky BA, Dufresne A. Immunotherapy in sarcoma: where do things stand? Surg Oncol Clin N Am. 2022;31(3):381–97.
10 Rizzo A, Nannini M, Astolfi A, Indio V, De Iaco P, Perrone AM, et al. Impact of chemotherapy in the adjuvant setting of early stage uterine leiomyosarcoma: a systematic review and updated meta-analysis. Cancers. 2020;12(7):1899.
11 Rizzo A, Pantaleo MA, Saponara M, Nannini M. Current status of the adjuvant therapy in uterine sarcoma: a literature review. World J Clin Cases. 2019;7(14):1753–63.

12 Santoni M, Rizzo A, Kucharz J, Mollica V, Rosellini M, Marchetti A, et al. Complete remissions following immunotherapy or immuno-oncology combinations in cancer patients: the MOUSEION-03 meta-analysis. Cancer Immunol Immunother. 2023;72(6):1365–79.
13 Veenstra R, Kostine M, Cleton-Jansen A, de Miranda NF, Bovée JV. Immune checkpoint inhibitors in sarcomas: in quest of predictive biomarkers. Lab Invest. 2018;98(1):41–50.
14 Dajsakdipon T, Siripoon T, Ngamphaiboon N, Ativitavas T, Dejthevaporn T. Immunotherapy and biomarkers in sarcoma. Curr Treat Options Oncol. 2022;23(3):415–38.
15 Astolfi A, Nannini M, Indio V, Schipani A, Rizzo A, Perrone AM, et al. Genomic database analysis of uterine leiomyosarcoma mutational profile. Cancers. 2020;12(8):2126.
16 Wang L, Li L, Chen D, Yang L, Li SK, Cheng C. Low-grade Myofibroblastic sarcoma: clinical and imaging findings. BMC Med Imaging. 2019;19(1):36.
17 Chan JYK, Gooi Z, Wong EWY, Ng SK, Tong MCF, Vlantis AC. Low-grade myofibroblastic sarcoma: a population-based study. Laryngoscope. 2017;127(1):116–21.
18 Kuhnen C, Homann HH, Mentzel T. [Myofibroblastic sarcoma of the thoracic wall. Change in appearance in tumour recurrence]. Pathologe. 2003;24(2):128–35.
19 Zhao R, Wang J, Zhang H, Chi Y, Bi N. High-grade myofibroblastic sarcoma of the pleura: a case report and literature review. Thorac Cancer. 2020;11(10):3011–4.
20 İçmeli ÖS, Alpay LA, Gündoğuş B, Türker H, Şen A. Inflammatory myofibroblastic tumor: a rare tumor of the lung. Eur Clin Respir J. 2014;1:25390.
21 Xu L, Yang Y, Wang Z, Wang XJ, Tong ZH, Shi HZ. Malignant pleural mesothelioma: diagnostic value of medical thoracoscopy and long-term prognostic analysis. BMC Pulm Med. 2018;18(1):56.