

OPEN

# Postoperative Radiotherapy for the Treatment of Solitary Fibrous Tumor With Malignant Transformation of the Pelvic

## *A Rare Case Report With Literature Review*

Chao Gao, MS, Yong Zhang, MD, Ming Jing, MD, Wei Qu, MD, Jia Li, MD,  
Xiang-Rong Zhao, MS, and Yong-Hua Yu, PhD, MD

**Abstract:** Solitary fibrous tumor of the pelvic is an uncommon neoplasm with nonspecific symptoms. Reports of malignant transformation are especially rare. We report a case of solitary fibrous tumor in pelvic. A unique feature of our case compared with previously reported is that this patient relapsed with malignant transformation and had significant response to radiotherapy. The patient was initially treated with surgery, followed by postoperative dimensional conformal intensity modulated radiation therapy (dynamic MLC VRIAN 23EX Linac, inversely optimized by the Eclipse system) to provide a radical cure for residual tumor.

In this case, there were no signs of recurrence after six and a half years of further follow-up, indicating that postoperation radiotherapy may be an effective treatment for SFT with malignant transformation in pelvic.

(*Medicine* 95(2):e2433)

**Abbreviations:** CT = computed tomography, CTV = clinical tumor volume, IMRT = intensity-modulated radiation therapy, PTV = planning target volume, RT = radiation therapy, SFT = solitary fibrous tumor.

### INTRODUCTION

Solitary fibrous tumor (SFT) is generally a benign neoplasm, the reported incidence of malignant SFTs varies from 7% to 60%, and the pelvis is a rare localization of SFT.<sup>1</sup> Although nearly all SFTs have low malignant potential, malignancy can occur, especially if they grow to a large size or in the case of repeated recurrence.<sup>2,3</sup> There are 2 forms of malignant transformation; one is malignant or high-grade SFT, and the other is de novo occurrence of malignant SFT.<sup>4</sup>

Editor: Giuseppe Di Lorenzo.

Received: August 29, 2015; revised: December 10, 2015; accepted: December 11, 2015.

From the Radiation Oncology Ward 2, Shandong Cancer Hospital and Institute (CG, YZ, WQ, JL, X-RZ, Y-HY); School of Medical and Life Sciences, Shandong Academy of Medical Sciences, Jinan University (CG, X-RZ); and Department of Dermatology, JiNan Dermatoses Prevention and Control Hospital, Jinan, Shandong, China (MJ).

Correspondence: Yong-Hua Yu, Department of Radiation Oncology, Shandong Cancer Hospital and Institute, 440 JiYan Road, JiNan, Shandong, China (e-mail: sdyonghuayu@163.com)

Funding: the study is supported by Shandong Province Science and Technology Development Plan No. 2014GSF118176.

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript.

No writing assistance was utilized in the production of this manuscript.

The patient has consented for the publication of the present case report.

Copyright © 2016 Wolters Kluwer Health, Inc. All rights reserved.

This is an open access article distributed under the Creative Commons Attribution License 4.0, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. ISSN: 0025-7974

DOI: 10.1097/MD.0000000000002433

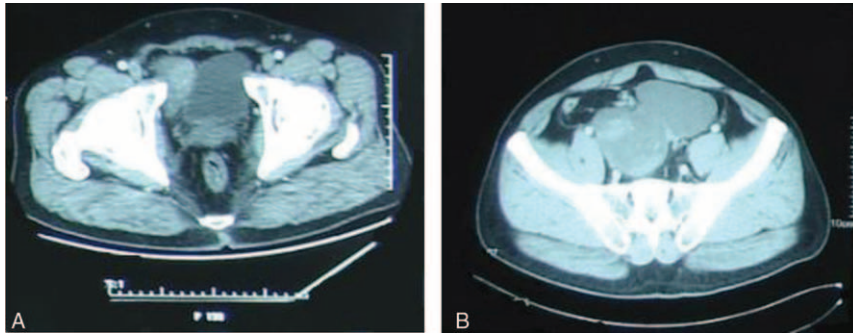
To our knowledge, the report of malignant transformation after recurrence of the SFT in pelvic is extremely rare. The main treatment for SFT is surgery. Herein, we report an SFT patient with postoperative recurrent malignancy transformation in pelvic. He was treated by radical surgical resection and subsequently underwent intensity-modulated radiation therapy (IMRT). It may provide a useful reference for the treatment of similar cases.

### CASE REPORT

A 58-year-old man was admitted to our hospital due to a pelvic mass, which was found by ultrasound in a private clinic in March 2007. Ultrasound demonstrated a large irregular marginated solid mass in the pelvic cavity. Computed tomography (CT) scan revealed a mass (5.5 cm in the longest diameter) in the cavity of the pelvic, the lesions border was clear, and no obvious swelling lymph nodes in double side basin wall and inguinal region (Figure 1A). Subsequently, the patient underwent surgical removal of the mass and the mass was removed completely. The surgery and postoperative period were uneventful. Pathologically, the tumor contained predominantly oval or spindle cells organized in a haphazard growth pattern (a so-called patternless pattern) (Figure 2A). Immunohistochemical stains revealed positive expression for CD34 (Figure 2B), Bcl-2, Ki-67, and Vimentin. Stains were negative for Desmin, S-100, SMA, and CD117. Finally, the tumor was diagnosed as SFT. Unfortunately, the patient refused any subsequent adjuvant treatment.

He accidentally hit a mass in the right lower quadrant in February 2009. On the physical examination, the mass was hard, inactive, and painful if touched it. Laboratory tests, including tumor markers (CA-125, CEA, and CA-19-9), were within the normal range. Pelvic CT revealed a tumor of ~7.5 cm in diameter, mixed density showing multiple soft tissue mass (Figure 1B). Subsequently, the patient underwent pelvic tumor resection again. During the surgery, the surgeons found the tumor, ~13 cm in diameter, had severe adhesion to the lower abdomen abdominal and the surrounding tissue. Thus, a portion of the bladder was included in the resection. Resection proceeded and the postoperative course was uneventful. Postoperative pathology showed spindle cell tumor with hemorrhage and necrosis, and tumor cells had a certain degree of nuclear atypia, high mitotic activity (Figure 3A). Immunohistochemically, the specimen was positive for CD34 (Figure 3B), Bcl-2 (Figure 3C), CD99, and vimentin, but negative for S-100, SMA, and CD117. Combining with the medical history, it was considered as malignant SFT.

Due to the patient with recurrent malignant transformation, then we conducted post-operative IMRT to eliminate residual tumors, and avoid recurrence and/or metastases. Three weeks



**FIGURE 1.** CT findings of the tumor in 2007. (A) CT showed a classical triangle soft tissue density shadow in the pelvic cavity; maximum cross-section was  $\sim 5.5 \times 2.5$  cm. Lesions border was clear; its signal was well-distributed. Double side basin wall and inguinal region did not see obvious swelling lymph nodes; CT findings of the tumor at the second recurrence in 2009. (B) CT showed an irregular soft tissue mass shadow in the pelvic cavity. Lesions border was not clear. Local and right side of the bladder wall had not clear boundaries. CT=computed tomography.

after the patient underwent operation, we developed a radiation treatment plan, and the patient underwent 3-dimensional conformal IMRT. The treatment machine was VRIAN 23 EX. LUNA TM 260 was used as the Eclipse planning system. The clinical tumor volume (CTV) was visualized on CT, and it was calculated including tumor bed. However, 0.3 cm outside of the CTV was defined as the planning target volume (PTV). We carried out the total PTV irradiation with a dose 60 Gy/30F, 2 Gy/F, 1 session/day, and 5 times/week. The DVH for each organ were as follows: bladder ( $D_{\max}$  65.8 Gy;  $D_{\text{mean}}$  34.8 Gy), femoral head-R ( $D_{\max}$  49.4 Gy;  $D_{\text{mean}}$  20.6 Gy), rectum ( $D_{\max}$  40.3 Gy;  $D_{\text{mean}}$  22.0 Gy). After radiation therapy, no other obvious radiation reaction was observed except the slight cystitis. The patient had refused adjuvant chemotherapy and has been followed up for six and a half years. There was no clinical evidence of disease recurrence.

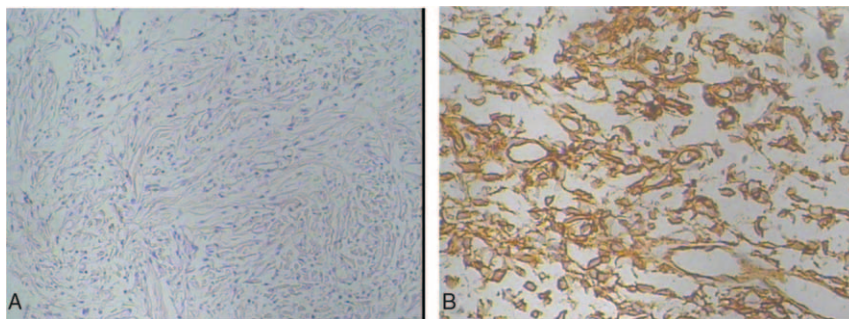
## DISCUSSION

SFT was first reported in 1931 by Klemperer and Rabin.<sup>5</sup> It is a rare neoplasm that is thought to originate from sub-mesothelial mesenchymal cells.<sup>6</sup> The majority of SFTs are benign; however up to 20% of tumors have been reported to be malignant.<sup>7</sup> Katsuno et al<sup>8</sup> reported that 6% of all SFTs originated from the pelvis. Men and women appear to be affected equally and the tumor appears to develop primarily in middle age to older individuals.<sup>9,10</sup> Systemic symptoms such as hypoglycemia, arthralgia, osteoarthritis, and clubbing have

also been documented.<sup>11,12</sup> In clinic, the symptoms of extra-pleural lesions is usually associated with the location of tumor, and these symptoms could disappear when the tumor is removed.

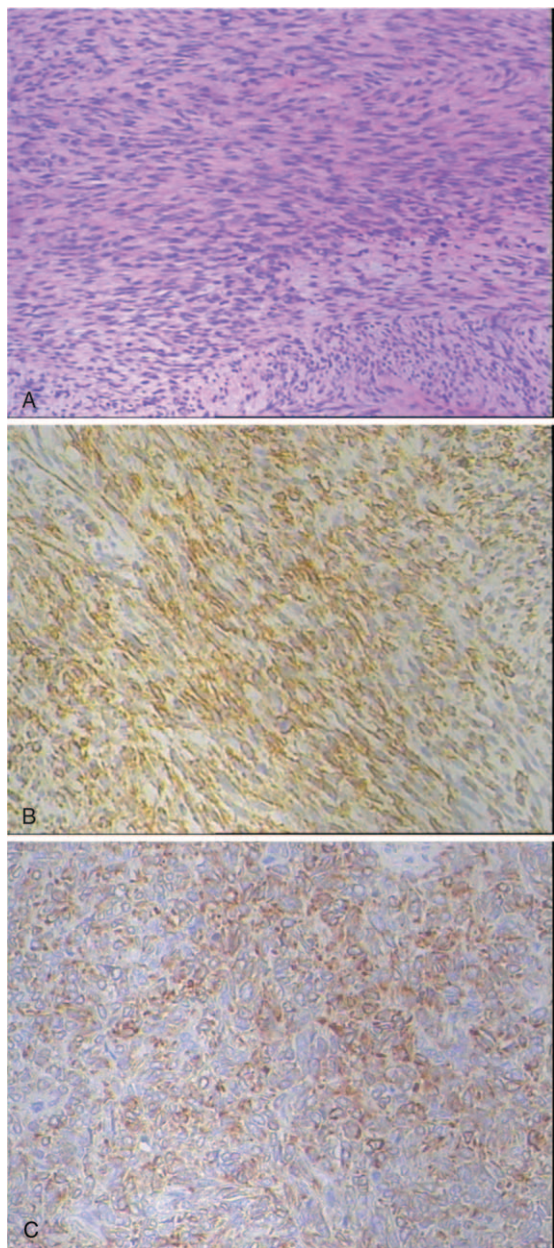
Definitive diagnosis of SFT is based on the characteristic of histological and immunohistochemical features. Histologically, SFT is composed of spindle cells with oval nuclei, typically arranged in “patternless” arrangement, separated by thin “strip-like” bundles of collagen.<sup>13</sup> The tumor may have noticeable but varying degrees of vascularity, and focal areas of blood vessels with a stag horn branching pattern characteristic of hemangiopericytomas are often found.<sup>14</sup> Immunohistochemistry, the tumor cells exhibit expression for vimentin, CD34, CD99, and Bcl-2, but no reactivity for cytokeratin, S-100 protein, actin, desmin, and calretinin.<sup>15,16</sup>

According to the previous reports, CD34 is strongly positive for diagnosis of SFT,<sup>17</sup> and Hasegawa et al<sup>12</sup> suggested the both of Bcl-2 and CD34 immunostaining for making differential diagnosis from spindle cell neoplasia. Although CD34 is a useful marker in diagnosis of SFT, 1 should bear in mind that its expression can be lost in high-grade tumours, in addition, overexpression of p53 and Ki-67 suggests the possibility of a malignant SFT, which relates to de novo or malignant transformation within a benign or low-grade.<sup>4</sup> England et al<sup>3</sup> considered neoplasms to be malignant if 1 or more of the following histologic features are present: (1) high cellularity, (2) high mitotic activity ( $>4$  mitoses per 10 high-power fields), (3) pleomorphism, (4) necrosis, and (5) hemorrhagic changes.



**FIGURE 2.** Histopathological findings of the primary tumor excised in 2007. (A) Spindle or oval cells with mild to moderate nuclear atypia, which shows a so-called patternless pattern (a: HE  $\times 100$ ). Immunohistochemical findings in 2007. (B) The specimen was positive for CD34.





**FIGURE 3.** Histopathological findings of the tumor at the second recurrence in 2009. (A) Histologic evidence to support malignant transformation in solitary fibrous tumor of pelvic includes high cellularity with pleomorphism and increased mitosis, HE  $\times$  100. Immunohistochemical findings in 2009. (B) The specimen was positive for CD34. (C) The specimen was positive for Bcl-2.

In the present study, the diagnosis of SFT was made according to the above characteristic immunohistochemical findings and histological features.

Currently, no standard therapy has been established for SFT with malignant transformation because of the rarity. The main method of treatment for SFT remains wide local excision of the tumor. Soft-tissue sarcomas have traditionally been managed by wide excisional surgery and radiation therapy, but in a study it was concluded that overall morbidity associated

with adjuvant radiation was not significantly higher than that with surgery alone.<sup>18</sup>

The treatment for unresectable malignant SFT has not been established yet. Radiation therapy (RT) alone can be considered for patients refusing or unsuitable for surgery, and it can attain 30% to 60% rate of control in sarcoma.<sup>19</sup> However, it is controversial if RT is therapeutic only for high-grade tumors or also for low-grade tumors.<sup>20,21</sup> Kawamura et al<sup>22</sup> reported a case of huge pelvic malignant SFT with lung metastasis, chemotherapy did not work whereas the tumor shrank 12 months after 50 Gy irradiation of the pelvic region. Moreover, in a series of 11 SFT treated with definitive RT without surgery, no patient had a local recurrence, and 9 were disease-free at 3 to 20 years from diagnosis.<sup>23</sup> Furthermore, Saynak et al<sup>13</sup> also reported RT alone achieved significant effect, which was consistent with Saynak M’s report.<sup>13</sup> On the contrary, Dietrich et al<sup>24</sup> indicated an accelerated progression of the solitary fibrous chest wall tumor in the course of irradiation. Whether the development of sarcomatous growth occurred as a result of RT remains speculative. Nevertheless, RT in SFT could be conceived when surgery is not suitable, as in meningeal, retroperitoneal, and pleural presentations, and pathologic signs of “malignancy” are present at the onset.

Postoperative adjuvant therapy with chemotherapy and/or RT has been used sporadically, but the benefit of these adjuvant therapies remains unproven. The literature is inconclusive in regard of adjuvant RT in SFT.<sup>25–27</sup> Postoperative RT was given due to the high-grade malignancy, narrow excision margins, large size and rapid growing, but there are no published series to substantiate its routine usefulness for this disease.<sup>28</sup> Xue et al<sup>29</sup> reported four and a half years after postoperative RT, no local recurrences were observed. Furthermore, Wushou et al<sup>30</sup> analyzed 227 SFT cases in the Surveillance, Epidemiology, and End Results database during the years of 2000 to 2009 and confirmed a survival benefit for patients treated with surgery in combination with adjuvant RT, whereas the effect was not appreciated with surgery alone. In another series, investigators found that the treatment protocol of combined adjuvant RT with surgery seemed to hinder tumor progression, but had no effect on overall survival.<sup>31</sup>

There are no standard chemotherapeutic indications or regimens for SFT. In some previous studies, Kawamura et al<sup>22</sup> reported that SFT had no response to paclitaxel (4 sessions, 60 mg/m<sup>2</sup>), and the tumor had continued to increase 22.2% in size in the pelvic CT scan. Gold et al<sup>2</sup> found that chemotherapy regimen of doxorubicin and cisplatin was also ineffective for the SFT patient. However, Grobmyer et al<sup>32</sup> revealed that combination of doxorubicin, ifosfamide, and mesna was associated with a significant improvement in disease-specific survival in patients with high-grade extremity soft tissue sarcomas. Stacchiotti et al<sup>33</sup> found that anthracyclines have a degree of antitumor activity in the range of soft tissue sarcoma chemotherapy, but ifosfamide monotherapy seemed to have lower activity. Furthermore, Park et al<sup>34</sup> found that combination therapy with temozolomide and bevacizumab is a generally well tolerated and clinically beneficial regimen for SFT patients. On the contrary, Stacchiotti et al<sup>35</sup> found that the temozolomide-bevacizumab combination did not induce a better therapeutic activity than temozolomide alone, and dacarbazine as a single agent has antitumor activity in SFT.

Several tyrosine kinase inhibitors have been reported, which have shown promise in treating SFT. For example, some previous studies reported that sorafenib has produced tumor responses in patients with SFTs.<sup>36,37</sup> Stacchiotti et al<sup>38</sup> found

that sunitinib is also active in SFT, and response can be long-lasting. Additionally, malignant SFT can express platelet-derived growth factor receptor beta strongly and has missense mutation of 18 exons, providing promising treatment target for unresectable malignant SFT.<sup>39</sup>

In the present study, we conducted postoperative IMRT to eliminate residual tumors, which can better control the primary tumor and avoid recurrence and/or metastases, but the patient refused adjuvant chemotherapy again. No recurrence was observed in the subsequent follow-up, indicating that the patient could be benefited from postoperative RT and clinicians can be referenced from this strategy.

Our patient was initially diagnosed as benign SFT. After radical surgery, he refused to receive the subsequent adjuvant therapy with chemotherapy and/or RT, and did not go to the hospital regularly for re-examination. Currently, he had a relapse. The diagnosis was malignant SFT. Therefore, the first treatment of SFT was clearly insufficient. Following surgery, postoperative RT and chemotherapy should be performed in order to better control the primary tumor and avoid recurrence or metastases.

## CONCLUSION

In this case report, we described an SFT growing in the pelvic, an infrequent localization, which presented a unique associated with recurrent malignant transformation. The absence of chemotherapy and/or RT could be the reason of relapse. This patient underwent postoperation RT after recurrence, no recurrences or metastases occurred during long-term follow-up. Thus, postoperation RT may be an effective treatment for SFT with recurrent malignant transformation in pelvic. Additionally, chemotherapy also should be performed for the greatest degree to prevent relapse. Owing to the possibility of repeated recurrences or malignant transformation, a prolonged follow-up may be advisable in this rare disease.

## ACKNOWLEDGMENTS

The authors specially thank Professor Yongsheng Gao (Department of Pathology, Shandong Cancer Hospital and Institute) for his help with the revision of the manuscript.

## REFERENCES

- Bugel H, Gobet F, Baron M, et al. [Solitary fibrous tumour of the kidney and other sites in the urogenital tract: morphological and immunohistochemical characteristics]. *Progres en Urologie*. 2003;13:1397–1401.
- Gold JS, Antonescu CR, Hajdu C, et al. Clinicopathologic correlates of solitary fibrous tumors. *Cancer*. 2002;94:1057–1068.
- England DM, Hochholzer L, McCarthy MJ. Localized benign and malignant fibrous tumors of the pleura. A clinicopathologic review of 223 cases. *Am J Surg Pathol*. 1989;13:640–658.
- Yokoi T, Tsuzuki T, Yatabe Y, et al. Solitary fibrous tumour: significance of p53 and CD34 immunoreactivity in its malignant transformation. *Histopathology*. 1998;32:423–432.
- Klemperer P, Coleman BR. Primary neoplasms of the pleura. A report of five cases. *Am J Ind Med*. 1992;22:1–31.
- Hu Y, Mahar TJ, Hicks DG, et al. Malignant solitary fibrous tumor: report of 3 cases with unusual features. *Appl Immunohistochem Mol Morphol*. 2009;17:451–457.
- Vossough A, Torigian DA, Zhang PJ, et al. Extrathoracic solitary fibrous tumor of the pelvic peritoneum with central malignant degeneration on CT and MRI. *J Magn Res Imaging*. 2005;22:684–686.
- Katsuno H, Maeda K, Hanai T, et al. Trans-sacral resection of a solitary fibrous tumor in the pelvis: report of a case. *Surg Today*. 2011;41:1548–1551.
- Robinson LA. Solitary fibrous tumor of the pleura. *Cancer Control*. 2006;13:264–269.
- Truong M, Munden RF, Kemp BL. Localized fibrous tumor of the pleura. *Am J Roentgenol*. 2000;174:42.
- Moran CA, Ishak KG, Goodman ZD. Solitary fibrous tumor of the liver: a clinicopathologic and immunohistochemical study of nine cases. *Ann Diagn Pathol*. 1998;2:19–24.
- Hasegawa T, Matsuno Y, Shimoda T, et al. Extrathoracic solitary fibrous tumors: their histological variability and potentially aggressive behavior. *Human Pathol*. 1999;30:1464–1473.
- Saynak M, Bayir-Angin G, Kocak Z, et al. Recurrent solitary fibrous tumor of the pleura: significant response to radiotherapy. *Med Oncol*. 2010;27:45–48.
- Zubor P, Kajo K, Szunyogh N, et al. A solitary fibrous tumor in the broad ligament of the uterus. *Pathol Res Pract*. 2007;203:555–560.
- Kanthan R, Torkian B. Recurrent solitary fibrous tumor of the pleura with malignant transformation. *Arch Pathol Lab Med*. 2004;128:460–462.
- Torres-Olivera FJ, Vargas MT, Torres-Gomez FJ, et al. Cytogenetic, fluorescence in situ hybridization, and immunohistochemistry studies in a malignant pleural solitary fibrous tumor. *Cancer Genet Cytogenet*. 2009;189:122–126.
- Hanau CA, Miettinen M. Solitary fibrous tumor: histological and immunohistochemical spectrum of benign and malignant variants presenting at different sites. *Human Pathol*. 1995;26:440–449.
- Ballo MT, Zagars GK, Cormier JN, et al. Interval between surgery and radiotherapy: effect on local control of soft tissue sarcoma. *Int J Radiat Oncol Biol Phys*. 2004;58:1461–1467.
- Tepper JE, Suit HD. Radiation therapy alone for sarcoma of soft tissue. *Cancer*. 1985;56:475–479.
- Clark MA, Fisher C, Judson I, et al. Soft-tissue sarcomas in adults. *N Engl J Med*. 2005;353:701–711.
- Yang JC, Chang AE, Baker AR, et al. Randomized prospective study of the benefit of adjuvant radiation therapy in the treatment of soft tissue sarcomas of the extremity. *J Clin Oncol*. 1998;16:197–203.
- Kawamura S, Nakamura T, Oya T, et al. Advanced malignant solitary fibrous tumor in pelvis responding to radiation therapy. *Pathol Int*. 2007;57:213–218.
- Jha N, McNeese M, Barkley HT Jr et al. Does radiotherapy have a role in hemangiopericytoma management? Report of 14 new cases and a review of the literature. *Int J Radiation Oncol Biol Phys*. 1987;13:1399–1402.
- Dietrich CG, Roeb E, Breuer E, et al. Solitary fibrous thoracic wall tumor. Progression with percutaneous radiotherapy. *Deutsche Medizinische Wochenschrift*. 2001;126:12–15.
- Dube VE, Paulson JF. Metastatic hemangiopericytoma cured by radiotherapy. A case report. *J Bone Joint Surg Am*. 1974;56:833–835.
- Friedman M, Egan JW. Irradiation of hemangiopericytoma of Stout. *Radiology*. 1960;74:721–730.
- Mira JG, Chu FC, Fortner JG. The role of radiotherapy in the management of malignant hemangiopericytoma: report of eleven new cases and review of the literature. *Cancer*. 1977;39:1254–1259.
- Colletta AA, Wakefield LM, Howell FV, et al. Anti-oestrogens induce the secretion of active transforming growth factor beta from human fetal fibroblasts. *Br J Cancer*. 1990;62:405–409.

29. Xue Y, Chai G, Xiao F, et al. Post-operative radiotherapy for the treatment of malignant solitary fibrous tumor of the nasal and paranasal area. *Jpn J Clin Oncol*. 2014;44:926–931.
30. Wushou A, Jiang YZ, Liu YR, et al. The demographic features, clinicopathologic characteristics, treatment outcome and disease-specific prognostic factors of solitary fibrous tumor: a population-based analysis. *Oncotarget*. 2015;6:41875–41883.
31. Melone AG, D'Elia A, Santoro F, et al. Intracranial hemangiopericytoma—our experience in 30 years: a series of 43 cases and review of the literature. *World Neurosurg*. 2014;81:556–562.
32. Grobmyer SR, Maki RG, Demetri GD, et al. Neo-adjuvant chemotherapy for primary high-grade extremity soft tissue sarcoma. *Ann Oncol*. 2004;15:1667–1672.
33. Stacchiotti S, Libertini M, Negri T, et al. Response to chemotherapy of solitary fibrous tumour: a retrospective study. *Eur J Cancer*. 2013;49:2376–2383.
34. Park MS, Patel SR, Ludwig JA, et al. Activity of temozolomide and bevacizumab in the treatment of locally advanced, recurrent, and metastatic hemangiopericytoma and malignant solitary fibrous tumor. *Cancer*. 2011;117:4939–4947.
35. Stacchiotti S, Tortoreto M, Bozzi F, et al. Dacarbazine in solitary fibrous tumor: a case series analysis and preclinical evidence vis-à-vis temozolomide and antiangiogenics. *Clin Cancer Res*. 2013;19:5192–5201.
36. von Mehren M, Rankin C, Goldblum JR, et al. Phase 2 Southwest Oncology Group-directed intergroup trial (S0505) of sorafenib in advanced soft tissue sarcomas. *Cancer*. 2012;118:770–776.
37. Domont J, Massard C, Lassau N, et al. Hemangiopericytoma and antiangiogenic therapy: clinical benefit of antiangiogenic therapy (sorafenib and sunitinib) in relapsed malignant haemangiopericytoma /solitary fibrous tumour. *Invest New Drugs*. 2010;28:199–202.
38. Stacchiotti S, Negri T, Palassini E, et al. Sunitinib malate and figitumumab in solitary fibrous tumor: patterns and molecular bases of tumor response. *Mol Cancer Therapeut*. 2010;9:1286–1297.
39. Rossi G, Schirosi L, Giovanardi F, et al. Pleural malignant solitary fibrous tumor with sarcomatous overgrowth showing PDGFRbeta mutation. *Chest*. 2006;130:581–583.