Cancer Research Journal
2022; 10(2): 26-29
http://www.sciencepublishinggroup.com/j/crj
doi: 10.11648/j.crj.20221002.11
ISSN: 2330-8192 (Print); ISSN: 2330-8214 (Online)

Analysis of the Efficacy of Anlotinib in the Late-Line Treatment of Advanced Leiomyosarcoma: A Case Report

Tai Zhao, Yajin Wang, Yuqing Du*

Department of Interventional Radiology, Shidong Hospital Affiliated to University of Shanghai for Science and Technology, Shanghai, China

Email address:
m13795480936_2@163.com (Tai Zhao), whyjj@163.com (Yajin Wang), du_yqsh@sina.cn (Yuqing Du)
*Corresponding author

To cite this article:
Tai Zhao, Yajin Wang, Yuqing Du. Analysis of the Efficacy of Anlotinib in the Late-Line Treatment of Advanced Leiomyosarcoma: A Case Report. *Cancer Research Journal*. Vol. 10, No. 2, 2022, pp. 26-29. doi: 10.11648/j.crj.20221002.11

Received: February 15, 2022; **Accepted**: March 15, 2022; **Published**: April 14, 2022

Abstract: Primary retroperitoneal leiomyosarcoma originated from smooth muscle tissue or mesenchymal cells with the potential to differentiate into smooth muscle cells, showing aggressive growth, easy to recur and metastasize after operation, with a 5-year overall survival rate of 28% - 40%. Multidisciplinary comprehensive treatment based on surgery is an effective means of leiomyosarcoma, while radiotherapy is mainly aimed at subclinical lesions and residual lesions. There is no standard treatment for advanced retroperitoneal leiomyosarcoma. How to effectively prolong the survival time of patients is worth discussing. *Aim:* To determine the comprehensive treatment of retroperitoneal leiomyosarcoma based on surgery, and to explore the effective prolongation of the survival time of patients with advanced retroperitoneal leiomyosarcoma. *Case Summary:* A female with pelvic leiomyosarcoma survived for 70 months after surgery, postoperative radiotherapy, local ablation and chemoembolization. Finally, multiple metastases of lung and liver occurred, abdominal distension and fatigue was hospitalized. After oral administration of anlotinib 12mg q1-14d, she survived for 10 months. *Conclusion:* Leiomyosarcoma needs multidisciplinary comprehensive treatment based on surgery. Late-line anti angiogenesis therapy with arotinib can improve the quality of life of patients and effectively prolong the progression free survival of advanced patients because of its mild adverse reactions, good tolerance and Oral convenience.

Keywords: Leiomyosarcoma, Surgery, Radiotherapy, Anlotinib Hydrochloride, Case Report

1. Introduction

Primary retroperitoneal leiomyosarcoma derives from smooth muscle tissue or mesenchymal cells with the differentiation potential to smooth muscle cells [1]. It occurs more commonly in people aged 40 to 70 years and in women, often grows aggressively and relapses easily after surgery. It can transfer to the lungs and liver through blood circulation, and the 5-year overall survival reported in the literature is 28%- 40% [2-5]. This report describes the case of multiple metastasis of liver and lung in a female patient with pelvic leiomyosarcoma, and discusses its effective treatment.

2. Case Presentation

2.1. Chief Complaints

A 45 year old female with pelvic leiomyosarcoma more than 5 years after operation, liver and lung metastasis more than 2 years, abdominal distension and fatigue was hospitalized.

2.2. Laboratory Examinations

Blood analysis showed normal leukocytes 4.65×109/L, hematocrit and platelet count were normal. Prothrombin and partial thromboplastin time were normal. Serum C-reactive protein increased at 19.2 mg/dl (normal range<10mg/dl). Blood biochemical analysis showed that serum albumin was slightly lower than 33.3g/l (normal range>40G/L). Renal function and urinalysis were normal.

2.3. Imaging Examinations and Final Diagnosis

Chest CT in September 2018 showed multiple lung metastases (Figure 1a), and contrast-enhanced abdominal MRI showed multiple liver metastases, a small amount of ascites, invasion of the right ureter, multiple lesions in the lower

abdomen, pelvic cavity and left groin area, which indicated tumor implantation metastasis and lymph node metastasis (Figures 2a, 3a). Clinical staging is pT2bN0M0, stage IV.

2.4. History of Present Illness

She presented to the hospital with complaints of left lower quadrant pain in November 2012, with no family history of tumor. Pelvic CT showed a retroperitoneal mass, and laparoscopic left pelvic tumor resection, intestinal adhesion dissection, vaginal fornix incision and suture under general anesthesia were performed in the same month. Close to the left ovary, a solid tumor, about 6*8cm in size, was found in the posterior peritoneum of the left pelvic wall, and the surface of the mass and the left adnexa area have adhered to the intestine. Postoperative pathology suggested grade II retroperitoneal leiomyosarcoma with necrosis, and immunohistochemistry results are VIM+, SMA+, Ki67 (10-20% positive), MSA+, EMA+, Des+, h-CALD+, CD117-, CD34-, DOG-1-, S-100-, GFAP-. The patient was diagnosed with pelvic leiomyosarcoma, pT2bN0M0, stage IIIc. After the surgery, radiation therapy with a dose of TD 50.4Gy/28f lesion area was performed in December 2012, and the GT regimen was sequentially given for six cycles.

In August 2015, a contrast-enhanced pelvic CT revealed recurrence at the rectouterine fossa, and trans-anal pelvic mass biopsy was performed. Pathology indicated spindle cell sarcoma with cellular atypia, which was considered to be the recurrence of leiomyosarcoma. ADM/DTIC chemotherapy was administered for three cycles to evaluate SD. Excision of the transabdominal presacral tumor, partial rectum, total uterus, and right adnexa, and terminal ileal prophylactic stoma were conducted in December. Postoperative pathology showed that malignant tumor of spindle cells in the presacral region had invaded the intestinal serosa, which, together with immunohistochemistry and medical history, was consistent with leiomyosarcoma.

In September 2016, multiple intrahepatic lesions were found, and a liver biopsy was performed. Pathological results suggested leiomyosarcoma liver metastasis. Radiofrequency ablation combined with TACE treatment was performed in October. TACE was performed on December 2, 2016, February 17 and April 21, 2017, to evaluate and review PD. Pazopanib was taken orally from December 2017 before drug resistance appeared two months later. Then, the treatment was adjusted to a combination of Pazopanib and Everolimus from February 2018. However, the drugs were discontinued one week later because the patient developed a persistent high fever, and anti-inflammation and supportive treatment was carried out accordingly.

2.5. Treatment and Outcome

Anlotinib hydrochloride, 12mg, qd, d1-14, q3w targeted therapy was started from September 20, 2018. The curative effect evaluation had been SD until June 2019 (Figures 1b, 2b, 3b). The patient died of failure on July 27, 2019, with a survival of 10 months.

The patient developed grade 2-3 oral mucosal ulcers during medication and received symptomatic treatment; moderate hypertension was under control with oral antihypertensive drugs without reduction or discontinuation. Morphine was given orally, from 10mg q12h to 40mg q12h, and the pain was well managed.

The patient's consent was obtained for publication of this case report and the associated images.

Figures (1-3) were the same patient's images.

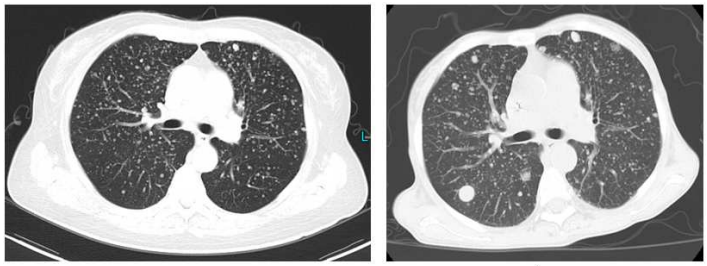


Figure 1. *a. Chest CT scan showed multiple miliary size metastases in both lungs of leiomyosarcoma of pelvis; b. After 9 months of treatment with Arotinib, CT scan showed a slight decrease in the number of multiple lung metastases and an increase in the size of some lesions.*

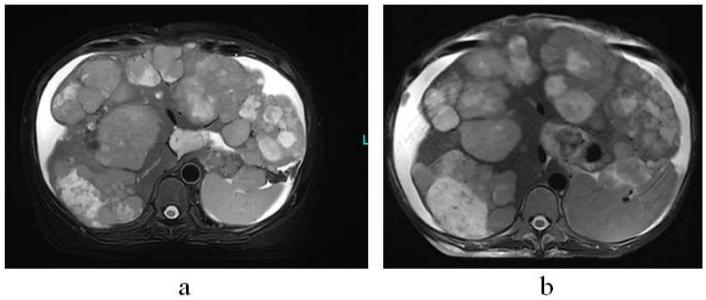
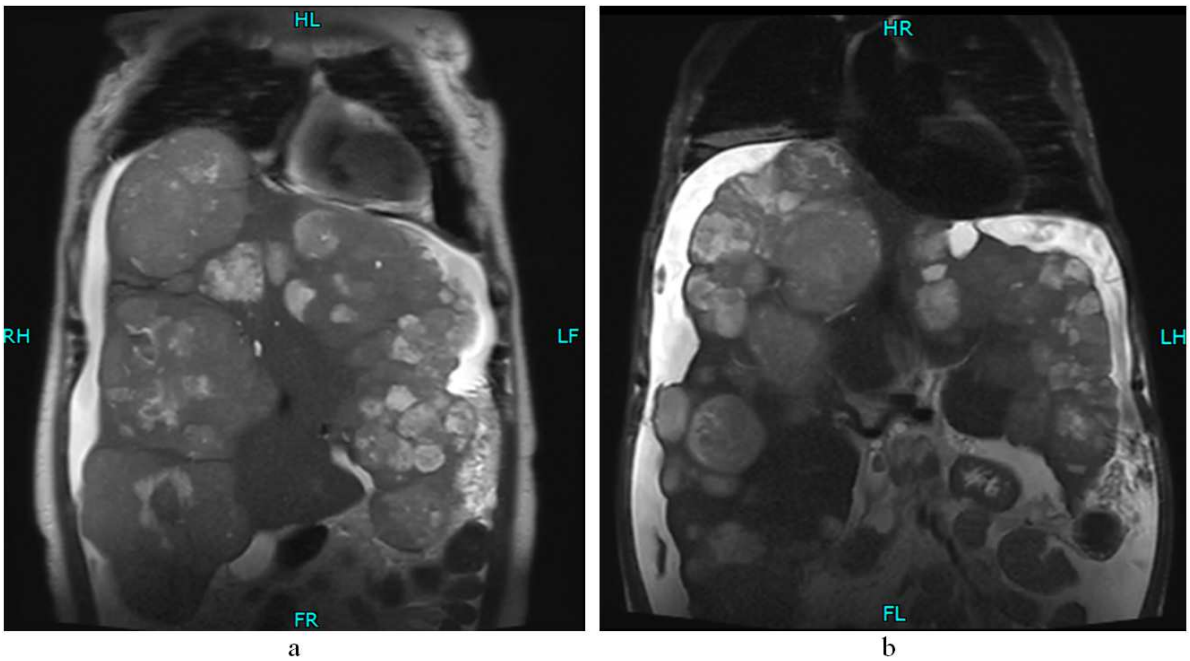


Figure 2. *MR a. AX T2WI showed multiple metastases of different sizes in liver and abdominal cavity with a small amount of ascites of leiomyosarcoma of pelvis; b. After 10 months of treatment with Arotinib, multiple metastases in liver and abdominal cavity increased slightly, and ascites increased slightly.*



a b

Figure 3. *MR a. COR T2WI showed multiple metastases of different sizes in liver and abdominal cavity with a small amount of ascites of leiomyosarcoma of pelvis; b. After 10 months of treatment with Arotinib, multiple metastases in liver and abdominal cavity increased slightly, and ascites increased slightly.*

3. Discussion

At present, leiomyosarcoma is believed to require multidisciplinary comprehensive treatment based on surgery. Surgical treatment should still be recommended for locally recurring tumors, solitary metastases, or distant metastases that can be resected in one or several stages, even if they are multiple [6]. Radiotherapy is mainly targeted at subclinical and residual lesions, and standardized postoperative radiotherapy can improve local lesion control, thereby improving survival and reducing relapse [7]. The patient underwent laparoscopic pelvic tumor resection, intestinal adhesion dissection, vaginal fornix incision and suture, and radiotherapy of the left pelvic lesion area after the surgery. 33 months after radiochemotherapy, recurrence was found at the rectouterine fossa, and transabdominal presacral tumor, partial rectum, total uterus and right adnexa excision was performed. Literature reported that for patients with unresectable leiomyosarcoma liver metastasis, drug-loaded microspheres TACE is used to treat liver metastasis after leiomyosarcoma surgery, and hepatic arterial embolization improved the survival of liver metastatic leiomyosarcoma [8].

Targeted therapy for advanced retroperitoneal leiomyosarcoma, literature has demonstrated that the progression-free survival of patients with advanced soft tissue sarcoma can be prolonged, with mild adverse reactions, good tolerance, and high clinical benefit rate [9, 10]. However, two months after the administration of Pazopanib, the patient developed drug resistance and was intolerant to Pazopanib and Everolimus. According to the second-line treatment of advanced soft tissue sarcoma by Anlotinib hydrochloride, PFS and OS were 12.4 months and 19.4 months, respectively [11, 12]. In combination with the patient's condition, Anlotinib hydrochloride 12mg q1-14d was selected and survival turned out to be 10 months. This patient underwent surgery-based comprehensive treatment and survived for 80 months.

As a novel small-molecule multi-target tyrosine kinase inhibitor developed by China, Anlotinib hydrochloride exhibits inhibition effects on tumor angiogenesis and tumor growth with obvious advantages in its mechanism of action. The 50% inhibiting concentration (IC_{50}) value for action on the above targets is lower and therefore safer. Anlotinib hydrochloride is administered 12 mg daily for two weeks and stopped for one week. This method of administration shows better tolerance and oral convenience, improving the quality of life without significant toxicity [12-14]. The patient was treated with oral Anlotinib hydrochloride for 10 months. The adverse effects include grade 1-2 hypertension, fatigue, and oral mucositis, which can be managed symptomatically.

4. Conclusion

Leiomyosarcoma needs multidisciplinary comprehensive treatment based on surgery. Late-line anti angiogenesis therapy with arotinib can improve the quality of life of patients and effectively prolong the progression free survival of advanced patients because of its mild adverse reactions, good tolerance and Oral convenience.

Conflict of Interest Statement

All the authors do not have any possible conflicts of interest.

References

[1] Wang Guanhuier, He Lianbo, Yang Kaiwei, et al. (2016). Primary retroperitoneal leiomyosarcoma: a clinical and pathological study of 11 cases. Chinese Journal of Urology, 37 (12): 916-918.

[2] Ramponi F, Kench JG, Simring DV, et al. (2012). Early diagnosis and resection of an asymptomatic leiomvosarcoma of the inferior vena cava prior to caval obstruction. J Vasc Surg, 55: 525-528.

[3] Chouliaras K, Senehi R, Ethun CG, et al (2019). Recurrence patterns after resection of retroperitoneal sarcomas: an eight-institution study from the US Sarcoma Collaborative, J. Surg. Oncol. 120: 340–347.

[4] Snow HA, Hitchen TX, Head J, et al (2018). Treatment of patients with primary retroperitoneal sarcoma: predictors of outcome from an Australian specialist sarcoma centre, ANZ J. Surg. 88: 1151–1157.

[5] Nao Kitasakia, Tomoyuki Abea, Akihiko Oshita, et al (2021). Long-term survival by repeat resection for metastases from primaryretroperitoneal leiomyosarcoma: A case report. International Journal of Surgery Case Reports 82: 105891.

[6] ZHAO Xudong, LI Peiyu, HUANG Xiaohui, et al. (2013). Prognostic factors predicting postoperative survival period in the treatment of primary retroperitoneal leiomyosarcoma. Chinese Journal of Surgery, 51 (10): 891-893.

[7] Constantinidou A, Jones RL (2018). Systemic therapy in retroperitoneal sarcomamanagement, J. Surg. Oncol. 117: 87–92.

[8] WANG Fuming, LIU Jingyu, YANG Jijin (2018). Drug-eluting beads for the treatment of hepatic metastasis following surgery of retroperitioneal leiomyosarcoma: report of one case. Journal of Interventional Radiology, 27 (4): 308-309.

[9] Yoo KH, Kim HS, Lee SJ, et al. (2015). Emcacy of pazopanib monotherapy in patients who had been heavily pretrealed for metastatic soft tissue sarcoma:a retrospective case series. BMc cancer, 15: 154-166.

[10] CHI Y, FANG Z, HONG X, et al (2018). Safety and efficacy of anlotinib, a multikinase angiogenesis inhibitor, in patients with refractory metastatic soft-tissue sarcoma. Clin Cancer Res, 24 (21): 5233-5238.

[11] ZHUANG Rong-yuan, WANG Zhi-ming, GUO Xi, et al (2019). The short-term efficacy and safety of anlotinib combined with chemotherapy in treatment of advanced soft tissue sarcoma. Chinese Journal of Clinical Medicine, 26: 378-381.

[12] Jiayong Liu, Zhengfu Fan, Shu Li (2018). Anlotinib hydrochloride capsules for advanced soft tissue sarcoma: single-center data analysis of a stage II multicenter clinical trial. Chinese Journal of Clinical Oncology, 45 (20): 1066-1070.

[13] Sun Y, Niu W, Du F, Du C, et al (2016). Safety, pharmacokinetics, and antitumor properties of anlotinib, an oral multi-target tyrosine kinase inhibitor, in patients with advanced refractory solid tumors. J Hematol Oncol, 9 (1): 105-106.

[14] LIN Li, KONG Fei, ZHANG Guifen, et al (2019). Clinical Efficacy and Safbty of Anlotillib in me TreatInent of Advanced Soft Tissue Sarcoma. JOURNAL 0F BASIC AND CLINICAL 0NCOLOGY, 32 (3): 223-225.