Int J Clin Exp Med 2021;14(6):2050-2053
www.ijcem.com /ISSN:1940-5901/IJCEM0114139

Case Report

Anlotinib in the treatment of lung metastasis of prostate cancer: a case report

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Received May 11, 2020; Accepted August 2, 2020; Epub June 15, 2021; Published June 30, 2021

Abstract: Anlotinib is a novel anti-angiogenic target tyrosine kinase inhibitor which showed excellent curative effects when treating non-small cell lung cancer. Castration-resistant prostate cancer with lung metastasis demonstrated poor prognosis after remission and low survival rate. But evidence is scarce whether anlotinib could inhibit the development of lung metastasis in prostate cancer patients. We report that a prostate cancer case with pulmonary metastasis improved after anlotinib treatment. The patient was administered 12 mg of anlotnib per day for every two weeks with a one-week interval. After 47 days, chest CT showed that the number and area of multiple metastases in both lungs decreased and bilateral pleural effusion reduced. The indexes of characteristic biochemical examination were significantly improved compared with values before treatment. Thus, for prostate cancer patients with pulmonary metastasis, anlotinib has the potentials to inhibit the growth of pulmonary metastatic tumors and improve the quality of life.

Keywords: Anlotinib, prostate cancer, pulmonary metastasis, castration-resistant prostate cancer, anti-angiogenic multitarget tyrosine kinase inhibitor

Introduction

Prostate cancer (PCa) is a leading cause of cancer-related deaths. The incidence of prostate cancer has been increasing over the past decades and contributed to serious burden of disease in China [1, 2]. Although endocrine therapy could control the condition in most patients, some patients develop castration-resistant prostate cancer (CRPC), with an extremely poor prognosis and a median survival of only one year [3]. Anlotinib is a novel small-molecule multitarget tyrosine kinase inhibitor (TKI) independently developed in China, which can exert anti-angiogenesis and anti-proliferation of tumor effects through inhibiting vascular endothelial growth factor receptor (VEGFR), platelet-derived growth factor receptor (PDGFR), fibroblast growth factor receptor (FGFR), c-kit and other targets [4, 5]. Previous studies have shown that anlotinib can significantly prolong the overall survival (OS) and progression-free survival (PFS) in patients with advanced non-small-cell lung cancer (NSCLC). However, the efficacy of anlotinib for pulmonary metastasis of prostate cancer has not been investigated. Here, we report a case of prostate cancer with pulmonary metastasis in which the metastasis eventually disappeared after anlotinib treatment.

Case presentation

A 62-year-old male patient was conscious, short of breath, and cyanotic on admission. This patient had prostate surgery one year ago and the postoperative pathology implicated prostate acinar adenocarcinoma (**Figure 1**). After surgery, the patient was treated with abiraterone and prednisone. No specific related past illness was found. The patient had smoked 20 cigarettes per day for 20 years and quitted for 15 years before admission. Admission examination showed a temperature of 38.3°C, pulse 115 beats/min, breathing 22 times/min, blood pressure 156/100 mmHg, and SpO_2 82% (oxygen absorption 1 L/min). The trachea was centered, and the thoracic cage showed an emphysematous chest. Double lung vocal

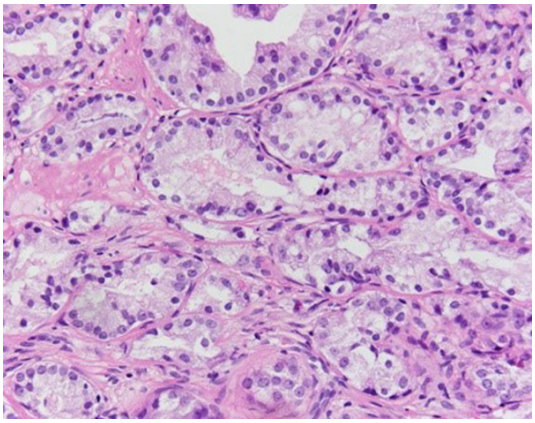

Figure 1. HE staining (×400) of surgical specimens of the patient's prostate revealed a prostatic acinar adenocarcinoma.

fremitus was reduced. The percussion of the lungs was hyper-resonant note, and the bilateral respiratory movement was weakened. Bilateral lung respiratory tone was low and dry, and wet rales could be heard in both lungs.

The plain CT scan of the lower abdomen showed no obvious enlargement of the prostate gland, inhomogeneous prostate density, and multiple patchy low-density shadows inside. A small amount of effusion was detected in the abdominal cavity and pelvic cavity. The chest CT scan showed increased texture in both lungs, and multiple nodules of different in the lung field (**Figure 2**). Pleural effusion was observed in the chest cavity. The blood gas analysis on admission reported that blood pH was 7.29, blood oxygen partial pressure 12.1 kPa, carbon dioxide partial pressure 11.9 kPa, and oxygen saturation 96%. The patient was diagnosed with pulmonary metastasis of prostate cancer considering his prior medical history.

After admission, the patient improved after receiving positive pressure ventilation with a noninvasive ventilator, anti-infection, anti-spasmolysis and phlegm dispersal treatments. And then hemorrhagic pleural fluid of 2300 ml was drained using the thoracic catheter. Both the epidermal growth factor receptor (EGFR) and anaplastic lymphoma kinase (ALK) gene mutations of the pleural effusion were negative. The patient took anlotinib 12 mg orally before breakfast per day after he and his family signed the informed consent form. Each course of treatment lasted for three weeks, including two weeks of treatment and one week of break.

In the third course, the patient experienced heartburn, poor appetite and weight loss, but became tolerable to anlotinib after treatment for gastric protection and gastric motility improvement. No complications were observed, such as damaged liver and kidney function or increased blood glucose level. 47 days after medication initiation, the chest CT showed fewer multiple lung metastases with smaller sizes and decreased pleural effusion. Chronic bronchitis and emphysema with multiple bullae of the lungs were observed (**Figure 2**). The blood gas analysis reported that blood pH was 7.44, blood oxygen partial pressure 18 kPa, carbon dioxide partial pressure 7.1 kPa, and oxygen saturation 99%. The patient's condition obviously improved compared with that before treatment.

Discussion

Multidisciplinary therapies such as chemotherapy, radiotherapy, immunotherapy and targeted therapy can improve the prognosis of advanced patients, but the overall survival rate did not increase as expected. Several studies have confirmed the safety and efficacy of abiraterone, which can significantly benefit both the progression-free survival time and the overall survival time of the disease [6, 7], but they also raise the concern for drug resistance. In the present case, after oral treatment with abiraterone prednisone for one year and four months, extensive lung metastasis and massive pleural effusion were observed, which may be partially explained by abiraterone resistance.

A consensus had gradually grown that the progression of prostate cancer could be related to PSA decline, tumor vascular remodeling and small cell/neuroendocrine differentiation, as well as activation of the androgen receptor (AR) signaling pathway [8, 9]. Among these biological mechanisms, tumor vascular remodeling provides an opportunity to treat prostate cancer since anlotinib can prevent tumor angiogenesis and inhibit tumor growth by potently inhibiting multiple targets, such as VEGFR, PDGFR, FGFR and c-Kit [10]. In the meanwhile, the semi-inhibitory concentration values of anlotnib for these targets are lower, which means greater safety in clinical practice.

In this case, the patient exhibited more tolerant to anlotinib than abiraterone and predni-

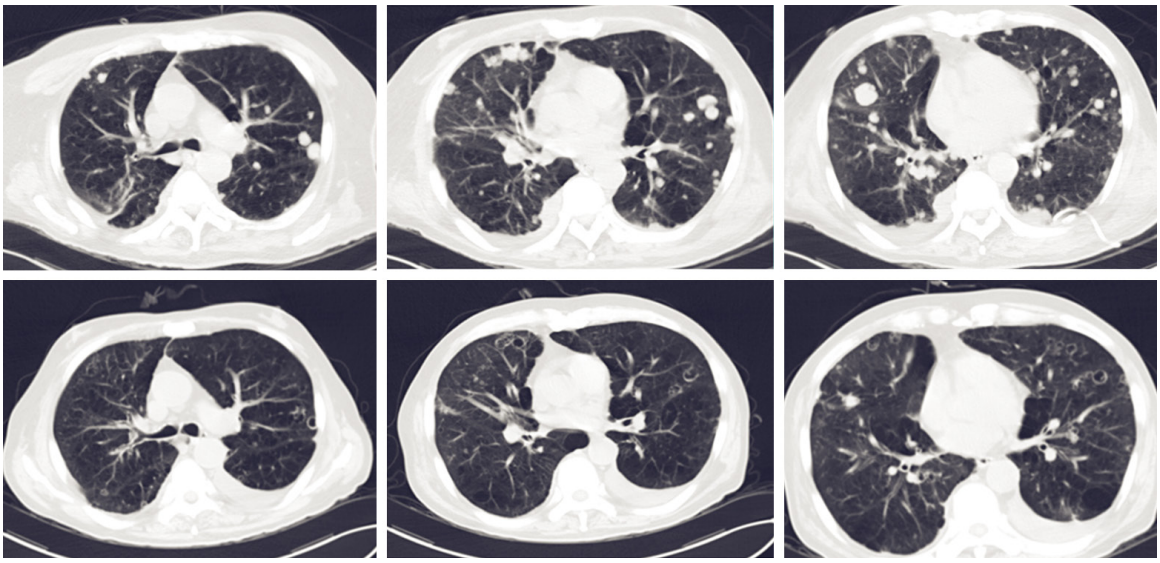

Figure 2. CT findings of the patient's chest before and after treatment with anlotinib. Double lung metastasis was shown before treatment, and reexamination after treatment showed that the metastatic nodules disappeared or shrank, accompanied by the formation of a cavity.

sone. The administration of oral anlotinib was more convenient, and it improved the quality of life without significant toxicity [11]. After treatment, the patient was able to walk 50 meters on his own after a 30-day follow-up through outpatient visit. Furthermore, ALTER-0303 is a clinical study of antilotinib as a third-line treatment for advanced NSCLC, and the results showed that the overall survival (OS) and progressive-free survival (PFS) of patients with advanced NSCLC can be significantly prolonged by anlotinib [12]. To date, targeted RTK inhibitors have been successfully utilized in the treatment of several cancer types [13]. As a novel inhibitor that targets multiple RTKs, anlotinib may have a therapeutic effect on prostate cancer by inhibiting the activation of VEGFR2, PDGFRβ, FGFR1 and downstream ERK signaling [14]. Besides, anlotinib has good membrane permeability, mild side effect and can be absorbed at a greater speed [15], so it eventually showed a better therapeutic effect. However, more high-quality, randomized trials should be conducted to confirm its therapeutic efficacy in pulmonary metastasis of prostate cancer.

Our article is the first to report that anlotinib was used for patients with recurrent pulmonary metastasis of prostate cancer. This case study failed to evaluate the efficacy of anlotinib in prostate cancer, but it provided a theoretical basis for future studies of anlotinib in prostate cancer and it warrants further studies whether anlotinib has better efficacy in treating pulmonary metastatic tumors.

Conclusion

For prostate cancer patients with pulmonary metastasis, anlotinib is convenient to take and can inhibit the growth of pulmonary metastatic tumors and improve the quality of life.

Acknowledgements

This study was supported by the fifth cycle key medical specialty construction project in Jinshan district, Shanghai (JSZK2015A08).

Disclosure of conflict of interest

None.

Abbreviations

NSCLC, non-small-cell lung cancer; CRPC, castration-resistant prostate cancer; EGFR, endothelial growth factor receptor; ALK, anaplastic lymphoma kinase; VEGFR, vascular endothelial growth factor receptor; PDGFR, platelet-derived growth factor receptor; FGFR, fibroblast growth factor receptor; OS, overall survival; PFS, progression-free survival.

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