Case of Treating Advanced Prostate, Bladder Double Primary Cancer with Anlotinib and Literature Review

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Abstract: Both prostate cancer and bladder cancer are common tumors in the genitourinary system[1]. While the incidences of both the two cancers are increasing, it is rare that the primary tumors of them occur at the same time in clinical practice .When both of them coexist at the same time, the treatment method will be complicated, and they often lose control after conventional treatment. Anlotinib is a novel small molecule multi-target tyrosine kinase inhibitor that inhibits vascular endothelial growth factor receptor, platelet-derived growth factor receptor, fibroblast growth factor receptor, stem cell factor receptor and other kinases.

1. Introduction

It has dual functions of anti-tumor angiogenesis and tumor growth inhibition, and has been clinically tested in multiple solid tumors, including non-small cell lung cancer, soft tissue sarcoma, gastric cancer, esophageal cancer, renal cancer, thyroid cancer, small cell lung cancer, colorectal cancer, etc., and have achieved certain results[2,3]. However, the treatment of prostate cancer and bladder cancer with anlotinib, especially for double primary cancer, has not been reported yet. One case of treatment of advanced double primary prostate cancer and bladder cancer with anlotinib in our hospital is reported below.

2. Clinical information

The patient, male, 61 years old, underwent B-ultrasound on 2016-11-5: multiple calcifications of the prostate, blood PSA 150ng/ml, FPSA 22.68ng/ml. 2016-11-8 making prostate puncture and postoperative pathology: prostate cancer, Gleason score of 8 points. 2016-11-15Pelvic MRI: prostate cancer, right suprapubic branch, upper left femur, partial acetabulum and humeral metastases; bilateral periorbital, pelvic mesangial lymphnodes enlargement . Bone scan: left humerus, upper left femur and right pubic symphysis concentrated foci, considering the possibility of metastasis. 2016-11-15, giving bicalutamide tablets 50mg 1 / day for endocrine therapy, zoledronic acid 4mg infusion for anti-bone metastasis therapy every 4 weeks. 2016-11-23 "Double orchiectomy". Radiation therapy for prostate cancer from 2017-05-10: DT 70Gy/35f. 2018-03-05 PET-CT: prostate cancer (see a high metastatic nodule in the left posterior, diameter 2.7cm, SUVmax=8.8) with retroperitoneal, right para-aortic and anterior sacral lymph node metastasis (SUVmax=8.5), multiple bone metastases (thoracic, bilateral tibia, right pubic symphysis and upper femur) showed osteogenic foci with increased FDG uptake, SUVmax=14.6). 2018-03-08 used docetaxel, prednisone chemotherapy for 3 cycles. Treatment with flutamide at 2018-06-13. 2018-07-09 CT showed tumor progression, and changed to abiraterone , prednisone from

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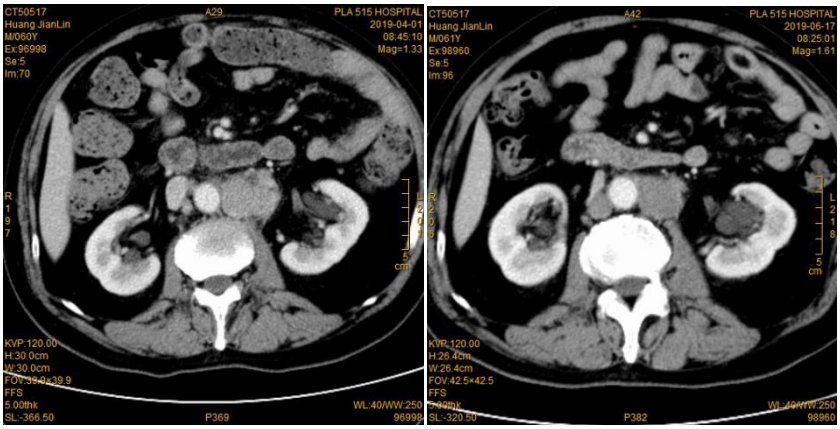
2018-07-16. 2018-09-10 CT: a slight increase in prostate lesions by the control of the front piece (2018.07.11), the lymph nodes enlarged in the abdominal pelvic cavity; the size of the bladder tumor was about 2.0cm × 2.0cm. The bladder occupational resection was performed, and the postoperative pathological diagnosis was myometrial invasive bladder urothelial carcinoma. 2018-10-19, 2018-11-16 used the chemotherapy regimen: Gemcitabine 1.8g d1, d8, cisplatin 130mg d2. 2018-11-26 CT showed tumor progression. In December 2018, abiraterone was discontinued. From 2019-01-21 begined enzalutamide treatment. Urinary incontinence symptoms appeared from 2019-02-04, 2019-02-19 CT showed that the tumor progressed, then stop enzalutamide oral. 2019-02-20 to 2019-04-30 TP regimen chemotherapy 4 cycles: paclitaxel liposome 210mg d1, cisplatin 60mg d1-2, during the period from 2019-04-04 to iropinib 12mg qd d1-14 Q3w treatment. 2019-06-17 Review of CT showed that the treatment of tumors was smaller than before, because the patient's tumor marker PSA was higher than before, and it was treated with anlotinib combined with flutamide 0.25g tid from 2019-06-18. 2019-08-12 patients with numbness and pain in the right lower extremity, CT scan: prostate cancer with bone, abdominal pelvic lymph node multiple metastasis after treatment changes, the control of the abdomen pelvic lymph nodes slightly increased; bone scan: multiple bones Increased intake, suggesting osteogenic metastasis. The flutamide was discontinued and continued to take anlotinib. From 2019-08-14, the right ankle joint metastasis gamma knife radiotherapy: 50% dose curve DT 500cGy × 5F, the patient's right lower limb numbness, pain relief after radiotherapy. Continued oral treatment with anlotinib until now. 2019-9-17 review CT: prostate cancer with bone, abdominal pelvic lymph node multiple metastasis treatment changes, control of the anterior pelvic lymph nodes decreased, each osteogenic metastases are similar, but PSA > 100.000ng / ml, Higher than before.

Appendix:

Comparison of curative effect of metastatic lymph nodes

Comparison 1:



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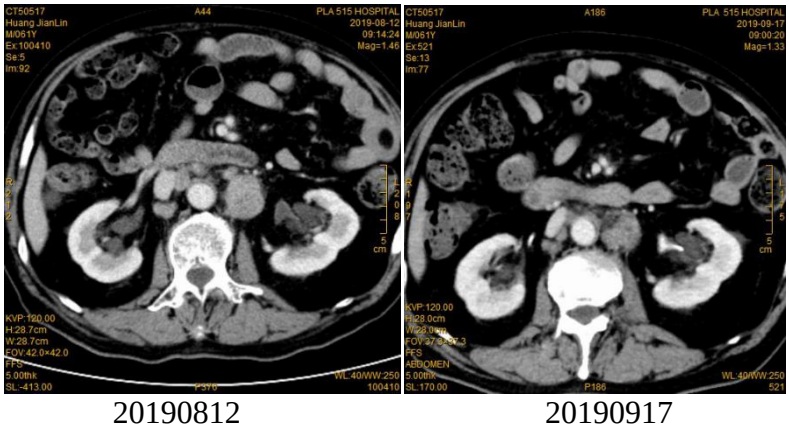

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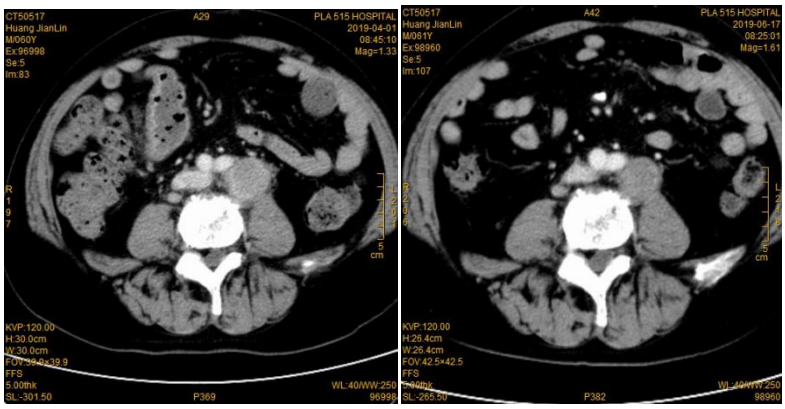
Comparison 2:



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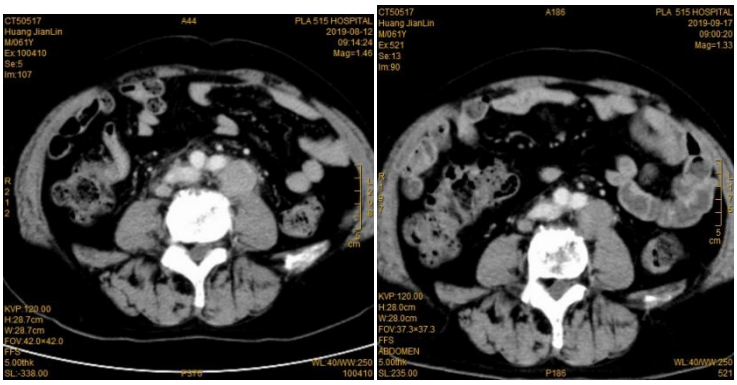

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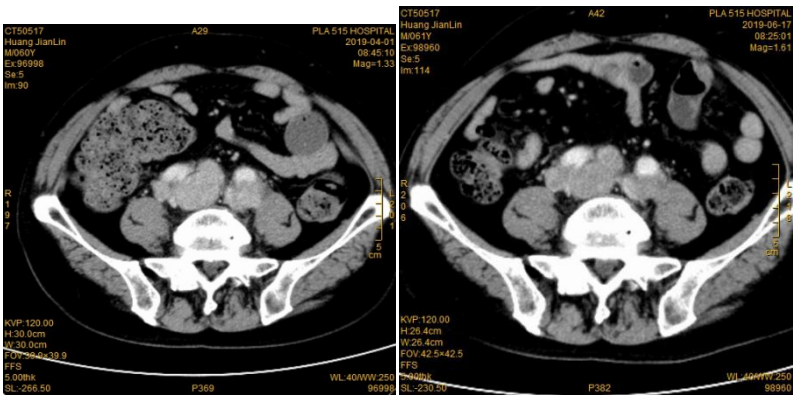
Comparison 3:



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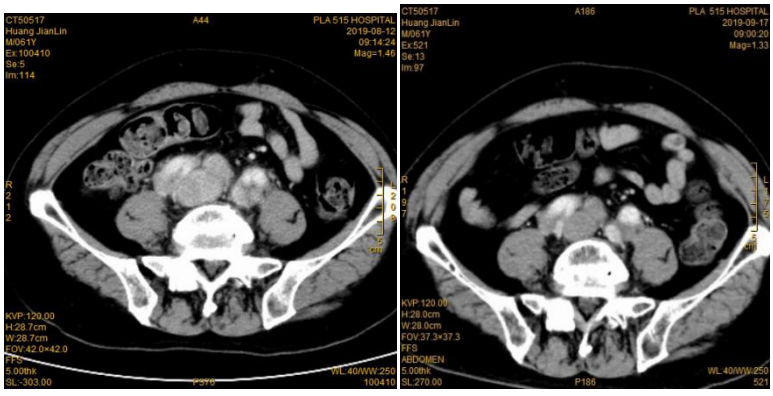

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3. Discussion

Prostate cancer is the most common tumor in men in Europe and America. In China, with the prolongation of life expectancy and the widespread application of PSA examination, the incidence rate has increased year by year, and currently ranks sixth in male tumors[4]. The treatment of

prostate cancer is mainly surgical treatment, radiation therapy, endocrine therapy and chemotherapy. Each treatment has its own indications and its own advantages and disadvantages. After all the above treatments, the tumor eventually loses control. Exploring a new treatment is imperative.

Bladder cancer is a common malignant tumor of the urinary system. The incidence rate in China is about 7/100,000, accounting for the second place in urinary tumors. It originates from the lining of transitional epithelial cells. Therefore, transitional cell carcinoma is the main pathological type, making up for about 90%, other rare types include squamous cell carcinoma, adenocarcinoma, small cell carcinoma, sarcoma and so on[4]. According to its clinical manifestations and prognosis, it can be divided into: superficial mucosa, muscle wall infiltration, and distant disseminated. The principle of treatment is mainly through surgery, radiotherapy, chemotherapy and other comprehensive treatments to control the tumor and preserve the bladder function as much as possible. Patients with distant metastasis will be treated with drugs, especially chemotherapy, in order to improve survival rate and prolong time to live.

Prostate cancer and bladder cancer are less likely to occur simultaneously or sequentially. A study by Moschini et al[5] showed that the cumulative incidence of bladder cancer in patients undergoing radical prostatectomy for 5 and 10 years was 0.75% and 1.26%; in patients receiving radiation therapy, the cumulative incidence of bladder cancer in 5 and 10 years was 1.63% and 2.34%, those who received radiotherapy had a higher incidence of bladder cancer than those who did not.

Two different origins of tumors, the characteristics of the disease and treatment methods have their own specific characteristics, generally conventional surgery, chemotherapy, radiotherapy, endocrine therapy often cannot take into account, the treatment effect is limited. Finding a treatment for the joint target of both has its practical significance.

Newborn tumor blood vessels provide various nutrients for tumor tissue and are essential for tumor growth and metastasis[6,7]. The main mechanisms regulating tumor angiogenesis include VEGFR, PDGFR and FGFR-mediated signaling pathways. The VEGFR-2 mediated signaling pathway is the most important and has the closest relationship with tumor angiogenesis[8]. Compared with other anti-angiogenic drugs, anlotinib can simultaneously inhibit three signaling pathways related to angiogenesis, completely block tumor angiogenesis, and also inhibit C-Kit-mediated signaling pathway and inhibit the occurrence and the development of various malignant tumors[9].

In this case, the patient is in advanced stage. After undergoing testicular excision for prostate cancer, endocrine therapy with bicalutamide, and radiotherapy for primary prostate, the lymph node of the abdomen is initially reduced, but resistance occurs one year or so. The effect of switching to flutamidee and abiraterone is not good. In September 2018, transurethral resection of bladder tumor was performed because of frequent urinary bladder cancer. The postoperative diagnosis of myometrial invasive bladder urothelial carcinoma, postoperative gemcitabine, cisplatin chemotherapy combined with enzalutamide endocrine therapy, the disease continues to progress (Abdominal lymph nodes, bladder masses reappear and increase), paclitaxel liposome, cisplatin chemotherapy three cycles to review the condition was stable, the fourth cycle of paclitaxel liposome, cisplatin chemotherapy began to combine with anlotinib. Because could not tolerate the side effect of chemotherapy, then stopped chemotherapy thus kept using anlotinib and add flutamide. The diameter of the lymph nodes metastasis in abdominal gradually kept shrinking, thus bladder carcinoma relatively stable, the level of PSA increasing, then stop flutamide, but anlotinib is still ongoing. The tumor shrinked again. During the course of the disease, zoledronic acid has been keeping on using for anti-bone metastasis. To relieve the pain caused by the bone metastasis of the sacroiliac joint , radiotherapy was carried out.

The initial treatment of patient is sensitive to endocrine therapy, suggesting that the lymph nodes of the abdominal cavity are derived from hormone-sensitive prostate cancer cells, and then there is drug resistance. It may be that hormone-resistant prostate cancer cells occupy a dominant position. Because patients also find bladder cancer at the same time, endocrine therapy insensitive, some of the enlarged lymph nodes in the abdominal cavity may be derived from bladder cancer cells.

Because the abdominal lymph node biopsy was not performed, the specific cause is difficult to determine. Because the efficacy of chemotherapy is not good and the side effect can not be tolerated, it is highly necessary to find a drug that can simultaneously target different sources of malignant tumors to control they further progress.

As an anti-angiogenic drug, anlotinib has a broad-spectrum anti-tumor effect, especially for angiogenic tumors. It has also shown good efficacy in lung cancer and alveolar soft tissue sarcoma, and entered into the guidelines of Chinese society of clinical oncology[10]. However, the treatment of prostate cancer, bladder cancer, especially the dual primary tumor patients have not been reported clinically. The author used anlotinib to treat the patient that got poor effect and intolerable side effect, and the patient has got relief for more than five months.

4. Conclusion

Anlotinib can be used to treate prostate cancer and bladder cancer, and the effect is satisfactory and the side effect is tolerable.

References

[1] Miao Yu, Fu Zhenyu, Sun Liguo et al. Clinical analysis of 9 cases of bladder cancer with prostate cancer [J], Jiangsu Medicine, 2015, 41 (17): 2074-2075.

[2] Wang Jun, Ran Fengming, Jin Bing. Clinical research progress of treatment with malignant tumor with anlotinib[J], Chinese Journal of Oncology, 2019,28(5):359-366

[3] Wang Ruiqing, Zhang Yanhua. Progress in clinical research of anti-tumor molecular targeting drug anlotinib[J], Chinese Journal of New Drugs, 2018,27(23):270-274

[4] Li Yexiong, ed. Radiation Therapy for Cancer [M]. Beijing: China Union Medical University Press, 2018: 1267-1340

[5] Moschini M, Zaffuto E, Karakiewicz PI, et al. External Beam Radiotherapy Increases the Risk of Bladder Cancer When Compared with Radical Prostatectomy in Patients Affected by Prostate Cancer: A Population-based Analysis [J]. Eur Urol, 2019, 75(2): 319-28.

[6] Jayson GC, Kerbel R, Ellis LM, et al. Antiangiogenic therapy in oncology current status and future directions [J]. Lancet 2016, 18(3): 321-323.

[7] El-Kenawi AE, El-Remessy AB. Angiogenesis inhibitors in cancer therapy: mechanistic perspective on classification and treatment rationales [J]. Br J Pharmacol, 2013,170(4): 712-729.

[8] Li J, Qin S, Xu J, et al. Apatinib for chemotherapy refractory advanced metastatic gastric cancer results from a randomized placebo controlled parallel arm phase IItrial[J]. J Clin Oncol, 2013, 31(26): 3219- 3225.

[9] Lin B, Song X, Yang D, et al. Anlotinib inhibits angiogenesis via suppressing the activation of VEGFR2, PDGFR and FGFR1 [J]. Gene, 2018, 654:77-86.

[10] China Society of Clinical Oncology Guidelines Working Committee Organized. Chinese Clinical Oncology Society (CSCO) soft tissue sarcoma diagnosis and treatment guidelines [M]. Beijing, People's Medical Publishing House, 2019: 80-84