

转移性前列腺癌伴恶性腹水一例报道

任尚青¹, 欧 勇¹, 李 安², 吕 倩¹, 钟 山³, 周 放¹, 范世达¹, 陈正军¹, 冯华林¹, 王 强¹,
罗 钺¹, 聂 钰¹, 何军娴¹, 王 东¹

(1. 四川省医学科学院·四川省人民医院机器人微创中心 四川 成都 610072;

2. 凉山彝族自治州第二人民医院泌尿外科 四川 西昌 615000;

3. 四川省医学科学院·四川省人民医院器官移植中心 四川 成都 610072)

摘 要 目前,临床上伴有胃转移、腹膜转移和恶性腹水的晚期前列腺癌很少见,且最佳治疗方案尚不清楚。本研究报道了一例伴有膀胱颈受累、盆腔淋巴结浸润的晚期前列腺癌患者,且肿瘤转移到骨、胃及腹膜等部位并伴有恶性腹水。前列腺癌腹膜转移和恶性腹水的预后极差,其主要的治疗方法为症状支持、腹膜穿刺引流、内分泌治疗和化疗。本研究通过报道一例伴有腹膜转移的晚期前列腺癌病例及回顾相关文献,为伴有恶性腹水的转移性前列腺癌临床研究提供参考借鉴。

关键词 前列腺癌;肿瘤转移;胃;腹膜;腹水

中图分类号 R697 **文献标识码** A **文章编号** 2096-7721 (2022) 02-0132-08

收稿日期: 2021-07-12 录用日期: 2021-11-10

Received Date: 2021-07-12 Accepted Date: 2021-11-10

基金项目: 电子科技大学·四川省人民医院“医工交叉联合基金”(ZYGX2021YGLH011)

Foundation Item: General Program of Medical Engineering Cross of Sichuan Provincial People's Hospital & University of Electronic Science and Technology of China(ZYGX2021YGLH011)

通讯作者: 王东, Email:wangdong_robot@163.com

Corresponding Author: WANG Dong, Email: wangdong_robot@163.com

引用格式: 任尚青, 欧勇, 李安, 等. 转移性前列腺癌伴恶性腹水一例报道[J]. 机器人外科学杂志(中英文), 2022, 3(2): 132-139.

Citation: REN S Q, OU Y, LI A, et al. Metastatic prostate cancer with malignant ascites: a case report[J]. Chinese Journal of Robotic Surgery, 2022, 3(2):132-139.

注: 任尚青, 欧勇为共同第一作者

Co-first Author: REN Shangqing, OU Yong

Metastatic prostate cancer with malignant ascites: a case report

REN Shangqing¹, OU Yong¹, LI An², LYU Qian¹, ZHONG Shan³, ZHOU Fang¹, FAN Shida¹, CHEN Zhengjun¹,
FENG Hualin¹, WANG Qiang¹, LUO Cheng¹, NIE Yu¹, HE Junxian¹, WANG Dong¹

(1. Department of Robotic Minimally Invasive Surgery Center, Sichuan Academy of Medical Sciences & Sichuan Provincial People's Hospital, Chengdu 610072, China; 2. Department of Urology, the Second People's Hospital of Liangshan Yi Autonomous Prefecture, Xichang 615000, China; 3. Department of Organ Transplantation Center, Sichuan Academy of Medical Sciences & Sichuan Provincial People's Hospital, Chengdu 610072, China)

Abstract At present, clinically advanced prostate cancer with gastric metastasis, peritoneal metastasis and malignant ascites is rare, and the optimal treatment is unclear. This study reported a case of advanced prostate cancer with bladder neck involvement, pelvic lymph node invasion, and metastasis to bone, stomach, peritoneum with malignant ascites. The prognosis of prostate cancer with peritoneal metastasis and malignant ascites is extremely poor, and the main treatment methods are symptomatic support, peritoneal puncture and drainage, endocrine therapy and chemotherapy. Herein, through a case report of advanced prostate cancer with peritoneal metastasis and the review of relevant literatures, a case of advanced prostate cancer with peritoneal metastasis was reported and relevant literature was reviewed to provide reference for clinical research of metastatic prostate cancer with malignant ascites.

Key words Prostate cancer; Tumor metastasis; Gastric; Peritoneal; Ascites

Prostate cancer is among the most common malignancies in men^[1], which poses a significant threat to public health. Worldwide, the incidence of prostate cancer ranks second among all male malignant tumors^[2]. With a well-arranged surveillance schedule and local treatment-based management, early-stage prostate cancer usually has a good prognosis, with the 5-year survival rate closing to 90%^[3]. At present, most newly diagnosed prostate cancer is locally advanced or extensively metastatic, and the patients cannot receive local radical treatment in China^[4]. The most common metastatic sites of metastatic prostate cancer are pelvic lymph nodes and bone, whereas tumor metastasis is uncommon to the stomach, peritoneum, and is not frequently

accompanied by malignant ascites. The patient's family gave consent to these studies and publication, and this report was approved by the Ethics committee of Sichuan Academy of Medical Sciences & Sichuan Provincial People's Hospital.

1 Case presentation

A 57-year-old male presented to the Department of Robotic Minimally Invasive Surgery Center complaining of frequent urination, urgency and dysuria, and the patient underwent transurethral resection of the prostate in July 2014. The postoperative pathological diagnosis revealed prostate adenocarcinoma (Gleason score 5+3=8). The patient underwent laparoscopic radical prostatectomy

after one year's combined androgen blockade (Bicalutamide+Goserelin), the definitive pathology report revealed prostate adenocarcinoma with a Gleason score of 5+4=9, and postoperative endocrine therapy was continued.

During the follow-up visit in February 2016, the patient underwent ultrasound examination and a mass was found in the bladder. The initial biopsy findings of the urinary bladder mass indicated poor differentiated carcinoma, and the transurethral resection of bladder tumor was performed. The postoperative pathological diagnosis revealed prostate adenocarcinoma metastasis. Subsequently, pelvic radiotherapy *stereotactic body radiation therapy* (SBRT) was performed for 36 times from May 2016 to June 2016, and regular follow-up was made. In June 2017, the patient was admitted to the hospital again due to abdominal distention. The CT examination showed a large amount of fluid in the abdominal cavity; The gastric wall of the cardia and the lesser curvature of the stomach was thickened and heterogeneous; The enlarged lymph node was identified in the abdominal cavity and retroperitoneum; Metastatic lesions were also found in multiple thoracic, lumbar, and sacral vertebrae (Figure 1). The operator repeated peritoneal drainage to collect pale yellow ascites, which were identified as abnormal cells that tended to be poorly differentiated cancer cells. The operator used docetaxel+prednisone chemotherapy and zoledronic acid for the prevention of bone related adverse events in the first phase of treatment, and the symptoms of abdominal distension were relieved and the patient's condition improved after one stage of treatment. In addition, chemotherapy (docetaxel+prednisone+cisplatin) from the second phase to the fourth phase was completed

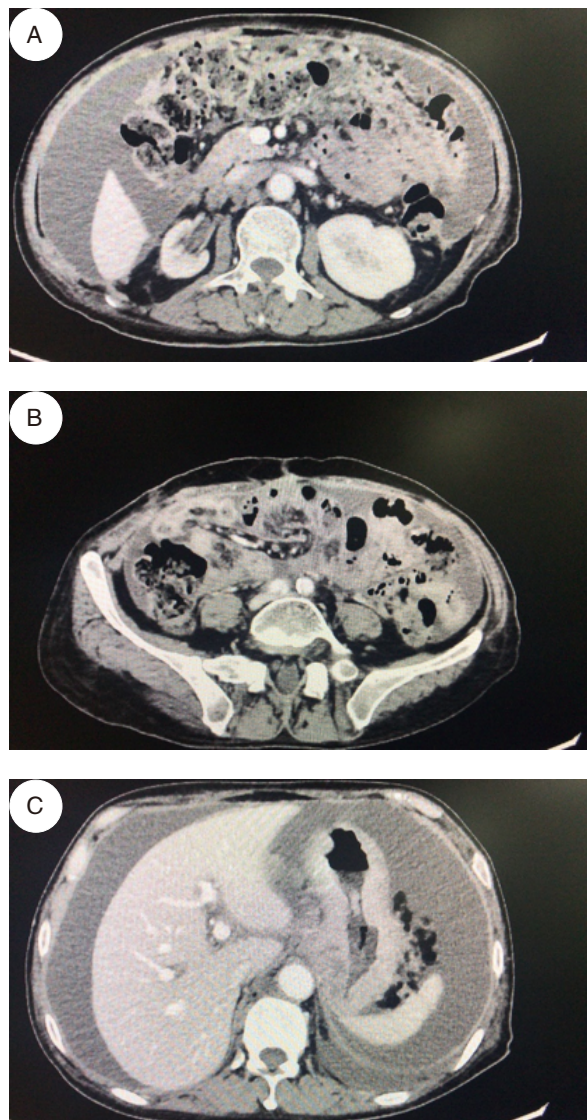


Figure 1 The patient's abdominal CT

A. Greater omentum and mesentery thickening with nodules; B. Parietal peritoneum thickening with nodules; C. Massive ascites.

from July 2017 to November 2017, with the addition of bevacizumab in the fourth phase. A gastroscopy was performed in December 2017, and multiple grayish neoplasms were observed in the bottom of the stomach and duodenal bulb. Immunohistochemistry of the biopsy showed pan-cytokeratin (PCK)(+), the epithelial membrane antigen(EMA) (+) and creatine kinase 7(CK7) (individual+), prostate specific antigen (PSA) (focal+), prosaposin (PSAP) (individual+),

androgen receptor (AR) (+) and CK20 (+), cluster of differentiation 56 (CD56)(+), caudal-related homeodomain transcription 2 (CDX-2) (-), paired box gene 8 (PAX-8) (-), which were considered as poorly differentiated prostate adenocarcinoma. Since then, the patient experienced multiple episodes of abdominal bloating exacerbation, accompanied by chest tightness and dyspnea. The patient eventually died of acute pulmonary edema in January 2018.

2 Discussion

The clinical manifestations of prostate cancer are various because it can metastasize to nearly every organ. In 1948, Arnheim first described the catalog of metastatic sites in patients with prostate cancer in a study of the autopsy results of 176 cases. The study founded the most common sites of metastasis of prostate cancer were bone, lymph nodes and lung. Rare metastases include adrenal glands, kidneys, brain, pancreas, genitals and breasts, malignant ascites or pleural effusion is extremely rare^[5]. In 2000, Bubendorf L et al. had reported 1 589 cases of prostate cancer suggested that 35% of the patients had blood-derived metastases, with the most common metastases in the bone (90%) and the less common metastases in the lungs (46%), liver (25%), pleura (21%) and adrenal gland (13%)^[6]. Skin, optic nerve, mandible, testicle, penis, pituitary gland, thyroid gland and salivary gland are some rare sites reported in the literature.

Peritoneal metastasis of prostate cancer with malignant ascites is rare, and only 20 cases have been reported in literatures^[7-25] (Table 1). The age of the patients ranged from 29 to 83 years, and

most of them had high-risk prostate cancer, with 6 cases of bone metastasis, 6 cases of lymph node metastasis, 1 case of rectal wall metastasis, 1 case of multiple visceral metastasis and 6 cases without other metastases (apart of peritoneal or omentum). Ascites was the first symptom in some patients, while the rest of the patients with ascites 1 to 16 years after the initial diagnosis. Among them, 3 cases presented with chylous ascites^[9,14,24], 1 case presented hemorrhagic ascites^[13], and the rest presented exudative ascites. 14 out of 20 cases received endocrine therapy or chemotherapy, and a total of 8 cases had responses, 5 cases responded to endocrine therapy, and 3 cases responded to chemotherapy. Responders lived for up to 18 months, while non-responders died within 1–4 months.

Gastric metastasis of prostate cancer is less common, and only a few reports suggest that metastatic prostate cancer affects the stomach^[26-34]. Most patients have varying degrees of upper gastrointestinal tract symptoms, such as nausea, vomiting, hematemesis and so on. On some occasions, the symptoms relieved in response to endocrine therapy or chemotherapy, but most patients had poor prognosis.

The pathogenesis of prostate cancer with ascites is still unclear, and the invasion of tumor cells into mesothelium is considered to be the main cause of peritoneal effusion. Rapoport A H et al.^[7] found that 13 of 523 cases of prostate cancer had peritoneal metastasis with peritoneal effusion, but no other metastases. However, studies of Broghamer W L Jr et al.^[35] suggest that prostate cancer with ascites may be caused by metastasis or reactive diseases, such as pancreatic cancer, lung cancer and gastric cancer. Megalli M R et al.^[36]

Table 1 Review of the literature of 20 cases with prostate cancer and ascites

Author/Year	Age	Other metastases (apart of peritoneal or omentum)	Treatment	Response of ascites to treatment	Outcome
Rapoport A H ^[7] 1968	76	Lymph nodes	5FU+thiotepa(intraperitoneal)	Progression	Death after 3 months
	45	Lymph nodes	Orchiectomy	Progression	Death
Megallli M R ^[8] 1973	58	None	Radiotherapy, Diethylstilbestrol	Remission	Alive within 6 months
Biegel Y ^[9] 1990	29	Bones	Refusal of therapy	Progression	Death after 1 months
Disdier P ^[10] 1990	78	None	Nilutamide	Remission	Normal
Catton P A ^[11] 1992	63	Lymph nodes, stomach, rectum, liver, spleen, adrenal gland, lungs, epicardium, pancreas	Orchiectomy, hormoneotherapy	Remission	Death after 15 months
Saif M W ^[12] 1999	70	None	None	Progression	Normal
Tsai J Y ^[13] 2001	68	Rectal wall	Interferon	Progression	Death after 4 months
Amin R ^[14] 2002	83	Lymph nodes	Hormonal withdrawal	Progression	Death after 18 weeks
Kehinde E O ^[15] 2002	76	None	TURP, Orchiectomy	Remission	18 months post-orchiectomy with no recurrent ascites
Lapoile E ^[16] 2004	80	Bones, others	None	Progression	Death after 4 months
Appalaneni V ^[17] 2004	60	Bones, Lymph nodes	Chemotherapy	Progression	Death after 6 weeks
Brehmer B ^[18] 2007	75	Lymph nodes	Goserelin, Bicalutamide	Remission	14 months without recurrence
Madaan S ^[19] 2007	75	Lymph nodes	Diethylstilboestrol	Progression	Death after 4 months
Zagouri F ^[20] 2009	75	None	Docetaxel	Remission	Normal
Benedict S P ^[21] 2010	67	None	Docetaxel	Remission	Normal
Ani I ^[22] 2013	57	Bones, Lymph nodes	Bicalutamide LHRH agonist	Stable disease	Normal
Petrakis D ^[23] 2015	76	Lymph nodes	Docetaxel	Remission	Alive within 10 months
Shimizu Y ^[24] 2015	72	Bones	Docetaxel	Progression	Death after 12 months
Papadatos S S ^[25] 2016	69	Bones	None	Progression	Death after 3 weeks

pointed out that ascites of prostate cancer can also be caused by second primary malignant tumors, of which gastrointestinal malignant tumors are the most common. Three cases of chylous ascites with diffuse lymph node metastasis had also been reported, which may be due to lymphatic hyperemia caused by a large number of cancer cells, resulting in chylous thorax and chylous ascites^[9, 14, 24].

It is crucial to judge the nature and etiology of ascites in these patients. Ascites may have multiple causes, it is necessary to distinguish metastatic ascites from ascites caused by other benign or malignant diseases, especially ascites caused by gastrointestinal tumors. Ascites exfoliated cells immunohistochemical staining, prostatic acid phosphatase, and prostate-specific antigen as specific markers can be used as an essential tool to identify malignant effusion^[12]. Peroxidase-antiperoxidase (PAP) immunohistochemical staining has specificity and sensitivity. PAP is positive in more than 95% of prostatic tissues and weak positive in about 3% of non-prostatic tissues, and PSA may also exist in anaplastic tumor cells with low PAP activity^[28]. The combination of PSA and PAP improves the sensitivity of diagnosis of prostate metastases. Therefore, the detection of ascites specific markers and the application of exfoliated cell immunohistochemical staining are helpful to differentiate ascites.

Abdominal distension, abdominal pain, and respiratory distress can be alleviated through ascites management, diet, diuresis, puncture, and drainage. Some patients may be relieved by endocrine therapy or chemotherapy. These therapies may prolong life expectancy and improve the quality of life. However,

the prognosis is poor, and most patients die within weeks to months.

In this study, the patient presented similar clinical manifestations. Ascites occurred three years after the diagnosis of prostate cancer. During this period, the patient received endocrine therapy. The presence of peritoneal metastasis, multiple lymph node metastasis, bone metastasis and gastric metastasis in the patient was confirmed by CT, ascites exfoliative cytology and gastroscopic biopsy. After the diagnosis of ascites, the patient underwent abdominal puncture and drainage, and was treated with docetaxel, cisplatin, and bevacizumab. However, the patient died of acute pulmonary edema in January 2018.

3 Conclusion

The prognosis of prostate cancer with peritoneal metastasis and malignant ascites is extremely poor. The main treatment modalities of this patient were symptomatic and supportive care, peritoneal puncture and drainage, endocrine therapy, radiotherapy and chemotherapy, etc. Patient distress could be relieved and patient's life be prolonged by these therapies. However, gastric and peritoneal metastatic prostate cancer is uncommon in clinical practice, and its treatment needs to be further optimized and explored.

Declaration

Availability of data and materials

All the data and material are from the patient's assay and examination of Sichuan Academy of Medical Sciences & Sichuan Provincial People's Hospital, which are real, credible and for availability.

Competing interests

The authors declared no potential conflicts of

interest with respect to the research, authorship and/or publication of this article.

Authors' contributions

REN Shangqing and OU Yong was responsible for writing and editing the article; LI An, ZHONG Shan, ZHOU Fang were responsible for reviewing the literature; LYU Qian, FAN Shida, CHEN Zhengjun, FENG Hualin, WANG Qiang, LUO Cheng, NIE Yu, HE Junxian were responsible for collecting the information of the current case. WANG Dong were responsible for the revision of the manuscript for important intellectual content. All authors have read and approved the manuscript.

Acknowledgements

I would like to show my gratitude to Dr. WANG Dong who has provided me with valuable guidance to this article.

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欢迎投稿 欢迎订阅 欢迎指导