

Metastatic prostate cancer presenting as generalized lymphadenopathy and progressing with inferior vena cava syndrome: A case report and literature review

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Abstract. The present study describes the case of a 71-year-old male patient that presented with generalized lymphadenopathy and a pelvic mass, but no signs of bone and visceral metastasis. Their total prostate-specific antigen level was >100 ng/ml. A biopsy of the pelvic mass, situated near the left iliac vessels, confirmed the existence of an adenocarcinoma originating from the prostate and a subsequent prostate biopsy indicated a Gleason score of 4+5. Endocrine treatment with bicalutamide and goserelin (androgen deprivation therapy) resulted in only a partial response of the left iliac metastatic lesions to the treatment. The subsequent treatment plan of androgen deprivation therapy and abiraterone plus docetaxel did not change the progression of the disease. The patient finally developed inferior vena cava syndrome. Subsequently, the patient declined both a re-biopsy of the prostate and enlarged cervical lymph nodes, and interventions by a vascular surgeon. To the best of our knowledge, the present study is the first documented case of a natural progression of metastatic prostate cancer with inferior vena cava syndrome.

Introduction

Metastatic prostate cancer presenting at initial diagnosis as a large pelvic mass with generalized lymphadenopathy is rare;

without prostate-specific antigen (PSA) screening, this can easily be mistaken for lymphoma (1). The occurrence of acute inferior vena cava syndrome, due to the progression of metastatic lymph nodes around the abdominal aorta and inferior vena cava, is also rare, with only three cases (2,3) documented in two references and no records regarding its natural progression. The present study describes a case of metastatic prostate adenocarcinoma, which manifested as generalized lymphadenopathy and ultimately led to death of the patient from acute inferior vena cava syndrome. A literature review in 2005 revealed that, in the MEDLINE database, there were only nine patients with prostate cancer who had initially presented with generalized lymphadenopathy (4). Most researchers consider Gleason scores a notable determinant of adenocarcinoma prognosis (1,5,6). The presence of generalized lymph node metastases does not influence the response of prostate cancer to androgen deprivation therapy (ADT) (5). To the best of our knowledge, the present study is the first to report on a case where metastatic lesions exhibited only a partial response to ADT in this type of prostate adenocarcinoma. Furthermore, this case is the first to detail the natural progression of metastatic prostate cancer with inferior vena cava syndrome.

Case report

A 71-year-old male patient presented with bilateral waist pain persisting for ~20 days and was admitted to the West China School of Public Health and West China Fourth Hospital (Chengdu, China), as a result, in February 2023. Although the patient experienced minor discomfort due to frequent urination, they had no notable difficulty urinating. Upon physical examination, substantial enlargement of the prostate and supraclavicular lymph nodes was observed. A series of routine tests was performed, including a routine urine and blood test, liver and kidney function tests, electrolyte level detection and coagulation profiling. Additionally, etiological screenings for pathogens, such as human immunodeficiency virus, syphilis and hepatitis B were performed. Each test yielded no marked abnormalities; however, the creatinine level was 133 μ mol/l (the normal reference range, 57-111 μ mol/l).

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Computed tomography (CT) with intravenous contrast of the chest and abdomen revealed multiple enlarged lymph nodes in the mediastinum, the bilateral supraclavicular fossa, inguinal regions, and surrounding the abdominal aorta, inferior vena cava, and both iliac arteries and veins. A mass was discerned between the prostate and the posterior wall of the bladder, along with bilateral renal hydronephrosis. Additionally, another mass measuring 8.9x4.1x6.3 cm was discovered adjacent to the left iliac vessels, as shown in Fig. 1. No signs of bone or visceral metastasis were observed. A cystoscopic examination revealed tumor invasion on the neck and trigone of the bladder, and both ureteral orifices were unobservable. The protruding mass was characterized by a smooth urothelial mucous membrane covering its surface. The absence of discernible bladder tumor characteristics, coupled with the anomalous prostate morphology and enhancement properties in the CT scan, primarily raised suspicions of prostate cancer infringing upon the neck and trigone of the bladder. PSA screening was subsequently performed and the total PSA level was >100 ng/ml (normal reference range, 0-4 ng/ml).

A biopsy of the large pelvic mass near the left iliac vessels was conducted, whereupon the puncture specimen revealed the presence of prostate-derived adenocarcinoma based on the findings of immunohistochemical (IHC) analysis. IHC analysis, performed as previously described (7), yielded the following profile: PSA (+), P504S (+), Nkx3.1 (+), INSM1 (-), CgA (low +), Syn (low +), P53 (+), ERG (-), Ki-67 (+, ~30%) (Fig. 2). In addition, hematoxylin and eosin (H&E) staining was performed according to a previously described protocol (7). Subsequently, bilateral renal drainage, and ADT treatment with bicalutamide (50 mg, orally administered, daily) and goserelin (10.8 mg, subcutaneous injection, once every 12 weeks) were commenced. An ultrasound-guided biopsy of the prostate, conducted at a different institution (Sichuan Modern Hospital, Chengdu, China), yielded a Gleason score of 4+5, according to the findings of H&E and IHC staining; this follows the 2014 International Society of Urological Pathology guidelines on Gleason Grading of Prostatic Carcinoma (8) (Fig. S1). After 3 months of treatment, the PSA levels declined to 6.96 ng/ml; however, they increased slightly to 7.85 ng/ml within 6 months. A follow-up abdominal CT scan with contrast revealed a notable reduction in the pelvic mass, but enlargement of the prostate lesion area and lymph nodes around the right iliac vessels (Fig. 3). In the venous phase of CT imaging, there was no enhancement observed in the segment of the inferior vena cava, spanning from the plane of the right renal vein to the bilateral external iliac veins. Additionally, multiple enlarged lymph nodes compressed these veins, indicating potential thrombosis within the lumen (Fig. 4). Consequently, on the basis of ADT treatment, the medication regimen was amended to goserelin (10.8 mg, subcutaneous injection, once every 12 weeks), abiraterone (1,000 mg, orally administered, daily), prednisone (5 mg, orally administered, twice a day) and docetaxel (120 mg, intravenously, every 3 weeks) with an anticoagulant (rivaroxaban; 20 mg, orally administered, once daily). After one treatment cycle, the PSA levels decreased to 5.34 ng/ml. However, the patient developed severe leg swelling, accompanied by a rapid and significant enlargement of the cervical lymph nodes after 2 weeks of this treatment. It was recommended that the patient undergo a re-biopsy of the

prostate and enlarged cervical lymph nodes, and interventions by a vascular surgeon were suggested; however, the patient declined due to previously unsatisfactory treatment outcomes and their limited financial resources. Within the next 3 weeks, the patient succumbed to severe pulmonary infection that exacerbated inferior vena cava syndrome-induced heart failure, ultimately causing circulatory collapse.

Discussion

The lymph nodes in the pelvic region are the most common sites for lymphatic metastasis in prostate cancer, followed by the periaortic lymph nodes. By contrast, the involvement of cervical and supraclavicular lymph nodes is rare (9). A literature review in 2005 revealed that in the MEDLINE database, there were only nine patients with prostate cancer who had initially presented with generalized lymphadenopathy (4). Furthermore, the present literature review, which used the PubMed database (pubmed.ncbi.nlm.nih.gov) to identify cases of prostate adenocarcinoma that initially presented with generalized lymphadenopathy over the past 20 years, identified 19 cases (5,10-22). The mechanism of lymph node metastasis may proceed as follows: The prostatic venous plexus, along with veins in the chest, abdomen and pelvis, may facilitate metastasis to the pelvic and periaortic regions. The potential pathway for metastasis to mediastinal and supraclavicular lymph nodes may involve upwards spread to the cisterna chyli and thoracic duct (1). Previous studies have suggested that neuroendocrine differentiation of prostate cancer, such as small cell and large cell prostate cancer, may initially present with generalized lymphadenopathy, with or without visceral metastases at diagnosis (23-25). Notably, metastatic prostate cancer presenting as generalized lymphadenopathy needs to be differentiated from malignant lymphoma. In the present case, at the initial consultation, the patient exhibited generalized lymphadenopathy without accompanying fever or weight loss. Alongside the enhanced CT findings at the initial visit, the differential diagnosis suggested metastatic urothelial carcinoma. Since bladder cystoscopy showed no typical characteristics of a urothelial tumor in the patient, prostate cancer was suspected, due to the mass protruding from the prostate into the bladder, which led to the invasion of the bladder trigone and the inability to identify the bilateral ureteral orifices. In addition, PSA screening indicated that the primary lesion may have originated from the prostate. Nevertheless, the large pelvic mass isolated from the prostate and adjacent to the left iliac vessels required further examination. Consequently, a biopsy of this mass was performed.

The final pathological findings confirmed that the primary prostate cancer had metastasized to the left iliac lymph node, resulting in a sizeable mass. Previous studies have documented some instances of subclavian vein thrombosis resulting from metastatic lymph node enlargement (26) and episodes of acute superior vena cava syndrome (27). Acute inferior vena cava syndrome is rare in metastatic prostate cancer; to the best of our knowledge, there have been only three documented cases (2,3). Kasimis *et al* (3) reported on the clinical features of two instances of inferior vena cava syndrome, but did not document the natural progression. Makusha *et al* (2) applied vascular stents to the patient with acute inferior vena cava syndrome, enabling effective relief of the obstruction and restoration of blood circulation.

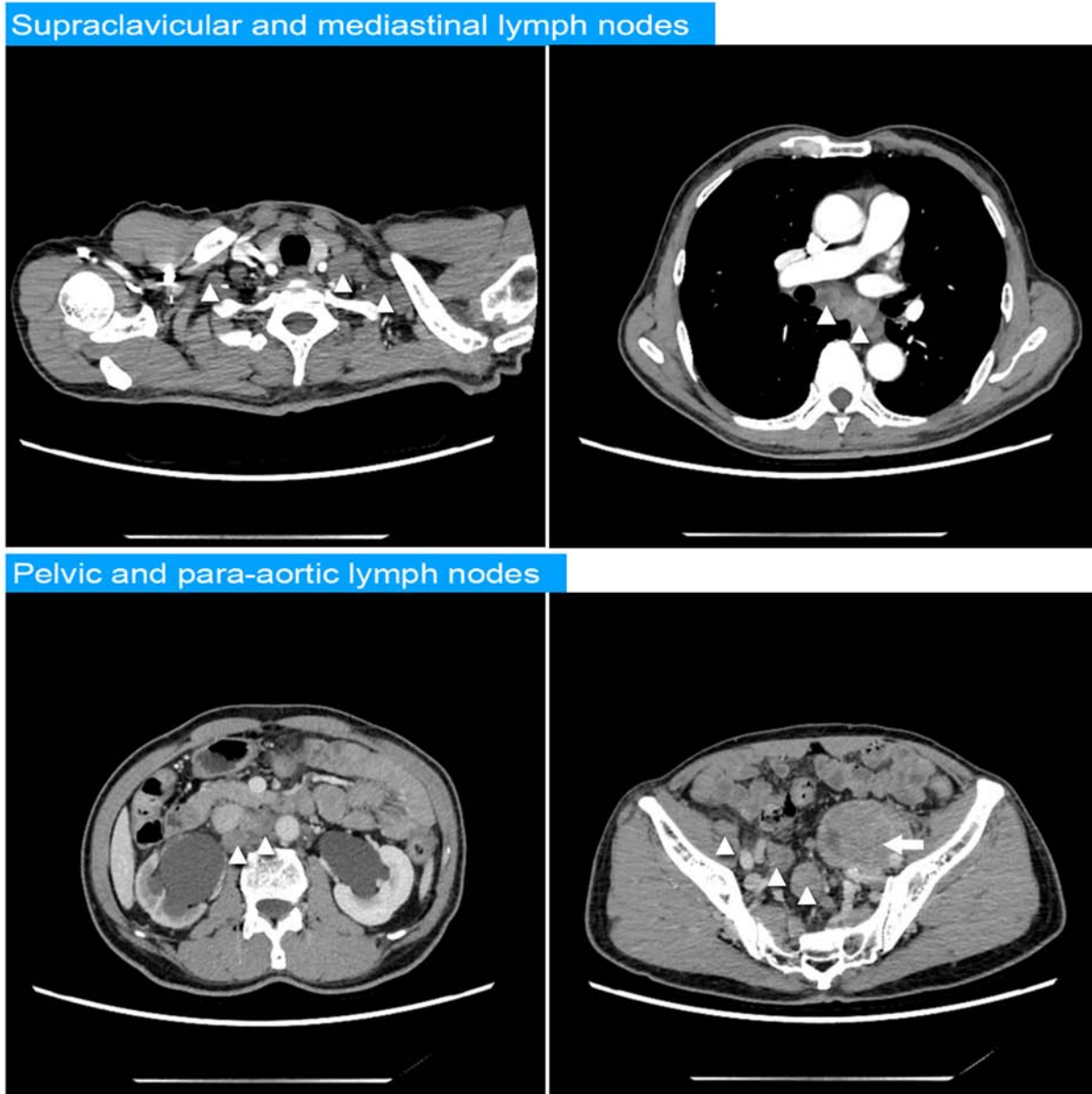


Figure 1. Generalized lymphadenopathy and the pelvic mass are shown on enhanced computed tomography arterial phase images; the arrow indicates the pelvic mass, and triangles indicate enlarged lymph nodes.

Considering the rapid progression of the disease and the ineffectiveness of therapies, the patient in this case chose a relatively palliative course of medication treatment: anticoagulation. The swelling in the lower extremities and scrotum progressively worsened over the next 3 weeks, accompanied by limited mobility, a large amount of skin exudation, infection and ulceration. Eventually, the patient died of circulatory failure induced by severe pulmonary infection and non-congestive heart failure.

An initial diagnosis of prostate cancer, accompanied by generalized lymphadenopathy, typically characterizes a cluster of markedly heterogeneous tumors. The limited data currently available suggest that these could include a variety of pathological types, such as adenocarcinoma (20), the co-existence of adenocarcinoma and small cell carcinoma (28), small cell carcinoma (23,29), large cell carcinoma (30), and the co-existence of adenocarcinoma and giant cell carcinoma (25). Notably, data on the prognosis of these cases are scarce. Nevertheless, most

researchers (1,5,6) consider the Gleason score in adenocarcinoma as a significant determinant of prognosis. The presence of generalized lymph node metastases does not influence the response to hormonal therapy, according to the previous studies (1,5,6). According to the present literature review, Gleason scores mainly range between 7 and 10 (1,5,6). In addition, neuroendocrine differentiated types of prostate cancer are often associated with generalized lymphadenopathy, and they exhibit no response to hormonal therapy, demonstrating a reaction to platinum-based chemotherapy instead (31). The prognosis and survival rates of these types of prostate cancer are poor (23). In the present case, a portion of the tumor tissue demonstrated a response to endocrine therapy. The enhanced CT scans, performed 6 months prior to and following endocrine therapy, demonstrated a notable decrease in the pelvic mass around the left iliac artery. Concurrently, a notable increase in metastatic lesions was observed surrounding the right iliac

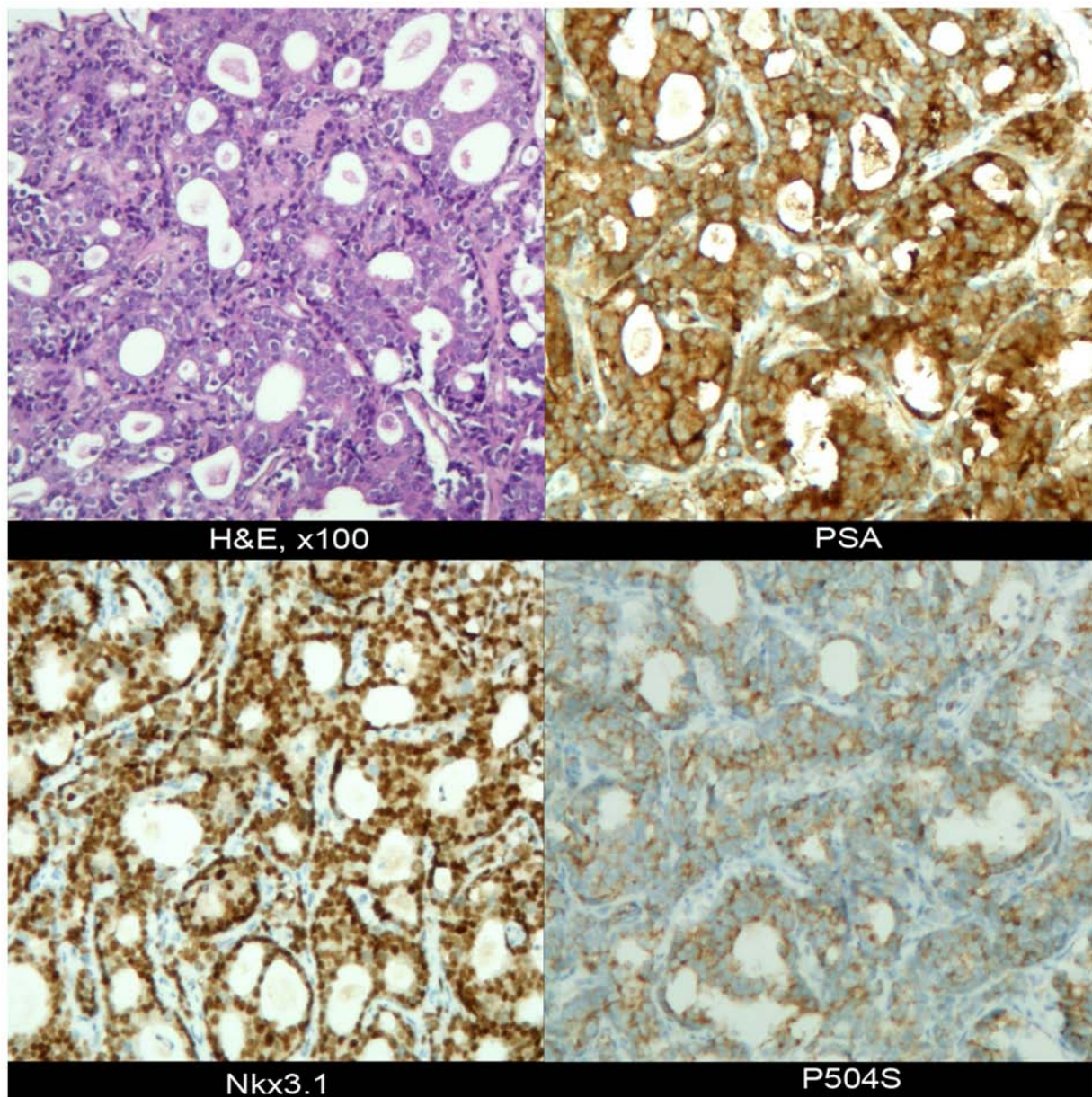


Figure 2. Pathological findings of the pelvic mass, as determined by H&E staining and immunohistochemistry (x100 magnification). H&E, hematoxylin and eosin; PSA, prostate-specific antigen.

artery and the abdominal aorta, alongside an enlargement of the primary prostate malignancy. A total of 6 months into the regimen, the PSA levels of the patient decreased from >100 to 7.85 ng/ml; however, imaging findings showed a marked progression of disease. Considering that the existing literature indicates a positive response to endocrine therapy in cases of prostate adenocarcinoma with generalized lymphadenopathy (5,6), the present study may be the first to report on a case where only some of the metastatic lesions in this type of prostate adenocarcinoma exhibited a response to ADT treatment. Current PEACE-1 (32) and ARASENS (33) studies have stipulated that the combination of ADT, neoadjuvant hormonal therapy and docetaxel may improve metastatic prostate cancer overall survival. In the present case, based on the ADT treatment with goserelin, the treatment plan was adjusted to goserelin, abiraterone and docetaxel with the PSA levels decreasing to 5.34 ng/ml, thus exhibiting a PSA response. However, the left

cervical lymph nodes rapidly increased in size, thus suggesting a heterogeneity in the malignant lesions and indicating that the treatment plan was ineffective for this potentially heterogeneous tumor. In prostate cancer, the most common type of differentiation is into neuroendocrine differentiated tumors. Notably, it is unclear if the primary tumor lesion was a heterogeneous tumor before or after ADT treatment. The patient refused to undergo a further cervical lymph node or prostate biopsy. Without further pathological support, platinum-based chemotherapy, which has been reported to benefit neuroendocrine differentiated tumors (31), was not administered. Eventually, the patient suffered from rapid progression of metastatic lymph nodes around the inferior vena cava, leading to inferior vena cava syndrome, and died from circulatory failure induced by a severe pulmonary infection and heart failure.

The clinical significance of the present case report is to document a case of metastatic prostate cancer initially presenting

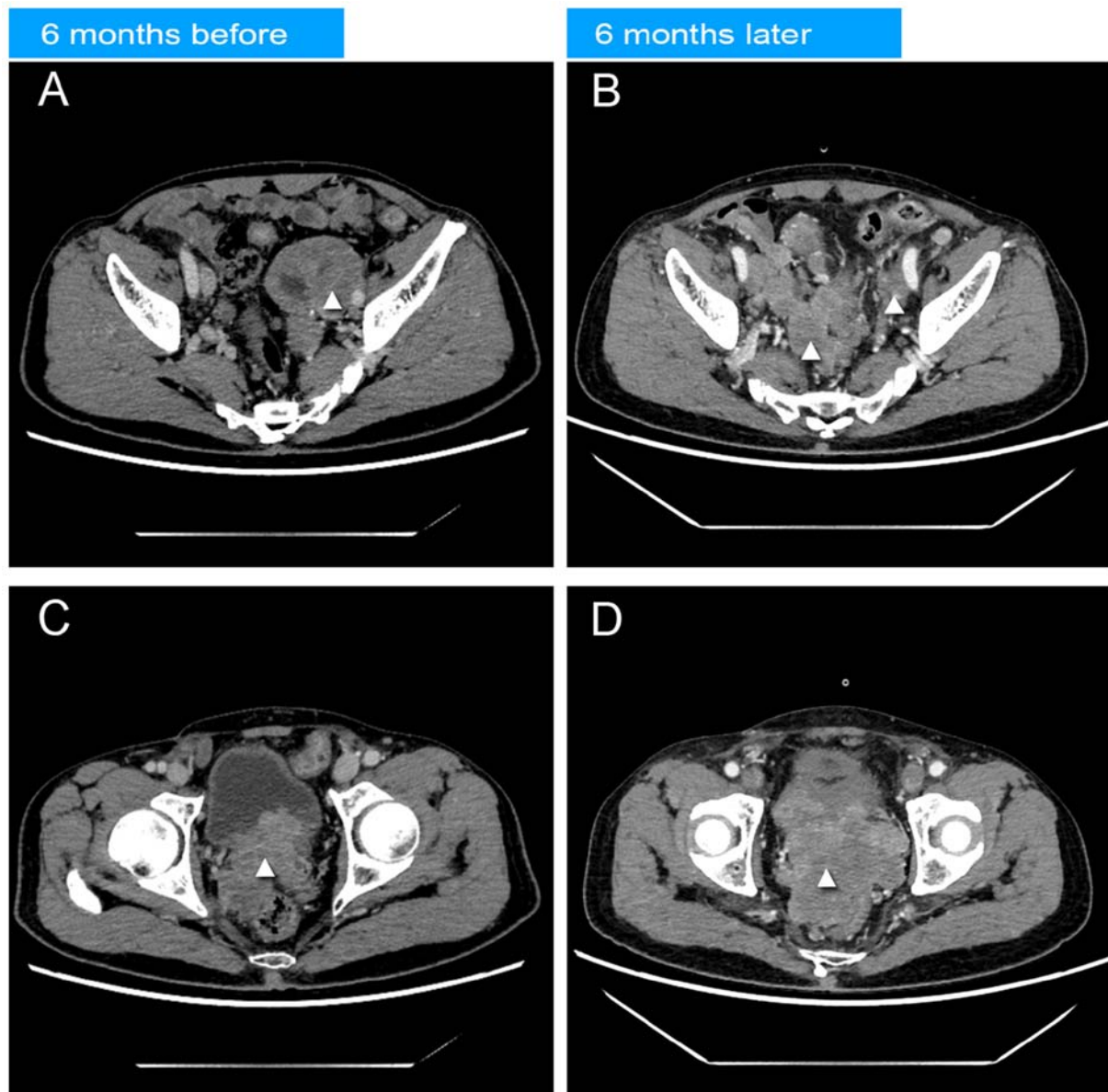


Figure 3. Enhanced computed tomography arterial phase images. The tumor lesion adjacent to the left iliac vessels diminished in size after 6 months of treatment, as illustrated in the transition from (A) to (B). The neoplastic lesions within the right pelvic region and the prostate exhibited growth, as evidenced from (C) to (D). Triangles indicate the tumor lesion.

as generalized lymphadenopathy, and to recommend vigilance regarding the concurrent presence of heterogeneous tumors, specifically those with neuroendocrine differentiation. To the best of our knowledge, the present study is the first to report on a case where only some metastatic lesions in this type of prostate adenocarcinoma exhibited a response to ADT treatment. The present study indicated that in the initial evaluation of the efficacy of endocrine therapy, combining PSA detection with imaging evaluation should be recommended, and that imaging assessment is indispensable in this type of prostate cancer. Furthermore, when there is no response, or only a partial response, of lesions to endocrine therapy, it is recommended that a re-biopsy be conducted of the prostate or metastatic lesions. Genetic testing of tumor tissue or circulating tumor cells may also provide relevant information. In particular, a re-biopsy of different sites can provide more detailed and comprehensive pathological results than prior specimens, such

as enlarged cervical lymph nodes or prostate tissues in this case. A re-biopsy at the identical site within a short space of time has no clinical value. Furthermore, to the best of our knowledge, the present case is the first to detail the natural progression of metastatic prostate cancer with inferior vena cava syndrome. This pathophysiological transformation resulted in an unfavorable survival prognosis for the patient, requiring immediate intervention. The present study provides an important prognostic and therapeutic reference for similar clinical conditions, and therefore may have clinical value. Finally, the literature review, from a pathological perspective, indicated that this specific type of prostate cancer is often comprised of a group of highly heterogeneous tumors. This insight provides a theoretical basis for our improved understanding of this specific type of prostate cancer, and the formulation of effective treatment strategies and subsequent follow-up plans. The currently available data are limited; therefore, more detailed

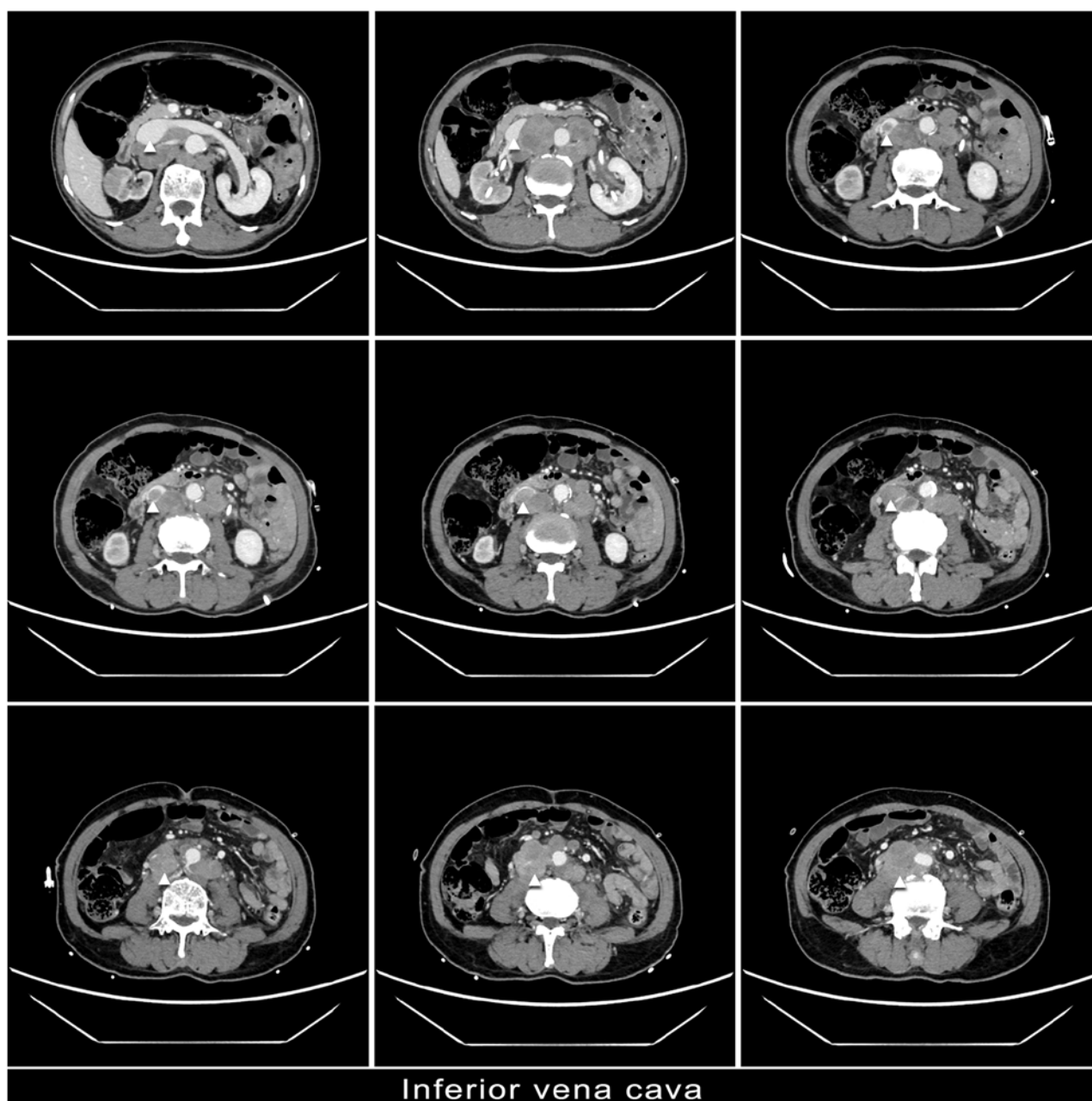


Figure 4. Enhanced computed tomography venous phase images. No enhancement was observed in the segment of the inferior vena cava, spanning from the plane of the right renal vein to the bilateral external iliac veins. Triangles indicate the inferior vena cava.

and similar studies on this specific disease in the future may verify the aforementioned conclusions.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

WW, CG, RW, XL, YL, GC, RR and FL were involved in data collection. WW, XL and RW contributed to the review of case materials, analyzed data and drafted the manuscript. CG developed the patient treatment strategies and established the follow-up protocols. WW, XL, RW and CG confirm the authenticity of all the raw data. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

The study was conducted according to the guidelines of The Declaration of Helsinki. The performance and publication of this study was approved by the Ethics Committee

of West China School of Public Health and West China Fourth Hospital, Sichuan University (Chengdu, China; approval no. HXSJ-EC-2024058). Written informed consent was obtained from the patient's family.

Patient consent for publication

Written informed consent was obtained from the patient's family for publication of the data and images in this case report.

Competing interests

The authors declare that they have no competing interests.

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