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Annals of Urology

ISSN 2767-2271

Case Report

Sustained Partial Response Of Metastatic Castration-Resistant Prostate Cancer With Bilobar Hepatic Involvement Treated With Intra-Arterial Hepatic Chemotherapy: A Case Report.

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Abstract

Metastatic castration-resistant prostate cancer (mCRPC) with liver metastases often has poor outcomes with conventional therapies showing limited effectiveness. This case report describes a 59-year-old man with mCRPC and extensive liver metastases who achieved a partial response through Intra-Arterial Hepatic Chemotherapy (IAHC). After progressing on standard hormonal therapy, radiotherapy, and two lines of chemotherapy, he received 12 cycles of IAHC with Carboplatin and Epirubicin, resulting in a 10-month progression-free survival (PFS). Further hepatic progression led to subsequent trans-arterial chemoembolization. Despite initial stability, disease progression occurred, leading to palliative care. The overall survival (OS) was 26 months from the onset of liver metastases. This case suggests IAHC may be a valuable option for selected mCRPC patients with liver metastases when conventional treatments fail, warranting further research.

INTRODUCTION

Prostate cancer is the second most common cancer among men worldwide. Despite advances in diagnosis and treatment, metastatic disease remains a therapeutic challenge, particularly when progressing to castration resistance. Hepatic metastases are a rare but severe manifestation of advanced prostate cancer, often associated with poor prognosis. In this report, we present a case of a patient diagnosed with mCRPC with bilobar hepatic involvement who sustained partial response after receiving IAHC.

CASE DESCRIPTION

In November 2020, an asymptomatic 59-year-old Caucasian man underwent prostatic biopsy for an elevated PSA level of 129 ng/ml. He was diagnosed with prostate acinar-type adenocarcinoma with a Gleason Score of 7 (4+3).

Patient's clinical conditions were good (ECOG PS 0) and his previous medical history was unremarkable.

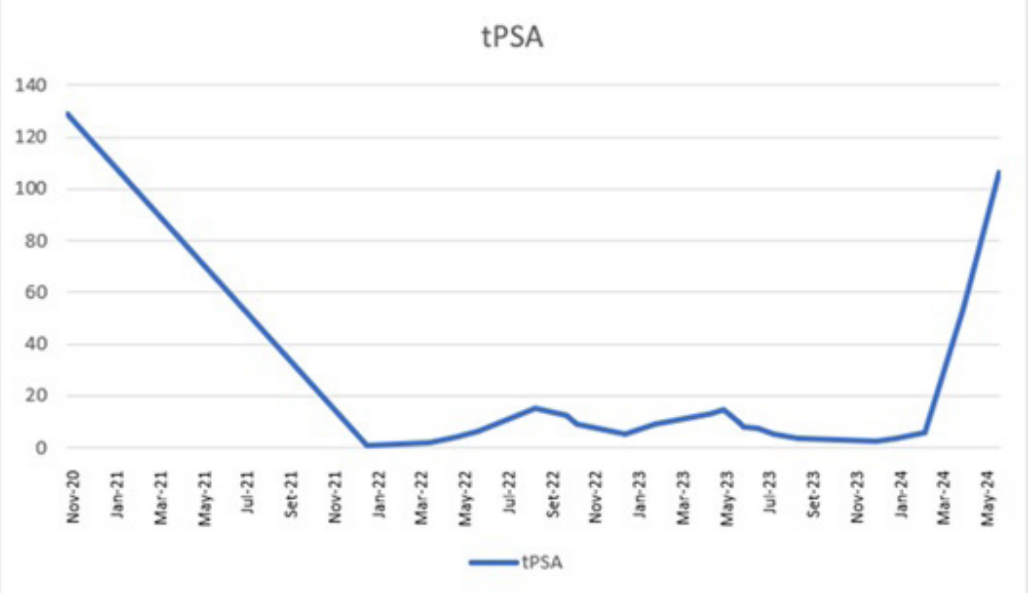
Contrast-enhanced total body CT scan showed enlargement of the prostate gland, invasion of bladder and distal sigma, involvement of regional lymph nodes and excluded the presence of distant metastases. Bone metastases were also excluded with bone scan.

Based on these findings, in December 2020 patient referred to Radiotherapy Department and initiated hormonal therapy with LHRH analogue (Leuprorelin acetate, 11,25 mg every 3 months) and antiandrogen (Bicalutamide, 50 mg/die). From May to July 2021, he underwent External Beam Radiation Therapy (EBRT) on prostate and seminal vesicles (60 Gy in 20 fractions) and on regional lymph nodes (44 Gy in 20 fractions). The nadir of PSA level was reached in January 2022 (0,96 ng/ml). In April 2022, patient referred to Emergency Department

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Received: 29-Mar-2025, Manuscript No. AOU-4700 **; Editor Assigned:** 01-Apr-2025 **; Reviewed:** 21-Apr-2025, QC No. AOU-4700 **; Published:** 30-Apr-2025, **DOI:** 10.52338/aou.2025.4700
Citation: Paola Pacetti, MD. Sustained Partial Response of Metastatic Castration-Resistant Prostate Cancer with Bilobar Hepatic Involvement Treated with Intra-Arterial Hepatic Chemotherapy: A Case Report. Annals of Urology. 2025 April; 10(1). doi: 10.52338/aou.2025.4700.
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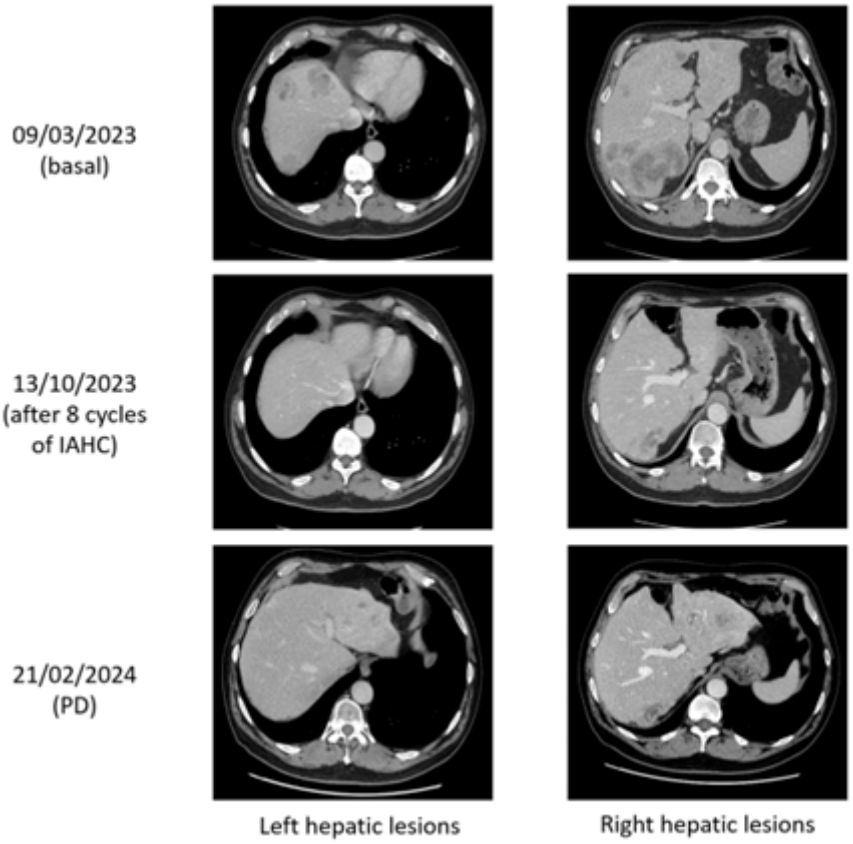
presenting with right iliac fossa pain, prompting an abdominal ultrasound, which revealed hepatic lesions.
Contrast-enhanced total body CT scan confirmed multiple bilobar hepatic lesions, the major ones located in segment IV and VI, and showed for the first time extra-regional abdominal lymphadenopathies.
A liver biopsy performed in May 2022 confirmed the localization of prostatic adenocarcinoma, so patient was addressed to our Oncologic Department in June 2022. Considering the radiological findings and the progressive PSA elevation from April to June 2022 (**Table 1**), the diagnosis of metastatic castration-resistant prostate cancer was made.

Table 1. Total PSA levels from November 2020 to May 2024.



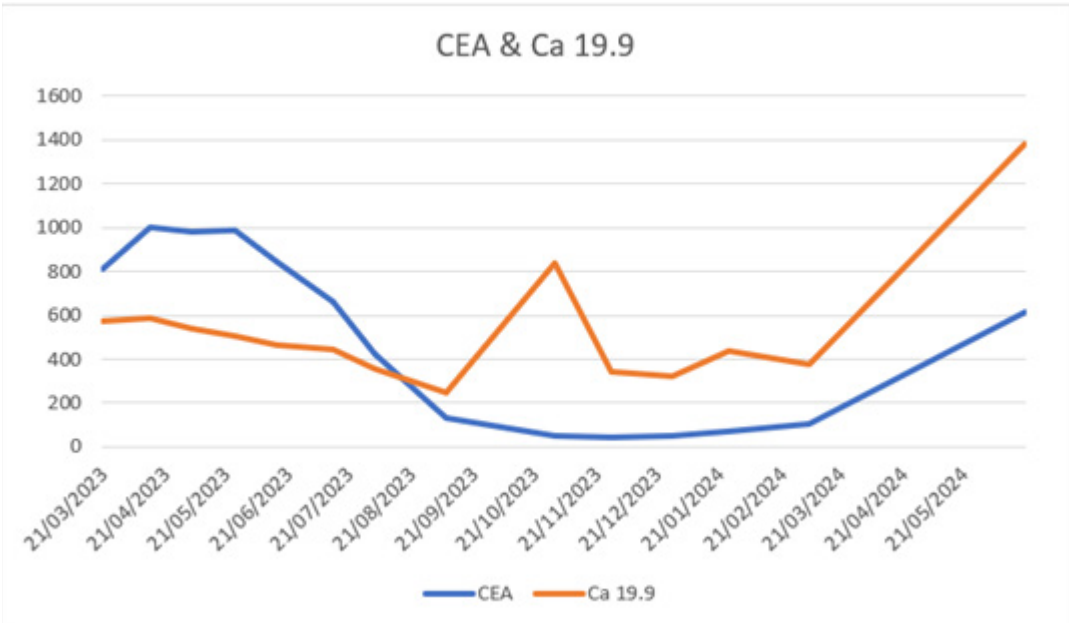
Considering the relatively young age of the patient (61-year-old), the good clinical conditions and the presence of visceral disease, a first-line chemotherapy with Docetaxel 75 mg/mq every 3 weeks was initiated. Bicalutamide was discontinued, while Leuprorelin acetate 11,25 mg every 3 months was maintained. Chemotherapy was administered for 5 cycles, with progressive resolution of pain in the right iliac fossa.
Nevertheless, in October 2022 pulmonary and nodal disease progression was observed while hepatic lesions were stable. PSA level reached 9 ng/ml.
Considering these findings and the persistent good clinical conditions (ECOG PS 0) we decided to switch to second-line chemotherapy with Cabazitaxel 20 mg/mq every 3 weeks. Patient received 6 cycles with initial good tolerance but referred intense asthenia after the 5th cycle, administered in February 2023.
On March 2023, he underwent a restaging total body CT scan which showed a numerical and dimensional increase of the multiple bilobar hepatic lesions (maximum diameter of 8 cm in the right lobe). Lymphadenopathies were unchanged (**Figure 1**).

Figure 1. CT scan of left and right hepatic lesions: basal, after 8 cycles of IAHC, progression of disease.



Concomitantly, patient's clinical conditions worsened (ECOG PS 2): he referred pain in the right iliac fossa, G1 asthenia and blood exams revealed elevation of liver function indices (AST 77 U/L, alkaline phosphatase 188 U/L, GGT 168 U/L) and tumour markers CEA (810 ng/ml), Ca 19.9 (572 ng/ml) and PSA (10 ng/ml) (**Table 2**).

Table 2. CEA and Ca 19.9 levels from March 2023 to May 2024.



Genetic testing for BRCA 1-2 resulted wild type, so target therapies were excluded.
After multidisciplinary discussion, considering the important liver progression, worsening of clinical conditions, the number of previous treatments received, and the poor response to them, along with the absence of other available effective therapeutic

options, it was decided to candidate the patient for Intra-Arterial Hepatic Chemotherapy (IAHC).

This procedure required angiography according to Seldinger technique with right femoral artery access. After angiographic study, the hepatic artery was cannulated, and Carboplatin (300 mg) and Epirubicin (100 mg) were infused.

The first cycle was administered in March 2023, then the patient received other 3 cycles every 3 weeks until May 2023.

After the fourth cycle his global quality of life improved (ECOG PS 0), but tumour markers were persistently elevated (PSA 9 ng/ml, CEA 986 ng/ml and Ca 19.9 504 ng/ml).

On May 2023, he underwent total body CT scan which showed stability of hepatic and nodal lesions. Colliquative necrosis was observed in both liver and lymph nodes, suggesting efficacy of treatment.

Consequently, patient received additional 4 cycles of IAHC from June to September 2023 which were globally well-tolerated, except for G2 leukopenia in June 2023.

From July to September 2023 a decreasing trend of PSA (3,5 ng/ml), CEA (132 ng/ml), Ca 19.9 (244 ng/ml) and liver function indices was observed.

On October 2023 total body CT scan showed partial response of hepatic lesions and stability of the nodal ones (**Figure 1**).

However, considering the important elevation of CEA at the end of October 2023 (841 ng/ml) and the progressive PSA levels reduction from May to September 2023 (14,8 ng/ml to 3,5 ng/ml), a liver re-biopsy was required to exclude the presence of primary hepato-biliary tumour. This procedure was conducted in November 2023 and reaffirmed prostatic adenocarcinoma localization.

Considering these findings, patient received additional 4 cycles of IAHC up to January 2024. For patient's personal reasons each cycle was administered every 4 weeks instead of 3 weeks.

Contrast-enhanced CT scan conducted in February 2024 demonstrated maintenance of response of right lobe liver lesions, but progression of the left lobe liver lesions (**Figure 1**). We explained these data considering a probable lower perfusion in the left hepatic sections due to vascular anatomical reasons.

These considerations, along with the total number of cycles (12 cycles of IAHC), made us to switch to trans-arterial chemoembolization (TACE) of the left lobe with BioPearl™ microspheres (3 ml) loaded with Doxorubicin (75 mg).

On March 2024 patient presented in good clinical conditions (ECOG PS 0), except for occasional pain in the left hemipelvis. TACE was performed on 05/03/2024. The day after the procedure patient referred intense pain on right hypochondrium which required intravenous morphine hydrochloride with progressive pain relief.

On 24 April 2024, the patient underwent a restaging total body CT scan that showed hepatic and nodal progression of disease.

Clinical conditions worsened (ECOG PS 2, G2 asthenia) and because of increased bilirubin level jaundice was observed.

Since patient referred pelvic pain radiating to lower limbs, bone scan was performed showing a lesion of the right sacroiliac synchrondrosis suspected for metastasis. PSA level reached 53,9 ng/ml.

Considering these findings, patient received palliative radiotherapy on the sacroiliac lesion and supportive therapy.

In May 2024, patient clinical conditions improved, and bilirubin levels normalized. Consequently, considering the improvement of clinical conditions and the absence of other available effective therapeutic options, in June 2024 metronomic vinorelbine (30 mg three times a week) was started.

Pain therapy was adjusted, introducing morphine in continuous infusion subcutaneously, with discrete relief.

Clinical conditions remained stable until the beginning of July 2024 when patient reported G2 asthenia and G2 anorexia (ECOG PS 2). Liver function indices and tumour markers worsened again, so vinorelbine was permanently discontinued, and patient died on 26/07/2024.

DISCUSSION

Liver metastases are found in approximately 25% of mCRPC and are considered the most lethal metastatic site in these patients, with a median OS of 10-14 months [1].

In fact, liver metastases in mCRPC seem to respond worse to conventional therapies (such as chemotherapy) than other metastatic sites of mCRPC [2-4]. So far, there are not standard treatments for prostate cancer liver metastases, so further research is needed.

As a result, for these patients there is a growing interest in locoregional therapies, such as percutaneous microwave ablation and radiofrequency ablation. These techniques have been experimented alone [5], in combination with each other [6] or with systemic therapies (i.e. Olaparib [7]), as described in some case reports.

We described a case of mCRPC with hepatic metastases treated with two lines of chemotherapy and then with intra-arterial hepatic chemotherapy which gave a sustained PFS (10 months), compared to the PFS reached during the previous standard treatments (3 months with Docetaxel and 5 months with Cabazitaxel).

We chose chemotherapy as first-line treatment instead of Enzalutamide because patient had received bicalutamide since the diagnosis, the disease was high-volume with visceral metastases, and he was relatively young and fit for chemotherapy.

The OS following the onset of liver metastases was 26 months (April 2022 – July 2024) which doubled the one reported in literature. [1]

At our knowledge this is the first case of IAHC in mCRPC with liver metastases which led to a durable control of disease.

CONCLUSION

This case underscores the complexity of managing advanced prostate adenocarcinoma with hepatic metastases and the therapeutic challenges encountered.
Further research into novel therapeutic modalities and biomarkers is warranted to improve outcomes in this patient population. A multidisciplinary approach incorporating systemic therapies, locoregional interventions, and genetic profiling remains essential for optimal disease management.

Acknowledgment
This research has received no external funding.

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