

Lutetium 177 PSMA Therapy for Metastatic Castrate Resistant Prostate Cancer: A Zambian Case Report

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Abstract

Targeted therapies such as Lutetium 177 PSMA therapy offer alternatives to the treatment of metastatic castrate resistant prostate cancer patients. Here, we present a 63 years old black Zambian male patient who initially diagnosed with high risk prostate cancer. The patient failed the initial treatments and presented with severe bone pains with spinal cord compression. He was then considered for PSMA lutetium therapy after multiple therapies and disease progression to metastatic castrate resistant setting. The patient's performance status improved dramatically after this treatment and was able to return to work without any pains and is fully ambulant. PSMA-targeted therapy is a promising approach in the management of metastatic castrate resistant prostate cancer. The access to such therapies is however limited especially in low limited resource areas which includes Zambia. There is however need to implement such therapies and also embrace the WHO 2030 rehabilitation vision in cancer survivors to improve their physical and quality of life.

Keywords: Metastatic castrate resistant prostate cancer • Prostate Specific Membrane Antigen (PSMA) based imaging and therapy • Lutetium 177 therapy

Highlights

- PSMA-targeted therapy represents a promising approach in the management of advanced prostate cancer.
- Access to advanced imaging techniques and targeted therapies can significantly improve outcomes in prostate cancer management, underscoring the need for more investment in healthcare infrastructure in countries like Zambia.
- Regular monitoring of serum PSA levels is crucial in assessing disease progression and response to therapy.
- We recommend embracing WHO 2030 rehabilitation vision in cancer survivors to improve patient outcomes especially physical function and quality of life.

Introduction

Prostate cancer is the most common non-cutaneous cancer in men, carrying a lifetime risk of 12.5% [1]. Globally, it ranks as the second most common incident cancer in men, following lung cancer, and stands as the sixth leading cause of cancer mortality in men [2]. Notably, international incidence and death rates exhibit significant variation, with high mortality rates observed in the Caribbean, parts of South America, and sub-Saharan Africa [3].

According to the world cancer research fund, Zambia is among the top ten countries with the highest mortality from prostate cancer [4]. The implications of these statistics are profound, particularly given the incidence and prevalence of metastatic Prostate Cancer (mPCa), which vary depending on factors such as age, ethnicity, and stage at diagnosis [5].

A study analyzing data from the national cancer database in the USA found an increase in the incidence of mPCa at diagnosis by 72% and 92% in men aged 55-69 years and 70-84 years, respectively, between 2004 and 2013 [6]. This same study noted that black men had a higher incidence of mPCa at diagnosis compared to white men. More recent data from the Surveillance, Epidemiology, and End Results (SEER) program showed that incidence rates of distant mPCa remained stable from 2004 to 2010, followed by a significant increase through 2018 in men aged 45-74 years [7].

Treatment options for metastatic Castrate-Resistant Prostate Cancer (mCRPC) have expanded in recent years, ranging from hormonal therapies to chemotherapy, immunotherapy, and the innovative Prostate-Specific Membrane Antigen (PSMA) based imaging and therapy [8]. PSMA is a type II integral membrane glycoprotein that is highly expressed in prostate cancer cells, providing a promising target for therapy [9].

Case Presentation

We present the case of a 63-year-old black Zambian male patient diagnosed as high-risk prostate cancer. The patient was first seen at Cancer Diseases Hospital (CDH) in Zambia in October of 2016 with a Gleason Score (GS) of 8 (4+4) and the initial Prostate-Specific Antigen (PSA) was 93.49 ng/ml. He presented with lower urinary tract symptoms and was otherwise stable with an ECOG The patient performance status of 1.

Clinical findings

initially presented with obstructive urinary tract symptoms. The patient's Digital Rectal Examination (DRE) showed an enlarged prostate bilaterally and fixed which was confirmed on CT scan as being enlarged and heterogeneous with enlarged pelvic, and para-aortic lymph nodes but no suspicious osseous lesions. Serum PSA initially reduced to 24 ng/ml after the initiation of Zoladex in private. At the beginning of 2018, disease progression was noted with a PSA of 67.43 ng/ml, and MRI showed lytic lesions to C5, T10 and L1 vertebral bodies without compression. Further PSA readings started increasing with more lytic and osteolytic lesions. The patient had severe back pains and MRI spine showed extensive spinal metastases and cord compression at L1 with a para-spinal soft tissue mass.

Timeline

- **2008:** Initial diagnosis made for high risk adenocarcinoma of the prostate at Washington University School of Medicine in St Louis Missouri in the USA with an initial PSA of 93.49 ng/ml and Gleason score of 8 (4+4). A PET CT only showed increased C-11 acetate uptake in the prostate gland greater on the left with mildly increased activity in several small inguinal lymph nodes bilaterally, likely reactive in nature. The bone scan was negative for osseous metastasis and no treatment given due to insurance reasons.
- **2016:** Patient seen in Zambia with a diagnosis of prostate cancer on Androgen Deprivation Therapy (ADT). The ADT and restaging was initially done from private hospital. The patient was then planned for hypofractionated radiotherapy which he went on to received. Docetaxel was later started upfront.
- **2016-2017:** Patient improves clinically and biochemically.
- **2018-2021:** The patient experienced progressive pelvic bone pains, and a steady rise in PSA levels from 5.02 in to 74.46. At this point abiraterone was started though the supply of the drug was not consistent as it was self-procured and not available in government hospitals. MRI scan was also done which showed lytic lesions to C5, T10 and L1 vertebral bodies without compression.
- **December 2021:** Due to the worsening symptoms, repeat MRI was done which showed extensive lytic lesions involving the spine with cord compression at L1 for which the patient received palliative radiotherapy.
- **January 2022:** The patient was referred to Apollo Hospitals in India for further management with Lu-177 PSMA therapy.
- **May 2022:** Upon arrival in India, the patient's PSA had risen to 100 ng/ml. A Gallium 68 PSMA PET CT was performed which revealed a small sized prostate gland with no significant abnormal PSMA uptake and multiple PSMA avid skeletal lesions. The patient was started on Lu-177 PSMA therapy.
- **September 2022:** The patient's PSA levels had decreased significantly to 0.733 ng/ml.
- **November 2022:** Follow-up PSMA PET CT demonstrated significant interval improvement, with some lesions showing complete resolution.
- **December 2022:** The patient underwent second cycle of Lu-177 PSMA therapy.
- **January 2023:** The patient continued to show improvement, with plans for one more cycle of Lu-177 PSMA therapy for which he awaits therapy due to non-availability of funds.

A follow-up PSMA PET scan in November 2022 demonstrated a significant interval improvement, with some lesions showing complete resolution (Figure 1).

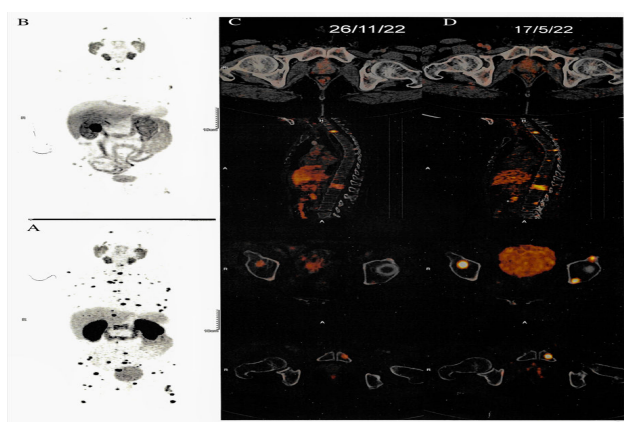


Figure 1. A and D, are the initial images which show extensive Ga-68 PSMA avid disease throughout the skeleton. B and C are post-therapy images demonstrating significant interval improvement in some lesions and complete resolution in others.

Therapeutic focus and assessment

The patient received the first Lutetium-177 therapy with 200 mCi on 30th May 2022 and the second with 180 mCi on 19th December 2022 at Apollo Hospital in India.

Rehabilitation

WHO has included rehabilitation in the Universal Health Coverage (UHC) target of the sustainable development goals as an essential health service and has since designated oncology as a priority area for rehabilitation 2030 initiative [10,11].

We instituted current guidelines that recommend Moderate-Intensity Continuous Training (MICT) aerobic exercise, Resistance Exercise (RES), and MICT plus RES (MICT/RES) performed two to three times per week for at least 12 weeks could result in improvements in Cancer Related Fatigue (CRF) and Quality of Life (QoL) of cancer survivors [12].

Follow-up and outcomes

Post-therapy, the patient experienced significant improvement in his pain symptoms and his serum PSA levels decreased markedly from 100 ng/ml in January 2022 to 0.733 ng/ml in September 2022. His overall condition and performance status also showed significant improvement. Although the patient is yet to receive one more cycle of therapy, the initial findings warrant attention, particularly as Zambia is in the process of implementing similar therapy strategies.

Patient perspective

The patient experienced a marked reduction in pain, regained some lost weight, and saw an overall improvement in his quality of life.

Discussion

This case highlights the potential benefits of PSMA-targeted therapy, specifically Lutetium-177 PSMA, in managing advanced prostate cancer in a resource constrained setting like Zambia [9,13]. Despite challenges such as the lack of consistent access to newer systemic treatments like Abiraterone, a considerable clinical improvement was observed in the patient's condition and quality of life.

Importantly, the patient's serum PSA levels, an indicator of prostate cancer progression, showed a significant decrease post-therapy [14]. This positive response aligns with outcomes noted in international studies, such as the VISION trial, which suggests that PSMA-targeted therapies could lead to improved overall survival and progression free survival [15,16].

In Zambia, the application of such advanced treatments is limited primarily due to the availability of sophisticated imaging techniques, such as Gallium-68 PSMA PET CT, which are crucial for making informed treatment decisions [16]. Yet, the encouraging outcome in this case offers hope, demonstrating that successful implementation and positive results with PSMA-targeted therapies are possible even amid these limitations.

Reflecting on the broader implications, this successful case underscores the urgent need for investment in advanced diagnostic and therapeutic strategies in Zambia. It serves as a reminder that the potential for improved overall survival and progression free survival, as indicated by robust studies like the VISION trial, could significantly change the landscape of prostate cancer treatment in Zambia, benefitting patients who otherwise may not have access to such treatments [15,17].

Thus, this case advocates for policies and initiatives aiming to increase the accessibility of advanced prostate cancer treatments in Zambia. It also highlights the critical importance of continued research and collaboration within the global oncology community to develop effective and accessible therapies for all patients, irrespective of their geographical location [18].

Conclusion

The preliminary findings of this case underscore the potential role of Lutetium 177 PSMA therapy in managing patients with mCRPC in Zambia. The case also highlights the importance of advocacy for policies and initiatives aiming to increase the accessibility of advanced prostate cancer treatments in Zambia. With the increasing burden of prostate cancer, especially in regions like Africa, there is an urgent need to improve access to advanced therapeutic options such as PSMA-based therapies.

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