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Review Article

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Prostate Cancer With Orbital Metastasis: A Case Series

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Abstract

Background: Orbital metastasis from prostate cancer is exceedingly rare, accounting for less than 1% of all orbital tumors. This case series aims to present four unique cases and highlight the clinical challenges and management strategies involved.

Methods: Four cases of prostate cancer with orbital metastasis were reviewed over a period from 2005 to 2024 at the University College Hospital, Ibadan, Nigeria. Data on clinical presentation, diagnostic imaging, treatment modalities, and patient outcomes were collected and analyzed.

Results: All patients presented with advanced-stage prostate cancer and had various systemic metastases at the time of orbital involvement. Common symptoms included proptosis, decreased visual acuity, and ocular pain. Diagnostic imaging such as MRI and CT scans played a crucial role in identifying orbital lesions. Treatment primarily involved palliative radiotherapy and hormonal therapy, with varying degrees of symptom improvement.

Conclusion: Orbital metastasis from prostate cancer poses significant diagnostic and therapeutic challenges. Early recognition and a multidisciplinary approach are essential for effective management and palliation. Despite aggressive treatment, the prognosis remains poor, underscoring the need for ongoing research and improved therapeutic strategies.

Keywords: Prostate cancer, Orbital metastasis, Case series, Palliative radiotherapy, Hormonal therapy

Research Highlights

- Rare Occurrence: Detailed analysis of four cases of prostate cancer with orbital metastasis.
- Diagnostic Challenges: Emphasis on the complexity and delays in diagnosing orbital metastases.
- Multidisciplinary Management: Insight into the palliative treatment strategies employed.
- Clinical Outcomes: Documentation of patient responses to various treatment modalities.
- Prognostic Implications: Discussion on the poor prognosis associated with such metastatic presentations.

Introduction

Prostate cancer is one of the most common malignancies among men, with a significant proportion developing metastases. It is the fourth most common cancer in both sexes combined and the second most common cancer in men. Almost 1.5 million cases of prostate cancer were diagnosed worldwide in 2022 **[1]**. It accounts for 15% of the cancers diagnosed in men **[2]**. In Nigeria, according to the GLOBOCAN report of 2022 **[3]**, prostate cancer is now the top male cancer, with about 12,000 diagnosed cases reflecting broader trends of rising cancer incidence in Nigeria. In the Ibadan cancer registry, it remains the most common male malignancy, with an increase in incidence **[4]**. About one fourth of patients present with advanced or metastatic disease at the time of diagnosis.

Prostate cancer can metastasize to many sites, either by direct local invasion, perineural invasion, hematogenous spread, or via lymphatic routes, with the skeleton being the most common metastatic site, accounting for up to 80% of all prostate cancer metastases **[6]**. Distant visceral metastases are seen in the pelvic lymph nodes, liver, and lungs.

Prostate cancer with orbital metastases is exceedingly rare, accounting for less than 1% of all orbital tumors **[7]**. Orbital metastases from prostate cancer typically present with non-specific symptoms, making early diagnosis challenging. The clinical presentations of these orbital metastases, in order of frequency, are decreased visual acuity, ocular pain, proptosis, retinal detachment, presence of a mass, uveitis (masquerade syndrome), secondary glaucoma, and osteoblastic lesions of the orbital wall **[8]**.

The rarity of orbital involvement often leads to a delay in diagnosis as these symptoms can mimic benign conditions such as orbital cellulitis or thyroid eye disease **[9]**. The distinguishing feature of orbital metastases is a rapid onset and progressive course with

combined motor and sensory deficits, non-responsive to antibiotics or steroids **[10]**.

The diagnosis of orbital metastasis from prostate cancer requires a high index of suspicion, particularly in patients with known metastatic disease. Imaging studies play a crucial role in identifying and characterizing orbital lesions. MRI is particularly useful due to its superior soft-tissue contrast, allowing detailed assessment of the extent of the orbital involvement and any intracranial extension **[11]**. CT scans are helpful in evaluating bony involvement and any coexisting skeletal metastases. A definitive diagnosis often requires a biopsy, which can be guided by imaging to minimize complications. The mechanism by which prostate cancer cells metastasize to the orbit is not well understood. Hematogenous spread is considered the most likely route, given the rich vascular supply of orbital tissues. Once in the orbit, tumor cells can invade the soft tissues, extraocular muscles, and, less commonly, the optic nerve. The rarity of orbital metastasis despite the high prevalence of prostate cancer suggests that specific molecular and micro environmental factors may influence the metastatic potential and organotropism of cancer cells **[12]**.

The treatment of orbital metastases from prostate cancer involves a multidisciplinary approach, aiming to control local symptoms and manage systemic disease. It is inevitably palliative, given that the hematogenous spread of cancer to the orbit is a sign of systemic disease and the involvement of other sites. Surgical intervention is generally not recommended, unless performed for diagnostic purposes (biopsy) in patients with no previous history of cancer, or as palliation (tumor resection or enucleation) in cases of unmanageable local symptoms.

The main treatment option is radiotherapy, with high rates (60%–80%) of clinical improvement of local symptoms and vision **[13]**. External-beam irradiation is the most common and accessible modality, with a total dose of 20–40 Gy delivered in fractions over 1–2 weeks. Stereotactic radiation therapy (SRT) has recently evolved as an alternative modality, in an effort to apply high doses of radiation to a well-defined volume with steep dose gradients outside the target volume **[14]**. A complex mixture of image-guided radiation using CT, MRI, and stereotactic localization defines stereotactic radiosurgery (SRS). Although not available in most treatment settings, SRT and SRS require a shorter treatment course compared with external-beam irradiation, thus contributing to a better quality of life.

Methods

A retrospective review of four cases of prostate cancer with orbital metastases seen over a period of 20 years (2005-2024) at the University College Hospital, Ibadan, Nigeria.

Case Report 1

The first patient was a 50-year-old retired police officer referred to the radiotherapy department of the University College Hospital in 2005 due to a six-month history of urinary retention, low back pain, and progressive lower limb weakness. Rectal examination revealed a hard, nodular prostate. A prostate biopsy showed moderately differentiated adenocarcinoma of the prostate with a Gleason score of 6 (3+3), and PSA was 712 ng/ml. Bone scintigraphy with Technetium 99M revealed sclerotic changes at L3-L5 with partial collapse of the L4 vertebra. He had bilateral orchidectomy and palliative external beam radiotherapy (EBRT) to the spine (20 Gy in 6 fractions over 2 weeks using a Telecobalt machine). The patient defaulted on follow-up visits after that.

Two years later, he presented with proptosis and diminished vision in the right eye, focal seizure involving the right hand, altered consciousness, and left lower limb swelling. Ophthalmological evaluation revealed proptosis, visual field loss, and loss of light perception in the right eye. Cranial CT scan revealed metastasis to the right orbit with intracranial extension. X-ray of the thoraco-lumbar region described moderately severe thoraco-lumbar spondylosis with osteoblastic deposits. Technetium 99M bone scan revealed multiple lesions, including a right periorbital lesion, while Doppler ultrasound described deep vein thrombosis (DVT) of the left leg. Abdomino-pelvic ultrasound was essentially normal. Other investigations (full blood count, electrolytes, urea & creatinine, and retroviral screening) were all normal. PSA was 138.9 ng/ml.

He was placed on steroids (dexamethasone) to reduce intracranial edema, subcutaneous Clexane & warfarin for DVT by the hematologist, and flutamide. EBRT to the whole brain with the posterior right orbital region was administered. The patient's clinical condition improved; the proptosis in the right eye regressed, vision was restored, and he was discharged home to continue follow-up visits. He was on regular three-monthly follow-up reviews for a period of 18 months with no ocular complaints before he defaulted. Six months later (2009), the patient was readmitted via the emergency department of the hospital with a history of about 7 hours of loss of consciousness with associated generalized tonic-clonic convulsion and abdominal distention. He was placed on mannitol for cerebral decongestion but died four hours later.

Case Report 2

The second case was a 60-year-old retired textile worker who presented at the urology clinic in February 2008 with a two-year history of difficulty with urination, six months of back pain, proptosis and pain in the right eye, and two weeks of weakness in the lower limbs. He was neither diabetic nor hypertensive. Clinical examination revealed proptosis of the right eye, reduced vision in the right eye, tenderness over the thoracolumbar spine, and paraparesis of the lower limbs. Digital rectal examination revealed normal anal sphincteric tone, enlarged firm to hard irregular prostate with obliteration of the median groove and right lateral sulcus. Abdominal-pelvic ultrasonography revealed an enlarged irregular prostate gland,

multiple pelvic lymphadenopathy, and bilateral hydronephrosis. Orbital ultrasonography revealed right orbital retrobulbar masses likely to be metastatic, while the total body bone scan (Technetium 99M) showed widespread osteoblastic lesions on the skull, right scapula, right humerus, ribs, spine, and femur. His PSA was 368.4 ng/ml, while electrolyte urea, creatinine, and full blood count were all within normal range.

Prostatic biopsy and histopathology revealed poorly differentiated adenocarcinoma of the prostate, Gleason's grade score 9 (5+4). He subsequently had a bilateral orchidectomy and was placed on flutamide 250 mg thrice daily and then referred for radiation therapy. A review by the ophthalmologist revealed right eye proptosis with associated diplopia in downward gaze and decreased visual acuity. The right orbit was tense and tender on palpation with increased resistance to retro displacement of the globe. The conjunctival vessels were hyperemic. A cranio-orbital CT scan revealed a right bulky intraconal mass in the cranial aspect of the right orbit measuring between 3 cm to 4 cm and multiple cerebral metastases with osteoblastic metastasis to the skull.

He received radiotherapy to the spine at 25 Gy in 6 alternate daily fractions over 2 weeks and had radiotherapy to the whole brain at 30 Gy in 10 daily fractions over 2 weeks using a Cobalt-60 machine. There was significant improvement in pain control over the orbit but no improvement in the right eye vision. He was also reviewed by the palliative team and seen periodically in the clinic. However, the disease subsequently progressed and the patient died six months after the diagnosis of orbital metastasis.

Case Report 3

The third case involves a 68-year-old man who began experiencing urinary difficulties in August 2012. His PSA level was noted to be 46 ng/dl. He underwent a prostate biopsy, which diagnosed prostate adenocarcinoma with a Gleason score of (3+4) = 7, and started flutamide. A CT scan of the abdomen was reportedly normal, and a bone scan did not show any bone metastases. He remained on flutamide until September 2014, after which his treatment was changed to Zoladex, resulting in a decrease in PSA to 0.31 ng/dl by November 2014.

Despite achieving castrate levels of testosterone, a rise in PSA was noted in July 2016. His treatment was changed back to flutamide in October 2016, which he continued until June 2017, when he started stilbestrol. His PSA increased from 61 ng/dl in November 2017 to 130 ng/dl in May 2018. A bone scan conducted in July 2018 revealed extensive osseous metastatic disease involving the axial and appendicular skeleton. A CT scan of the abdomen and pelvis without contrast in November 2018 showed a bladder mass inseparable from the enlarged prostate, bony metastases, pelvic lymph node enlargement, and mild left-sided hydronephrosis. However, a cystoscopy revealed a normal bladder.

He began enzalutamide in August 2018 and underwent palliative radiation to the pelvis and spine along with 6 cycles of Taxotere in March 2019. A repeat bone scan in July 2019 showed disease progression, with a PSA of 28 ng/dl. An MRI of the cervical spine showed features of osseous metastatic disease throughout the cervical spine, upper thoracic spine, and clivus, with involvement of the posterior elements and mild loss of height at T1 with epidural extension from T1 to T3. In December 2019, he presented with left periorbital swelling without pain or visual changes. Physical examination revealed left periorbital edema with a slight downward shift of the eye but no redness. Sclerae were nonicteric, and the mucous membranes were moist. The pharynx was non-injected, and there were no dentures or palpable adenopathy. Pain assessment was 2 (mild pain), and the ECOG score was 1 (symptomatic: ambulatory; restricted in strenuous activity). There was no bone tenderness to percussion over the spine or neck, but there was tenderness in both shoulders without redness, swelling, or warmth at the site. The patient was unable to raise his arms above shoulder height. Other systems were essentially normal. Blood profiles were normal except for a raised PSA of 132 ng/ml.

He received 6 courses of Cabazitaxel with Granulocyte Colony-Stimulating Factor and palliative radiotherapy to the left orbit (25 Gy in 6 alternate daily fractions over 2 weeks), which resulted in significant improvement in orbital symptoms. However, the patient died 8 months later.

Case Report 4

The fourth case is a 69-year-old retiree who presented with proptosis and pain in the right eye for the past three months, accompanied by diminished vision in the right eye, intermittent headaches, and dizziness. His past medical history revealed a diagnosis of prostate cancer in January 2017, initially presenting with urinary difficulty and lower back pain. His Gleason score was 8 (4+4), and his initial PSA was 250 ng/ml.

He underwent bilateral orchiectomy in February 2017 and started on androgen deprivation therapy (ADT) with flutamide, later switching to Zoladex in 2019 due to rising PSA levels. As of his latest check-up in June 2024, his PSA level was 340 ng/ml. A bone scan revealed extensive osteoblastic metastatic disease involving the axial and appendicular skeleton. A CT scan of the abdomen and pelvis showed no significant visceral metastases but confirmed bony metastases.

On examination, the patient was alert, oriented, and in mild distress due to ocular pain. His blood pressure was 140/85 mmHg, heart rate 82 bpm, respiratory rate 18 breaths/min, and temperature 36.8°C. An ophthalmic examination showed proptosis with limited movement, especially on downward gaze in the right eye, visual acuity reduced to hand motion, conjunctival hyperemia, and chemosis. The pupils were equal but non-reactive to light on the right side. The left eye

showed normal visual acuity and no signs of proptosis or conjunctival hyperemia.

An MRI of the brain and orbit revealed a right orbital mass with extension into the intracranial cavity, suggestive of a metastatic lesion. CT scans of the thorax, abdomen, and pelvis showed new visceral metastases. A bone scan confirmed widespread osteoblastic activity consistent with metastatic disease.

A diagnosis of ocular metastasis from prostate cancer with intracranial extension and widespread bone metastases was made. The patient was to continue on ADT with Zoladex, steroids, and analgesics. The case was to be discussed at a multidisciplinary meeting to consider commencing chemotherapy (docetaxel) and adding a second-line anti-androgen therapy (e.g., enzalutamide) due to rising PSA levels. Palliative radiotherapy to the right orbit and whole brain was recommended to control local symptoms and improve quality of life.

Discussion

Orbital metastasis is a rare feature of adult malignancies, accounting for only 2-9% of orbital tumors **[16,17]**. Both epithelial tumors, primarily adenocarcinomas from the lung, breast, stomach, thyroid, and kidney, and non-epithelial tumors like sarcomas, melanomas, and neuroblastomas, can metastasize to the orbit. Soft tissue metastases from the prostate are very rare **[18,19]**.

Two routes of metastasis to the orbit have been documented. The first involves pulmonary metastasis, where tumor emboli travel through the pulmonary circulation to the choroidal arteries and then into the ophthalmic artery. The second route includes prostatic or vertebral lesions seeding into Batson's plexus, which leads to the cranial venous sinuses and subsequently to the ophthalmic and vertex veins **[16,20]**.

Radiological studies can aid in diagnosing metastatic tumors. The most common CT scan findings are a well-defined, contrast-enhancing, intraconal mass and osteoblastic lesions. The patients under review had a CT scan-confirmed diagnosis. Diagnosis can also be achieved through cytological examination of fine needle aspiration material, ocular enucleation, or evisceration of the orbit, with frequent cytological findings including nuclear crowding, microglandular groups, nuclear and nucleolar enlargement, and variable pleomorphism.

The treatment of prostatic metastases to the orbit is palliative and does not extend survival. And it includes chemotherapy, hormonal therapy, radiation therapy, or a combination of these. Hormonal therapy is effective in 70% to 80% of patients, with an average response duration of about 18 months. Androgen ablation is preferred for hormone-naïve patients. Additionally, local radiation therapy has proven effective and is often used for symptom palliation in certain cases.

De Potter and colleagues reported a complete ocular response after combining hormonal therapy with radiotherapy to the uvea **[21,22]**. Enucleation of the mass is rarely used and is considered for cases of complete blindness or intractable pain, with marked symptom relief noted in over 80% of patients following radiation therapy **[23]**.

Among the four patients under review, all received hormonal therapy, and three also received radiation therapy. The fourth patient is currently being evaluated for treatment. The first patient responded well to flutamide and whole-brain irradiation, resulting in restored vision in the affected eye. The second patient had a poor response, while the third patient showed improvement in ocular symptoms but passed away seven months later. The fourth patient is still undergoing treatment.

Despite aggressive treatment, the prognosis for patients with orbital metastases from prostate cancer remains poor, with a median survival of less than a year post-diagnosis of orbital involvement **[6]** This underscores the importance of early detection and comprehensive management of prostate cancer to potentially delay the onset of metastatic disease

The prognosis for patients with metastatic disease to the orbit is poor. Various studies reported an overall median survival rate of 7.4-24.5 months **[16,17,19,24]**.

Conclusion

Orbital metastasis from prostate cancer, although rare, presents significant diagnostic and therapeutic challenges. A high degree of clinical suspicion, appropriate imaging, and timely biopsy are critical for an accurate diagnosis. Management requires a multidisciplinary approach to address both local and systemic disease, with a focus on palliation and maintaining quality of life.

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Statement of Ethics: This study did not fall under the scope of the ethics requirements of UI/UCH-EC.

Conflict of Interest Statement: The authors declare that they have no conflicts of interest.

Author Contributions

Dr. Oladeji A. A.: Conceptualized the study, led the writing of the manuscript, and acted as the corresponding author.

Dr. Jatto J.: Contributed patient data for the second case and documented clinical findings.

Dr. Ntekim A. I.: Provided critical revisions and proofread the manuscript.

Dr. Edijana B. O.: Collated data and cases for the study.

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Data Availability Statement

The data for this article are available upon request and can be accessed at the Record Department, University College Hospital (UCH), Ibadan, Nigeria.

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