

# Orbital metastases of prostatic carcinoma in a tropical African population

\*O. B. Shittu and J. O. Ogunbiyi

*Urology Division, Department of Surgery and Pathology Department  
College of Medicine, University of Ibadan and  
University College Hospital, Ibadan*

## Summary

We have reviewed the cases of orbital metastases from carcinoma of the prostate gland seen in the University College Hospital, Ibadan over an 11 year period, 1990 – 2000. During the period, seven cases of orbital metastases that presumably arose from carcinoma of the prostate were seen.

Four of the patients died of progression of the primary disease over a variable period ranging between 2 weeks and 30 months of diagnosis and treatment, two were lost to follow up and one is alive 46 months after initial diagnosis of orbital metastases from carcinoma of the prostate and treatment.

**Keywords:** *Orbit, Metastases, Prostate, Cancer, Nigeria.*

## Résumé

Nous avons fait le bilan des cas des métastases orbitales de la carcinome de la glande sexuelle masculine vus au college hospitalo universitaire, Ibadan au cours d'une période de onze ans, 1990 – 2000.

Pendant cette période, sept cas des métastases orbitales qui vraisemblablement se sont présentés à cause de la carcinome de la glande sexuelle masculine ont été vus.

Quatre des patients étaient mort à cause de la progression des maladies primaires au cours d'une période variable entre 2 semaine et 30 mois du diagnostic et du traitement, on a perdu des soins post-hospitaliers chez deux patients et un patient est vivant 46 mois après le diagnostic premier de la métastase orbitale de la carcinome de la glande sexuelle masculine et traitement.

## Introduction

Involvement of the orbit by metastatic tumours is seen occasionally but these are generally uncommon. In addition, unilateral orbital metastases are reported but generally they are probably predominantly bilateral. On the contrary direct spread to the orbit from tumours of adjacent structures occur commonly and this is especially so with intraocular tumours that are often seen in children.

Among adults, orbital metastases are most commonly of epithelial origin and it would seem that orbital metastases are site specific, being not just a part of bony metastases<sup>1,2,3,4,5,6</sup>. Several epithelial tumours have been documented to show orbital metastases, including oesophageal<sup>7</sup>, breast<sup>8</sup>, pancreatic<sup>9</sup> and lung<sup>10</sup> cancers. Metastatic carcinoma to the orbit constitutes only between 2.3, and 7% of all orbital tumours<sup>11,12</sup>.

Prostatic carcinoma is one of the most common tumours in adult men and it often leads to widespread metastases to the axial skeleton and viscera<sup>13</sup>. When prostatic carcinoma presents with metastasis in the orbit, it is usually a late event and often the patient is in the terminal stages of the disease<sup>3,4</sup>. However, the orbital presentation preceded the diagnosis of prostate

cancer in 60% of the cases reported in the series by Boldt and Nerad<sup>3</sup>.

In Nigeria, we have recently observed an increase in the incidence of prostatic carcinoma<sup>14</sup> but the extent of lesions has not been closely studied even though there is a suggestion that our cases have predominantly presented late.

The aim of this paper is to present 7 cases of prostatic carcinoma with orbital metastases, which to our knowledge is the first, published report on this subject from this environment.

## Patient's characteristics

Case no 1. C. O. with hospital number 909816 was a 60-year old civil servant who presented with a 2- year history of back pain, gradual swelling of both legs and diplopia.

There was proptosis of left eye at presentation and the prostate gland was hard and irregular.

Total serum acid phosphatase (SAP) was 62.0KA unit/l (normal 1-4KA unit/l) while the prostatic fraction was 26.8KA unit/l (normal 0-1KA unit/l) at presentation. Eye examination revealed left optic disc atrophy and restriction of the peripheral fields.

An ultrasound examination of the orbit revealed a retrobulbar mass that was bowing the rectus muscle laterally, but the eye bulb was normal in shape and size. Ear examination revealed severe mixed hearing loss on the left side due to metastasis in left facial bone.

A tru-cut biopsy of the prostate revealed adenocarcinoma of the prostate gland. A biopsy of the orbital mass was not done because of the risk to the eye.

He had bilateral orchidectomy and radiotherapy to the prostatic bed, with regression of leg swelling, regression of the proptosis and improved vision in the left eye and better hearing in the left ear. Prostate gland became flat and patient put on weight. He relapsed 20 months after orchidectomy with worsening vision in the left eye and metastasis in left shoulder. He could not afford the cost of medication for total androgen blockade. His condition gradually got worse and he died 34 months after orchidectomy.

Case no. 2, G. F with hospital number 939123 was a 53 year old store-keeper who presented with low abdominal pain and low back pain of 4 months duration. He was quite ill at presentation and there were multiple hard and irregular masses in the pelvis as well as a hard and irregular prostate gland.

There was also proptosis of the left eye, diplopia and weakness and numbness of the tongue with deviation of the tongue to the left. He had weakness of the left hypoglossal nerve and the left lateral rectus muscle of the eye. The level of prostate specific antigen (PSA) was 140ug/l (normal 0-4ug/l) and CEA was 0ug/l (normal 0-10ug/l). Spine X-ray showed sclerosis of the lumbosacral spine. Biopsy of the prostate confirmed adenocarcinoma, gleasson grade 5. Ultrasound of the orbit showed an echogenic mass separate from the eye-ball. He had bilateral orchidectomy done with regression of the proptosis and improvements in the vision in the left eye, left XIIth

\*Correspondence

nerve palsy and regression of the abdominal and pelvic masses. He was however lost to follow-up soon after.

Case no. 3 D. O. with hospital number 951674 was a 64-year old carpenter and farmer who was under the care of physicians with an assessment of sepsis syndrome. The PSA was elevated at 103.4ug/l.

The prostate gland was enlarged and irregular and extended to the pelvis. Biopsy of prostate showed adenocarcinoma of the prostate. He had bilateral orchidectomy and got better that he was well enough to be discharged from hospital. He developed proptosis of the left eye 4 months after orchidectomy, presumably from orbital metastasis from prostate cancer as this regressed with the use of an anti-androgen. He was however lost to follow-up shortly afterwards.

Case no. 4 J.O.S with hospital number 961139 was a 64-year old academic who presented with proptosis of the left eye 5 months after starting Zoladex for advanced carcinoma of the prostate. In addition he also complained of back pain radiating to the legs. He had radiotherapy to the spine about 4 weeks before presentation. He was quite ill and weak in both legs. Power in the legs was grade 3. Ultrasound of the orbit showed a retro-bulbar mass of mixed echoes suggestive of secondary deposits. He was commenced on anti--androgens, but there was no significant improvement and he died 6 weeks afterwards.

Case no. 5 A. A. with hospital number 240578 was a retired university administrator who presented with a 3-months history of low back pain that radiated to the back of the legs occasionally. The prostate gland was enlarged and irregular. The total serum acid phosphatase was 5.5KA unit (normal 1-4 KA units), while the prostatic fraction was 2.3KA unit (normal 0-1 KA unit). Biopsy of the prostate gland confirmed invasive adenocarcinoma. He had bilateral orchidectomy done. He became asymptomatic until 17 months later when he presented with paraplegia, and X-ray confirmed spinal metastasis with wide osteoblastic changes in the spine. He had radiotherapy to the spine with relief of pain but no improvement in neurological status. Three months later he developed proptosis of the left eye. An orbital ultrasound showed distortion of the retrobulbar space by a retrobulbar space-occupying lesion, suggestive of a metastatic deposit. He was commenced on anti androgen therapy with little improvement in the proptosis.

However the general clinical condition continued to deteriorate with recurrent anaemia that became resistant to multiple transfusions. He died 30 months after he had orchidectomy.

Case no. 6 was S. L. with hospital number 9227916 a 66-year old legal practitioner, who presented 18 months after transurethral resection of the prostate (TURP) and bilateral orchidectomy for locally advanced carcinoma of the prostate gland with haematuria and radicular pain in the left leg. X-ray confirmed osteoblastic secondaries in the L5 spine, sacrum and right pubic ramus. Symptoms improved after a course of palliative radiotherapy to the bony metastases. He was asymptomatic until 7 months later when he developed paraplegia, pathological fracture of the right humerus and proptosis on the right. Ultrasound showed a mixed echogenic mass in the retrobulbar space consistent with a secondary deposit. The clinical condition gradually deteriorated and he died two weeks after.

Case no. 7 with hospital number 292645 was A. A, a 7-year old university don who presented with two weeks history of generalised bone pain and inability to walk. He was paraplegic. PSA was greater than 30ug/l (normal 1-4ug/l and bone marrow biopsy was consistent with metastatic adenocarcinoma. He had bilateral orchidectomy, and he commenced active physiotherapy. He gradually regained the ability to walk

over the following 12 months.

He however developed pain and poor vision in the right eye 18 months after orchidectomy. Examination revealed proptosis of the right eye with loss of vision in the eye, while orbital ultrasound revealed an echogenic orbital mass. He was treated with anti-androgens and external radiotherapy to the right orbit. He responded well, the PSA remains at less than 1ug/l about 20 months after radiotherapy.

## Discussion

Osseous metastases from carcinoma of the prostate gland constitute the most common form of distant spread<sup>15</sup>. The most frequent sites involved are the pelvis, spine, femurs and ribs<sup>15</sup>. The orbit is rarely involved. It is note worthy that up to 1989; only 28 cases of oculo-orbital metastases of prostate cancer had been reported in the literature<sup>16</sup>. Urological malignancies in general and prostate cancers in particular are especially uncommonly metastatic to the orbit and an orbital tumour as the primary manifestation of occult carcinoma of the urological system is even more unusual<sup>2,17</sup>.

One of the largest series of eye and orbit metastases reported is that of Ferry and Font<sup>5</sup> in which the prostate was the site of primary tumour in only 3 cases(1.3%)

In yet another series, the same authors found that only between 3.5 and 4% of metastatic tumours to the orbit were from prostatic primaries<sup>6</sup>.

Fredman examined 112 patients (141 eyes) with metastatic tumours of the eyes and orbit and found the breast to be the most common primary site<sup>18</sup>. The prostate was the 5th most common neoplasm to involve the eye in that study. The median survival time (MST) after choroidal metastases for all stages of breast cancer was 314 days<sup>13,18</sup>. Eventually about half of those diagnosed with cancer of the prostate develop advanced, metastatic disease and androgen-deprivation therapy will at best only buy some time for the patient, as there is no cure once the disease has spread beyond the gland itself. Bloch and Gartner<sup>19</sup> found 4 cases of prostatic carcinoma out of a series of 112 metastatic tumours in the eye and orbit. Three cases preferentially involved the orbit while 1 case involved both the orbit and the eye. In the series as a whole, 11.6% of patients presented with ocular metastases before the primary tumour was diagnosed.

The longest survival of all patients was 9.2 years, and it was concluded that the prognosis was very poor for patients with orbital tumour metastases.

In the series described here, two patients were lost to follow-up, four died of disease (DOD) over a variable period (2 weeks to 30 months). The last patient is alive 46 months after the initial diagnosis and treatment.

Although bony metastasis is quite prominent in advanced prostate cancer, it would seem that metastases to the orbit especially worsens the prognosis<sup>19</sup>.

Considering the increasing detection rate of prostate cancer in our environment<sup>14, 20</sup>, it is important to clarify prognostic parameters in order to select the optimal treatment modality for a patient.

Several prognostic factors have been considered in the outcome for prostate cancer and these have varied with respect to whether the cases are localised cancer or with metastatic disease<sup>21</sup>. These factors are related to each other in a rather complex fashion. For example some studies suggested a positive relationship between increasing height and poor prognosis but this was later found to be more so if there was a positive family history of prostate cancer<sup>22</sup>. In another instance an in-

crease intake of animal fat as a proportion of total caloric intake was shown to be associated with advanced prostate cancer<sup>23</sup>.

In yet another study, co-morbidity was found to be the most important prognostic factor, especially for those aged under 70 years. At 60 years, patients with one concomitant disease were twice as likely to die than those with no co-morbidity (95% confidence interval, Ci, 1.0 - 4.3), whereas the hazard ratio HR was 7.2 (3.1 - 16.6) for two or more diseases<sup>24</sup>. This was not caused by a reduced use of curative treatment for these patients. At the age of 74 years, co-morbidity was no longer a significant prognostic factor. Co-morbidity seems most important when evaluating the risk of early death<sup>24</sup>. The response to initial endocrine therapy might be a good prognostic parameter in addition to the histopathological features of the primary tumour<sup>25</sup>. Poor differentiation of the tumour was also an important prognostic factors at all ages; this became increasingly apparent 2 years after diagnosis (HR 3.4, CI 1.5 - 7.7<sup>24</sup>).

In our center we are limited by diagnostic modalities to the use of clinical staging and biopsy histology grading in determining treatment applied. At other times we are limited by the patient's ability to procure medications.

There are several points against using Gleason grade to prognosticate especially since these grading systems do not reliably predict the lethal potential of a tumour in an individual patient, or the responsiveness of an individual to various forms of therapy. Even, initial response to androgen ablation could not be relied upon as a good prognostic indicator, as demonstrated by one of our patients, who regained full power in both legs after orchidectomy having been previously paraplegic. But he went on to develop orbital metastasis with visual loss, although he subsequently responded again to treatment with anti-androgens, as evidenced by the normalization of the PSA. Probably more cases need to be seen and followed up to evaluate this situation among our patients. The value of the degree of differentiation is even more difficult to discuss because it is known that most of the patients here present late. No clear information on relative differentiation has been previously documented. Yet if we have only 7 cases over an 11 year period showing orbital metastasis and this is supposed to be an indicator of advanced disease that would be inconsistent in our environment. During this same period, 627 confirmed cases of carcinoma of the prostate gland were seen, giving an incidence of 0.01%. Even though we could not confirm the orbital metastases histologically because of the location, on the basis of the clinical findings and response to treatment there is no doubt in our minds that these are orbital metastases from prostatic carcinoma. It would be important therefore to clearly document the nature of prostate cancer that is seen in this environment.

Two of our patients had ophthalmologic review during the course of their management as canvassed by Hingorani and others<sup>4</sup>. These authors are of the view that assessment and management of these patients by an ophthalmologist are essential since the ophthalmologist can offer accurate monitoring and charting of the degree of proptosis and ophthalmoplegia to assess progress and the response to treatment. In addition, an expert examination is required to diagnose certain ophthalmological complications of orbital space occupying lesion such as corneal exposure and optic nerve compression which are amenable to treatment, and which can improve comfort, vision and the quality of life<sup>4</sup>.

## References

1. Harstein ME, Grove AS Jr, Woog JJ. The role of the integrin

family of adhesion molecules in the development of tumours metastatic to the orbit. *Ophthalmic Plastic & Reconstructive Surgery* 1997; 13(4): 227 - 238.

2. Wijerman PC, Boeve ER, Mickish GHJ, Simonsz HJ, Schroder FH. Orbital tumours as a first indication of urological malignancies. *BJUrol*. 1997; 7: 288 - 289.
3. Boldt HC and Nerad JA. Orbital metastases from prostate carcinoma. *Arch ophthalmol* 1988; 106: 1403 - 8
4. Hingorani M, Davies A, Nischal K and Aclimandos WA. Prostatic orbital metastases and the role of the ophthalmologist. *BJUrol* 1996; 78: 642 - 658.
5. Ferry AP, Font RL. Carcinoma metastatic to the eye and orbit I. A clinicopathologic study of 227 cases. *Arch Ophthalmol* 1974; 92: 276 - 86.
6. Font RL, Ferry AP. Carcinoma metastatic to the eye and orbit. *Cancer* 1976; 36: 1326 - 1335.
7. Collins MH, Wojno TH, Grossniklaus HE. Metastatic oesophageal carcinoma to the orbit. *Am J Ophthalmol*. 1999; 127(2): 228 - 9.
8. Kuzma BB and Goodma JM. Slowly progressive bilateral enophthalmos from metastatic breast carcinoma. *Surgical neurology* 1998; 50 (6): 600 - 602.
9. Geeta N, Chandralekha B, Kumar A, Ittiyavirah AK, Ramadas K, and Joseph F. Carcinoma of the pancreas presenting as an orbital tumour: a case report. *Am J Clin Oncol* 1998; 21(5): 532 - 3.
10. Shields JA, Shields CL, Eagle RC Jr, Gunduz K, Lin B. Diffuse ocular metastases as an initial sign of metastatic lung cancer. *Ophthalmic surgery and lasers* 1998; 29(7): 598 - 601.
11. Silva D. Orbital tumours. *Am J Ophth*. 1998; 65: 318.
12. Henderson JW (ed). *Metastatic carcinoma in orbital tumours*. Philadelphia, WB Saunders company. 1973 chap 16 pg 474.
13. Tertzakian GM, Herr HW, Mehta MB. Orbital metastasis from prostatic carcinoma. *Urology* 1982; 19: 427 - 429.
14. Ogunbiyi JO, Shittu OB. Increase incidence of prostate cancer in Nigerians. *J Natl. Med. Assoc.* 1999; 91(13): 159 - 164.
15. Ivker M, Keesal S, Leberman P. The pelvic lymphatics and vertebral veins in the osseous metastasis of carcinoma of the prostate: A preliminary report. *J Urol*. 1961; 86: 650 - 654.
16. Rigot JM, Duret MH, Custier P, Mazeman E. 2 cases of Oculo-orbital metastases of a prostatic epithelioma. *Ann Urol. (Paris)* 1989; 23: 43 - 45.
17. Reifler DM, Kini SR, Liu , Little RH. Orbital metastasis from prostatic carcinoma. *Arch Ophthalmol* 1984; 102: 292 - 295.
18. Fredman MI, Folk JC. Metastatic tumours of the eye and orbit. Patient survival and clinical characteristics. *Arch Ophthalmol* 1987; 105: 1215 - 1219.
19. Bloch RS and Gartner S. The incidence of ocular metastatic carcinoma. *Arch Ophthalmol* 1971; 85: 673 - 675.
20. Osegbe DN. Prostate cancer in Nigerians: facts and non-

- facts. *J Urol* 1997; 157: 1340 – 1343.
21. Hamdy FC. Prognostic and predictive factors in prostate cancer. *Cancer Treat Rev.* 2002 June 27; 3: 143 – 51.
  22. Norrish AE, McRae CU, Holdaway IM, Jackson RT. Height related risk factors for prostate cancer. *British Journal of Cancer* 2000; 82: 141 – 145.
  23. Hayes RB, Ziegler RG, Gridley G, Swanson GM, Schoenberg JB, Silverman DT, Brown LM, Pottern LM, Liff J, Schwartz AG, Fraumeni JF Jr, Hoover RN. Dietary factors and risks for prostate cancer among blacks and whites in the United States. *Cancer Epidemiol biomarkers Prev.* 1999 8 1: 28 – 34.
  24. Post PN, Hansen BE, Kil PH, Janssen-Heinen ML, Coebergh JW. The independent prognostic value of comorbidity among men aged <75 years with localised prostate cancer: a population-based study. *BJU Int.* 2001. Jun 87; 9: 821 – 6.
  25. Okada Y, Shichiri Y, Ogawa O, Yoshida O. Prognostic factors of prostatic cancer. *Gan To Kagaku Ryoho.* 1995; 22:13; 1999 – 2005.