# A report of orbital metastasis from a urinary bladder adenocarcinoma

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A 60-year-old man presented with sudden-onset proptosis of the left eye and intermittent diplopia of 2 months duration. Ophthalmic examination revealed bilateral eyelid retraction, left eye proptosis and a firm, non-tender mass (2 cm × 1.5 cm) in left supero-medial orbit with restricted extraocular movements. Contrast-enhanced computed tomography showed a well-defined, enhancing antero-medial orbital mass which was removed via anterior orbitotomy approach. The histopathology/immunohistochemistry showed adenocarcinoma; metastasis of urothelial origin. The oncology consultation and metastatic workup revealed a urinary bladder carcinoma with distant metastasis. Our patient expired within 6 months of diagnosis. The ophthalmic symptoms due to orbital metastasis may be the first presentation of some cancer patients.

**Key words:** Eyelid retraction, orbital metastasis, proptosis, restriction of extraocular movements, urinary bladder adenocarcinoma

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Orbital metastasis is an uncommon clinical entity present in 2%-5% of cancer patients.[1-3] Approximately 25% of orbital metastasis present with an occult primary, that is, before the diagnosis of primary malignancy is established.[1-3] The presenting ophthalmic features include proptosis, diplopia, orbital mass and reduced visual acuity. In males, the prostatic (12%) and lung carcinoma (8%) are common primary sites, whereas in females, the breast carcinoma (53%) tops the list.[1-3]

The orbital metastasis of urinary bladder carcinoma is rare and occurs late in the disease process.[4-6] Additionally, the delayed diagnosis imposes a greater management challenge which is frequently associated with a poorer prognosis.[1,7] Moreover, the trivial systemic symptoms of the patients often get missed, adding to this perplexing scenario.[4-7] This necessitates a detailed clinical history, thorough local and systemic examination with radiological support, specifically in elderly, presenting with acute onset of orbital features.

Our patient was an elderly male with unilateral proptosis of short duration and restriction of ocular movements with a contrast-enhancing anterior orbital mass. The histopathology of the excised mass revealed a tumor of metastatic origin enabling us to diagnose the primary cancer.

## Case Report

A 60-year-old male patient presented with left eye protrusion, diminution of vision and redness of 2 months duration. It was associated with pain, watering and intermittent double vision since 2 weeks. There was no history of significant weight loss, abdominal pain or swellings over other parts of body. He was chronic smoker, occasional alcoholic and was under treatment for hypertension and coronary artery disease. On ophthalmic examination, the best corrected visual acuity was



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6/6 and 6/12 in right and left eyes, respectively. The left eye showed proptosis of 4 mm (Leudde's exophthalmometery), widened vertical palpebral fissure and mild inferolateral globe dystopia [Fig. 1a and b]. The patient had bilateral upper and left lower eyelid retraction. The palpation revealed a firm, non-tender, localized and immobile mass of 2 × 1.5 cm in the left superomedial orbit. The adduction and elevation of the left eye were limited [Fig. 1c and d].

At presentation, a contrast-enhanced computed tomography scan of orbits revealed a well-defined, homogenous mass, abutting left globe with marked contrast enhancement [Fig. 2a]. The anterior portion of medial rectus appeared thickened and the optic nerve was not discernible [Fig. 2b]. A working diagnosis of orbital lympho-proliferative disease was kept and a left anterior orbitotomy with in-toto mass excision was performed. The excised mass was sent for histopathological examination.

The slides showed tumor cells arranged in nests and clusters with interconnected trabeculae and intervening fibrovascular tissue [Fig. 3a and b] with morphologic features of an epithelial malignancy. On immunohistochemistry, the cells showed strong expression for cytokeratin 7 [Fig. 3c] and diffuse, strong nuclear positivity for GATA 3 [Fig. 3d], thereby confirming urinary bladder as the likely primary origin. The cells were negative for prostate specific antigen (PSA) excluding prostate gland as primary [Fig. 3e].

A metastatic workup including a chest X-ray, ultrasound abdomen and a positron-emission tomography (PET) scan was subsequently requested. The PET scan showed high metabolic activity and FDG uptake in left orbit, para-aortic lymph nodes, urinary bladder and prostate region, suggestive of metastasis. The oncology opinion revealed a urinary bladder carcinoma. The bilateral eyelid retraction was thought to be part of a paraneoplastic syndrome leading to the thyroid associated ophthalmopathy like effects of antibodies on the orbital receptors.[8] The patient expired within 6 months of the diagnosis of orbital malignancy.

## Discussion

The median survival of patients with orbital metastasis is 6-9 months.[1,2,7] Transitional cell carcinoma (TCC) is a common urinary bladder malignancy of which, 10%-15% are invasive.[4-7] Of the invasive TCC, around 50% cause distant metastasis to the common sites such as lymph nodes, lungs, bones and rarely to orbit, via the Batson valveless venous plexus.[7,9] Urinary bladder adenocarcinoma is the third most common histological variant accounting for 0.5%-2.0% of all urinary bladder carcinomas.[10] The adenocarcinomas are almost always invasive, have a poorer prognosis and regardless of the treatment modality; the five-year survival rate is 0%-31%.[10]

To the best of our knowledge based on the review of literature (English language), this is possibly the first case report of urinary bladder adenocarcinoma with orbital metastasis. We have compiled the previous reported cases of orbital metastasis from urinary bladder carcinoma (urothelial origin) [Table 1]. Of total 17 patients (including our case), 14 (82.4%) were males. The mean age at presentation was 67 years (range 45-78 years) and the time period between the onset of ophthalmic symptoms and detection of primary urinary bladder carcinoma ranged from 3 days to 11 years. However, in six cases, the ophthalmic symptoms appeared prior to or simultaneously with the primary carcinoma.

The clinical presentation of orbital metastasis depends on the orbital or periorbital structures involved. The common symptoms include pain, globe protrusion, diplopia, redness and decreased visual acuity all in rapid progress.[1,3] Diplopia (88.2%) was the most common presenting complaint followed by proptosis (70.6%) and diminution of vision or vision loss in 8 (47.1%). The other prominent features were limitation of ocular movements, blepharoptosis and pain while occasionally optic disc edema, exudative retinal detachment, uveitis, choroiditis, secondary glaucoma and widening of palpebral fissure.[3] Of 17 patients mentioned in Table 1, the majority ($n = 12$) died at a mean duration of 3.2 months after the diagnosis of orbital metastasis, and 5 have not clear final status.

A high index of suspicion is critical for an early diagnosis of the orbital metastasis. The above mentioned ophthalmic features, tailored laboratory investigations, appropriate radiology (for extent, dimensions and vascularity) and metastatic workup may provide sufficient diagnostic clues. A PET scan provides sufficient radiological evidence of a metabolically active lesion or tumor with its possible sites of metastasis.

Minimally invasive diagnostic techniques such as ultrasonography guided a fine needle aspiration cytology or an incisional tissue biopsy, from the primary and/or metastatic site, may provide conclusive evidence of the suspected condition. The pathological diagnosis is necessary for initiating anti-cancer treatment in the form of chemotherapy, radiotherapy or immunotherapy.[7,9,10] The immunohistochemical studies

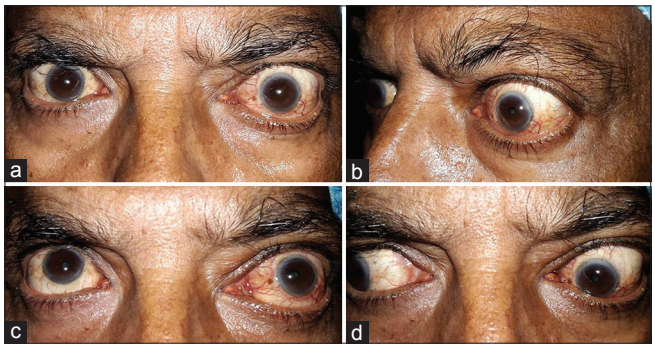


**Figure 1:** (a) Primary gaze photograph shows bilateral upper eyelid retraction, down and out protrusion of left eye, conjunctival congestion and bilateral temporal flare. (b) Oblique view shows the degree of protrusion and eyelid retraction of left eye. (c) The elevation of the left eye appears limited. (d) The adduction of the left eye appears limited

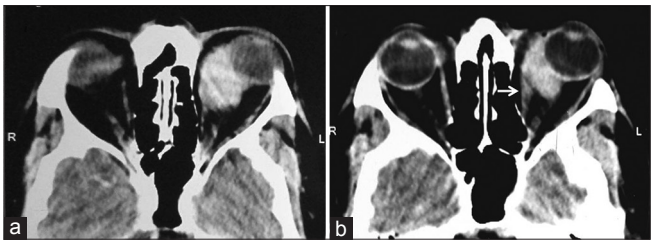


**Figure 2:** (a) Axial section of contrast-enhanced CT scan (superior orbit) shows a well-defined mass of 2.3 × 2.7 × 8.0 cm abutting left globe with marked contrast enhancement. (b) Mid-orbit level axial scan shows thickened proximal medial rectus muscle with an intraconal retrobulbar component of mass lesion

from the metastatic tumor site and its comparison with the primary tumor may be necessary for a definitive diagnosis.[6] In conclusion, a sudden-onset proptosis with ocular movement restriction should incite a high-index of suspicion for orbital metastasis, especially in elderly.

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**Table 1: Reported cases of orbital metastasis from urinary bladder carcinoma**

| Sl. No. | Author/year | Age (years)/ gender | Time interval between onset of ophthalmic symptoms and detection of urinary bladder carcinoma | Ophthalmic features | Treatment | Period from ophthalmic symptoms to death | Results/ final outcome |
|---|---|---|---|---|---|---|---|
| 1 | Smiley/1965 | 75/M | Orbital lesions appeared simultaneously | Diplopia, proptosis, vision loss | Not mentioned | Not mentioned | Not mentioned |
| 2 | Seimiya/1971 | 55/M | 5 months | Left sided swelling, pain (bilateral) | Radiotherapy | 8 months | Death |
| 3 | Krauss/1982 | 64/F | 15 months | Diplopia, proptosis, pain | Radiotherapy | 1 month | Death |
| 4 | Prats/1989 | 58/M | Orbital lesions appeared simultaneously | Diplopia, proptosis, ptosis, hypoesthesia of trigeminal nerve, vision loss | Not mentioned | 4 months | Death |
| 5 | Anguro/1991 | 61/M | 11 months | Diplopia, proptosis | Not mentioned | 1 month | Death |
| 6 | Felip/1991 | 58/M | Orbital lesions appeared simultaneously | Diplopia, ptosis, hypoesthesia of trigeminal nerve, vision loss | Radiotherapy | 3 months | Death |
| 7 | Felip/1991 | 62/M | 3 years | Diplopia, proptosis, vision loss | Refused for treatment | Not mentioned | Not mentioned |
| 8 | Hugkulstone/ 1994 | 45/M | Orbital lesions appeared simultaneously | Diplopia, left conjunctival mass, red eye (bilateral) | Not mentioned | 5 months | Death |
| 9 | Scott/1995 | 73/M | 3 years | Diplopia, proptosis, pain | Radiotherapy + retrobulbar alcohol injection + steroid | 13 days | Death |
| 10 | Fynn-Thompson/2003 | 68/M | 11 years | Diplopia, proptosis, vision loss | Not mentioned | 1 month | Death |
| 11 | Chua/2004 | 78/F | 4 years | Diplopia, red eye | Radiotherapy + Chemotherapy | 1 month | Death |
| 12 | Souza Filho/2004 | 53/M | 3 weeks | Diplopia, proptosis, vision loss | Not mentioned | 1 month | Death |
| 13 | Shikishima/ 2006 | 74/M | 3 years | Diplopia, proptosis, red eye, pain, vision loss | Radiotherapy + Chemotherapy | 7 months | Death |
| 14 | Lin/2007 | 60/M | 8 months | Diplopia, blurred vision, proptosis, chemosis of conjunctiva, global extraocular movements restriction | Chemotherapy | Not mentioned | Not mentioned |
| 15 | Magrath/2014 | 57/F | 3 days | Proptosis, decreased vision, global extraocular movements restriction | Palliative care | Not mentioned | Not mentioned |
| 16 | Genc 2017 | 67/M | Orbital lesions appeared simultaneously | Limitation of movements, diminution of vision | Palliative chemotherapy + radiotherapy | Not mentioned | Not mentioned |
| 17 | Current case | 60/M | 1 year | Decreased vision, proptosis, widened palpebral fissure, restriction in ocular motility, diplopia, palpable orbital mass | Chemotherapy | 6 months | Death |

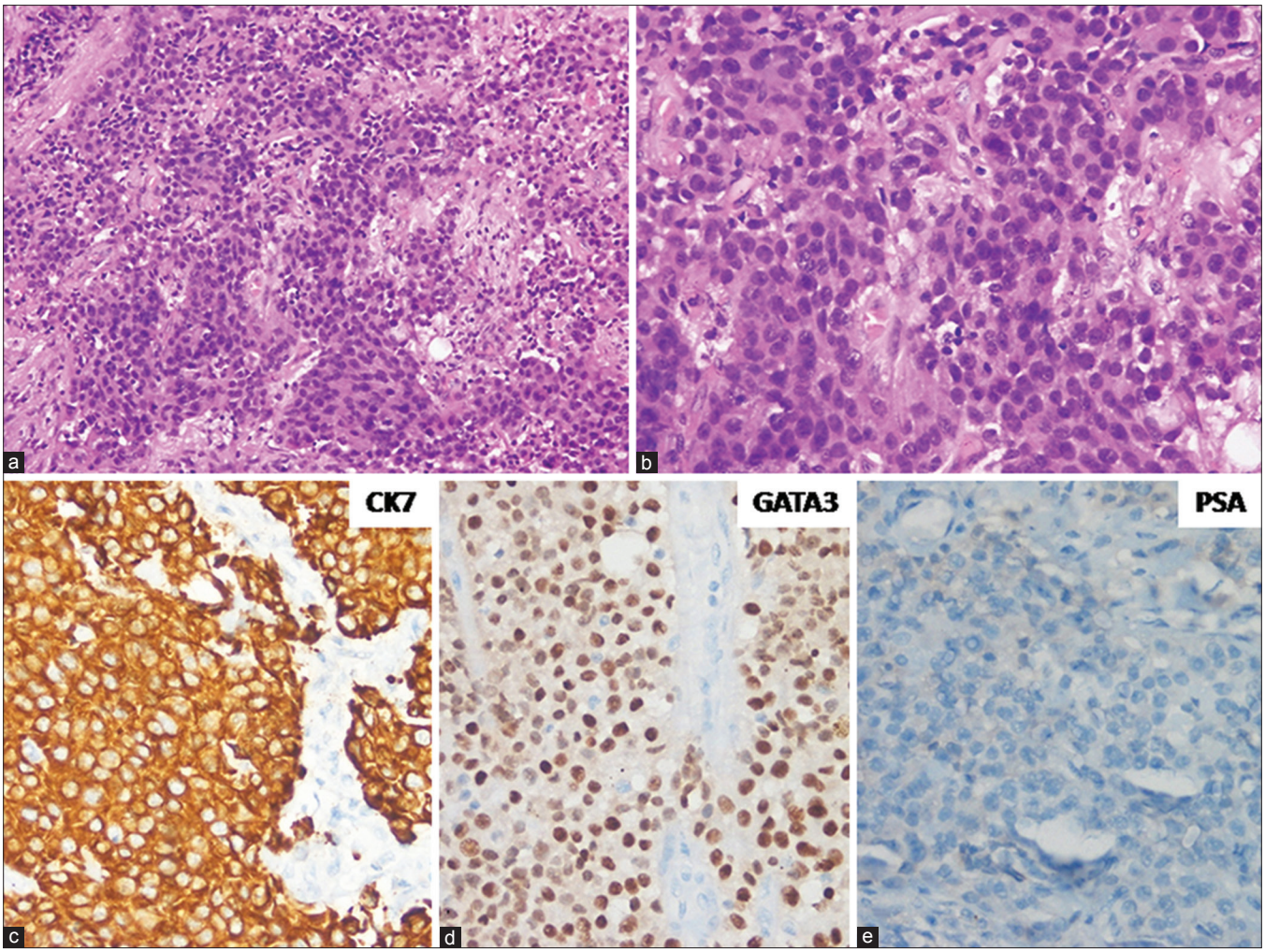


**Figure 3:** (a) Low magnification demonstrating tumor cells arranged in nest and trabeculae (H and E × 200). (b) Moderately pleomorphic, round to oval cells with moderate cytoplasm (H and E × 400). (c) Diffuse strong positivity for cytokeratin 7 (immunoperoxidase × 400). (d) Diffuse nuclear positivity for GATA 3 (immunoperoxidase × 400). (e). Tumor cells were negative for PSA (immunoperoxidase × 400)

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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### Conflicts of interest

There are no conflicts of interest.

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