Genitourinary malignancy presenting as an ocular metastasis: A case report and review of the literature

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Abstract

Metastases to the eye or orbit as the initial presentation of genitourinary malignancy are unusual and can be a diagnostic challenge. We report an 81-year-old man who presented with pain and proptosis in an eye that had been blind for 50 years. Radiologic investigations identified a mass involving the left globe and orbit. Histology of the enucleation specimen was consistent with a metastatic poorly differentiated carcinoma suggestive of a prostate primary. With the constellation of obstructive urinary symptoms, an abnormal digital rectal examination, elevated prostate-specific antigen and a positive bone scan, androgen deprivation therapy was initiated for metastatic prostate cancer. After an initial response to treatment, the patient's disease progressed in a manner atypical for prostate cancer. After describing our case, we review the literature on ocular and orbital metastases and their relation to genitourinary malignancies.

Introduction

Between 2% and 5% of cancer patients will develop an ocular or orbital metastasis. In 25% of these, it is the presenting sign of malignancy.[1-4] Frequently, this presents a diagnostic challenge and represents a poor prognosis.[5] We present an unusual case of proptosis as the index sign of malignancy and review the literature surrounding orbital and ocular metastases in prostate cancer and renal cell carcinoma (RCC).

Case report

In January 2006, a highly functional 81-year-old man wth a history of peripheral vascular disease developed proptosis and pain in the left eye, which had been blind for 50 years due to unrelated causes.

Magnetic resonance imaging (MRI) with gadolinium revealed a 2.7-cm homogenously enhancing left orbital mass encasing the optic nerve, extending along the lateral aspect of the globe and displacing it medially (Fig. 1a). Brain imaging was non-contributory. High resolution computed tomography (CT) of the orbits confirmed no bone involvement (Fig. 1b).

With a working diagnosis of melanoma or meningioma, left enucleation and debulking was performed. The orbital mass was centrally cored and decompressed internally, leaving the peripheral margins of the tumour intact. The specimen was a firm white mass extending over the posterior sclera and encasing the optic nerve. The tumour involved the anterior chamber, ciliary body, choroid and sclera, with extension into the episcleral and orbital soft tissues. Immunophenotyping was positive for pankeratin, vimentin, CD20, P504S and prostate-specific antigen (PSA), and negative for CK7, CK20 and prostate specific acid phosphatase (PSAP). RCC and androgen receptor antibodies were not available at that time. The pathologic assessment described a poorly differentiated adenocarcinoma consistent with a prostate primary.

The patient was seen at our institution 2 months later. He reported obstructive urinary symptoms. A firm irregularity of the right prostate was palpable, consistent with T2b disease. His PSA was 8.9 μg/L. Baseline bone scan showed increased uptake in the left fourth rib, but no bony orbital involvement (Fig. 2). Given the constellation of urinary symptoms, abnormal digital rectal examination (DRE), elevated PSA, pathology and bone scan findings, the patient was started on leuprolide and flutamide for metastatic prostate cancer. He did not have a prostate biopsy.

Two months following the first leuprolide injection, his PSA had declined to 0.6 μg/L. The patient's ophthalmologist noted a dramatic improvement with decreased intraorbital pressure and improved cosmesis. Given the degree of local response, further surgical intervention was not necessary and the patient continued with anti-androgen therapy.

The patient did well for about two years, when he developed impending spinal cord compression. His PSA was 0.36 μg/L and a CT identified a 9.6 × 4.8-cm expansile

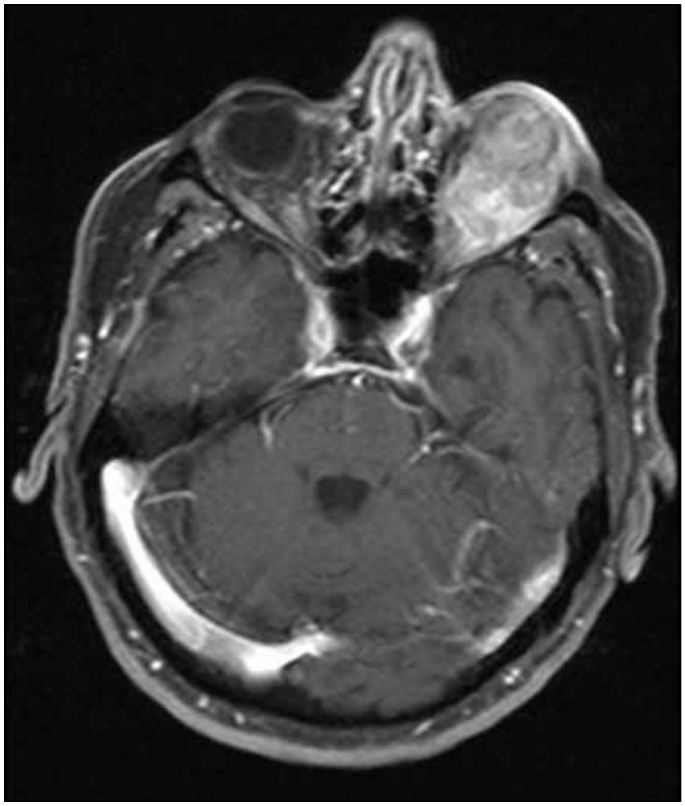

Fig. 1a. Axial T2-weighted magnetic resonance imaging.

lytic lesion involving the left fourth rib and T4 vertebral body with a large soft tissue component. Given this unusual radiologic presentation, a biopsy was performed. The morphologic findings were similar to those of the ocular specimen. Palliative radiotherapy was administered.

Three months later, a CT of the chest, abdomen and pelvis identified progression of the irradiated rib lesion; PSA was 0.3 μg/L. The putative radioresistance and low PSA at the time of radiologic progression prompted pathology review. The ocular sample was morphologically consistent with a clear cell neoplasm with acinar and papillary architecture. Immunohistochemistry studies directed at PSA, previously reported as positive, were reviewed as negative, with minimal expression. The prostate acid phospha (PAP) was negative. Additional testing revealed epithelial membrane antigen (EMA) and RCC expression, minimal androgen receptor expression, and no E-Cadherin or CD57 expression. These findings were reported as metastatic poorly differentiated adenocarcinoma with RCC as the most likely primary site. The rib biopsy showed similar histopathologic features.

Abdominal ultrasound and CT identified three renal cysts: a 7-mm cyst within the left kidney and two cysts measuring 1.3 cm and 2.0 cm within the right kidney. The lesions were classified as Bosniak II. Review of a CT angiogram and Doppler ultrasound performed 7 months prior as a preoperative assessment for femoral-femoral bypass confirmed

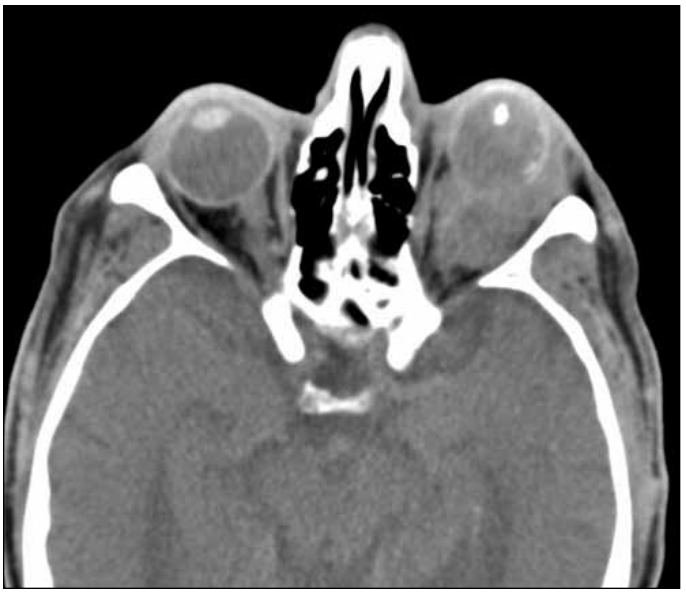

Fig. 1b. High resolution axial computed tomography scan.

that the cysts had been present and were stable in size. Unfortunately, the patient's disease continued to progress; neither confirmatory prostate nor renal biopsy were deemed clinically appropriate. He died in November 2008 and no autopsy was performed.

Discussion

Epidemiology and pathophysiology

Metastases to the orbital or ocular region typically develop in the setting of diffuse metastatic disease and occur in 2% to 5% of all cancer patients; however, it can be the presenting sign of malignancy in up to 25% of cases.[1,6] The prognosis is poor with a median survival of 6 to 9 months.[5]

The most commonly reported primary sites are breast (28%-59%), lung (8%-12%) and prostate (3%-10%).[1,7] Of the 48 published cases of orbital and ocular metastases secondary to prostate cancer since 1975, 38% were initial presentations.[7,8-19] RCC is a rare cause of intraocular and orbital metastases, accounting for 3% of metastatic orbital tumours.[20,21] Shome and colleagues identified 71 cases of intraocular and orbital metastasis from RCC between 1934 and 2004.[20] We identified an additional 6 cases.[22-26] Of these 77 cases, 47% were the primary presentation of malignancy.

Metastases to the eye and orbit typically occur through hematogenous spread via the carotid and ophthalmic artery. Genitourinary cancers may access this route via pre-existing pulmonary metastases or through Batson's plexus.[27] This valveless venous plexus connects the pelvic veins to the vertebral veins.[28] Tumour cells within the plexus may access the cranial venous sinuses and, subsequently, the ophthal-

mic veins via changes in venous pressure.[29] Prostate cancer cells most frequently metastasize to the orbital bone, while RCC shows a predilection for orbital soft tissue.[1,20]

Clinical presentation and diagnosis

The clinical presentation of metastases to the orbital region depends on the structures affected. For example, pain, diplopia and decreased visual acuity may be present if the orbital bone, soft tissue or globe is affected, respectively. These symptoms may progress over weeks to months.[1,30] Examination may reveal proptosis, ptosis, ophthalmoplegia or red eye. Complications include retinal detachment, uveitis, papilledema and secondary glaucoma.[1,2,8,29]

Appropriate investigations require consideration of the patient's clinical status and goals. If the patient has a previously-confirmed cancer diagnosis, it would be reasonable to defer further workup in favour of immediate treatment. However, a primary presentation of malignancy in a relatively healthy individual requires investigation. Ophthalmologic assessment can confirm a clinical suspicion of neoplasm, determine baseline visual acuity and institute measures to prevent sight-threatening complications.[15,31] Ultrasound can assess lesion location, size and characteristics. CT best delineates bony orbital disease, while MRI describes soft tissue and optic nerve involvement.[1,6,8]

In the search for a primary site, a thorough history, examination and review of past medical records should be performed. Radiologic investigations may suggest a primary or locate other sites of metastases more amenable to biopsy. If a careful systemic workup does not identify a primary, fine needle aspiration of the lesion is recommended which is diagnostic in 90% of cases. Potential risks include vision loss, bleeding, infection and dissemination of tumour cells.[1,5,31] Alternatively, if the tumour is accessible and well-circumscribed, excisional biopsy could be considered.[2]

Treatment

Treatment is aimed at providing local control to preserve vision, cosmesis and comfort.[1,29,31] Serial observation is appropriate in asymptomatic patients with slow-growing tumours that do not threaten vision. Chemotherapy or hormonal therapy can be used in the setting of widely metastatic disease. If systemic therapy fails, local treatments should be considered.[5]

A variety of local therapies are available including plaque brachytherapy, phototherapy and surgery; however, no randomized trials have been performed.[1,5,8,10,32] Currently, the mainstay of treatment is palliative external beam radiotherapy, typically 20 to 40 Gy over 1 to 2 weeks.[1,5] Tumour and symptom response have been demonstrated in 63% to 83% of cases; however, half of these studies were performed in breast cancer and the generalizability of these results to other histologies is uncertain.[33-38] Potential side effects include skin erythema, conjunctivitis, corneal ulceration, cataract formation, retinopathy and neuropathy.[1,33,34]

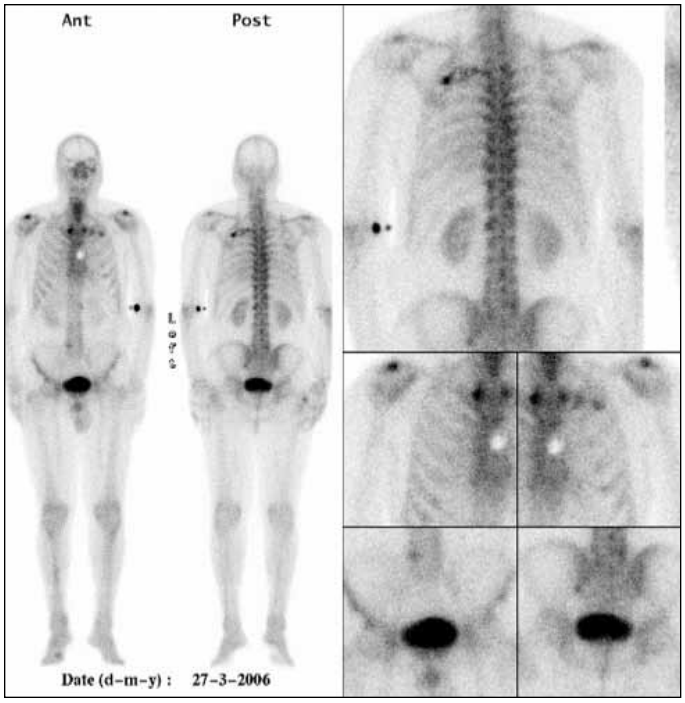

Fig. 2. Baseline bone scan. Findings were significant for increased uptake in the left fourth rib and degenerative changes within the acromia, sternocostal joints and lumbar spine, but negative in the orbit.

When response to the above modalities is incomplete, surgical debulking can improve cosmesis and visual acuity.[31] Enucleation has not been shown to prolong survival and should be reserved for uncontrolled tumour growth, a sightless eye or intractable symptoms.[1]

Our case: A diagnostic dilemma

We present a puzzling case of an 81-year-old man whose initial presentation of malignancy was proptosis secondary to an orbital tumour. He was originally treated for metastatic prostate cancer; however, due to an unusual clinical course, pathology review was performed and evidence for a RCC metastasis was identified. As with all pathologic information, correlative clinical evidence must be considered.

Our patient's presentation with obstructive urinary symptoms, abnormal DRE, elevated PSA and bone metastases was suggestive of prostate cancer. Although metastatic disease with an initial PSA less than 10 μg/L is uncommon and the positive predictive value of DRE in the setting of elevated PSA is only 46%, the diagnosis of prostate cancer was supported by local tumour response to androgen deprivation therapy.[39,40]

RCC, on the other hand, is well-known for its ability to metastasize to unusual locations, has no association with PSA, is relatively radioresistant and has been reported to undergo spontaneous regression.[41-43] Although three Bosniak II cysts were identified, the difficulty in distinguishing between Bosniak II (benign) and Bosniak III (suspicious for malignancy) lesions is well-documented.[44-46] However, the three-year survival of untreated stage IV RCC is less than 5%;[47] our patient lived for 34 months after his initial diagnosis. Also, spontaneous regression of RCC metastases typically occurs following a nephrectomy.[43]

Interestingly, about 25% of patients with RCC have multiple primary tumours; prostate cancer is one of the most common concomitant malignancies.[48] Unfortunately, without tissue samples from the prostate or kidney, the only certain diagnosis is metastatic poorly differentiated adenocarcinoma.

Conclusion

Metastases to the orbital region are occasionally the primary presentation of cancer and represent a diagnostic challenge. Suspicion of malignancy in this anatomic site requires a rational clinical approach. Referral to an ophthalmologist and thorough investigation if no primary is evident is often warranted. In an older male with visual complaints and urinary symptoms, the genitourinary system should be evaluated as a potential primary site as prostate cancer is one of the main sources of orbital metastases. Although prognosis is generally poor, both local and systemic treatment options exist to address symptoms and preserve visual acuity.

Competing interests: None declared.

This paper has been peer-reviewed.

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