CASE REPORT

Insidious enemy: downside to prolonged survival in prostate cancer

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SUMMARY

An 83-year-old man, a prostate cancer survivor of 10 years with multiple vertebral metastases presented with sudden onset of double vision. On examination he was found to have an isolated partial left abducens palsy with no other neurological deficits. Despite having microvascular risk factors, given his history of prostate cancer, a MRI brain scan was requested to look for a neurological cause. The scan revealed a metastatic lesion in the clivus encasing the cavernous sinus and carotid artery. He was referred to his oncologist for further management, however he opted out of further treatment and succumbed to his illness a month later. This case report includes a literature review of cases with clivus metastases secondary to prostate cancer. It highlights the importance of carefully examining eye movements and having a high index of suspicion for the subtlest sign that may suggest brain metastases in elderly patients with prostate cancer with prolonged survival.

BACKGROUND

Prostate cancer is the most common type of cancer and the second most common cause of cancer death among UK men as per the cancer research UK 2014 statistics report. Despite the aforementioned, brain metastasis from prostate cancer has been detected in less than 1% of all patients with prostate cancer.¹⁻³ This could suggest resistance of brain parenchyma to establishment of metastatic foci by prostate carcinoma cells, underreporting or undetected metastatic cases.^{4,5} We report a rare case of a patient with prostate cancer presenting with an isolated sixth cranial nerve (CN6) palsy as the only presenting symptom for clivus metastasis.

CASE PRESENTATION

An 83-year-old man presented with a 3-week history of sudden onset of horizontal diplopia on left gaze with no double vision on primary position. He denied having had headaches, facial numbness or cranial nerve associated neurological symptoms. He was diagnosed in 2006 with moderate to poorly differentiated prostate cancer (Gleason Score 4+5) with bony metastases for which he was initially treated with goserelin acetate, a gonadotropin-releasing hormone agonist, and additionally bicalutamide, an antiandrogen, 4 years following diagnosis. He had stable prostatic specific antigen (PSA) levels until 2012 when he had steadily increasing levels despite trials of bicalutamide, diethylstilbestrol and later abiraterone. He was also being treated

for hypertension and gout. Additionally, he had a history of diverticulosis and recurrent colorectal polyps with signs of low grade dysplasia warranting an early anterior resection in 2012. Interestingly, 2 out of 10 lymph nodes harvested during the anterior resection yielded tumour cells which were secondaries from the previously diagnosed prostate cancer rather than colorectal. As this was a colorectal adenocarcinoma confined within the muscularis propria with no lymph node involvement (clinical stage T2NO), the patient did not require any adjuvant treatment. In 2014, he had also been found to have further bony metastases confirmed on CT scan. He had a course of radium-223 and a further course of palliative radiotherapy to the lumbosacral spine in 2015. By the time he was seen by the ophthalmology team a year later, he was only on low dose dexamethasone as a result of failure to respond to all aforementioned treatments and was suffering from extreme exhaustion presumed to be secondary to actively dividing cancer cells. He was deemed unfit for chemotherapy and therefore was referred for supportive care at a hospice.

Neuro-ophthalmological examination revealed partial restriction of left lateral rectus muscle. His pupils were equal and reactive bilaterally. Visual acuity was 6/9 in both eyes. Cover test revealed left esotropia measuring 10 prism dioptres for distance. A prism was not required as the patient was coping well without it. Examination of the anterior and posterior segments of the eyes was satisfactory.

In view of his subtle presentation, our initial diagnosis was isolated incomplete left CN6 palsy likely secondary to a microvascular mononeuropathy event. His blood tests for inflammatory markers were normal. There was no deterioration in his double vision on further follow-up with the orthoptist 10 days later. Nevertheless, given his history of metastatic prostate cancer, we proceeded with MRI brain and orbit. The MRI revealed a metastatic lesion in the clivus encasing cavernous sinus and left carotid artery with minimal fascia in between the right carotid artery and the lesion (figure 1).

INVESTIGATIONS

MRI brain.

DIFFERENTIAL DIAGNOSIS

Microvascular mononeuropathy isolated CN6 palsy.

CrossMark

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Figure 1 MRI brain, sagittal view, showing clivus metastasis.

OUTCOME AND FOLLOW-UP

He was referred to the oncologist for further management. However, he became progressively weaker and decided to opt out of further treatment. He passed away a month later.

DISCUSSION

Brain metastases from prostate cancer, although rare, often at diagnosis have extensive bone and soft tissue dissemination.⁵ Notably, the most common primary site for cancer metastases to the clivus is the prostate.⁶ The CN6 runs along the clivus, between the pons and the cavernous sinuses, therefore, a

metastatic lesion to the clivus can be responsible for unilateral or bilateral CN6 palsy.

We performed a literature search including PubMed, MEDLINE and Embase databases to identify all cases of patients presenting with sixth nerve palsy as a consequence of clivus metastases from prostate cancer. We used the search terms 'clivus metastasis, clivus neoplasm, clivus tumour, 6th Nerve palsy, abducens nerve palsy, prostate cancer, prostate metastatic disease, prostate ca, prostatic adenocarcinoma, prostate metastasis and prostate carcinoma'. The initial search revealed 20 results. These were screened and narrowed down to 11 reports which were relevant to this review, all of which were case reports or small case series.

Based on our literature review, most case reports described prostatic cancer metastasis to skull base with involvement of multiple cranial nerves. There were only nine reported cases of isolated CN6 palsy as the single initial presenting symptom of clivus metastasis. Table 1 summarises the results of our literature review.

Brain metastasis, on average, manifests 60 months after the initial diagnosis of prostate cancer.² This is a terminal event ensued by death, in a majority of the cases, in less than a year.⁷ Prolonged survival in patients with prostate cancer increases the risk of brain metastasis and we should be prepared to detect central symptoms promptly in order to diagnose these metastases early.⁸

To date there is limited information on treatment of clivus metastases from prostate cancer as patients present late in the context of multiple metastases. Radiotherapy with or without use of steroids has been shown to be effective in resolving clinical symptoms either completely or at least partially.^{9 10} The role of hormone therapy is unknown especially since many patients will have hormone-refractory disease at the time of presentation. Endoscopic resection can be challenging because of the anatomical location of the bony clivus close to critical structures including the brainstem, basilar artery, internal carotid artery and cranial nerves. With the advancement of neurosurgical

Table 1 Schematic description of epidemiological, histopathology and prognostic data from literature review and our patient

Author	Age (years)	Interval from prostate cancer diagnosis (months)	Presenting symptoms	Treatment	Survival (months)	Histopathology of clivus lesion (transsphenoidal biopsy)
Pallini <i>et al</i> ⁶	50	0	Diplopia (CN6 palsy)	Transsphenoidal tumour resection, palliative radiotherapy, chemotherapy	6	Metastatic adenocarcinoma of the prostate
Pallini <i>et al</i> ⁶	70	120	Diplopia (CN6 palsy)	Transsphenoidal tumour resection, palliative radiotherapy, chemotherapy	3 (as of 2008)	Metastatic adenocarcinoma of the prostate
Mcdermott <i>et al</i> ⁹	53	17	Diplopia (CN6 palsy)	Radiotherapy	2	NA
Mcdermott <i>et al</i> ⁹	58	39	Diplopia (CN6 palsy)	Radiotherapy	31	NA
Malloy ¹⁰	70	3	Diplopia (CN6 palsy)	Radiotherapy	24 (as of 2008)	NA
Heidenreich <i>et al</i> ¹²	50	0	Diplopia (CN6 palsy)	Androgen ablation as palliative therapy	NA	Metastatic adenocarcinoma of the prostate
O'Boyle <i>et al</i> ¹³	71	0	Diplopia (CN6 palsy)	Androgen ablation, transsphenoidal tumour resection, palliative radiotherapy	NA	Metastatic adenocarcinoma of the prostate
Ransom <i>et al</i> ¹⁴	NA	31	Diplopia (CN6 palsy)	Androgen ablation	4	NA
Pollanz <i>et al</i> ¹⁵	52	48	Diplopia (CN6 palsy)	Chemotherapy, radiotherapy	3	NA
Patient A	83	120	Diplopia (CN6 palsy)	Androgen ablation, palliative radiotherapy, dexamethasone	1	NA

CN6, sixth cranial nerve.

NA, not available

approaches, surgical resection with adjuvant radiotherapy and chemotherapy have also been proposed, though there are limited data on the impact on survival.^{6 11} Needless to say, extensive research will be pivotal in providing us with better management strategies and prognostic values in patients with prostatic cancer with clivus metastasis.

We report this case for its rare occurrence in the hope that medical professionals alike will be more alert in recognising the subtlest sign of brain metastasis among patients with prostate cancer, especially the elderly and the long-term survivors. Furthermore, timely diagnosis and apt treatment can improve quality of life and survival.

Learning points

- ▶ This case proves that sixth cranial nerve palsy in elderly patients is not always caused by microvascular insufficiency, especially in the context of a previous history of malignancy.
- ▶ Even the subtlest neurological deficit in long-term prostate cancer survivors should be investigated thoroughly.
- ▶ Early detection and management of brain metastasis is made possible with high-end imaging and surgical techniques like MRI, transsphenoidal biopsy and tumour resection.

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