

Intracranial Meningeal Carcinomatosis in Metastatic Castration Resistant Prostate Cancer: Will Extension of Survival Increase the Incidence?

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Clinical Practice Points

- Prostate cancer is known to commonly metastasize to the bone, while visceral organ metastases are seldom seen in advanced castration-resistant prostate cancer (CRPC). Intracranial meningeal carcinomatosis or dural metastases from prostatic adenocarcinoma is extremely rare.
- Here we present a case of an 81-year-old man with CRPC and bone metastases who developed meningeal carcinomatosis after longer than expected survival after 2 lines of chemotherapy and an autologous antigen-presenting cell-based immunotherapeutic agent.
- Longer survival from docetaxel-based chemotherapy, and recently approved (sipuleucel-T, cabazitaxel, and abiraterone acetate) and emerging novel agents (MDV-3100 and radium-223), coupled with better imaging technology may render meningeal involvement more common. Early identification may forestall serious neurological deficits.

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Introduction

Prostate cancer is known to commonly metastasize to the bone, while visceral organ metastases are seldom seen in advanced CRPC. Intracranial meningeal carcinomatosis or dural metastases from prostatic adenocarcinoma is extremely rare.

Case Report

We present an 81-year-old man with a history of prostate cancer and leptomeningeal metastases. He was diagnosed to have CRPC with extensive bone metastases coupled with a prostate-specific antigen (PSA) = 894 ng/mL diagnosed 18 months earlier. He had received docetaxel in combination with prednisone for 6 cycles in conjunction with zoledronic acid. Upon progression, he was offered a clinical trial evaluating a novel autologous antigen-presenting cell-based vaccine. He experienced an improvement in pain during the trial and progressed approximately 6

months after starting this agent. He was switched to ketoconazole plus hydrocortisone and responded partially for approximately 5 months. He then progressed and received a cycle of cabazitaxel chemotherapy. At that time, he complained of numbness in the left side of his face and a mild headache. Magnetic resonance imaging (MRI) evaluation of the brain with and without contrast revealed findings consistent with meningeal carcinomatosis. Figure 1 shows the axial (top panel) and coronal section (bottom panel) where the left temporal and frontal subdural space exhibit a maximal thickening of 6 mm and postcontrast enhancement. He underwent a craniotomy and dural biopsy, which demonstrated findings consistent with metastatic prostate carcinoma. Figure 2 shows poorly differentiated carcinoma with vesicular nuclei and a few mitoses invading the dura mater (top panel, right lower corner) consistent with high grade prostatic adenocarcinoma, and the bottom panel shows neoplastic cells positive by immunohistochemistry (IHC) for pancytokeratin. IHC for PSA was negative (image not shown). He was given corticosteroids and a plan for cranial radiotherapy was made. Meanwhile, he suffered a generalized seizure and phenytoin was begun. Given his poor performance status, the patient decided to go home with hospice and palliative care. He died in approximately 2 weeks.

Discussion

Prostate cancer is known to commonly metastasize to the bone, while measurable soft tissue and visceral metastasis to the liver, lungs, and other sites are seldom seen in the advanced castration-resistant

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Intracranial Meningeal Carcinomatosis and Extension of Survival in MCRPC

Figure 1 MRI of the Brain. Axial (Top Panel) and Coronal Section (Bottom Panel) Show That the Left Temporal and Frontal Subdural Space Exhibit a Maximal Thickening of 6 mm and Postcontrast Enhancement

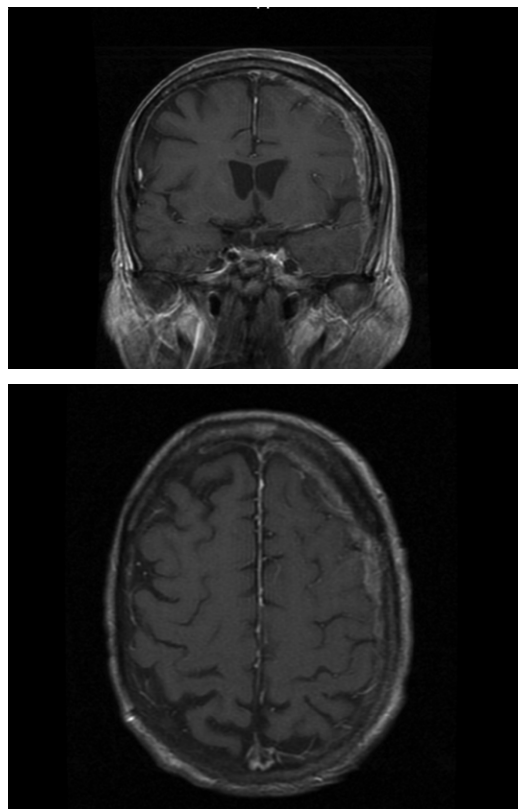
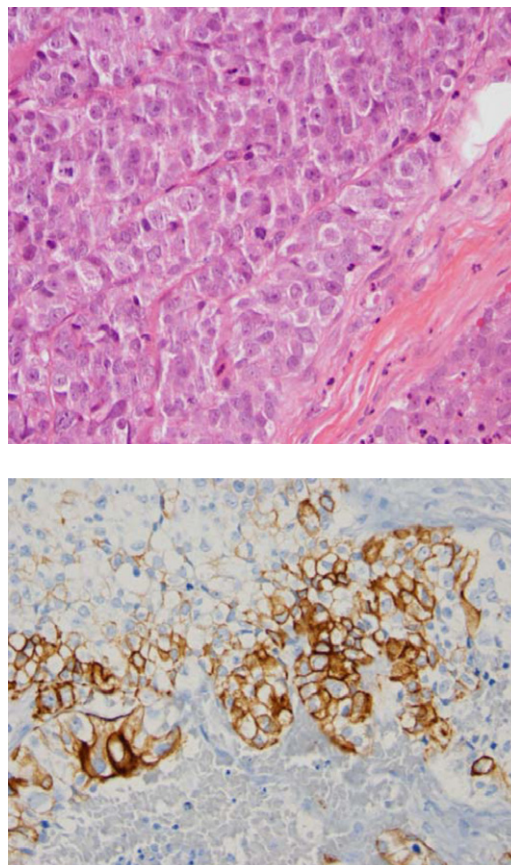


Figure 2 Pathologic Features of Dural Biopsy. Poorly Differentiated Carcinoma With Vesicular Nuclei and a Few Mitoses Invading the Dura Mater (Top Panel, Right Lower Corner) Consistent With High Grade Prostatic Adenocarcinoma. Bottom Panel, Neoplastic Cells Positive by Immunohistochemistry for Pancytokeratin (Hematoxylin and Eosin Stain; Magnification $\times 400$)



state. Intracranial meningeal carcinomatosis or dural metastases from prostatic adenocarcinoma are extremely rare and have been described in less than 30 cases in the literature.^{1,2} However, subclinical intracranial metastases may be more common. Of 126 autopsied cases with prostate cancer, 14 (11.1%) demonstrated intracranial metastases, including 5 previously asymptomatic patients.³ Pathology revealed moderately to poorly differentiated tumor in 11 of 14 cases.³ In another study of 16,280 patients with prostate cancer, 131 had intracranial metastases that were diagnosed either with computed tomography/MRI scan ($n = 53$) or on autopsy ($n = 78$). Only 21% of these 131 cases had dural metastases while the rest had intraparenchymal metastases.⁴ Another report identified 38 antemortem cases of intracerebral metastases among 7994 patients with prostate cancer.⁵ Even intraparenchymal metastases may be subclinical in many cases as illustrated by a study of 91 patients with prostate cancer who underwent autopsy, of whom 4 had intracerebral metastasis, but premortem diagnosis had been made in only 1 of these patients.⁶ Furthermore, small-cell cancer of the prostate or subsequent small-cell differentiation of adenocarcinoma may lead to central nervous system (CNS) metastasis.⁷ Adenocarcinoma was the most common

histologic type followed by small cell cancer squamous cell, rhabdomyosarcoma, and ciribriform cell carcinoma. Intriguingly, in another study of dural metastases from any primary, a different distribution of primary sites was observed compared with earlier series.⁸ Notably, prostatic dural metastases occurred more commonly in the autopsy series (7 of 27 cases) compared with the surgical series (1 of 33 cases).

Prostate cancer may metastasize to the meninges through direct invasion from adjacent vertebral or skull bone, either hematogenously or lymphatically. Generally, leptomeningeal and brain metastases are late events in the evolution of a malignancy. Given the recent appearance of more cases of prostatic dural metastases in the literature, one may hypothesize that extension of survival observed because of recent advances in systemic therapy, such as sipuleucel-T, cabazitaxel, and abiraterone acetate, is increasing the incidence of leptomeningeal involvement. Indeed, in 1 retrospective study, the

