# *Solitary brain metastasis after recurrent adenocarcinoma of the prostate*

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*Prostate cancer is rarely metastatic to visceral organs, and even less commonly to the brain. Recent data suggests brain metastasis from prostatic adenocarcinoma occur in 0.16% of patients, and almost universally in the setting of very high-volume disease. We present a man with an abruptly symptomatic brain lesion that developed at a PSA value of 1.5 ng/mL with no other known metastatic disease and required emergent neurosurgical resection. The patient had been initially treated with radiotherapy for Grade Group 4 prostate cancer in 2005 with a long period of PSA suppression.*

**Key Words:** prostate cancer, brain metastasis, pathology, radiology, recurrence

## Introduction

In 2019 in the United States, there will be an estimated 164,690 new cases of prostate cancer (19% of all male cancer incident cases) and an estimated 29,430 prostate cancer mortalities (9% of all male cancer deaths).[1]

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Prostate cancer metastasis are most commonly identified in bone with a reported incidence of 7.7% and 16.6% at 1 and 5 years respectively.[2] Visceral spread is less common. There are several interrelated factors leading to differing pathophysiology between visceral and bone metastases including intrinsic cellular factors, the tumor microenvironment, and systemic factors.[3] Prostate cancer metastasis directly to the brain is an increasingly rare phenomenon. A 2003 series found only 0.63% of metastasis from prostate adenocarcinoma to occur in the brain, and more recent series observe brain metastasis occurring less commonly at 0.16% of total prostate cancer metastatic sites.

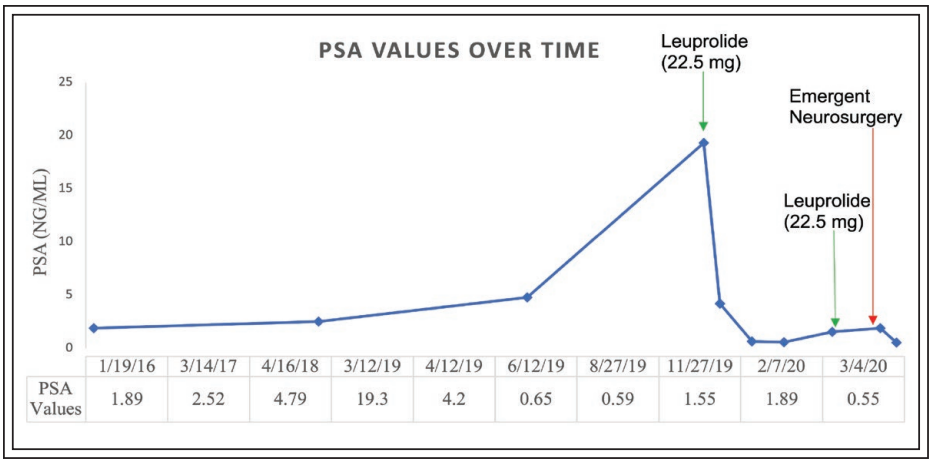


**Figure 1.** Patient's pre-leuprolide PSA trend over time; calculated PSA doubling time was 13.0 months. Leuprolide was administered on 3/12/19 (green arrow). The patient presented with neurologic symptoms leading to emergent neurosurgical resection on 2/7/20 (red arrow).

Brain metastasis in this disease are rare, and generally occur in the setting of high-volume systemic disease. When prostatic-origin brain metastasis are present, data predict coincident bony spread in 95% of afflicted patients, nodal metastasis present in 86%, and a synchronous visceral metastasis rate of 76%.[4] Patients experiencing brain metastasis often present with nonspecific neurologic symptoms. Survival after a diagnosis of metastatic prostate cancer to the brain averages 2.8 months.[5,6] Solitary brain metastasis appears to be vanishingly rare and a careful differential is necessary if pathology is not immediately available.

## Case report

We present an 81-year-old man who had been treated for Gleason 4+4 prostate cancer with radiotherapy and single-dose of androgen deprivation in 2005. After a long convalescent period with excellent follow up and PSA control, this patient came to our institution in 2018 with a PSA that had recently risen to 4.8 ng/mL and a palpable prostate nodule. He underwent prostate biopsy which showed local recurrence of high-grade prostate adenocarcinoma. A fluciclovine-positron scan was performed which showed no extra-prostatic spread. Initial plans for ablative cryotherapy were discarded after his PSA accelerated to 19.3 ng/mL. Leuprolide was administered with excellent PSA response, Figure 1. He presented to an outside hospital in January 2020 with acute neurologic symptoms. His PSA was measured at 1.45 ng/dL approximately 7 weeks prior. Imaging at the outside hospital demonstrated a brain lesion likely responsible for the acute changes, Figure 2. Emergent neurosurgical resection was performed, which confirmed metastatic adenocarcinoma of prostate, Figure 3. The patient has since recovered well from surgery with no other evidence of metastasis.

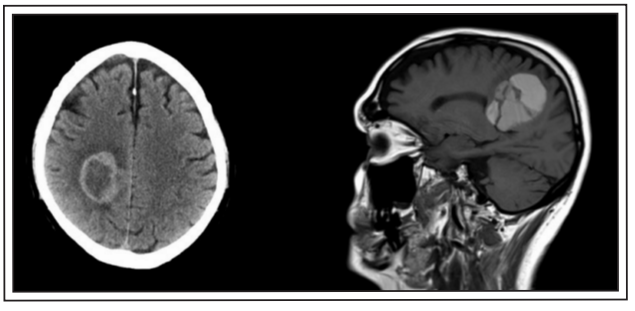

**Figure 2.** MRI of mass occupying brain lesion compressing the corpus callosum and right lateral ventricle not previously seen on fluciclovine PET scan.

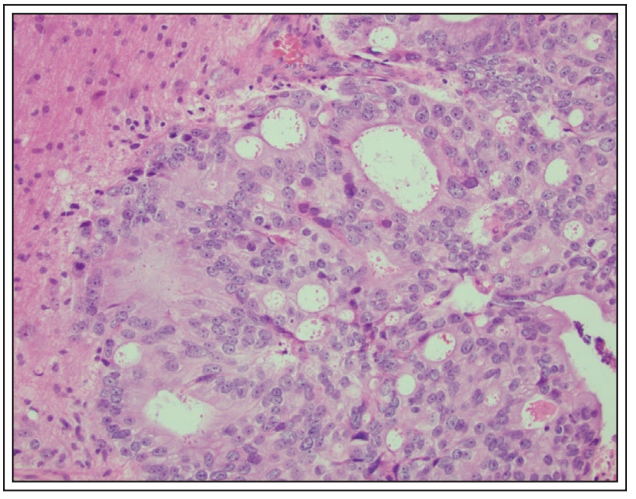

**Figure 3.** Brain: adenocarcinoma with cribiform architecture. H&E stain, high Power. NKX3.1 immunostain showed nuclear reactivity with absence of TTF-1 and GATA-3 supporting a prostatic origin.

## Discussion

We present an extremely rare case of pathologically confirmed solitary brain metastasis from castrate-sensitive adenocarcinoma of the prostate. The underlying biology of metastasis is complex. Different malignant transformations occurring in poorly differentiated cancer appear to confer the ability to travel hematogenous and to selectively inhabit unrelated tissues. Intrinsic cellular factors, the tumor microenvironment, and systemic factors all combine to influence the destination of metastasis.[7] In this instance, it appears that a combination of malignant transformation, ionizing radiotherapy and time allowed the development of a CNS-trophic mutation that is quite unusual for prostate cells.

The pathway of metastasis in our patient is clearly quite unusual and highlights the rarely explored relationship between prostate cancer cells and the central nervous system (CNS). Computed tomography and magnetic resonance imaging are commonly used in the diagnosis of brain metastases but given the vanishingly-low likelihood of CNS spread, directed imaging is only suggested in the setting of neurologic symptoms as illustrated here.[8]

This case is particularly unusual in that our patient had no previously identified metastatic disease despite evaluation with fluciclovine-positron scanning, and experienced this event at a point relatively early in the course of this disease while he still demonstrated hormone sensitivity of the tumor and a low PSA value. The most common sites of metastasis for prostate cancer are bone, distant lymph nodes, liver, and thorax, none of which have been found in this patient. Symptomatic patients primarily complain of localized bony pain or lower urinary tract symptoms, illustrating the importance of careful review of systems with symptom-guided regional imaging during follow up.[9] Brain metastases typically occur in the context of widespread metastatic disease, and while it is even more uncommon to have the brain as the only site of metastatic prostate cancer, symptoms must be identified and pursued appropriately.[10]

As discussed, metastatic prostate cancer to the brain is a rare but morbid event. Early diagnosis and direct management are key for optimal prognosis and long term survival. Additional understanding of the biology of metastatic tropism and growth is a key to combat all malignancies, and analysis of unique cases such as the one presented may provide insight to better understand, predict and prevent the spread of cancer. □

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