

Central Nervous System Metastases from Prostate Cancer: Two Cases Report

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ABSTRACT

Intracranial metastases from prostate cancer are unusual. It appears frequently in advanced castration-resistant prostate cancer. Their prognosis is very poor and median of survival does not exceed 4 months at maximum. Few systemic treatments cross the blood brain barrier. We report two cases of patients with two different localisations of intracranial metastases from adenocarcinoma of prostate cancer.

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Introduction

Central nervous system (CNS) metastases can develop from any primary cancer, the predilection for distant spread varies by cancer type. CNS localisations from prostate cancer is a rare disease. The prognosis remains very poor, as it typically indicates a disseminated malignancy.

Case report 1

A 70 years old man: diagnosed with prostate adenocarcinoma in 2009, treated with radical prostatectomy (pT3bN1M0-ISUP5) followed by adjuvant radiotherapy and two years of Androgen Deprivation Therapy (ADT). The post-radiotherapy PSA was 0.32 ng/ml. On July 2015, PSA =5 ng/ml, multiple metastasis on lymphatics and bones, treated with abiraterone acetate. On April 2016, PSA =38ng/ml, tumoral progression and multiple metastasis of liver and lung, treated with six cycles of chemotherapy, Docetaxel, then maintenance with ADT (LH-RH analogues). On January 2017, the patient was admitted to the hospital for confusing with vomiting and headache. Brain-CT objectified multiples parenchymatous cerebral metastasis (Figure-1). A whole brain radiotherapy was performed (30 Grays in 10 fractions) with clinical response, followed by 6 cycles of Docetaxel with a tumoral extra-cranial progression, apparition of pleural and surrenal metastasis, treated with abiraterone acetate with biochemical response: PSA at 1.08 Vs 5 ng/ml, despite this biochemical response, the disease was on progression. NSE and Chromogranin rates were normal. A surrenal biopsy confirmed the absence of a neuro-endocrine component. The other sites were not accessible for biopsy. A chemotherapy by Cabazitaxel has been initiated and maintained for six months followed by Enzalutamide. On June 2018, the patient was treated with a bi-chemotherapy: Carboplatin-Etoposide, six cycles administrated with stability of all metastasis. Because of poor performance status (PS=4),

treatments were stopped. The patient died in April 2019, that means 26 months after metastasis brain diagnosis.

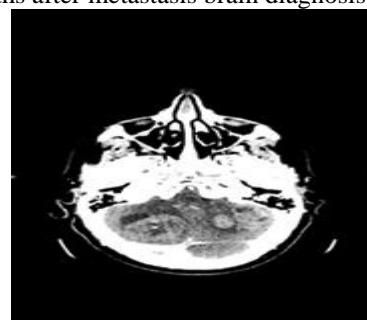


Figure 1A

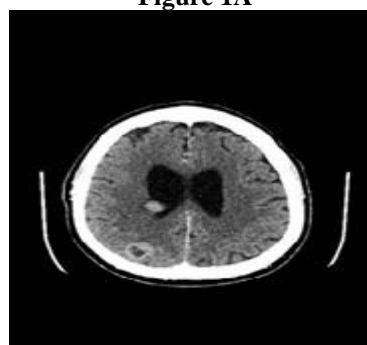


Figure 1B

Figure 1. A CT of the brain revealed multiple secondary lesions in the cerebellum (A) and in parenchymatous cerebral (B).

Case report 2

78 years old man diagnosed with prostate adenocarcinoma (ISUP 4) in 2015, with synchronous metastasis on bones, lung and lymphatics, and initial PSA=2696 ng/ml, treated by ADT (LH-RH analogues) plus Denosumab with nadir of PSA at 882 ng/ml. On September 2015, biochemical progression,

treated by abiraterone acetate+Prednisone+ADT. On May 2017, biochemical and radiological tumoral progression; treated by Enzalutamide until June 2017 when the patient was admitted to the hospital with disorder behavior and confusion.

Brain-CT objectived pachymeningitis by local extention from bone cranial metastasis (Figure-2). Whole Brain irradiation (30 grays in 10 fractions) was done . PSA at 3450ng/ml. Because of poor performance status, supportive and palliative care were decided, and the patient died four months later.

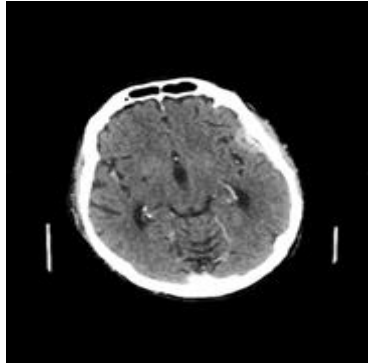


Figure 2A



Figure 2B

Figure 2 . CT of the brain objectived pachymeningitis by local extention from bone cranial metastasis.

Discussion

Prostate carcinoma is the most common malignancy among men in the world. It is the third leading cause of death from cancer. An estimated 174,650 new cases of prostate cancer will be diagnosed in 2019, accounting for 20% of new cancer cases in men.

Prostate carcinoma is typically metastasizing to the axial skeleton and pelvic lymph nodes. Intracranial metastases are uncommon in prostate carcinomas. Bone, lung, and liver are the most frequent sites of distant prostate cancer metastases. Bubendorf et al (1) showed that metastasis to the spine is independent of lung metastasis, its involvement occurred in smaller tumors (4 to 6 cm) as compared with the maximum spread to lung (6 to 8 cm) and liver (> 8 cm). In this same autopsy series, spine metastases were found in 87% of the patients with metastatic prostate cancer, this could be explained by the affinity of prostate carcinoma cells to bones. This study has failed in demonstrating brain metastasis. Autopsy series are a useful tool to show the frequency and mechanisms of intracranial metastasis in prostate cancer. (1)

The main pathways form of prostate carcinoma dissemination are: hematogenous spread , either by the caval system or by the Batson plexus or and local extention from bone cranial metastasis.(1)

Prostate carcinoma represents the main source of dural metastases. Kleinschmidt- De Masters and al. considered prostate carcinoma to be the primary tumor involving

secondary to the dura mater, followed closely by breast carcinoma. The review by Lynes and al found intracranial metastatic of prostate carcinoma in 67% of the patients involving the dura mater , whereas an autopsy series by Taylor and all. reported the frequency of 85%.(2)

According to multiple sources and database from 1982 to 2018, we selected patients with intraparenchymal metastases from prostate adenocarcinoma proven either on autopsy or stereotactic biopsy. In 75 to 86% , brain metastasis of prostate carcinoma were solitary.

However, a recent study of MSKCC reports 29% of solitary brain metastasis, probably because magnetic resonance imaging (MRI) is most often used, enabling the detection of multiple brain metastasis. (3)

The most common symptoms at presentation include headache (50%), focal weakness (40%), confusion or altered mental status (30%), seizures (15%), and ataxia (10%), and these symptoms tend to worsen with time as the tumor grows and the surrounding edema exerts a mass effect on nearby structures. Occasionally, brain metastases are asymptomatic detected with choline PET/CT (Sneed et al., 2008).

PSMA PET/CT imaging appears to have superseded F18 FDG PET/CT, CT and MR imaging not only in the staging of Prostate cancer but also in the detection of PSMA-avid disease and is increasingly being used for restaging recurrent prostate cancer (3).

Brain metastases are typically a late manifestation of disease, 24 to 47 months from the primary diagnosis of prostate adenocarcinoma, 31 to 45 months if small cells carcinoma.(4)

There are multiple treatment modalities: Surgery, radiotherapy, and chemotherapy, in addition to corticosteroids for symptom-based therapy. However, patient-specific factors determine what treatment options can be used. Surgery cannot be used if poor performance status, elder patients and technically, when multiple foci of brain metastases exist and in dural metastasis.(5)

Different dose-fractionation schedules in radiotherapy are used with any difference of efficacy.(20 Gy in 5 fractions or 30 Gy in 10 fractions) .(6) These options range from 1-week programs with lower total doses and higher doses per fraction to more protracted programs lasting up to 4 weeks with higher total doses but lower doses per fraction. Previous studies suggested that patients with a short expected survival should be treated with a short Whole Brain Irradiation (WBI) program for a best quality of life. In contrast, longer WBI programs were reported to result in improved local (intracerebral) control and survival in the group of patients with the longest estimated survival time.

Unfortunately, patients with brain metastasis of prostate carcinoma are never included in studies , so we don't have any data of efficacy of chemotherapy or new generation hormonotherapy.

Cabazitaxel cross the blood brain barrier more than Docetaxel. A recent clinical case report described 3 CRPC patients treated with cabazitaxel plus whole brain radiotherapy, where cabazitaxel was highly active and well-tolerated. (6)

Enzalutamide must be avoided in patient with risk factors of seizure (0 to 0.6%). (7)

There is no neurologic toxicity with Abiraterone Acetate , despite , there is no data of its efficacy.

The prognosis remains very poor. The mediane survival time does not exceed one month. However, with

corticosteroids, median survival times improved to 2–2.5 months, and with whole-brain radiotherapy (WBRT), median survival times improved to 3–6 months.(8)

In our case report, the survival time was very different between the two cases (5 months versus 27 months).

Conclusion

Intracranial metastasis of prostate cancer is a rare condition, occurring in patient with advanced stage and widespread metastatic disease. The prognosis is poor and therapeutic is limited. Clinical trials should be encouraged in order to open more perspectives.

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