

# Cerebral Metastasis as First Systemic Event in a Patient with Prostate Adenocarcinoma

## *Metástase cerebral como primeiro evento sistêmico em paciente com adenocarcinoma da próstata*

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### Abstract

Prostate adenocarcinoma (PAC) is the second most common malignant tumor in men, and it is usually diagnosed because of its symptoms and/or because of an increase in the value of the prostate-specific antigen (PSA) in asymptomatic patients. The lymph nodes and the bones are the most common sites in which metastases occur, while the brain is a rare site, with metastases occurring in < 2% of the cases, and usually only after the aforementioned sites have been affected. Considering the brain as the only site where a metastasis can occur, the incidence is of 0.15%. We present the case of a 63-year-old male diagnosed with PAC, with a Gleason score of 7 (3+4), who underwent radiotherapy and anti-hormonal therapy in 2012. After biochemical recurrence early in 2015 (PSA: 8 ng/mL), he was re-staged, and the bone and node metastases were excluded. The patient then resumed the hormone therapy with bicalutamide. He was admitted in August 2015 to the emergency department of our institution with headache and behavioral changes. The imaging study revealed a single right temporo-parieto-occipital lesion, which was then resected. The histological analysis confirmed it to be a PAC brain metastasis. The patient went through a cycle of brain radiotherapy, and evolved favorably after one year of follow-up.

### Keywords

- ▶ prostatic neoplasms
- ▶ brain tumors
- ▶ neoplasm metastasis

### Resumo

O adenocarcinoma da próstata (ACP) é a segunda neoplasia maligna mais comum em homens, sendo habitualmente diagnosticada por meio de seus sintomas e/ou pelo aumento do valor do antígeno prostático específico (APE) em doentes assintomáticos. As metastizações óssea e ganglionar são as mais frequentes, sendo o cérebro um local raro de disseminação desta neoplasia, ocorrendo em menos de 2% dos casos, e geralmente surgindo apenas após a disseminação nos locais previamente descritos. Considerando o cérebro como único local de metastização, a incidência é de 0,15%. Os

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**Palavras-chave**

- ▶ neoplasias da próstata
- ▶ tumores cerebrais
- ▶ metástase neoplásica

autores apresentam o caso de um homem de 63 anos com diagnóstico de ACP, com pontuação 7 (3 + 4) na escala de Gleason, submetido a radioterapia e bloqueio hormonal em 2012. Por recidiva bioquímica (APE de 8 ng/mL) no início de 2015, o paciente foi re-estadiado, tendo-se excluído as metastizações óssea e ganglionar. Ele reiniciou a hormonoterapia com bicalutamida. Em agosto de 2015, foi admitido no serviço de urgência de nossa instituição com um quadro de cefaleias associadas a alterações no comportamento. O estudo imagiológico revelou uma lesão cerebral temporo-parieto-occipital direita única, e o paciente foi submetido a uma craniotomia com remoção completa; o diagnóstico histológico revelou tratar-se de metástase de ACP. O paciente foi posteriormente submetido a radioterapia cerebral, apresentando uma evolução favorável após um ano de acompanhamento.

**Introduction**

Prostate adenocarcinoma (PAC) is the second most common malignant tumor in men<sup>1</sup> after lung cancer (of all histological types), with 32 cases per 100 thousand people per year.<sup>2</sup> Elderly men, African-Americans and men with family history of PAC are the most well-established risk groups.<sup>3</sup> The diagnosis is based on a combination of clinical signs (hematuria, urinary complaints or retention, back pain) that are usually late findings, and an elevated level of prostate-specific antigen (PSA), with prostate biopsy as the next diagnostic tool when PSA levels are > 4 ng/mL.<sup>4</sup>

Distant lymph nodes and the bones are the most common metastatic sites in a list that includes the liver, the thorax (lungs, pleura and mediastinum), the adrenal glands and the kidneys.<sup>5</sup> The brain is a rare site for PAC dissemination, and it is only affected in 2% of the cases,<sup>1</sup> usually after the aforementioned sites have already been invaded by tumor cells (primary metastases are exceedingly rare, and few cases have been described in literature). Occurring late in the natural history of PAC, brain metastasis entail a poor prognosis, with the mean survival rate described in literature being around 1–7.6 months, and 1-year survival rates of < 20%.<sup>5</sup>

Though data on the subject is scarce, the case of the surgical treatment of a single metastasis followed by radiotherapy has been described as beneficial to the patient, in line with the procedures performed for other single brain metastases of different histological origins.

**Case Presentation**

In February 2012, a then 59-year-old male presented in a routine blood work a PSA level of 5.0 ng/mL, with no associated symptoms or signs. A transrectal prostatic biopsy was performed, revealing a PAC, with a combined Gleason score of 7 (3+4). At that moment, the doctors decided to implement 38 weeks of external beam radiotherapy plus hormonotherapy, which resulted in the normalization of the PSA levels.

The patient remained in remission until December 2014, when an exam to control the PSA levels revealed the patient had a level of 8.0 ng/mL; therefore, he resumed the hormone therapy with bicalutamida. He underwent a bone scintigraphy, which revealed no bone disease, and a computed tomography

(CT) scan of the thorax, abdomen and pelvis, which also revealed no distant disease.

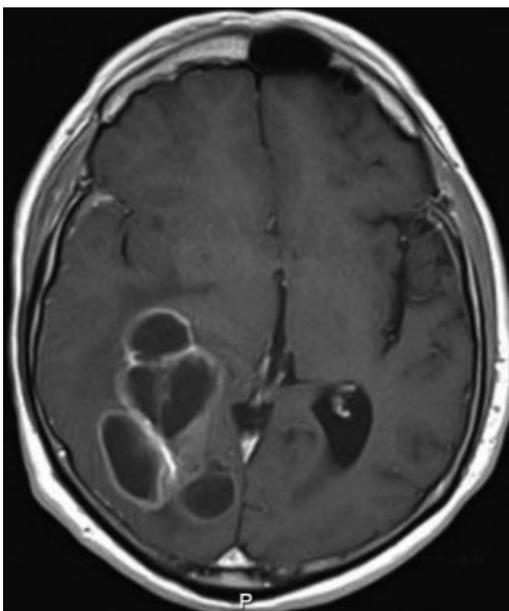
In late August 2015, he presented to the emergency department of our center with a 6-week long history of headache and increasingly frequent episodes of confusion. Objectively, he was fully conscious and properly aware of time and space, displayed no focal deficits, and had a normal cranial nerve upon examination.

The contrast-enhanced CT scan showed a right temporo-parietal lesion, cortical/subcortical in topography, 8 cm in diameter, with an important mass effect and midline shift. The left lateral ventricle was dilated, but without any overt signs of hydrocephalus (▶ Fig. 1). The magnetic resonance imaging (MRI) scan confirmed the findings of the CT scan, further displaying the cyst nature of the lesion (▶ Fig. 2). The lesion was round, with a well-defined capsule that enhanced with gadolinium, and did not appear to infiltrate the white matter.

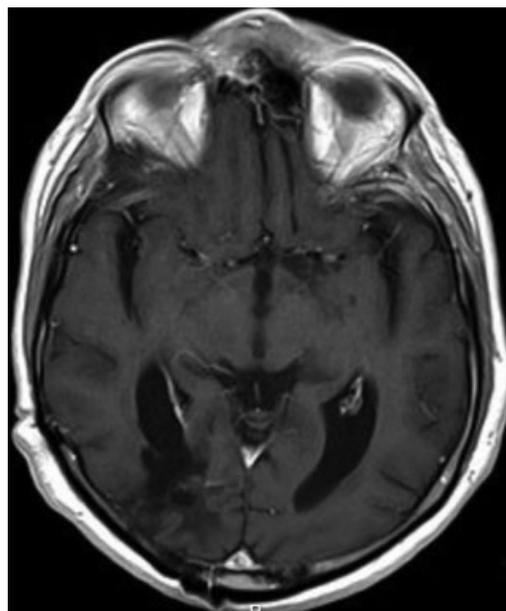
Considering it was a single lesion in a previously autonomous patient with recent symptoms not attributable to other pathologies, and that we had found no other primary tumor likely to be the source of this metastasis, we decided to



**Fig. 1** Contrast-enhanced computed tomography (CT) scan of the patient, showing a multiloculated lesion, with a significant midline-shift.



**Fig. 2** Gadolinium-enhanced T1-weighted magnetic resonance imaging (MRI) scan confirming the lesion.



**Fig. 4** Gadolinium-enhanced T1-weighted MRI performed 12 months after metastasis removal, showing no traces of secondary disease at the site.

perform a right parietal craniotomy with the goal of ascertaining the origin of the lesion. A histological examination disclosed an adenocarcinoma. The immunohistochemistry was positive for cytokeratins and PSA antibodies, supporting the diagnosis of PAC metastasis (→ **Fig. 3**).

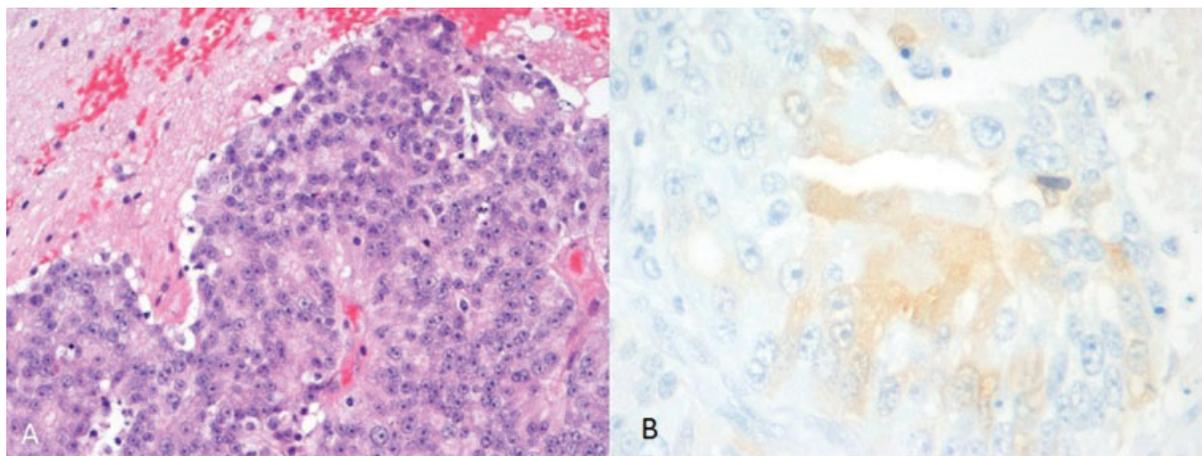
We decided the patient should undergo brain radiotherapy along with full androgenic blockade (bicalutamide plus luteinizing hormone releasing hormone [LHRH] analogues).

After 16 months of follow-up, the neurological exam of the patient was normal, his PSA levels were < 0.03 ng/ml, and the control MRI showed no evidence of recurrence or of new brain metastases. A repeat CT scan of the torso and pelvis did not reveal any distant disease at these topogra-

phies, and the latest MRI follow-up also displayed no signs of secondary disease (→ **Fig. 4**).

## Discussion

Due to advancements in treatment, patients with PAC are expected to present survival rates at 5 and 10 years of close to 100% and 87% respectively.<sup>2</sup> However, as McCutcheon et al showed in their series,<sup>6</sup> one of the few sizeable series on the subject, secondary brain lesions in PAC are a sign of an advanced disease, with a mean survival rate of 9.2 months, despite the aggressive treatment. With a recorded survival of 17 months, our patient is beyond the numbers of that series,



**Fig. 3** (A) Hematoxylin and eosin (H&E) stain, high magnification. Adenocarcinoma (lower right) and surrounding cerebral parenchyma (upper left). Tumor cells with abundant and clear cytoplasm; round nuclei; large and prominent nucleoli. (B) Prostate-specific antigen (PSA) antibody immunohistochemistry. Positive neoplastic cell stain.

and that confirms the progress made since 1999 in the treatment of these patients. It is worthy of note that the PSA levels were in a descending curve when the brain disease was discovered, displaying the limitations of using PSA levels as a tool to spark an investigation for metastasis.

Though reported cases are rare, most authors performed tumor removal followed by an adjuvant treatment, radiotherapy and hormonal manipulation for single PAC brain metastases, which is in line with what is performed for other tumors. Such an approach is associated with longer survival, better quality of life and fewer recurrences in terms of brain disease when compared with radiotherapy alone,<sup>7</sup> as was the case with our patient, who had a disease-free survival rate greater than the average previously described in the literature.

#### Conflicts of Interest

The authors have no conflicts of interest to declare.

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