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Clinical Case

Metastatic prostate cancer with negative MRI-targeted prostate biopsies: case report

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Abstract

This article presents the case of an asymptomatic patient with ascending PSA and suspected prostate cancer, who underwent two MRI-targeted prostate biopsies, both of which were negative for this neoplasm. PSMA PET/CT revealed secondary bone implant, while the biopsy of the metastatic lesion showed prostate adenocarcinoma. Docetaxel-based chemotherapy associated with androgen deprivation was performed. Despite the high accuracy of MRI-targeted prostate biopsy, diagnosis can occasionally be difficult, and PSMA PET/CT can help to detect distant lesions and aid the diagnosis.

Keywords: Prostate Neoplasms; Image-Guided Biopsy; Positron Emission Tomography combined with Computed Tomography; Carcinoma of unknown primary.

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Introduction

The prostate-specific antigen (PSA) level is used for screening and follow-up of prostate cancer treatment.[1] However, PSA may be elevated in other clinical conditions, such as prostatitis, benign prostatic hypertrophy and other neoplasms, making prostate biopsy mandatory for the definitive diagnosis of prostate cancer.[1] Even with MRI-guided prostate biopsy, diagnosis can occasionally be difficult. This article reports a case of a patient with metastatic prostate cancer who underwent two cognitive biopsies, both of which were negative.

Clinical case

A 64-year-old asymptomatic male patient underwent screening for prostate cancer, with an initial PSA of 6.11ng/mL. Digital rectal examination showed a palpable nodule on the middle third of the left lobe. Prostate MRI revealed an estimated weight of 35g, with a nodular lesion with irregular contour in the left peripheral zone, with hyposignal on T2, diffusion restriction and early enhancement by venous contrast, measuring 2cm, and probable extra-prostatic extension (PIRADS 5), without pelvic lymphadenopathy. An MRI-targeted transrectal prostate biopsy combining with systematic biopsy was performed, with 15 fragments in total, whose diagnosis was chronic prostatitis and prostatic hyperplasia. A new PSA was performed, which showed an increase to 30.03ng/mL. A second MRI-targeted transrectal prostate biopsy, with 17 fragments, was performed with the same histopathological result. The PSA remained on an upward curve, reaching 70.18ng/mL after the second biopsy and 768.60ng/mL after the last pre-treatment PSA. PET/CT PSMA was performed, showing a hyperplastic prostate, without evidence of focal lesions indicating prostate cancer and detectable by this method and without lymphadenopathy. In addition, the scan showed bone lesions with abnormal PSMA overexpression, suggestive of secondary implants, located in the sternum, 1st and 9th right costal arches, 2nd and 5th left costal arches, vertebral bodies C5, C6, D4, D5, D8, D9, D11, L2, L3, as well as in the iliac, anterior portion of the left acetabulum and the intertrochanteric line of the femur on the same side (Figure 1).

The case was discussed in a multidisciplinary session of the Urology service of the Pedro Ernesto University Hospital (HUPE/UERJ), which includes a radiologist, a pathologist and an oncologist. Subsequently, a bone biopsy of the lesion in the left iliac bone was performed (Figure 2). The histopathological result was metastatic adenocarcinoma, and the immunohistochemistry was positive for PSA and PSMA, suggesting a primary prostatic site.

Therefore, T3aN0M1b metastatic prostate cancer and androgen deprivation therapy, associated with

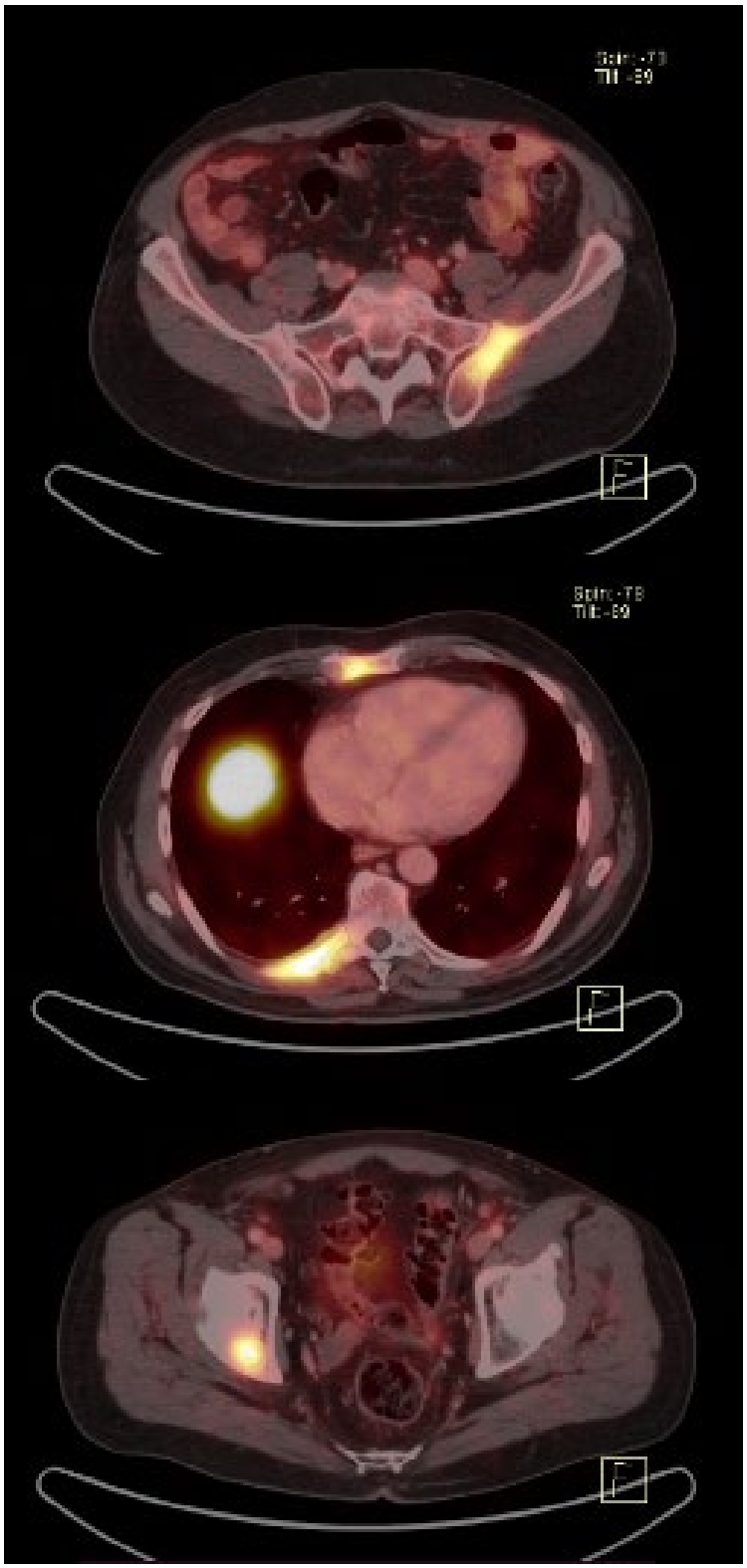

Figure 1. PET/CT PSMA with bone lesions showing abnormal PSMA overexpression, suggestive of secondary implants, located on the left iliac (A), sternum and right costal arch (B) and right iliac (C)

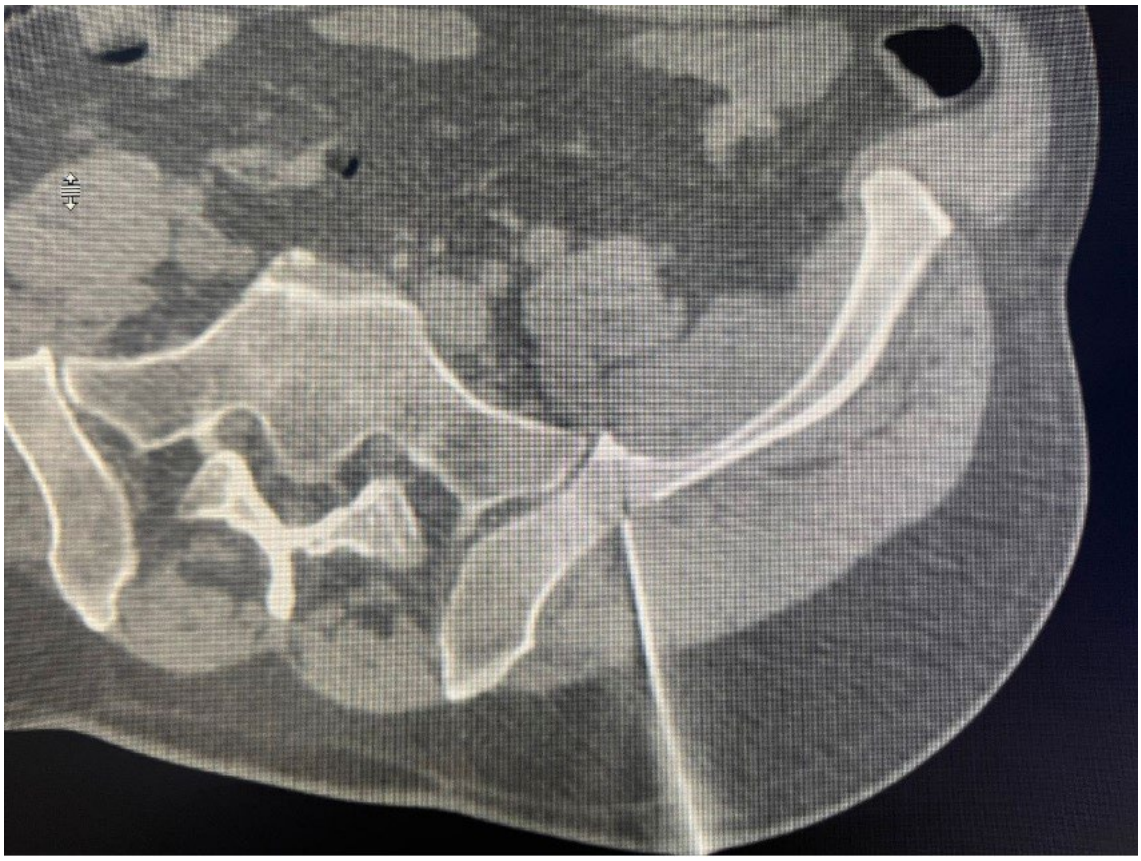

Figure 2. Computed tomography (CT) showing puncture site in osteoblastic lesion on the left iliac bone

docetaxel-based chemotherapy, was initiated. After one month of androgen deprivation, the PSA had dropped to 4.56ng/mL. Up to the time of publication of this paper, two chemotherapy sessions had been performed, the last PSA was 0.11ng/ml and the patient remained asymptomatic.

Discussion

Carcinoma of unknown primary (CUP) are a heterogeneous group of metastatic cancer in which the primary tumor is not identified after standard investigation. In historical series, CUP accounted for 3-5% of all cancers; however, this number has been decreasing in recent publications, and is now about 2%.[2] This epidemiological change is due to technological advances in diagnosis and clinical practice.

In cases of patients with bone metastasis and elevated PSA, the most common primary sites are prostate and lung, followed by liver, kidney, thyroid and colon[3]. When there is osteoblastic bone metastasis associated with very high PSA levels, the patient can be considered as having prostate cancer and start treatment without histopathological results.[1]

In the present clinical case, the investigation of metastatic neoplasia and the diagnosis of prostate adenocarcinoma were only possible due to prostate cancer screening since the patient is asymptomatic. The objective of this strategy advocated by the European Association of Urology (EAU) and the Brazilian Society of Urology (SBU) aims to reduce the specific mortality of this cancer and increase overall survival. Screening should be offered to asymptomatic men over 50 years of age, informing the patient about the risks and benefits of early diagnosis.[1,4]

In patients with suspected prostate cancer who have never had a prostate biopsy, MRI of the prostate is indicated prior to the procedure. MRI-guided transrectal biopsy increases the detection rate of ISUP≥2 cancer when compared to systematic biopsy, with a detection

rate of 1.09 to 1.46,[5,6] and can reach 96% accuracy when both are combined,[7] in contrast to the 77% accuracy of systematic biopsy by itself.[8]

When the first biopsy is negative and a high suspicion of prostate cancer persists, one possible strategy is to repeat the biopsy with an increased amount of fragments of the clinically relevant lesion identified on MRI. In two retrospective studies, patients were divided into 3 groups, with one, three and five fragments biopsied from the lesion identified on MRI. The one- and three-fragment groups diagnosed 63-75% of prostate cancers and the five-fragment group detected 90-93%.[9,10] These percentages are likely influenced by the location and size of the index lesion, in addition to the experience of the physician performing the biopsy.

In the present case, the diagnosis of prostate cancer was not possible with transrectal prostate biopsy using the recommended strategy of associating MRI-guided biopsy with systematic biopsy. In the second biopsy, the strategy of increasing the number of fragments of the index lesion from three to five was adopted, which continued to show a negative result for cancer. It is worth mentioning that the exams were performed by an experienced physician.

In view of the increase in PSA, prostate MRI with clinically significant lesion and digital rectal examination suggestive of prostate cancer, a PSMA PET/CT was performed. It is a more accurate test than CT of the abdomen and bone scintigraphy for the staging of high-risk prostate cancer, both for evaluation of lymph node and bone metastasis.[11] Although its use is recommended only for the staging of prostate cancer according to the guidelines, evidence exists that the prostatic MRI associated with PSMA PET/CT increases the sensitivity of the diagnosis,[12] including clinical reports of patients undergoing radical prostatectomy without histopathologycal confirmation prior to surgery.[13] In the present case, once a lesion with PSMA overexpression was identified, a positive lesion biopsy was performed with confirmation by immunohistochemistry of adenocarcinoma prostatic primary cancer.

To our knowledge, this is the first case described in the literature of a diagnosis of metastatic prostate cancer confirmed by immunohistochemistry with two previous negative cognitive biopsies. Other cases of metastatic prostate cancer with successive negative biopsies have been described in the literature.[14-17] These patients had PSA at diagnosis that ranged from 56 to 4222ng/mL, with an association of transrectal, perineal and endoscopic resection biopsies, being negative for prostate cancer. The documented cases include reports of bone, lymph node and ureteral metastases.

Even with the development of new diagnostic methods, CUP remains a challenge for clinical practice. MRI-targeted prostate biopsy has increased the accuracy of the exam for the diagnosis of prostate cancer, but there are cases, such as the one presented in this study, in which diagnosis is not possible with serial exams. When faced with asymptomatic patients with high PSA and a negative prostate biopsy, further investigation is an option when the risks and benefits of new complementary exams are well understood.

Conclusion

The prostate cancer screening associated with the PSMA PET/CT and metastatic lesion biopsy aided the diagnosis of prostate cancer, even with negative transrectal MRI-targeted repeat prostate biopsies.

References

1. EAU Guidelines. Edn. presented at the EAU Annual Congress Amsterdam 2022. ISBN 978-94-92671-16-5.
2. Rassy E, Pavlidis N. The currently declining incidence of cancer of unknown primary. Cancer Epidemiol. 2019;61:139. doi: 10.1016/j.canep.2019.06.006.
3. Katagiri H, Takahashi M, Inagaki J, et al. Determining the site of the primary cancer in patients with skeletal metastasis of unknown origin: a retrospective study. Cancer. 1999;86(3):533. doi: 10.1002/(sici)1097-0142(19990801)86:3<533::aid-cncr24>3.0.co;2-1.
4. Brazilian Society of Urology. Counseling for the early diagnosis of prostate cancer. 2020 Oct 10. Available from: https://portaldaurologia.org.br/medicos/noticias/aconselhamento-para-o-diagnostico-precoce-do-cancer-de-prostata/
5. Kasivisvanathan V, Rannikko AS, Borghi M, et al. MRI-Targeted or Standard Biopsy for Prostate-Cancer Diagnosis. N Engl J Med. 2018;378:1767. doi: 10.1056/NEJMoa1801993. Epub 2018 Mar 18.
6. van der Leest M, Cornel E, Israel B, et al. Head-to-head Comparison of Transrectal Ultrasound-guided Prostate Biopsy Versus Multiparametric Prostate Resonance Imaging with Subsequent Magnetic Resonanceguided Biopsy in Biopsy-naive Men with Elevated Prostate-specific Antigen: A Large Prospective Multicenter Clinical Study. Eur Urol. 2019;75:570. doi:

10.1016/j.eururo.2018.11.023
7. Bryk, DJ, Llukani E, Taneja SS, et al. The Role of Ipsilateral and Contralateral Transrectal Ultrasound-guided Systematic Prostate Biopsy in Men With Unilateral Magnetic Resonance Imaging Lesion Undergoing Magnetic Resonance Imaging-ultrasound Fusion-targeted Prostate Biopsy. Urology. 2017;102:178. doi: 10.1016/j.urology.2016.11.017
8. Roehl KA, Antenor JA, Catalona WJ. Serial biopsy results in prostate cancer screening study. J Urol. 2002;167(6):2435-39. doi: 10.1016/S0022-5347(05)64999-3.
9. Zhang M, Milot L, Khalvati F, et al. Value of Increasing Biopsy Cores per Target with Cognitive MRI-targeted Transrectal US Prostate Biopsy. Radiology. 2019;291:83. doi: 10.1148/radiol.2019180712. Epub 2019 Jan 29.
10. Lu AJ, Syed JS, Ghabili K, et al. Role of Core Number and Location in Targeted Magnetic Resonance ImagingUltrasound Fusion Prostate Biopsy. Eur Urol. 2019;76:14. doi: 10.1016/j.eururo.2019.04.008. Epub 2019 Apr 30.
11. Hofman MS, Lawrentschuk N, Francis RJ, et al. Prostate-specific membrane antigen PET-CT in patients with high-risk prostate cancer before curative-intent surgery or radiotherapy (proPSMA): a prospective, randomised, multicentre study. Lancet. 2020;395:1208. doi: 10.1016/S0140-6736(20)30314-7. Epub 2020 Mar 22
12. Emmet L, Buteau J, Papa N, et al. The additive diagnostic value of prostate-specific membrane antigen positron emission tomography computed tomography to multiparametric magnetic resonance imaging triage in the diagnosis of prostate cancer (PRIMARY): a prospective multicentre study. Eur Urol. 2021;80:682:689. doi: 10.1016/j.eururo.2021.08.002
13. Meissner VH, Rauscher I, Schwamborn K, et al. Radical prostatectomy without prior biopsy following multiparametric magnetic resonance imaging and prostate-specific membrane antigen positron emission tomography. Eur Urol. 2022;82:156–60. doi: 10.1016/j.eururo.2021.08.002
14. Nakata S, Nakano K, Takahashi H, et al. A case of prostate cancer diagnosed pathologically by bone metastatic site biopsy. Nippon Hinyokika Gakkai Zasshi. 2005;96(4):507–510. doi: 10.5980/jpnjurol1989.96.507.
15. Fukumoto R, Soda T, Uehara M, et al. A case of prostate cancer diagnosed by lymphadenectomy. Hinyokika Kiyo. 2012;58(10):557–560. PMID: 23235279
16. Ueda Y, Higuchii Y, Hashimoto T, et al. Prostate cancer diagnosed through the biopsy of the bone metastatic lesion; a case report. Hinyokika Kiyo. 2007 May;53(5):327-30. Japanese. PMID: 17561720.
17. Iwamura H, Hatakeyama S, Tanaka Y, et al. A case of metastatic cancer with markedly elevated PSA level that was not detected by repeat prostate biopsy. BMC Res Notes. 2014 Jan 29;7:64. doi: 10.1186/1756-0500-7-64.