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Radiation-Induced Brain Necrosis: The Role of The PSMA PET/CT Evaluation - Case Report

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ABSTRACT

This is a case of a 69-year-old patient with Prostate Cancer (PCa) who underwent PSMA PET in three different evaluation scenarios: Biochemical Relapse (BCR), response assessment and differential diagnosis between Radiation-induced Brain Necrosis (RBN), and neoplastic tissue viability. PSMA PET showed superiority compared to conventional imaging exams in all scenarios and impacted on the management of the patient.
Keywords: *PSMA, PET/CT, Prostate Cancer, Biochemical Relapse, Response Assessment, Radiation Necrosis*

Introduction

Prostate Cancer (PCa) is the most common malignant tumor in men, after non-melanoma skin cancer, representing 30% of diagnoses of the disease in the country. National Cancer Institute data (INCA) estimates 72.000 new cases/yearly of PCa for the 2023-2025 triennium (INCA, 2023). The PSMA role in the scenarios of primary staging and biochemical relapse (BR) has already been acknowledged by robust research and by dependable guidelines such as NCCN's (NCCN, 2023). Since the availability of systemic therapy options has been increasing, especially for metastatic castration-resistant PCa (mCRPC), the need for an accurate imaging method for response assessment and also report standardization regarding criteria evaluation became evident. The molecular information provided by PSMA PET has been showing promising results in the therapy response analysis and outstanding superiority compared to conventional imaging exams, due to its limitations and likewise by the ability to evaluate the patient with only one imaging method. The following case report shows the importance of a reliable imaging exam in the evaluation of a patient with PCa on the biochemical recurrence (BCR), response assessment and differential diagnosis between residual neoplastic tissue and radiation-induced brain necrosis (RBN).

Case Report

Biochemical Relapse (BCR)

69 years old, smoker, high-risk PCa diagnosed at 61 years old with initial PSA of 325.4ng/mL and Gleason 9 (4+5). The patient underwent radical prostatectomy and extended pelvic lymphadenectomy. The anatomopathological report showed extracapsular extension, perineural impairment, infiltration of the bladder surgical margins, and of the seminal vesicles. Radiotherapy of the prostate bed and adjuvant hormonal blockage (HB) were performed with proper PSA level reduction. After 2 years of follow-up, the persistence of undetectable PSA levels led to the HB withdrawal and then intermittent HB was prescribed.

The follow-up was discontinued by the COVID-19 pandemic and, seven years after the initial treatment, the PSA level increased to 131ng/mL. The imaging investigation of the BR was performed with PSMA PET which showed no evidence of disease in the abdomen or in the thorax whatsoever. A single bone lesion was identified on the skull, with extra-axial impairment of the frontal, temporal, and parietal regions, infiltration of the diploe, and extension to the meningeal plans and adjacent encephalic parenchyma. Complementary brain MRI was also performed, and no other lesions were detected. The patient underwent radiotherapy and Androgen Deprivation Therapy (ADT) with Enzalutamide and Degarelix association was prescribed (Fig. 1).

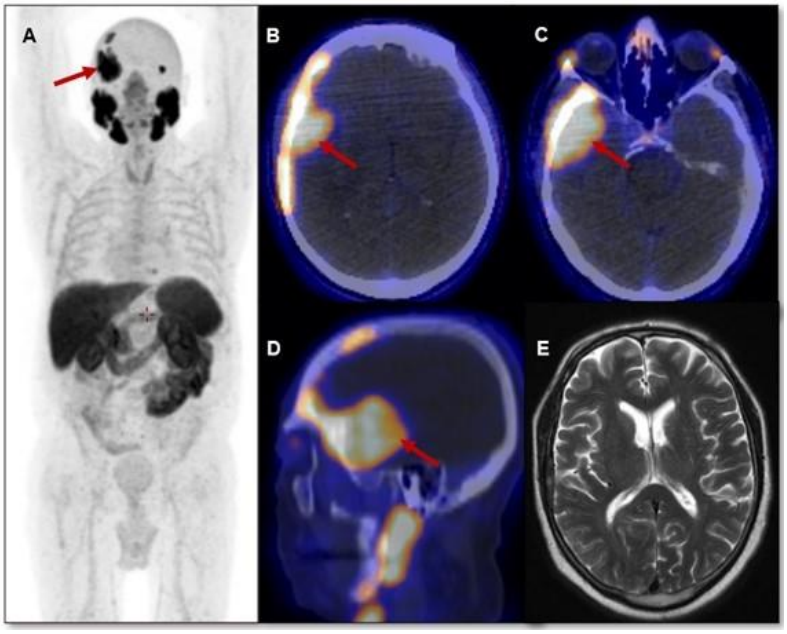

Figure 1: BCR investigation Imaging findings: A, B C and D) Maximum Intensity Projection (MIP), axial and sagittal fusion images of PSMA PET, respectively, showing the skull lesion with SUVmax = 27.59 (red arrow); E) Brain MRI axial T2 showing expansive extra-axial lesion with impairment of the pachymeninx and mainly the temporal lobe with hemorrhagic foci and vasogenic edema.

Response Assessment

After the completion of the treatment and 5 months from the PET for BR investigation, the patient underwent PSMA and brain MRI to assess treatment response. At that time, PSA was 0.02ng/mL.

The images showed a significant PSMA molecular expression decrease and extension reduction of the metastatic lesion on the skull. The same findings were reported on the MRI: significant shrinkage of the skull lesion, resolution of the hemorrhagic foci, and of the edema that surrounded the extension of the metastasis to the brain and meninx.

These imaging exams and the PSA decrease indicate a satisfactory response to treatment, at least partially (Fig. 2).

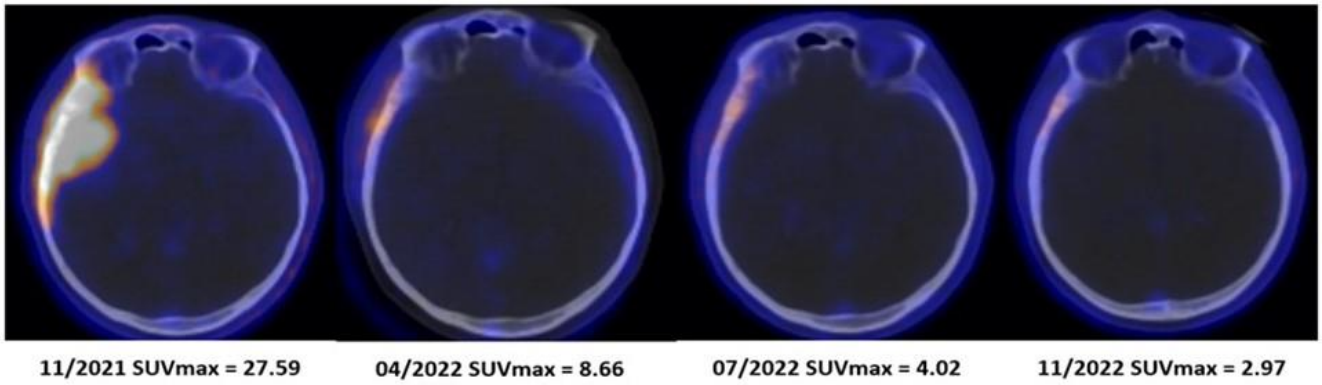

Figure 2: PET PSMA and response assessment: axial fusion images show progressive decrease of the SUVmax and of the skull lesion extension: A) Baseline study November / 2021 SUVmax = 27.59; B) April / 2022 SUVmax = 8.66; C) July / 2022 SUVmax = 4.02 and D) November / 2022 SUVmax = 2.97.

Radiation-Induced Brain Necrosis (RBN) X Residual Neoplastic Tissue

During follow up, the PSA level remained low and stable, however, the patient reported persistent headaches, sometimes severe. No other symptoms were reported, the neurologic exam did not show abnormalities and the PSA level was 0.02ng/mL. The patient underwent an MRI which pointed out an increase in the right temporal lobe lesion size, with central necrosis and vasogenic cerebral edema return. The perfusion phase indicated a predominance of necrotic tissue.

Another PET PSMA was performed and showed a minimum concentration of PSMA at the lesion and the appearance of temporoparietal hypodensity. There were no other areas of PSMA abnormal expression nor new concentration foci.

Despite the low level of PSA and imaging findings, the symptoms were getting worse, and the patient underwent a neurosurgery approach after a multidisciplinary debate. The anatomopathological analysis reported necrotic tissue consistent with RBN (Fig. 3).

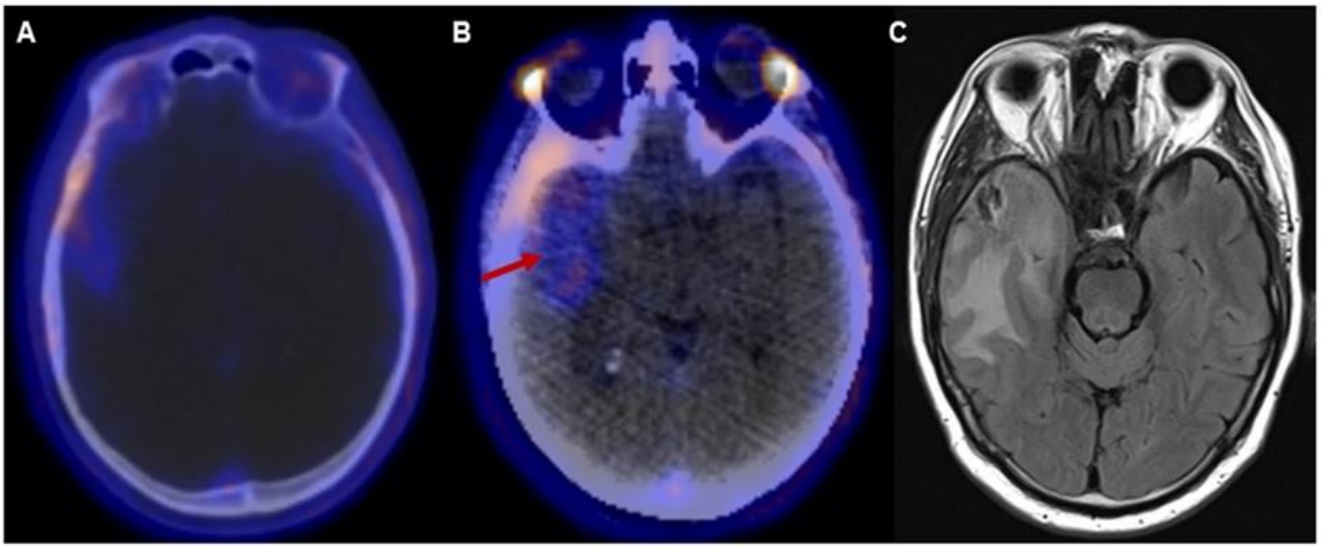

Figure 3: Headache investigation: A and B) axial fusion PET images show minimum concentration of PSMA in the skull lesion and appearance of temporoparietal hypodensity with SUVmax = 2.78; C) Brain MRI axial T2 shows increase of the right temporal lobe lesion size, with central necrosis and vasogenic cerebral edema return.

Discussion

PSMA PET has already proven its value on the primary staging and BCR investigation of the PCa with a significant impact on the management decision (Donswijk *et al*., 2020; Pozdnyakov *et al*., 2022) The superiority over conventional imaging (Alipour and S. Hofman 2019; Pyka *et al*., 2016) exams was acknowledged by comprehensive guidelines such as NCCN2 whose panel does not consider conventional imaging as a prerequisite since 2020.

In this case, there is no doubt that PSMA was instrumental in locating and determining the extent of PCa recurrence. Cranial metastasis as a single lesion is not the most common recurrence scenario and, as the patient did not present unequivocal symptoms nor neurological complaints, PSMA, as a whole-body examination, probably saved time in this investigation.

Towards response assessment, PSMA has been showing a notable potential due to molecular information associated with anatomic features of the lesions, the whole-body analysis, and the ability to evaluate soft tissue and bone foci of metastasis (Thomas *et al*., 2017). Beyond that, it is already known the lower sensitivity and specificity of bone scintigraphy compared to PSMA and, despite the development of

computerized bone scan indexes for response evaluation, the residual bone remodeling represents a limitation on this scenario (Pyka *et al*., 2016; Thomas *et al*., 2017; Petersen *et al*. 2021).

It is important to state that, since 5 to 8% of the patients may not overexpress PSMA, a baseline PET is essential to determine the receptor expression status before using this tool to analyze the therapy response (Baum and Nanni 2017; Noto *et al*., 2018; Kase *et al*., 2022).

With respect to the response assessment of this patient, PSMA provided reliable information that agreed with the clinical evolution and also with PSA levels.

In order to validate the indication of PSMA PET in this scenario, consensus statements and criteria interpretation have been proposed to guarantee agreement and standardization of the report (Shagera *et al*., 2021; Gafita *et al*. 2023).

Finally, concerning the differential diagnosis between RBN and neoplastic tissue viability on the brain component of the skull lesion, PSMA was able to reliably favor RBN, based on the stable and low tracer expression and the anatomic features of the lesion, besides the agreement with the PSA level.

Brain lesions in PCa are uncommon with an approximate incidence of 0,18%, according to McBean R, *et al*. (2021). The distinction between RBN and residual or recurrent viable tumor cells is a specific situation and there is little data available about the role of PSMA. Another report with a similar case pointed out the value of the PSMA PET evaluation and there are studies that indicate a potential use of this tracer, however, regarding gliomas (Rayamajhi *et al*., 2023; Thomas *et al*. 2017).

In conclusion, PSMA PET is a dependable tool for the evaluation of the patients with PCa already acknowledged for primary staging and BCR investigation with other potential roles.

Ethics Approval

The participant signed an informed consent form authorizing the use of his clinical and imaging data under proper confidentiality.

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