False-positive mpMRI and true-negative $^{68}$Ga-PSMA PET/CT xanthogranulomatous prostatitis: a case report

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Background: Xanthogranulomatous prostatitis (XGP) is a rare disorder of the prostate. It presents as a hard fixed nodule on digital rectal examination (DRE), and may cause obstructive urinary symptoms and elevated serum prostate-specific antigen (PSA) levels, therefore mimicking prostate cancer (PCa) clinically and biochemically. Radiological features of XGP overlap with those of PCa, and the 2 conditions cannot be distinguished by pelvic multiparametric magnetic resonance imaging (mpMRI). $^{68}$Ga-labelled prostate-specific membrane antigen ($^{68}$Ga-PSMA) with positron emission tomography/computed tomography (PET/CT) has shown its potential in the initial diagnosis and staging of PCa; however, the imaging characteristics of XGP on $^{68}$Ga-PSMA PET/CT have yet to be reported.

Case Description: We report the case of a 56-year-old man who had slowly progressing dysuria for 10 years, which was significantly worse for 1 week, and a PSA level of 49.19 ng/L. Ultrasound revealed a hypoechoic lesion in the left periphery of the prostate, which was hypointense with capsular irregularity on axial T2-weighted imaging (T2WI), hyperintense on the diffusion weighted imaging (DWI), and hypointense on the apparent diffusion coefficient (ADC) maps resulting in a Prostate Imaging-Reporting and Data System (PI-RADS) score of 5. The patient was highly suspected of having high-risk PCa and underwent a $^{68}$Ga-PSMA PET/CT for staging. The PET/CT images showed no PSMA uptake in the involved region. Considering that a small proportion of cases of PCa do not express PSMA, a subsequent targeted biopsy was performed, guided by mpMRI. Histopathological examination showed a large number of foamy macrophages in the neutrophile granulocyte infiltrate, and XGP was finally diagnosed. After treatment with antibiotic levofloxacin, the patient’s PSA returned to normal, and his dysuria symptoms had disappeared at the 2-month follow-up.

Conclusions: Non-uptake of PSMA in a lesion may still provide information for a diagnosis by exclusion or regular follow-up checks in patients that are highly suspected to have PCa in clinic or on mpMRI.

Keywords: Prostate cancer (PCa); prostate-specific membrane antigen (PSMA); positron emission tomography/computed tomography (PET/CT); case report; xanthogranulomatous prostatitis

Submitted Dec 02, 2021. Accepted for publication Mar 06, 2022.
doi: 10.21037/tau-21-1068
View this article at: https://dx.doi.org/10.21037/tau-21-1068

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Introduction

There is increasing interest in the use of images to guide the diagnosis and staging of prostate cancer (PCa). Multiparametric magnetic resonance imaging (mpMRI) is a well-established imaging modality in PCa assessment (1). It can identify suspicious lesions and improve the yield of a transrectal ultrasound-guided biopsy (2,3). However, mpMRI is limited by its low specificity, and other conditions such as benign prostatic hyperplasia nodules, acute and chronic prostatitis, and granulomatous prostatitis are difficult to differentiate from PCa in terms of imaging features (4).

68Ga-labelled prostate-specific membrane antigen (68Ga-PSMA) with positron emission tomography/computed tomography (PET/CT) is an important advance for imaging PCa. Despite being mostly used for secondary staging, it is especially beneficial for detection accuracy in primary staging due to its advantages in sensitivity and specificity (5,6). Several recent studies have also evaluated the benefit of 68Ga-PSMA PET/CT to be used in the first-line diagnosis of PCa with initial high serum prostate-specific antigen (PSA) (7,8). Studies have combined the role of PET/MRI in the detection PCa, suggesting that PET/MRI could further improve the diagnostic accuracy of clinically significant PCa and avoid overtreatment of non-prostate cancer, such as xanthogranulomatous prostatitis (XGP) (9-12).

A rare prostate disorder, XGP can present as a hard fixed nodule on digital rectal examination (DRE), and can cause low obstructive urinary symptoms and an elevation of serum PSA levels, therefore mimicking PCa clinically and biochemically (13). The most common sites of xanthogranulomatous inflammation are the kidneys and gallbladder (14). Radiological features of XGP overlap with those of PCa, and the 2 conditions cannot be distinguished by mpMRI (15). In the literature, only one case has been reported showing abnormally high fluorodeoxyglucose (18F-FDG) uptake of xanthogranulomatous pyelonephritis on PET scan (16). However, the imaging characteristics of XGP based on 68Ga-PSMA PET/CT have not yet been reported.

We present a case report of a patient who was suspected to have PCa due to their results of a positive ultrasound, mpMRI, and his clinical features, but who was subsequently reported to have XGP based on a histopathological examination. We present the following case in accordance with the CARE reporting checklist (17) (available at https://tau.amegroups.com/article/view/10.21037/tau-21-1068/rc).

Case presentation

A 56-year-old man had experienced slowly progressing dysuria for 10 years, which became significantly worse for 1 week. A DRE revealed an enlarged prostate. He had previously presented with benign prostatic hyperplasia and had a history of hyperlipidemia for more than 10 years. There were unremarkable in the patient’s past medical and family history. The detected serum PSA level increased from 1.01 ng/mL to 49.19 ng/mL. Urine microscopy results showed negative for nitrite and leukocyte esterase and a normal range of white blood cells per high power field (WBC/HPF). An ultrasound revealed a hypoechoic lesion in the left peripheral zone (Figure 1A,1B) with hypointense lesions with capsular irregularity on axial T2-weighted imaging (T2WI), hyperintense on the diffusion-weighted imaging (DWI), and hypointense on the apparent diffusion coefficient (ADC) maps resulting in a Prostate Imaging-Reporting and Data System (PI-RADS) 5 in mpMRI (Siemens Healthineers, Erlangen, Germany; mpMRI scanning protocol included axial T1-weighted imaging, axial-sagittal-coronal T2WI imaging, DWI, ADC maps, and dynamic contrast-enhanced imaging-DCE) (Figure 1C-1E).

The patient was highly suspected of having high-risk PCa and underwent a 68Ga-PSMA PET/CT for staging. The 68Ga-PSMA/CT can detect smaller amounts of prostate cancer cells compared to MRI or 18F-FDG PET. 68Ga-PSMA was synthesized from precursor PSMA-617 of Huayi Isotopes Co., Ltd. (Jiangsu, China). The patient received an intravenous injection of 160.6 MBq 68Ga-PSMA, then underwent PET/CT scans after 59 minutes by using a GE Discovery PET/CT 690 Elite scanner (General Electric Healthcare, Waukesha, WI, USA). The PET/CT images showed no PSA uptake in the involved region (Figure 1F-1H). Considering that a small proportion of patients with PCa do not express PSMA (18), a subsequent targeted biopsy was performed, guided by ultrasound and mpMRI. Histopathological examination showed a large number of foamy macrophages in the neutrophil granulocyte infiltrate, no evidence of malignancy was noted, and XGP was finally diagnosed (Figure 1I-1K) (19). After treatment with the antibiotic levofloxacin, the patient’s PSA returned to normal, and his dysuria symptom had disappeared at the 2-month follow-up. The timeline for the case is detailed in Figure 2.

The patient was very satisfied with his treatment.

Study protocols were accorded with recommendations of the Commission of Medical Research Involving Human
Subjects at Region of Xiangya Hospital, Central South University. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Figure 1 Ultrasound, mpMRI, 68Ga-PSMA PET/CT images and histopathological examination of the patient. Ultrasound revealing a hypoechoic lesion in the left periphery of the prostate (A, B) showing hypointense with capsular irregularity on axial T2-weighted imaging (T2WI) (C), hyperintense on the diffusion weighted imaging (DWI) (D), and hypointense on the apparent diffusion coefficient (ADC) maps (E) resulting in a Prostate Imaging-Reporting and Data System (PI-RADS) score of 5. Positron emission tomography/computed tomography (PET/CT) images showed no prostate-specific membrane antigen (PSMA) uptake in the involved region (F, CT; G, PET; H, fusion). Location of the lesion on the ultrasound, mpMRI and 68Ga-PSMA PET/CT images was indicated by orange arrows. Histopathological examination showed a large number of foamy macrophages in the neutrophile granulocyte infiltrate (I, hematoxylin and eosin, original magnification ×40; J, hematoxylin and eosin, original magnification ×200; K, hematoxylin and eosin, original magnification ×200).

Figure 2 The timeline of this case. mpMRI, multiparametric magnetic resonance imaging; 68Ga-PSMA PET/CT, 68Ga-labelled prostate-specific membrane antigen with positron emission tomography/computed tomography.
Discussion

Clinical evidence shows that the use of mpMRI can improve PCa diagnosis, reduce unnecessary prostate biopsies and non-significant PCa overtreatment (20). The $^{68}$Ga-PSMA PET/CT has been growing interest in targeted imaging of recurrent PCa and staging of high risk PCa due to its advantages in sensitivity and specificity. Several recent studies have also evaluated the benefit of $^{68}$Ga-PSMA PET/CT to be used in the first-line diagnostic setting of PCa, and they concluded that $^{68}$Ga-PSMA PET/CT could further improve the diagnostic and measurement accuracy of PCA detection and total gross volume estimation. A combination of mpMRI and PSMA-based PET images could also improve the ability to detect clinically significant PCa for PI-RADS 3 lesions, this may be beneficial for early and correct diagnosis of PCa that require aggressive treatment (9). The rare prostate disease of XGP can mimic the characteristics of PCa (13). The clinical presentation and imaging features of this case were highly suggestive of PCa, as reported in the initial evaluation of mpMRI, but the patient was found to have XGP. To our knowledge, this is the first $^{68}$Ga-PSMA PET/CT imaging of an XGP case report that showed a false positive result on mpMRI and a true negative result on $^{68}$Ga-PSMA PET/CT imaging.

The histopathological type of xanthogranulomatous inflammations remains rare and their classification is controversial. Xanthogranulomatous inflammations are observed more frequently in the kidneys and gallbladder and rarely in the prostate. The etiology and pathogenesis of XGP remain unclear. Some etiologic agents have been reported for xanthogranulomatous inflammations including hyperlipidemia, infections caused by some pathogenic microorganism or bacterial toxin, and prostatic hyperplasia. It has been reported that XGP is associated with abscesses (14). The patient’s ultrasonography did not reveal any features of abscess, nor did he have any signs or symptoms that would suggest an abscess. Bacterial toxins, cell debris, and prostatic secretions flow into the prostatic stroma through the disrupted epithelium, triggering a localized inflammatory response. In the present case, the man had a history of hyperlipidemia and benign prostatic hyperplasia, and the correlation between this history and XGP needs to be further explored.

The XGP diagnosis, in this case, was made by pathological examination of the lesion. The pathological feature of XGP was a nonspecific granuloma infiltrated by a large number of inflammatory cells, which was mainly composed of foamy macrophages containing numerous fat droplets, and might also contain other chronic inflammatory lymphocytes and plasma cells. Inflammatory cells combined with hyperplasia of fibrous tissues to form tumor-like nodules or lesions. These specific features—the histiocytes—cause some prostate MRI features including low signal intensity lesions with capsular irregularity on axial T2WI, hyperintense on the DWI, and hypointense on the extracapsular extension and rim-enhancing areas of ADC maps, which make XGP difficult to distinguish from PCa (15). Additionally, due to the aggregation of inflammatory cells in xantogranulomatosis, a PET/CT study reported a case of abnormal uptake of $^{18}$F-FDG in the left kidney xanthogranulomatous pyelonephritis that mimicked a tumor (16).

Currently, no imaging study has described how to differentiate between XGP and PCa. Until now, only a few cases of the MRI features of XGP have been reported. The $^{68}$Ga-PSMA PET/CT characteristics of XGP have never been reported in the literature. Our case showed no high uptake of PSMA in the XGP lesion area, which was a distinct difference from PCa. The possible explanation for this finding might be related to the pathology of XGP, that is, PSMA is not highly expressed in normal prostate epithelial cells or prostatic inflammatory lesions. The PSMA is expressed by the great majority of PCa lesions and is positively correlated with PSA, and $^{68}$Ga-PSMA PET/CT has become the investigation of choice in biochemical recurrence and high risk PCa owing to its superior performance. However, a small number of patients with high inter- or intra-lesional heterogeneity present PSMA-negative tumor phenotypes. Nevertheless, according to recent studies, the combination of mpMRI and $^{68}$Ga-PSMA PET/CT achieved a satisfactory detection rate for clinically significant PCa and significantly reduced unnecessary prostate biopsies. Therefore, this combination is a promising strategy for accurately diagnosing PCa. As shown in this case, a non-uptake of PSMA in the lesion may provide information for a diagnosis by exclusion or with regular follow-up checks in patients that are highly suspected of PCa on mpMRI.

Clinically, the most common symptoms of XGP include lower urinary tract obstruction and urinary frequency, similar to benign prostate hyperplasia. In our case, dysuria may have been associated with both benign prostate hyperplasia and XGP. In addition, granulomatous prostatitis may stimulate prostate tissue causing a transient increase in serum PSA levels, but it would decrease as the
inflammation resolves. In this case, the patient’s serum PSA level was significantly elevated at 49.19 ng/mL at the onset of symptoms and returned to normal at the patient’s last follow-up after effective treatment.

To date, the management of XGP patients has remained conservative. As mentioned above, the course of XGP is benign and can resolve spontaneously. Conservative treatment should be considered in principle, with antibacterial drugs as the first choice, and alpha blockers and corticosteroids may be helpful. Surgical management, including transurethral resection of the prostate or prostatectomy, is appropriate if lower urinary tract obstruction symptoms are obvious and/or if conservative treatment has failed. This patient did not require prostate surgery because his dysuria was well controlled after the antibiotic levofloxacin treatment, and his serum PSA values returned to normal. Research has shown that 19% of nonspecific granulomatous prostatitis patients develop PCAs (21), therefore, those with persistently elevated serum PSA values require close follow-up.

**Conclusions**

The disease XGP is rare, benign, and inflammatory. We have reported a case that was considered to be PCA initially on account of clinical and radiology resemblances. We also showed the ⁶⁸Ga-PSMA PET/CT appearances, which had not been reported before. Non-uptake of PSMA in a lesion may still provide information for a diagnosis by exclusion or in regular follow-up checks in patients that are highly suspected of PCa in clinic or on mpMRI. Distinguishing XGP from PCa by using only mpMRI remains a challenge. PSMA-based PET combined with mpMRI may be useful in this situation to identify and characterize suspicious prostatic lesions before biopsy or definitive treatment. Our report reinforces the current recommendations on the use of PSMA-based PET as a meaningful diagnostic tool for prostate lesions.

**Acknowledgments**

**Funding:** This work was supported by the National Natural Science Foundation of China (No. 91859207).

**Footnote**

**Reporting Checklist:** The authors have completed the CARE reporting checklist. Available at https://tau.amegroups.com/article/view/10.21037/tau-21-1068/rc

**Conflicts of Interest:** All authors have completed the ICMJE uniform disclosure form (available at https://tau.amegroups.com/article/view/10.21037/tau-21-1068/coif). The authors have no conflicts of interest to declare.

**Ethical Statement:** The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Study protocols were accorded with recommendations of the Commission of Medical Research Involving Human Subjects at Region of Xiangya Hospital, Central South University. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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Cite this article as: Tang Y, Yang J, Zhou C, Li J, Hu S. False-positive mpMRI and true-negative 68Ga-PSMA PET/CT xanthogranulomatous prostatitis: a case report. Transl Androl Urol 2022;11(4):561-566. doi: 10.21037/tau-21-1068