Urologia Internationalis

Case Report

Urol Int 2021;105:520–524
DOI: 10.1159/000512378

Received: July 3, 2020
Accepted: October 13, 2020
Published online: February 3, 2021

Multiparametric MRI Lesion Classified as Prostate Imaging-Reporting and Data System 5 but Histopathologically Described as Benign: A Case Report and Review of Literature

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Keywords
Prostate cancer · PI-RADS classification · Multiparametric MRI · MRI/Ultrasound fusion-based targeted biopsy · BPH

Abstract
Introduction: Prostate cancer (PCa) is the most common malignancy in men. The multiparametric MRI (mpMRI) significantly improved the diagnostic approach of PCa. Although PCa is highly likely to be present in prostate imaging-reporting and data system (PI-RADS) 5 lesions, there are up to 18% of PI-RADS 5 lesions with benign histopathology after targeted biopsy. ***Case Description:*** We present the case of a 66-year-old man who was referred to our hospital for MRI/ultrasound fusion-based targeted biopsy due to an elevated PSA and a PI-RADS 5 lesion described in the mpMRI. After 2 consecutive biopsies, the mpMRI target showed no malignancy. The lesion was described as PI-RADS 2 two years later. ***Conclusion:*** This case demonstrates the risk of false-positive classified PI-RADS 5 lesions in the mpMRI and the challenge in some cases to distinguish between BPH nodules and cancer. Until today, a limited amount of studies exists concerning this issue. However, further studies are required to evaluate further characteristics associated with a higher possibility of histopathologically benign findings in PI-RADS 5 lesions.

Introduction

Prostate cancer (PCa) is the most common malignancy in men [1]. Standard of care in diagnostics of PCa is generally the ultrasound-guided transrectal biopsy [2]. In the past years, however, the multiparametric MRI (mpMRI) gained importance in detection of clinically significant cancer and led to a reduction of unnecessary biopsies and treatment. Several studies showed that clinical assessment of prostate MRI may not only improve detection of PCa but also serves as image guidance for surgery, focal therapy, and radiotherapy. Furthermore, studies showed improved efficiency of MRI/ultrasound fusion-based biopsy in detecting clinically significant PCa [3–5].

In mpMRI, lesions suspicious of PCa are classified according to the prostate imaging-reporting and data system (PI-RADS) published in 2012, adjusted as PI-RADS Ver-

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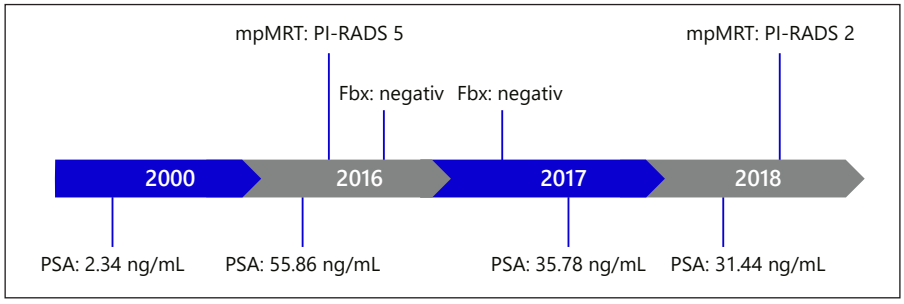

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Fig. 1. Chronological presentation of diagnostic approach.

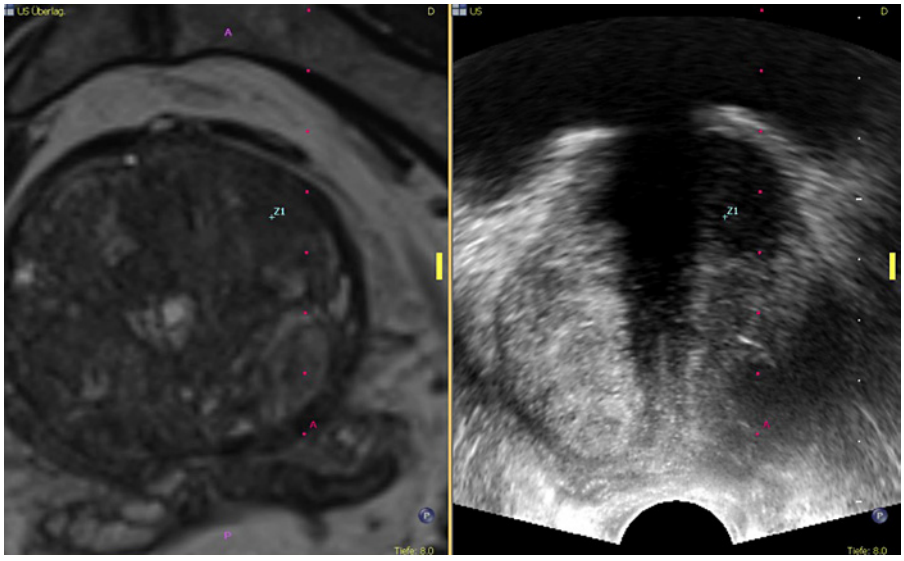

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Fig. 2. Image fusion of the lesion in side-by-side view showing the lesion in the mpMRI in the anterior part of the prostate (marked with Z1) and the corresponding hypodense lesion in the B-mode ultrasound imaging (marked with Z1). Due to the fusion system, the image is reversed right to left.

sion 2 (V2) in 2015, respectively [6, 7]. The mpMRI combines anatomical, functional, and physiological information using 3 different sequences: the T2 – weighted, diffusion-weighted, and dynamic contrast-enhanced imaging.

Lesions are characterized in 5 categories according to their likelihood for the presence of clinically significant PCa [7]. The overall detection rate for PCa in PI-RADS 5 lesions is described between 82 and 94% in current literature [3, 4, 8–10]. False-positive results in PI-RADS 5 lesions are mostly caused by prostatitis and benign hyperplasia [7]. However, the morphology of prostatitis in mpMRI appears commonly more diffuse and not as focal as cancer [7]. The number of benign histopathology of lesions in mpMRI described as PI-RADS 5 is rated between 13 and 18% in the current literature [8–10]. Factors associated with negative outcome after targeted biopsy are not clearly characterized to this date.

In this report, we present the case of a patient who was referred to our hospital for MRI/ultrasound fusion-based targeted biopsy of the prostate due to a clinically high suspicion for PCa (elevated PSA and PI-RADS 5 lesion in the mpMRI) but benign pathologically findings in the mpMRI target. Two years later, the former PI-RADS 5 lesion in the mpMRI was classified as PI-RADS 2.

Case Presentation

A 66-year-old man was referred to our institution for MRI/ultrasound fusion-guided biopsy of the prostate. The patient's history revealed an elevated PSA of 55.86 ng/mL at the time of presentation. Sixteen years earlier, the PSA level was 2.34 ng/mL. In between, no PSA levels were obtained. Therefore, a mpMRI was performed. In Figure 1, the PSA-values, mpMRI's, and biopsies obtained are outlined chronologically. MpMRI of the prostate showed a suspicious lesion in the anterior part of the prostate located apically in the transitional zone described as PI-RADS 5 lesion. The diameter of the lesion was 2.2 cm. The lesion was assessed and categorized according to the PI-RADS classification version 2 [7]. The total volume of the prostate was measured with 115 mL using the ellipsoid formula. Consecutively, PSA density was 0.47. Digital rectal examination (DRE) showed no induration of the prostate. The patient underwent a 12-core randomized tran-

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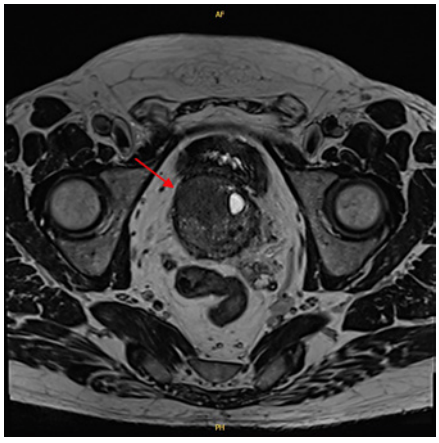


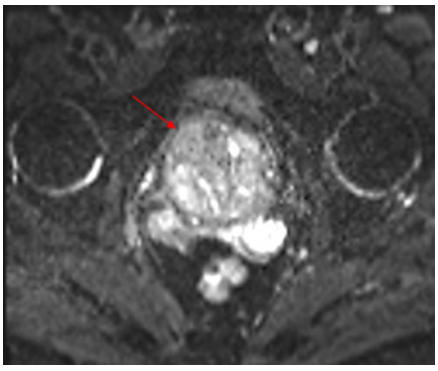
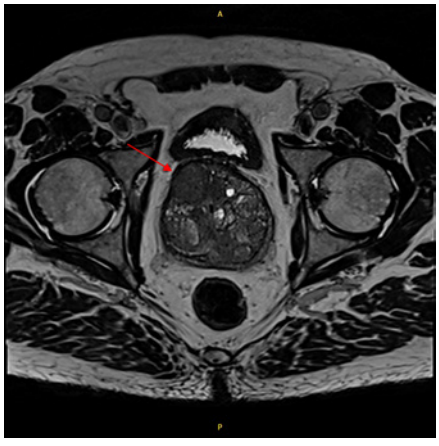


Fig. 3. Lesion in the mpMRI (T2-weighted sequence) classified as PI-RADS 5 located in the anterior part of the prostate at the right side marked with a red arrow.

Fig. 4. Lesion in the mpMRI (ADC map) classified as PI-RADS 5 with signs of slight diffusion restriction marked with a red arrow.



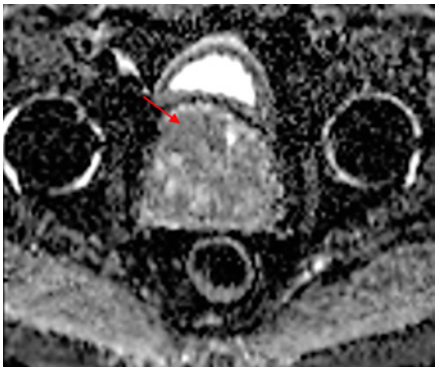


Fig. 5. Lesion in the mpMRI (T2-weighted sequence) described as a BPH nodule classified as PI-RADS 2 located in the anterior part of the prostate on the right side marked with a red arrow.

Fig. 6. Lesion in the mpMRI (ADC map) described as a BPH nodule classified as PI-RADS 2 with no signs of diffusion restriction marked with a red arrow.

srectal ultrasound-guided biopsy of the prostate and additional 3 cores of the mpMRI target.

In Figure 2, the fusion of the PI-RADS 5 lesion in the mpMRI with the B-mode ultrasound imaging is displayed. Image fusion was done software-assisted using the Philips Percunav® device on an Epiq 7 ultrasound system (Philips Medical Systems, Bothell, WA, USA). The registration was realized with plane wise fusion of the ultrasound and mpMRI image data using the T2-weighted axial mpMRI sequence. The fusion biopsy as well as the 12-core randomized biopsy was performed transrectally using an end-fire probe with the Philips Epiq 7 (Philips Medical Systems, Bothell, WA, USA) scanner. The standard biopsy consisted of 12-cores collected from the lateral and medial aspects of the base, mid, and apical parts of the prostate of the left and right lobe. The histopathologic evaluation showed no malignancy but signs of benign prostatic hyperplasia and hardly any signs of chronic inflammation. Due to the persistence of an elevated PSA of 55.86 ng/mL and a lesion described in the mpMRI associated with clinically significant PCa highly likely being present, a second biopsy was taken 4 months later. This time, 4 cores were taken from the target additionally to the 12-core randomized biopsy. Again, no malignancy was found histopathologically. The histopathological report revealed signs of chronic prostatitis and benign prostatic hyperplasia with round cells consisting of plasma cells and lymphocytes as well as basal cell hyperplasia. Even though PSA levels persisted on a high level between 32 and 56 ng/mL, the patient refused further biopsies. Two years later, mpMRI was reassessed again at a PSA level of 31.44 ng/mL. The mpMRI was obtained in the same radiological institution as 2 years before, and the same radiologist with a long experience in interpretation of mpMRI's of the prostate did the report. The volume of the prostate was still measured around 115 mL. PSA density declined to 0.27. This time, the lesion formerly described as PI-RADS 5 was now classified as PI-RADS 2 according to the PI-RADS classification system version 2 [7]. In the first mpMRI, a PI-RADS 5 lesion was described in the anterior part of the transitional zone with a diameter of 2.2 cm (Fig. 3). The lesion showed only a slight restriction in the diffusion-weighted sequence (Fig. 4) and no washout phenomenon in the perfusion-weighted sequence. However, according to the T2-weighted sequence, it was classified as PI-RADS 5. Two years later, the lesion showed no increase in diameter and in contrast to the previous mpMRI the margins were now more clearly circumscribed (Fig. 5) with no signs of diffusion restriction (Fig. 6). Therefore, the lesion was then described as a BPH nodule and classified as PI-RADS 2. Two years later, histopathology after holmium laser enucleation of the prostate confirmed those findings, showing no signs of malignancy, respectively.

Discussion

MpMRI significantly increased the detection rate of clinically significant PCa [3–5, 11]. MpMRI prior to biopsy of the prostate proved to reduce the number of men undergoing biopsy and to increase the detection rate of clinically significant PCa. The number of clinically significant cancers missed by MRI/ultrasound-guided biopsy is low and described between 0 and 10% [5, 12–14].

According to the PRECISION trial, the detection rate for PCa in PI-RADS 3 lesions is 34%, for PI-RADS 4 lesions 69%, and for PI-RADS 5 lesions 94% [4]. Other studies describe rates for malignancy in PI-RADS 5 lesions between 83 and 97% for low and intermediate-risk PCa and 62–81% for clinically significant PCa (Gleason 7a or greater) [3, 8, 9, 15]. Although the detection rate of PCa is high in PI-RADS 5 lesions, cases of benign findings have been described [10, 16].

It is generally known that inflammation within the prostate can mimic PCa in the mpMRI [7, 10, 16, 17]. As prostatitis can lead to early contrast enhancement, low ADC values appear as hypointense lesions in the mpMRI similar to cancer [16, 17]. Not only prostatitis can mimic PCa but also BPH nodules [10, 17, 18]. BPH nodules can show features similar to PCa including restricted diffusion, low intensity in T2, and early contrast enhancement [10, 17, 18]. In our case, the lesion fulfilled these criteria. It was located in the transitional zone showing moderate restriction in the diffusion-weighted sequence and almost no washout phenomenon. Furthermore, looking at the T2-weighted sequence the lesion was not clearly encapsulated. This limitation of the mpMRI was described from the American Society of Radiology earlier [7]. BPH nodules located in the transitional zone and blurred margins can be hard to distinguish from lesions suspicious of cancer [7]. Two years later, however, the lesion in the presented case showed clear margins and was, therefore, classified as PI-RADS 2.

The pitfalls in interpretation are less challenging in PI-RADS 5 lesions than in PI-RADS 3 or 4 lesions, as the lesions are more apparent and greater in size. However, there are some pitfalls which need to be considered when interpreting MRI imaging of the prostate leading to false-positive PI-RADS 5 lesions.

For example, Sheridan et al. [10] showed in a prospective series of 98 patients that one of 5 PI-RADS 5 lesions (18%) is histopathologically benign. They identified characteristics which were associated with histopathologically benign findings in MRI/ultrasound fusion-based targeted biopsy [10]: low PSA density and/or tumor located at the apex or base [10]. On histopathological level, most of the benign PI-RADS 5 lesions were benign prostatic hyperplasia nodules or inflammatory changes [10]. This is similar to our case, in which the histopathology revealed signs of BPH. This was concordant to the classification of the lesion in the mpMRI 2 years later.

Other studies describe rates up to 46.3% for false-positive MRI lesions and developed normograms for predicting benign pathology on MRI/ultrasound fusion-based targeted biopsy [19]. Factors predicting benign pathology include age, PSA, prostate volume, and PI-RADS score [19].

The coherence of clinically significant PCa and high PSA density is already well known and several studies on this topic exist [20–23]. PSA densitiy greater than 0.15 ng/mL is associated with a higher risk of clinically significant PCa [21]. PSA density is supposed to distinguish more precisely between malignant and benign findings than PSA level alone [23]. Recent studies suggested the combination of PSA density and PI-RADS score to select patients for biopsy and showed that PSA density combined with mpMRI imaging can improve the negative predictive value of PI-RADS scoring [19, 21]. In our case, PSA density was elevated up to 0.47 ng/mL, which according to the current literature is highly suspicious for clinically significant PCa, although in our case histopathology revealed no malignancy. However, final proof of definitive whole organ histopathology would only be possible if radical prostatectomy would have been done.

In conclusion, this case report shows risk factors for benign histopathology in PI-RADS 5 category lesions on mpMRI. Further studies are necessary to evaluate factors predicting negative outcome of targeted biopsy.

Conflict of Interest Statement

The authors declare that they have no conflicts of interest.

Statement of Ethics

All procedures performed in this case report involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. All subjects have given their written informed consent to publish details or photos of the case.

Funding Sources

No funding was obtained.

Author Contributions

Apfelbeck Maria: project development, data collection, data analysis, and manuscript writing and editing. Schlenker Boris: manuscript editing. Chaloupka Michael: data collection and manuscript editing. Stief Christian: project development and manuscript editing. Clevert Dirk André: project development, data collection, data analysis, and manuscript editing.

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