Published in final edited form as:

J Comput Assist Tomogr. 2014 ; 38(2): 274–276. doi:10.1097/RCT.0b013e3182aac58a.

Changes Observed in Multiparametric Prostate MRI Characteristics Correlate with Histopathological Development of Chronic Granulomatous Prostatitis Following Intravesical BCG Therapy

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Abstract

Administration of Bacillus Calmette-Guerin (BCG) has been shown to cause granulomatous prostatitis, a rare inflammatory process that can be mistaken for prostate cancer (PCa). We present a case of a 78-year-old male on active surveillance (AS) for PCa with a subsequent diagnosis of high-grade urothelial carcinoma. Following intravesical BCG therapy, he developed chronic granulomatous prostatitis (CGP). We present serial MRI and biopsy data demonstrating the time interval between BCG administration and the manifestation of CGP.

Keywords

Granulomatous prostatitis; intravesical BCG; prostate neoplasms; magnetic resonance imaging; ultrasound

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DISCLOSURES:

J. Logan has nothing to disclose.

Dr. Walton-Diaz has nothing to disclose

Dr. Rais-Bahrami has nothing to disclose.

Dr. Merino has nothing to disclose

Dr. Turkbey has nothing to disclose.

Dr. Choyke has nothing to disclose.

Dr. Pinto has nothing to disclose.

INTRODUCTION

CGP is an uncommon and benign inflammatory condition of the prostate that can mimic prostate cancer (PCa) both clinically and radiographically. The diagnosis of CGP is based on histology and is classified further into non-specific, specific/infectious, or allergic granulomatous prostatitis; the non-specific subtype is the most common.¹ Non-specific CGP is found in 0.44% of radical prostatectomy (RP) specimens and 0.29–3.3% of transrectal ultrasound (TRUS)-guided biopsies.^{2, 3} Despite this low incidence, the diagnosis of CGP is becoming more frequent due to the increased use of TURP, repeated and/or more extensive prostate biopsies, and intravesical administration of Bacillus Calmette-Guerin (BCG) therapy for high-risk urothelial carcinoma.

Although the exact number of men who will develop CGP following intravesical BCG therapy is unknown, rates have been estimated to range between 1.3 and 40%.^{4, 5} Clinically, the symptoms are vague but include urinary frequency, dysuria, and acute retention. Further complicating its differentiation from PCa, CGP can present with a transient serum increase in PSA, symptoms of prostatitis, and nodular or diffusely firm enlargement of the prostate, leading to an increased suspicion of cancer based upon DRE. CGP management is typically supportive, as symptoms in the majority patients will resolve spontaneously.

CASE REPORT

A previously healthy 78-year-old male with an elevated serum PSA level (4.7 ng/ml) was diagnosed with Gleason 3+3= 6 prostate adenocarcinoma in 5% of a single core obtained via standard extended sextant 12-core TRUS-guided prostate biopsy. This patient elected to be managed on an active surveillance protocol which integrates the use of serial multiparametric prostate magnetic resonance imaging (MP-MRI). One year after his initial diagnosis, he developed gross hematuria and workup revealed a 4cm high-grade urothelial carcinoma without muscle invasion managed with a comprehensive TURBT and subsequent 6-week course of intravesical BCG therapy. A subsequent MP-MRI revealed no distinct peripheral zone lesions but areas suspected to represent benign prostatic hyperplasia in the transitional zone based upon T2W and DW MRI sequences (Figure 1a–b). PSA at this time was 9.4 ng/ml. A repeated standard of care extended sextant 12-core TRUS-guided biopsy revealed Gleason 3+3 = 6 disease with 30% and 20% in 2 cores within the left base peripheral zone. No evidence of prostatitis or granulomatous disease was identified within the biopsy cores evaluated at this time including both targeted and standard 12 core specimens (Figure 2a). Additionally, retrospective review of this area revealed no imaging pathology in the corresponding anatomical locations on the MP-MRI study. With these clinical, imaging, and pathology findings, the patient elected to continue active surveillance for management.

During his follow up, his serum PSA level rose to 10.7 ng/ml and a follow-up MP-MRI (approximately 14 months after the initial MP-MRI study) was performed. This revealed a new lesion in the left mid-base peripheral zone, whereas findings in the remainder of the prostate gland were stable (Figure 1c–d). The newly visualized left mid/base peripheral zone lesion was sampled under MR/US fusion guidance and histopathologic evaluation revealed

chronic granulomatous prostatitis (CGP) at that location (Figure 2b). Additionally, random 12 core biopsy demonstrated Gleason 6(3+3) disease in 40% and 30% in 2 cores in the left base, which again appeared normal on the MP-MRI. The patient continued on active surveillance and his follow-up has been uneventful with a three-month follow-up PSA of 7.55 ng/ml.

DISCUSSION

With the inability to definitively differentiate CGP from prostate cancer on TRUS,¹ the use of MP-MRI has garnered increasing curiosity and use. However due to the infrequency of CGP, MRI data on CGP appearance relies on small patient series. Ma and colleagues⁶ were among the first look at MRI features of CGP and demonstrated in six patients who underwent MRI following BCG administration, five patients were diagnosed with CGP and had MR findings of nodular and diffuse hypointense lesions on T2W—findings which were indistinguishable from prostate tumors located in the peripheral zone. Furthermore, because MR characteristics were not the focus of the study, only T2W images were acquired.

Suzuki and colleagues performed T2W, T1W, and DWI MRIs on ten patients who proven cases of CGP and categorized differences seen on all MRI phases. Notable findings from this study included six of ten patients who demonstrated CGP in with a diffuse shape, lower signal intensity (SI) than bone marrow on T2W, and higher SI on DWI.⁷ The other observed characteristics included 3 CGP lesions that were nodular in appearance but did not have congruence in their SIs for either T2W or DWI. Another recent report of 5 patients found a slight decrease in mean Apparent Diffusion Coefficients (ADC) derived from diffusion weighted MRI for CGP versus prostate cancer with moderate dynamic contrast enhancement (DCE) of CGP lesions, again overlapping with PCa.⁸ MR spectroscopic imaging reports have included even fewer patients and have thus been unable to describe conclusive findings.⁹ For these reasons, prostate biopsy remains the only definitive method for distinguishing CGP from PCa.

Further complicating the story of BCG-induced CGP development is the timing during which the granulomatous process develops. Cases have reported CGP detection via TRUS or cystoprostatectomy ranging anywhere from 2–45 months after completion of a course of intravesical BCG; because of the incidental discovery of CGP, these ranges have remained broad.^{9, 10} In the case we present here, we were able to document the time interval between the administration of BCG and the development of imaging changes by MRI. These indicate that CGP development takes greater than 12 months following BCG-therapy completion to appear and may be seen at or before 24 months post-BCG administration. This information becomes important for clinicians as serial MRI of the prostate becomes more widespread. As our case indicates, it is important for clinicians to consider that newly developing prostate lesions have the potential to be related to CGP, especially in patients who have completed BCG therapy within the previous 12 months.

Acknowledgments

This research was supported by the Intramural Research Program of the NIH, National Cancer Institute, Center for Cancer Research and the Center for Interventional Oncology. NIH and Philips Healthcare have a cooperative

research and development agreement. NIH and Philips share intellectual property in the field. This research was also made possible through the NIH Medical Research Scholars Program, a public-private partnership supported jointly by the NIH and generous contributions to the Foundation for the NIH from Pfizer Inc, The Leona M. and Harry B. Helmsley Charitable Trust, and the Howard Hughes Medical Institute, as well as other private donors. For a complete list, please visit the Foundation website at <http://www.fnih.org/work/programs-development/medical-research-scholars-program>.

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Figure 1.

78 year-old male who was undergoing active surveillance for Gleason 3+3 = 6 prostate cancer with subsequent diagnosis of high grade urothelial carcinoma and managed with intravesical BCG therapy. Axial T2W MRI (A) and ADC maps of DW MRI (B) as a baseline shows no distinct lesion in the peripheral zone but a benign prostatic hyperplasia of the transitional zone. Axial T2W MRI (C) and ADC maps of DW MRI (D) obtained 14 months after the baseline MRI demonstrate a hypointense lesion within the left mid-base peripheral zone (arrows in C and D). This lesion underwent MRI/TRUS fusion guided biopsy and histopathology was consistent with chronic granulomatous prostatitis.

Figure 2.

A) High power view of the patient's initial fusion biopsy with a single core displaying Gleason 3+3 = 6 prostate adenocarcinoma and no evidence of prostatitis. B) High power view of patient's second fusion biopsy 24 months post-BCG initiation with a single core now displaying Gleason 3+3 = 6 disease with evidence of CGP.