Short Communication

A positive magnetic resonance spectroscopic imaging with negative initial biopsy may predict future detection of prostate cancer

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ABSTRACT

Current diagnostic modalities for early prostate cancer (PCa) lack sufficient sensitivity and specificity. Magnetic resonance spectroscopic imaging (MRSI) detects biochemical changes in tissues that may predate histological changes that can be diagnosed on a biopsy. Men with MRSI suggestive of malignancy but negative biopsy may thus be harboring cancer that manifests at a later date. We report the first case in our cohort of men with positive MRSI but negative initial biopsy who, 6 years after the initial MRSI, were detected to have PCa despite a "normal" prostate specific antigen (<4.0 ng/ml).

Key words: Biopsy, magnetic resonance spectroscopic imaging, prostate cancer, prostate specific antigen

INTRODUCTION

Serum prostate specific antigen (PSA) based screening for detection of early prostate cancer (PCa) is associated with overdiagnosis and the value of PSA screening remains controversial.[1] Multiparametric magnetic resonance imaging (MRI), which is the combination of various MR techniques including conventional T2-weighted (T2W) imaging, diffusion-weighted imaging (DWI), dynamic contrast-enhanced (DCE) MR imaging and magnetic resonance spectroscopic imaging (MRSI), is emerging as an important diagnostic tool for detection, localization, staging, and evaluation of treatment outcomes.[2,3] MRSI identifies biochemical changes within the tissue that may predate the appearance of histological changes that are currently used to diagnose PCa.[4] It is thus possible that patients with MRSI suggestive of malignancy may not have biopsy detectable PCa at the time of MRSI but may develop histological cancer at a later date. We have been evaluating MRSI prior to biopsy as a diagnostic modality for PCa since 1999 and have followed up patients with positive MRSI but negative biopsy for their outcomes. We report the first case in our series that developed PCa in a follow up after an initial positive MRSI but negative biopsy, despite the serum PSA returning to normal (<4.0 ng/ml).

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CLINICAL CASE

A 56-year-old man presented with lower urinary tract symptoms (LUTS) and elevated serum PSA (8.53 ng/ml) in October 2004. His digital rectal examination revealed a grade 2, benign enlargement of the prostate. He underwent an MRSI study followed by a transrectal ultrasound (TRUS)-guided sextant and focused biopsy as per a previously described protocol.[5] The MR investigations were carried out at 1.5 T using a whole-body MR scanner (Siemens, Erlangen, Germany) using a pelvic-phased array coil in combination with an endorectal surface coil. After acquisition of scout images in three orthogonal planes, the position of the endorectal coil was checked on sagittal images. Following this, T1-weighted (T1W) transverse and T2W images in transverse, sagittal, and coronal planes were acquired covering the entire prostate using turbo spin-echo sequence (TR=5000 ms, TE=98 ms, FOV=280, matrix size=256 × 256, slice thickness=5 mm, without the interslice gap). The MRSI parameters used were TR=1300 ms, TE=120 ms, voxel size = 5 × 5 × 5 mm^3, average=3, with a total acquisition time of 17 min. 3D ^1H MRSI spectral grid was superimposed on

a T2W image of the prostate and two suspicious voxels demonstrated elevated levels of choline (Cho) and decreased citrate (Cit), indicative of malignancy [Figures 1a and b]. The metabolite ratio [Cit/(Cho+Cr)] for these voxels were 0.027 (right periphery mid) and 0.061 (left periphery mid), where Cr refers to creatine. The biopsy did not reveal malignancy on any of the cores sampled.

His repeat PSA values were 6.04 ng/ml in 2005, 4.31 ng/ ml in 2006 and with no follow-up for 4 years, 4.0 ng/mL in 2010. He was managed for his symptoms and consented for a repeat MRSI study in 2010. The repeat MRSI study was carried out using the same parameters as the 2004 study. This study revealed four voxels suspicious for malignancy with [Cit/(Cho+Cr)] ratios varying from 0.147 to 0.27 [Figures 2a and b]. Although the PSA had returned to normal, due to the persistently abnormal MRSI, the patient consented for a repeat TRUS-guided biopsy (12 cores including four from the focused areas) that revealed adenocarcinoma from the right peripheral base. With a diagnosis of clinical T1c, N0, M0 PCa, the patient underwent a robotic radical prostatectomy that confirmed a Gleason score 3+3 adenocarcinoma.

DISCUSSION

The use of serum PSA to screen men for PCa is fraught with a high false-positive rate. There is thus need to substratify men with raised PSA into those who are more likely to have cancer than others and therefore require a biopsy.

Among men with raised PSA, MRI techniques may help identify a subset that requires treatment.[6-8] T2W-MRI and MRSI are the most commonly used MR techniques in detection of PCa. Among the newer MR techniques, DWI is sensitive to restriction of the water molecule diffusion and provides contrast based on the translational motion of water protons in biological tissues. DCE-MRI is capable of assessing microvascular properties. All these techniques have shown the potential value in distinguishing malignant from benign prostate.[9,10] MRSI-guided prostate biopsies may improve the biopsy yield and improve concordance between the biopsy and radical prostatectomy Gleason scores.[5,11]

In our patient, it is possible that the tumor existed even in 2004 since there are suspicious areas in the MRI. The lesion was not visible on the TRUS and the biopsy (sextant plus focused) could have missed the tumor. This is an inherent limitation of the biopsy and one of the reasons that we now perform 12 core biopsies as standard.

It is proposed that metabolic changes predate histologic changes and this fact provides a window of opportunities for detecting early disease. Our patient had a "normal" PSA on his follow-up and may not have been advised a repeat biopsy. Normalizing PSA after an initial increase is a well-known phenomenon and, in fact, has been a significant finding

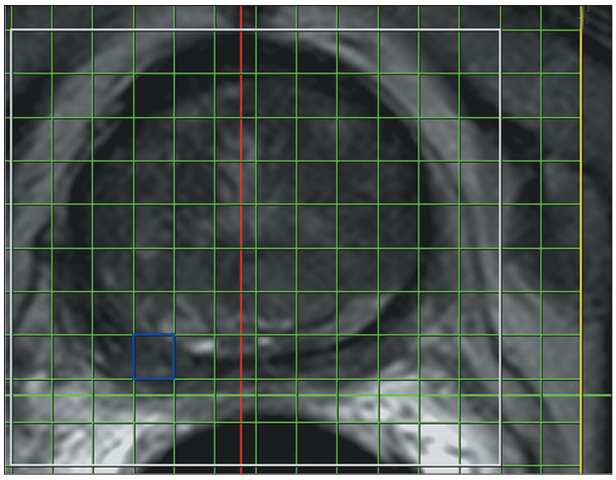

Figure 1a: 3D ^{1}H MRSI spectral grid superimposed on a T2-weighted (without fat-sat) image of the prostate in 2004. A small incidental neurofibroma is noted

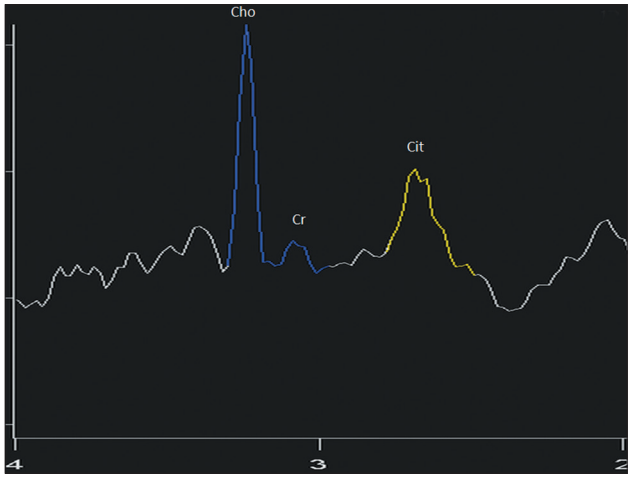

Figure 1b: MR spectrum obtained from the voxel showing increased Cho and decreased Cit

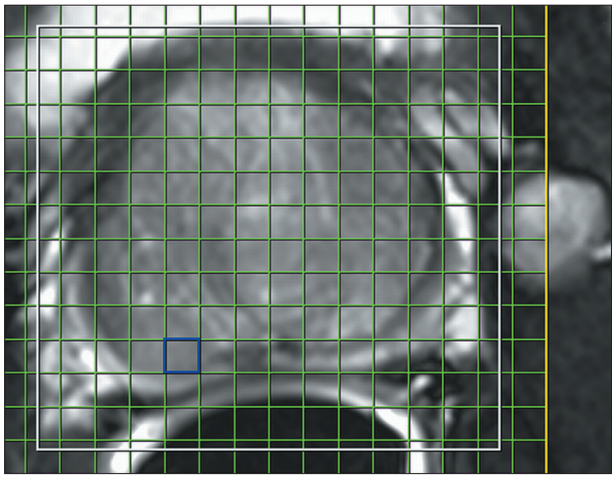

Figure 2a: 3D ^{1}H MRSI spectral grid superimposed on a T2-weighted (fat-sat) image of the prostate in 2010

in our cohort of men.[3] Such men would normally not be considered candidates for a repeat biopsy. In view of our previously reported findings in men with negative MRSI and

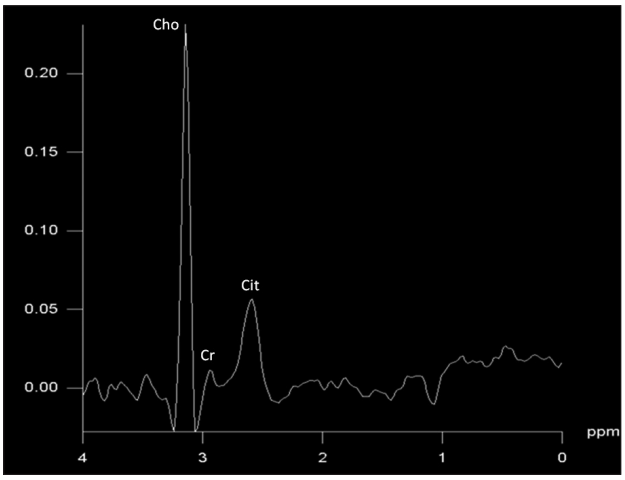

Figure 2b: MR spectrum obtained from the voxel showing elevated Cho and decreased Cit, indicative of cancer

negative biopsies,[3] the current report suggests that MRSI may become an important variable in deciding which patients with a negative initial biopsy should be followed-up more closely. The finding of malignancy supports our hypothesis of MRSI changes predating histologic ones and continued follow-up of our cohort of men with negative biopsies with positive MRSI may further strengthen the evidence.

Considering upto 20% chance of detecting cancer on repeat biopsy in a patient with a negative initial biopsy, it is quite possible that the detection of cancer in our patient was purely by chance and not, in any way, related to the positive MRSI. The importance of this case lies in the fact that his PSA actually declined to normal levels and this patient would not have been a candidate for repeat biopsy, were it not for the positive MRSI. It is not possible to define a role for MRSI in following up positive cases purely on the basis of this single case report but it lends credence to the need for further evaluation of this modality.

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