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Mucinous Adenocarcinoma of the Prostate: MRI and MR Spectroscopy Features

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Abstract

OBJECTIVE—The purpose of this study was to investigate the MRI and MR spectroscopy features of mucinous adenocarcinoma of the prostate.

CONCLUSION—MRI and MR spectroscopy do not appear to provide the ability to reliably detect the lakes of extracellular mucin seen in mucinous adenocarcinoma of the prostate.

Keywords

MRI; mucinous adenocarcinoma; neoplasm; prostate; MR spectroscopy

Mucinous (or colloid) adenocarcinoma of the prostate is a subtype of prostate cancer that is characterized by large pools of extracellular mucin that by definition compose at least 25% of the tumor volume [1]. Mucinous adenocarcinomas represent approximately 0.4% of all prostate adenocarcinomas [2,3]. Traditionally, mucinous adenocarcinoma of the prostate has been considered to be more aggressive than the more common nonmucinous prostate adenocarcinoma [1], although this notion has been challenged [2,4]. Given these considerations, the 2005 International Society of Urological Pathology Consensus Conference on Gleason Grading of Prostatic Carcinoma suggests that these tumors should be classified as Gleason score 8 (4 + 4) [5]. Thus, mucinous adenocarcinoma would be considered a high-risk finding that could well influence therapeutic decisions and approaches. Unfortunately, the diagnosis of mucinous adenocarcinoma of the prostate is often difficult to make before prostatectomy [1,6] because the amount of tissue obtained with biopsy may not be representative of the entire tumor, and this subtype may not be recognized because of its rarity and lack of overt aggressive cytologic features.

Endorectal MRI and MR spectroscopy have emerged as relatively accurate and powerful methods of evaluating prostate cancer [7,8], raising the possibility that there might be MR features that would suggest the diagnosis of mucinous adenocarcinoma of the prostate and allow noninvasive diagnosis and more appropriate therapeutic management. An early small series of patients with mucinous adenocarcinoma of the prostate suggested these tumors have high T2 signal intensity rather than the usual decreased T2 signal intensity of nonmucinous adenocarcinoma of the prostate [9]. To our knowledge, the MR spectroscopy findings in mucinous adenocarcinoma of the prostate have not been reported. Therefore, we undertook

this study to investigate the MRI and MR spectroscopy features of mucinous prostate adenocarcinoma.

Materials and Methods

Subjects

This was a retrospective single-institution study approved by our institutional review board with waiver of informed consent. The study was compliant with requirements of the HIPAA. We performed a computerized search of our radiology and hospital information systems for the period from 1999 to 2005 to identify patients who met the following inclusion criteria: endorectal MRI and MR spectroscopy of the prostate performed for biopsy-proven prostate cancer; radical prostatectomy specimen obtained within 180 days of imaging, with step-section evaluation of the specimen and creation of detailed tumor maps showing the size, location, and histopathologic features of all malignant foci; no interval treatment between MRI and prostatectomy.

One hundred one patients fulfilled these criteria. Two were excluded because of unavailable histopathologic slides ($n = 1$) or MR images that were not retrievable ($n = 1$). Ninety-nine eligible patients remained in the study. Medical records of patients with mucinous adenocarcinoma of the prostate were reviewed to exclude a primary mucinous tumor elsewhere in the body.

Imaging Technique

Images were acquired on a 1.5-T MRI scanner (Signa, GE Healthcare) using the body coil for excitation and a pelvic phased-array coil in combination with a balloon-covered endorectal coil (BPX-15 Prostate Endorectal Coil, Medrad) for signal reception. Thin-section high-spatial-resolution axial and coronal T2-weighted fast spin-echo images were obtained with the following parameters: TR/effective TE, 5,000/96; echo-train length, 16; slice thickness, 3 mm; gap, 0 mm; field of view, 14 cm; matrix, 256×192 ; frequency-encoded direction, anteroposterior; and number of excitations, 3. Three-dimensional MR spectroscopy data were acquired using a water- and lipid-suppressed double spin-echo point-resolved spectroscopy sequence that used spectral-spatial pulses for the two 180° excitation pulses [10–12]. The spectral-spatial pulses allowed sharp volume selection as well as frequency selection to reduce the water resonance and suppress lipid resonances. Data sets were acquired as $16 \times 8 \times 8$ phase-encoded spectral arrays (1,024 voxels with a spatial resolution of $0.24\text{--}0.34\text{ cm}^3$) with TR/TE of 1,000/130 and a 17-minute acquisition time.

Histopathologic Review

The radical prostatectomy specimens were all marked with ink and fixed overnight in 10% neutral buffered formalin. Axial step sections were obtained at 3- to 4-mm intervals in a plane perpendicular to the prostatic urethra. In most cases, the apical margin, bladder (base) margin, step sections adjacent to these margins, and alternate sections between these margins were all sliced into quarters and submitted entirely for histopathologic evaluation. In a few cases, a whole-mount step-section technique was performed. One pathologist with 12 years of experience reviewed all slides and was unaware of the MRI and MR spectroscopy results. The reader measured and recorded the size, location, and histopathologic features of all cancer foci on a standardized diagram of the prostate, including the percentage of extracellular mucin in relation to the tumor volume.

MRI and MR Spectroscopy Interpretation

A consensus panel consisting of two radiologists and a spectroscopist with 4, 12, and 17 years of experience, respectively, reviewed the MRI and MR spectroscopy studies of patients with a histopathologic diagnosis of a mucinous adenocarcinoma. At the time of imaging interpretation, readers were aware of the final histopathologic diagnosis. All images were reviewed on a PACS workstation (Impax, Agfa HealthCare). For each histopathologically proven mucinous tumor, the consensus panel characterized the corresponding area on T2-weighted MR images as hypointense, isointense, or hyperintense in relation to the adjacent normal peripheral zone and measured the largest axial perpendicular diameters of visible lesions.

On MR spectroscopy, the spectroscopic voxels were considered usable for analysis if they contained at least 75% of peripheral zone tissue, did not incorporate the urethra and ejaculatory ducts, and were not substantially contaminated by water and lipid. Voxels were scored using the 5-point scale previously described by Jung et al. [13]. MR spectroscopic images were classified as positive (neoplastic metabolism, scores 4 and 5), equivocal (score 3), or negative (normal, scores 1 and 2, or atrophic metabolism).

Correlation between MR images and histopathologic diagrams was made using as guidance distinctive anatomic landmarks seen at histopathologic examination and on transverse T2-weighted MR images, such as the ejaculatory ducts, urethra, prostatic capsule, surgical pseudocapsule, and prominent nodules of benign prostatic hyperplasia.

Results

A tumor was considered mucinous if at least 25% of the tumor volume was composed of extracellular mucin [3] and such a tumor was diagnosed in three of 99 patients (3%) in our series.

The first patient was a 46-year-old man who presented with a prediagnostic prostate-specific antigen (PSA) of 7.6 ng/mL. On histopathology, the largest diameter of the tumor, which was located in the right mid-gland, measured 1.2 cm, and approximately 80% of the total tumor volume was composed of lakes of extracellular mucin. The lesion was isointense to the peripheral zone on MRI, and MR spectroscopy findings were negative (Fig. 1).

The second tumor was diagnosed in a 52-year-old man. His PSA at the time of diagnosis was 4.6 ng/mL. This tumor was diagnosed in the left midgland and measured 0.9 cm in its largest transverse diameter. Approximately 75% of its volume was composed of lakes of extracellular mucin. This tumor was also indistinguishable from the peripheral zone on MRI and had negative MR spectroscopy findings (Fig. 2).

The third patient was a 64-year-old man with a PSA of 6.2 ng/mL. The tumor was located in the right midgland to the base; it measured 1.2 cm in maximum transverse diameter and approximately 25% of its volume was composed of extracellular mucin. A focus of low signal intensity on T2-weighted images was identified (0.8 cm in maximum diameter) with positive metabolic features on MR spectroscopy. However, when histopathologic findings were correlated with imaging, it was noted that MRI showed only about two thirds of the lesion. The anterior aspect of this tumor, which represented most of the extracellular mucin lakes identified on histopathology, was occult at MRI and MR spectroscopy (isointense to the peripheral zone on T2-weighted MRI and without malignant metabolism) (Fig. 3).

Discussion

Our study supports the impression that mucinous adenocarcinomas of the prostate may not carry the usual characteristics of nonmucinous tumors on T2-weighted MRI (low signal intensity) and MR spectroscopy (increased choline and decreased citrate peaks), presumably because of the large volume of extracellular mucin they harbor. Our results concur with the description provided by Outwater et al. [9] in which mucinous adenocarcinomas presented with high signal intensity on T2-weighted images. This characteristic, described in other mucinous tumors seen elsewhere in the body [14,15], seems to render prostate mucinous adenocarcinomas occult against the high T2 signal intensity of the normal peripheral zone background. However, to our knowledge, this is the first description of the MR spectroscopy findings seen in this subtype of prostate cancer. We were unable to detect any malignant metabolism in areas where lakes of extracellular mucin were identified at histopathology, making two of our cases completely invisible on MR spectroscopy.

The analysis of our cases raises an additional question. It is not unusual to identify variable amounts of intraluminal mucin in nonmucinous prostate adenocarcinoma specimens, and some tumors present with less than 25% of their volumes composed of lakes of extracellular mucin. Could this fact at least in part explain why some prostate adenocarcinomas are not detected on MRI and MR spectroscopy? Further and larger studies that control for factors known to influence tumor detection—e.g., tumor volume—and investigation of the correlation between the amount of mucin seen in cancer and imaging accuracy are necessary to answer this question.

Our study has limitations. First, this was a retrospective study, and we likely incurred a selection bias because we included only patients who underwent radical prostatectomy. It is possible that these were patients with more localized disease and, consequently, our results would not be generalizable to patients with larger and more extensive mucinous adenocarcinomas. However, these tumors are more likely to contain larger pools of extracellular mucin, and one would expect to identify the same imaging features we describe. Second, as in many case series, our sample size is small and may not represent all mucinous adenocarcinomas; however, the MRI features we describe agree with those previously reported [9], suggesting that our MR spectroscopy findings are valid. Third, we did not include a control group in our study. A case-control study would allow us to compare the incidence of the MRI and MR spectroscopy findings seen in patients with mucinous adenocarcinoma and other groups of patients, for instance, those with nonmucinous adenocarcinomas or men without cancer. Nonetheless, because of the small number of patients with mucinous tumors, we would not be able to perform a meaningful statistical analysis to draw any definite conclusions from such study. Last, although histopathologic examination with tumor maps is considered the standard of reference for radiologic tumor detection, it can be difficult to correlate the location of histopathologic and imaging findings. Most of our histologic step sections were quartered during processing, the standard procedure at our institution at the time these patients underwent surgery, instead of being prepared as whole-mount sections.

In conclusion, MRI and MR spectroscopy do not appear to be able to reliably detect the lakes of extracellular mucin seen in mucinous adenocarcinomas of the prostate. This raises the question of whether the presence of mucin in some nonmucinous tumors is responsible for the less than optimal detection of cancer with both MRI and MR spectroscopy. Further and larger studies are needed to test this hypothesis.

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Fig. 1.
 46-year-old man with mucinous adenocarcinoma of prostate in right midgland.
A, Histologic specimen shows tumor (*outline*).
B, MR image shows tumor isointense to peripheral zone.
C, MR spectroscopy image shows negative findings.

Fig. 2.
 52-year-old man with mucinous adenocarcinoma of prostate in left midgland.
A, Histologic specimen shows tumor (*outline*).
B, MR image shows tumor is isointense to peripheral zone.
C, MR spectroscopy image shows negative findings.

Fig. 3.
 64-year-old man with mucinous adenocarcinoma of prostate in right midgland.
A, Histologic specimen shows tumor (*outline*).
B, Only posterior aspect of tumor (*arrow*) is identified as focus of low signal intensity on MRI.
C, On MR spectroscopy, only posterior medial voxel shows malignant metabolism (*arrow*).