

## Primary follicular lymphoma of the prostate presenting with elevated PSA and a PI-RADS 3 lesion on MRI: A case report

Hanna Jia<sup>a</sup>, Daniel Roberson<sup>b,\*</sup>, Xunda Luo<sup>c</sup>, R. Caleb Kovell<sup>b</sup>, Lee Hartner<sup>d</sup>, Joseph F. Harryhill<sup>b</sup>

<sup>a</sup> Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA

<sup>b</sup> Division of Urology, Department of Surgery, University of Pennsylvania Health System, Philadelphia, PA, USA

<sup>c</sup> Department of Pathology and Laboratory Medicine, University of Pennsylvania Health System, Philadelphia, PA, USA

<sup>d</sup> Division of Hematology and Oncology, Department of Medicine, University of Pennsylvania Health System, Philadelphia, PA, USA

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### ABSTRACT

Prostate cancer is the most common malignancy diagnosed in men. PI-RADS 3 lesions on multiparametric MRI, when histologically proven malignant, overwhelmingly represent prostatic adenocarcinoma. Primary lymphoma of the prostate, especially follicular lymphoma, is exceedingly rare. To our knowledge, its presentation with a PI-RADS 3 lesion and elevated PSA has not been previously described. We report the case of a 68-year-old, healthy male presenting with elevated PSA and lower urinary tract symptoms found to have a PI-RADS 3 lesion. Prostate biopsy revealed low-grade follicular lymphoma, and staging showed no other lesions. The patient is currently being managed with close surveillance.

### 1. Introduction

Primary lymphoma of the prostate is rare, making up less than 0.1% of all prostate cancers.<sup>1</sup> Follicular lymphoma, an indolent B cell lymphoma comprised of the malignant counterparts of germinal center B cells, is a rare subset of lymphomas that has been described in the prostate. Imaging of the prostate via multiparametric MRI (mpMRI) has become increasingly utilized in the work-up of elevated prostate specific antigen (PSA), but the appearance of follicular lymphoma on mpMRI has not yet been reported. We report the first published case, to our knowledge, of primary follicular lymphoma of the prostate presenting with an elevated PSA and a Prostate Imaging Reporting & Data System (PI-RADS) 3 lesion on mpMRI.

### 2. Case presentation

A 68-year-old otherwise healthy male initially presented with an elevated PSA of 4.5 µg/L, an increase from 2.8 µg/L 6 months prior and worsening lower urinary tract symptoms. Physical exam was unremarkable including a digital rectal exam revealing a smooth and symmetric, moderately enlarged prostate with no induration or nodules.

Family history was noncontributory. Repeat serum PSA, measured three months after his presenting PSA, was 10.71 µg/L, with a 4K score of 37%, and PSA density of 0.137 µg/L/cc. Prostate mpMRI revealed a 78 cc gland with a 7mm PI-RADS 3 lesion in the anterior right transition zone at the mid-gland, with no concern for extraprostatic extension, pelvic lymphadenopathy or osseous metastases (Image 1).

Prostate biopsies revealed dense small lymphocytic infiltrate in 3 of 7 cores, concerning for low-grade non-Hodgkin's lymphoma. Immunohistochemistry confirmed a dominant population of B cells positive for CD20, PAX5, CD10, BCL6, and BCL2, and negative for CD5 and SOX11, with a proliferative (Ki67+) index of 5%. No centroblasts were noted. B cells are associated with intact CD21<sup>+</sup> follicular dendritic cell meshworks. In total, these findings were diagnostic for low-grade (WHO grade 1–2 of 3) follicular lymphoma (Image 2).

Following discussion at our university based, multidisciplinary GU oncology board the patient was referred to medical oncology for a full staging workup and further care. Staging CT imaging of the neck, chest, abdomen, and pelvis showed no evidence for intrathoracic or intra-abdominal lymphadenopathy, and a 1.7cm level 4 neck lymph node most consistent with benign lymphadenopathy.

The options of observation versus definitive local therapy were

\* Corresponding author. Division of Urology, Department of Surgery, University of Pennsylvania Health System Perelman Center for Advanced Medicine, West Pavilion, 3rd Floor 3400 Civic Center Blvd, Philadelphia, PA, 19104, USA.

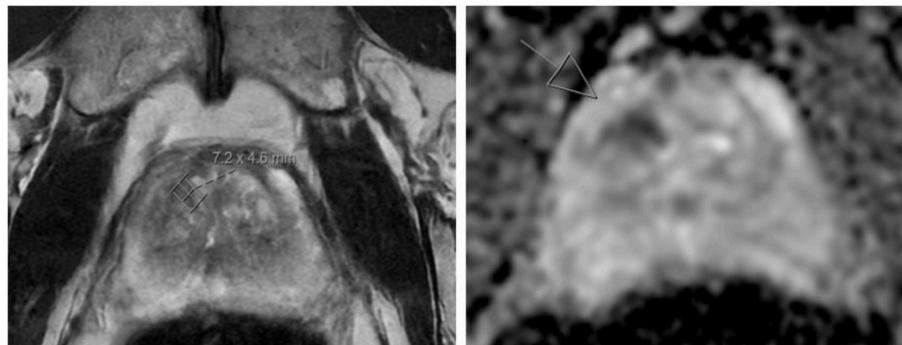
E-mail address: [Daniel.roberson@penntmedicine.upenn.edu](mailto:Daniel.roberson@penntmedicine.upenn.edu) (D. Roberson).

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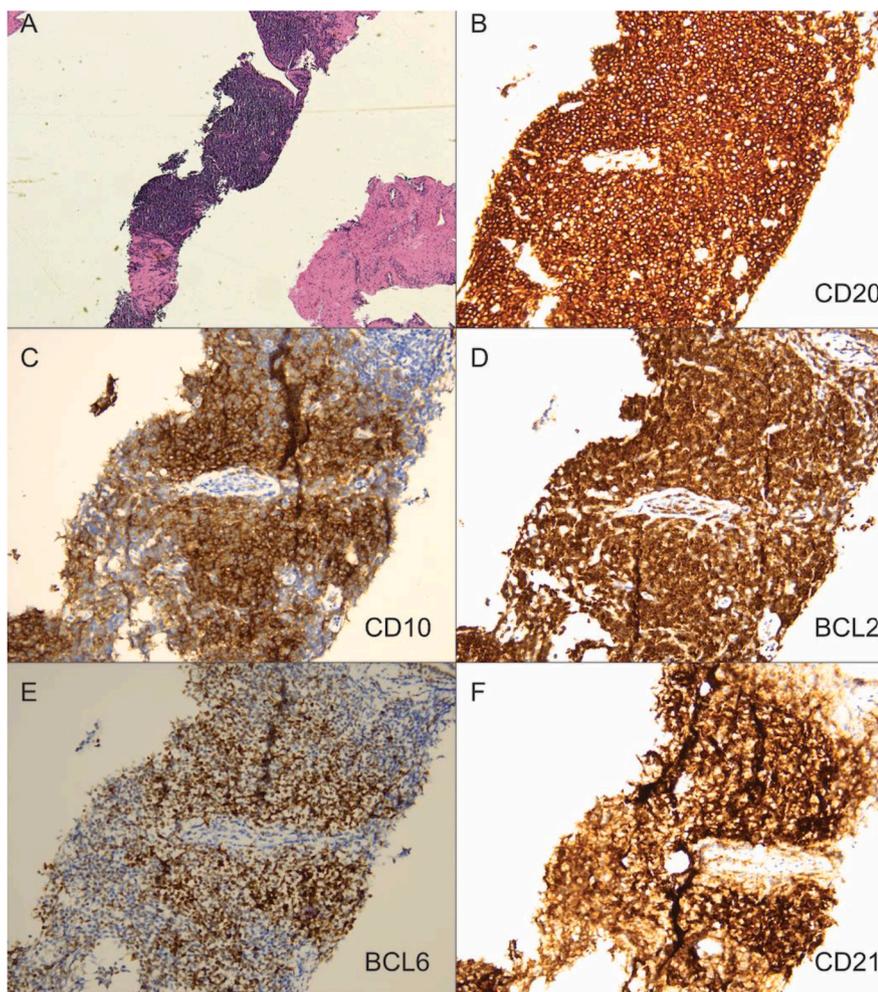
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**Fig. 1.** Multiparametric MRI of the prostate. The image on the left is a representative cross section from the T2 weighted axial sequence that shows the size and location of the PI-RADS 3 lesion in the right mid-gland transition zone. It measured 7.2mm × 4.6mm in this view. The image on the right is the diffusion weight imaging sequence with the arrow pointed to the lesion in question.



**Fig. 2.** Prostatic tissue involved by follicular lymphoma in needle biopsies. Routine HE stain (A) showing prostatic tissue with a vaguely nodular infiltrate of monotonous small lymphocytes with irregular nuclei, condensed chromatin, and scant cytoplasm, predominantly in a follicular growth pattern. Immunohistochemical stains show a dominant population of B cells that are positive for CD20 (B), PAX5 (not shown), germinal center markers CD10 (C) and BCL6 (E), and aberrant BCL2 expression (D) indicating the presence of a translocation involving the *BCL2* gene. Follicular dendritic cell meshwork is highlighted by CD21 stain (F). CD3 (not shown) and CD5 (not shown) stain scattered small T-cells. The proliferative index of the lesion determined by Ki-67 stain (not shown) is approximately 5%.

discussed with the patient. Surveillance would consist of follow-up imaging, serial physical examination and laboratory studies. Although there is no clear standard in such a case with little precedent, an alternative of definitive local therapy with radiation as treatment for follicular lymphoma could be considered; bone marrow biopsy would be necessary for complete staging before proceeding. To monitor for local disease progression, interval follow up with repeat mpMRI and prostate biopsies in 6–12 months should be considered.

### 3. Discussion

Primary prostatic lymphoma is markedly rare, representing only 0.1% of lymphomas and 0.09% of prostatic malignancies.<sup>1</sup> Patients present most commonly with obstructive voiding symptoms such as frequency, urgency, and dysuria.<sup>2</sup> These nonspecific clinical features make it difficult to generate an index of suspicion and differentiate it from other causes of lower urinary tract symptoms, including benign prostatic hyperplasia or prostatic adenocarcinoma. Thus, the overwhelming majority of cases of primary prostatic lymphoma are

diagnosed incidentally on biopsy, transurethral resection, or prostatectomy. Histologically, diffuse large B-cell lymphoma is the predominant histological subtype found in the prostate. Other reported subtypes include small lymphocytic lymphoma, mucosa-associated lymphoid tissue, follicular lymphoma, mantle cell lymphoma, and Burkitt lymphoma.<sup>3</sup>

In this case, our patient presented initially with a rising PSA and obstructive voiding symptoms. Suspicious findings on multiparametric MRI culminated in prostate biopsy, which demonstrated primary follicular lymphoma of the prostate. This particular histologic type makes up only 12% of primary prostatic lymphoma,<sup>3</sup> and has been rarely reported in the literature. In addition, several other aspects of this case make it unique. First, this is the only published case to our knowledge of follicular lymphoma presenting as a PI-RADS 3 lesion. While mpMRI of the prostate is now increasingly used to evaluate men at risk for prostate cancer, no primary studies have examined how prostatic lymphoma appears on mpMRI. This is largely due to rarity of disease and the fact that most reported cases were published before mpMRI became more ubiquitous. Second, PSA is typically within or near normal limits in cases of prostatic lymphoma, with patients presenting with a mean PSA of 3.5–5.3 µg/L.<sup>2,3</sup> At the time of mpMRI and biopsy our patient had a PSA of 10.71 µg/L. We hypothesize that this patient's PSA elevation was due to the inflammatory and infiltrative processes related to the prostatic lymphoma, rather than the lymphoma itself. However, other possibilities include the secretion of binding factors by the lymphoma that could increase the half-life of PSA, or of modifier proteins that could stimulate the overproduction of PSA.<sup>4</sup>

The clinical course of primary prostatic lymphoma is believed to be relatively indolent and patients can remain asymptomatic for years.<sup>5</sup> In addition, because of the low-grade nature of our patient's prostatic lymphoma and negative full body staging studies, we plan to manage him conservatively for now. This will include close surveillance with physical exam, repeat imaging, and laboratory studies, all in short intervals. If repeat imaging continues to show an isolated lesion in the prostate, we plan to discuss with our patient definitive local treatment in order to reduce the risk of disease progression.

#### 4. Conclusion

To our knowledge, this is the first reported case of primary follicular lymphoma of the prostate presenting with an elevated PSA and a PI-RADS 3 lesion on MRI. While exceedingly rare, it is important for genitourinary surgeons, oncologists, and pathologists to be familiar with

the clinical features of primary prostatic lymphoma.

#### Consent

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 upon request.

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Oncology or General Urology.

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