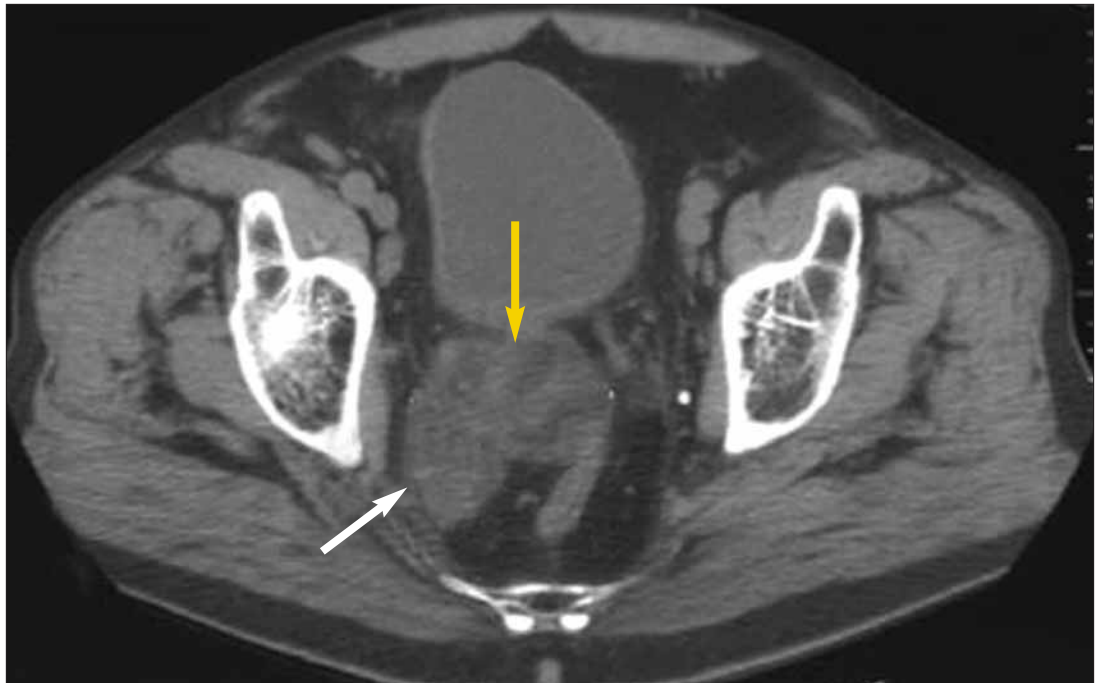


Primary Lymphoma of the Prostate in a Patient Infected With HIV

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Figure 1 – CT scan of the pelvis demonstrates an infiltrating mass of the prostate (yellow arrow) with extension into the right seminal vesicle (white arrow).



A 66-year-old HIV-positive man was referred to the urology service complaining of right lower quadrant abdominal pain, constipation, intermittent diarrhea, urinary frequency, hesitancy, dysuria, stranguria, severe nocturia, and constant bladder pressure for 1 month. Findings from his physical examina-

tion were unremarkable except for a nodular indurated prostate.

The complete blood cell count as well as levels of serum electrolytes, blood urea nitrogen, and creatinine were normal. The prostate-specific antigen (PSA) level was 0.14 ng/dL (normal, 0 to 4 ng/dL). His lactate dehydrogenase level was elevated at 459 IU/L (normal, 0 to 180 IU/L), and his CD4⁺ cell count was decreased at 360/ μ L (normal, 490 to 1740/ μ L).

Urinalysis showed 6 to 10 red blood cells and “too many to count” white blood cells per high-power field. Re-

sults of the urine culture were negative. A CT scan showed a right-sided mass within the prostate that infiltrated outward and resulted in ipsilateral ureteral obstruction (Figure 1).

Cystourethroscopy revealed an enlarged prostatic urethra covered by shaggy gray-white fibrinous exudate. A stent was placed in the right ureter. Transrectal ultrasound-guided core needle biopsies of the prostate revealed a diffuse large B-cell lymphoma (Figures 2 and 3).

Histologically, there was nearly complete replacement of the prostatic

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parenchyma, involvement of the seminal vesicles, and extensive infiltration of the extraprostatic adipose tissue by the lymphoid proliferation. Extensive tumor necrosis was observed; however, viable, loosely aggregated, enlarged neoplastic cells were interspersed between the necrotic areas. There was no glandular architecture and no cellular cohesion. Focal perineural invasion was noted. The neoplastic cells showed an increased nuclear-to-cytoplasmic ratio with irregularly shaped nuclei containing coarse, irregular nuclear chromatin. Mitotic figures, including atypical forms, were easily identified.

The neoplastic cells were strongly and diffusely immunoreactive with CD45RB (leukocyte common antigen) and CD20 (B-cell marker), but nonreactive with CD3 (T-cell marker), CD15 (LeuM1), CD30 (Ki-1), bcl-2, keratin, prostate acid phosphatase, and PSA. The CD4:CD8 ratio was not assessed because of nearly complete replacement by malignant B cells. Results of an additional workup, including a bone marrow biopsy, were negative.

Which of the following statements is correct?

- A. Primary lymphoma of the prostate is more common than secondary lymphoma of the prostate.
- B. Diffuse large B-cell lymphoma is the most common primary lymphoma of the prostate.
- C. Typically, primary lymphoma of the prostate is associated with elevated serum levels of PSA.
- D. There is no role for radical surgical extirpation in the management of primary lymphoma of the prostate.

(Turn the page for answer.)

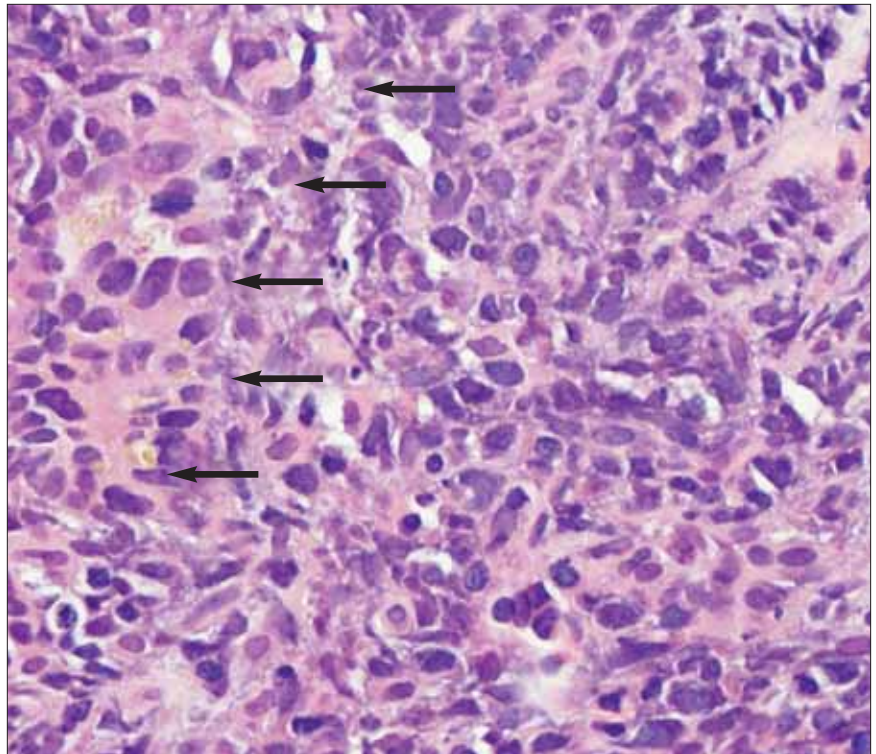


Figure 2 – In a biopsy specimen of the prostate, there is a diffuse arrangement of remarkable enlarged lymphoid cells with a high nuclear-to-cytoplasmic ratio, prominent nucleoli, and increased mitotic figures (right side). Invasion into the seminal vesicle is shown on the left (arrows) (hematoxylin-eosin, original magnification $\times 300$).

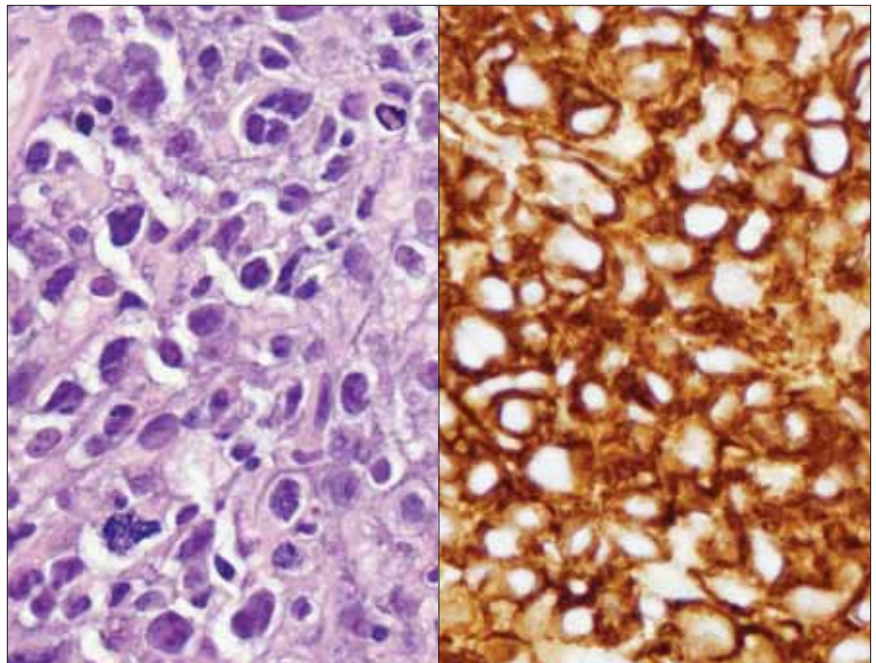


Figure 3 – Large, irregular, dyscohesive, atypical cells with mitotic figures are seen at left in prostate tissue (hematoxylin-eosin, original magnification $\times 300$). At right, CD20 immunoreactivity in the neoplastic cells confirms the diagnosis of B-cell lymphoma (original magnification $\times 300$).

Challenges in Urology

Primary Lymphoma of the Prostate in a Patient Infected With HIV

Discussion

Diffuse large B-cell lymphoma is the most common primary lymphoma of the prostate (option B) is correct. According to Bostwick and coworkers,¹ the diagnosis of primary lymphoma of the prostate can be established if 3 criteria are met:

- Lymphoma must be limited to the prostate and adjacent soft tissue.
- Lymph node involvement should be absent at presentation.
- Other tissues or organs must be free of lymphoma for at least 1 month.

Primary lymphoma of the prostate is more common than secondary lymphoma of the prostate (option A) is not correct. Secondary prostatic lymphoma is far more common. The incidence of prostatic lymphoma ranges from 0.1% to 0.2% of all those with lymphoma.^{2,3} Conversely, lymphoma involves the prostate or lower urinary tract secondarily in 8% to 20% of patients with lymphoma.^{4,6} Lymphoma is known to occur more frequently in HIV-infected persons, and it is the second most common tumor seen in those with HIV, after Kaposi sarcoma.⁷ In patients with HIV infection, lymphoma has been reported in uncommon extranodal sites, such as the orbit, mandible, skin, salivary gland, oropharynx, heart, lung, liver, rectum, muscle, bone, kidney, gonad, adrenal gland, and placenta.⁸ We were unable to find a report of an HIV-infected person with primary lymphoma of the prostate in a review of the English language literature.

Regardless of whether the patient is immunocompromised, the diagnosis of primary prostatic lymphoma is usually made by the pathologist because the symptoms and signs of lymphoma of the prostate are nonspecific. When symptoms occur, obstructive and irritative urinary complaints with or without hematuria are usually reported.^{1,6,9}

Typically, primary lymphoma of the prostate is associated with elevated serum levels of PSA (option C) is not cor-

rect. The PSA level is usually normal in patients with primary lymphoma of the prostate, but false elevations in PSA have been reported.¹⁰ Djavan and associates¹⁰ postulated that a falsely elevated PSA level may be caused by a coexisting prostate cancer, abnormal secretion of an unknown protein that increases PSA levels, or excess secretion of α -antichymotrypsin that causes a prolonged serum PSA half-life. Tomaru and coworkers¹¹ reported a case of primary lymphoma of the prostate in which the PSA level was 903 ng/dL; they theorized that the PSA level was elevated by "destruction and regeneration of the prostatic gland."

There is no role for radical surgical extirpation in the management of primary lymphoma of the prostate (option D) is not correct. There are reports of management of primary prostatic lymphoma with radical prostatectomy and radical cystoprostatectomy; however, multimodal approaches using radical surgery, systemic chemotherapy, and external beam radiation are often used.^{9,12,13} Although cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) combination chemotherapy is standard, other regimens have shown promise. Hematopoietic growth factors, such as rituximab, can ameliorate cytopenia associated with chemotherapy.^{7,13} The addition of highly active antiretroviral therapy improved outcomes in HIV-infected persons who were treated with systemic chemotherapy.⁶

Outcome

Based on findings from the evaluation of the patient, his lymphoma was designated as clinical stage 1_E, according to the Modified Ann Arbor staging system.^{14,15} He was referred to the oncology and radiation oncology services for further therapy.

Six courses of CHOP chemotherapy and rituximab were given. Interval CT scans revealed a partial response to treatment without the development

of lymph node disease. External beam radiation therapy (30 Gy divided over 15 treatments) was administered. The stent was removed 6 weeks later. The prostatic fossa was nearly normal, except for minimal patchy areas of gray exudate that extended from the bladder neck to the midprostatic urethra.

One year later, the patient's GI and urinary complaints have resolved. His lymphoma has remained stable without any additional intervention. ■■

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