## **RESIDENT'S CORNER**

# Aggressive prostate cancer masquerading as acute prostatitis

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Prostatitis is a common cause of prostate-specific antigen (PSA) elevation but can masquerade underlying prostate cancer. We present a case of a man with undiagnosed prostate cancer whose initial PSA elevation of > 999.0 ng/mL was initially ascribed entirely to

#### Introduction

Prostate-specific antigen (PSA) elevation in the setting of prostatitis must be interpreted with care. Even though prostatitis does cause PSA elevation, inappropriately allocating all PSA elevation to the acute presentation may leave a concomitant process, such as prostate cancer, unexplored. We present a case of a man with undiagnosed prostate cancer whose initial PSA elevation of > 999.0 ng/mL was initially ascribed entirely to prostatitis.

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Address correspondence to Dr. Judd W. Moul, DUMC Box 3707 Med Ctr, Duke University Medical Center, Durham, NC, 27710 USA prostatitis. In the setting of possible prostatitis clinicians should avoid the knee jerk reaction to blame the totality of PSA elevation on prostatitis. A greatly elevated PSA may be a sign of an underlying prostate cancer and should be explored in the proper clinical setting.

**Key Words:** PSA elevation, prostatitis, prostate cancer, screening PSA

#### Case report

A 68-year-old male presented to his primary care physician (PCP) with 4 days of worsening dysuria and incomplete emptying while denying fever or chills. Digital rectal exam (DRE) revealed a boggy and tender gland with firmness in the lower right lobe. Urinalysis showed 2+ blood and neither nitrites nor leukocyte esterase were present. The patient was diagnosed with bacterial prostatitis and started on 4 weeks of ciprofloxacin. He returned to his PCP 2 weeks later with persistent lower urinary tract symptoms. DRE revealed no tenderness but continued firmness in the right lobe and a nodule on the same side. Labs showed alkaline phosphatase of 175 U/L, a PSA of > 999.00 ng/mL and an absence of an elevated white blood cell count. Urinalysis again revealed 2+ blood and the absence of both nitrites and leukocyte esterase. Urine culture demonstrated < 1000 colony-forming units (CFU). He was maintained on ciprofloxacin and a CT was also ordered for possible nephrolithiasis by his PCP. One week later he was referred to Urology for refractory prostatitis.

In Urology clinic, the patient's DRE revealed a boggy, tender prostate with a right-sided induration. Additional urine culture showed 1,000-10,000 CFU/mL of gram-negative organism. A working diagnosis of prostatitis was maintained, and the patient was switched to trimethoprim/sulfamethoxazole for the remainder of his antibiotic treatment and told to follow up in 3 months.

CT abdomen and pelvis did not show nephrolithiasis but revealed prominent enlarged lymph nodes of the iliac chain, Figure 1a, and pelvic sidewall with periaortic nodes up to 1.3 cm and sclerosis of the axial and proximal appendicular skeletons, Figure 1b. At this point, there was concern for metastatic prostate cancer and the patient was counseled about undergoing a prostate biopsy. Trans-rectal ultrasound guided (TRUS) biopsy was performed 12 days later revealing extracapsular extension and perineal invasion with 8 of 12 cores positive for Gleason 4 + 5 = 9 adenocarcinoma and the remaining cores positive for Gleason 4 + 4 = 8adenocarcinoma. Staging nuclear medicine bone scan showed multiple osseous lesions from the calvarium and ribs to the pelvis and bilateral femurs that were compatible with metastatic disease, Figure 1c. Physical exam, biopsy, CT and bone scan results rendered a diagnosis of prostate cancer consistent with cT4N1M1b disease.

Degarelix was started as soon as biopsy pathology returned. In total 7 weeks passed from initial presentation to initiation of androgen deprivation therapy (ADT). The patient reported almost immediate improvement in voiding after initiation of ADT. PSA nadir of 3.22 ng/mL was achieved 5 months later. Despite a rising PSA while on ADT the patient continues to void well and endorses high quality of life.

#### Discussion

Here we present an uncommon presentation of metastatic prostatic cancer. The patient was initially referred to urology for what appeared to be a case of treatment resistant acute bacterial prostatitis. A low index of suspicion for prostate cancer and marginalization of severely elevated PSA in the setting of a boggy prostate show how prostate cancer may be mistaken for prostatitis.

While a hallmark of prostate cancer is an abnormal rise PSA, interpretation of a rising PSA can be confounded by a handful of benign conditions: benign prostatic hyperplasia, trauma, and prostatitis, among others. PSA is not often obtained in the setting of prostatitis unless there is an abnormal DRE, as in our case, or by coincidence as part of routine prostate cancer screening.<sup>1</sup> The American Academy of Family Physicians (AAFP) recommends against obtaining a PSA as part of initial work up for prostatitis and attributes a "C" rating to its use.<sup>2</sup> The European Association of Urology (EAU) and American Urological Association (AUA) do not comment on the use of PSA in the work up of acute prostatitis. Despite the lack of evidence supporting the diagnostic utility of PSA in prostatitis, PSAs are still ordered on occasion and physicians must know how to properly interpret a high value. A marked elevation in the correct clinical setting may be a sign of a concomitant cancer and requires further investigation.



**Figure 1.** Imaging at diagnosis. **(a)** Nuclear medicine Tc-99m bone scan: showing multiple foci of tracer uptake. **(b)** CT abdomen/pelvis without contrast: showing sclerosis involving the superior aspect of L5 vertebral body. **(c)** 1.3 cm nodal involvement of external right iliac chain.

While there are no guidelines on how to use total PSA in prostatitis, multiple studies describe an expected range of PSA values. Hara et al evaluated 20 individuals diagnosed with acute prostatitis and reported a maximum PSA of 77.0 ng/mL,<sup>3</sup> and other studies have shown the minimum PSA value to be as low as 4.1 ng/mL.<sup>4</sup> In a larger cohort of 115 individuals, Ahn et al observed an average PSA of 16.8 ng/mL (interquartile range 6.5-36.3 ng/mL) in men with acute prostatitis.<sup>5</sup> Finally in a study by Game et al, a cohort of 31 patients hospitalized with prostatitis, it was found that PSA peaked on day 3 of infection with a mean of 20.08 ng/mL (std.  $\pm$  19.35).<sup>6</sup> While our patient's PSA was > 999.00 ng/mL, these studies show that a PSA does not have to be in the hundreds to prompt further evaluation of underlying prostate cancer. Even though these studies lack uniformity, they help illustrate that the average PSA elevation in prostatitis is often in the 20's with an upper limit well below 100.

Since the downgrading of prostate cancer screening in 2012 by the U.S. Preventative Services Task Force (USPSTF), late stage disease as seen in our patient has become more common.<sup>7</sup> In hindsight, he had constitutional symptoms that were pointing toward something greater than prostatitis from the beginning. The nodule palpated on DRE and a markedly elevated PSA also pointed towards prostate cancer. The immediate improvement of his lower urinary tract symptoms once ADT was started further begs the question if there was ever prostatitis. The 7-week span from presentation to initiation of treatment likely did not change the long term prognosis for our patient. However, even with diffusely metastatic disease data shows a significant decrease in 5-year survival as PSA advances from the 100-200 ng/mL range to 200-500 ng/mL and again once PSA is > 500 ng/mL.<sup>8</sup> Thus, the timely diagnosis of even advanced metastatic prostate cancer may help improve overall survival.

### Conclusion

We report a case of metastatic prostate cancer masked by symptoms of acute prostatitis. The patient presented with an extremely elevated PSA and abnormal DRE that should have raised greater concern for prostate cancer. Attributing significant PSA elevation solely to prostatitis and not considering a concomitant process could result in delay of the diagnosis of prostate cancer. It is imperative that clinicians continue to consider possible prostate cancer when patients present with markedly elevated PSA in the setting of what appears to be acute prostatitis.

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