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CASE REPORT

Case Report of Mesorectal Failure in the Treatment of Prostate Adenocarcinoma

James L Shen, PhD John G Roubil, MD, Linda Ding, PhD, Julie Trifone, CMD, Carla Bradford, PhD, Fenghong Liu, Phd, Yankhua Fan, PhD, I-Lin Kuo, PhD, Camelia Bunaciu, MS, Salvatore Larosa, MS, Suhong Yu, PhD, Abdulnasser Khalifeh, PhD, Jonathan Saleeby, MS, Harry Bushe, MS, Maryann Bishop-Jodoin, Med, Thomas J. FitzGerald, MD

*TJ.Fitzgerald@umassmemorial.org

ABSTRACT
Prostate cancer afflicts a substantial portion of the male population with increasing incidence each decade after the age of 40. Standard of care for localized disease at presentation includes prostatectomy and/or radiation therapy which can include management of pelvic lymph nodes. However, the selection of lymph nodes treated by radiotherapy remains variable among practitioners including individual practitioners in the same institution. We present a patient with prostate adenocarcinoma who underwent radical prostatectomy with adjuvant radiotherapy for lymph node involvement and developed mesorectal failure secondary to metastatic spread to untreated tissue.

Keywords: Prostate cancer, Radiation therapy, Mesorectal

Introduction

Prostate cancer is the second most common cancer in men in the world. One out of every 8 men is expected to be eventually diagnosed with prostate cancer.[1] Evaluation for patients initially diagnosed with localized prostate cancer involves tumor-nodes-metastasis (TNM) staging, evaluation of tumor grade, prostate-specific antigen (PSA) level measurement, and risk stratification when considering additional treatment options. Treatment options range from active surveillance and androgen deprivation therapy (ADT) for very-low to low-risk tumors to radical prostatectomy and/or radiotherapy. In the event of lymph node metastases, patients are typically treated with definitive radiotherapy with ADT, although younger patients with higher functional status and minimal regional lymph node involvement can also receive radical prostatectomy and ADT with or without radiotherapy.[2-4]

Contouring of metastatic lymph nodes confirmed by positron emission tomography–computed tomography (PET/CT) is standard of care, with Radiation Therapy Oncology Group (RTOG) guidelines recommending delineation of positive lymph nodes for boost. Other indications include extra-prostatic and/or seminal vessel involvement and positive margins after prostatectomy.[5] However, guidelines on whether additional lymph nodes should be contoured and treated remain less well defined, especially in patients with node positive disease at presentation as the pattern of failure may be altered secondary to retrograde flow through pelvic lymphatic channels or interruption of tissue planes by surgery. As such, the decision to preemptively treat other lymph nodes typically remains up to the discretion and experience of the practitioner who will assign tissues at risk based on pre-determined guidelines of care. Here, we present a case report of a patient diagnosed with prostate adenocarcinoma with positive pelvic lymph nodes, was treated with hormonal therapy, underwent prostatectomy with adjuvant hormone image-guided, intensity-modulated radiation therapy (IGT/IMRT) for lymph node involvement who developed secondary mesorectal lymph node metastases.

Case Presentation

The patient is a 62-year-old male who had a prostatectomy in March 2018 for adenocarcinoma. At the time of his initial diagnosis, his Gleason score was 7 (4+3) in the right lobe (3 core biopsies), and 8 (4+4) in the left lobe (2 core biopsies). Of the 12 biopsies, 8 were positive. His prostate was measured to be 19 cubic centimeters (cm^3) in volume by ultrasound. He was pre-treated with androgen suppressive hormonal therapy with Firmagon and Lupron prior to robot-assisted surgery by Urology, due to magnetic resonance imaging (MRI) findings of extracapsular extension and seminal vesical asymmetry (this prevented post-resection grading). His PSA prior to resection was 12.94, and 1.2 after surgery.

Surgical pathology showed tumor involvement in 30 percent involvement of the 3.8 x 3.5 x 2.5 cm gland. Extraprostatic disease was noted by the right neurovascular bundle. Surgical margins were ultimately negative, however 2 lymph nodes from the right external iliac and obturator region were positive for metastatic disease. The largest of these lymph nodes was 2.5 mm. As a result, his surgical staging was T3N1 adenocarcinoma.

He was continued on hormonal therapy after surgery, but initially deferred radiation treatment while recovering from his prostatectomy. He ultimately received comprehensive post-operative adjuvant volumetric modulated arc therapy (VMAT) radiation therapy with a total dose of 6600 cGy to the prostate bed and sentinel lymph nodes. The plan included 5000 cGy in 200 cGy fractions to the prostate bed and lymph node drainage regions with a 1600 cGy boost to the prostate bed (Figure 1). Treatment was delivered approximately one year post prostatectomy.

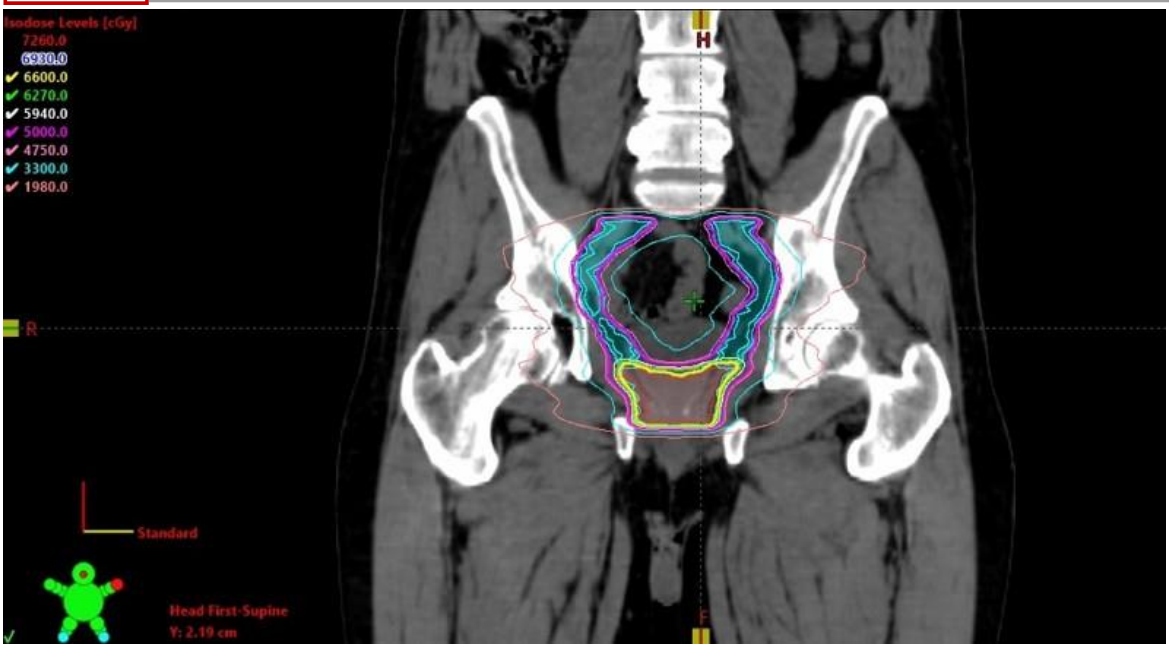

Figure 1. Initial fields of radiation therapy directed to the prostate bed and draining lymph node region.

The patient did well for two years with undetectable PSA. PSA increased to 0.1 and increased to 1.2 over one year. He underwent Axumin PET/CT imaging which revealed a positive, left meso-rectal lymph node (Figure 2). The area was treated with 6000 cGy in 300 cGy fractions, and the meso rectum was treated with 4000 cGy in 200 cGy fractions, over a 1 month (Figure 3). The patient tolerated therapy without complications and continues to do well.

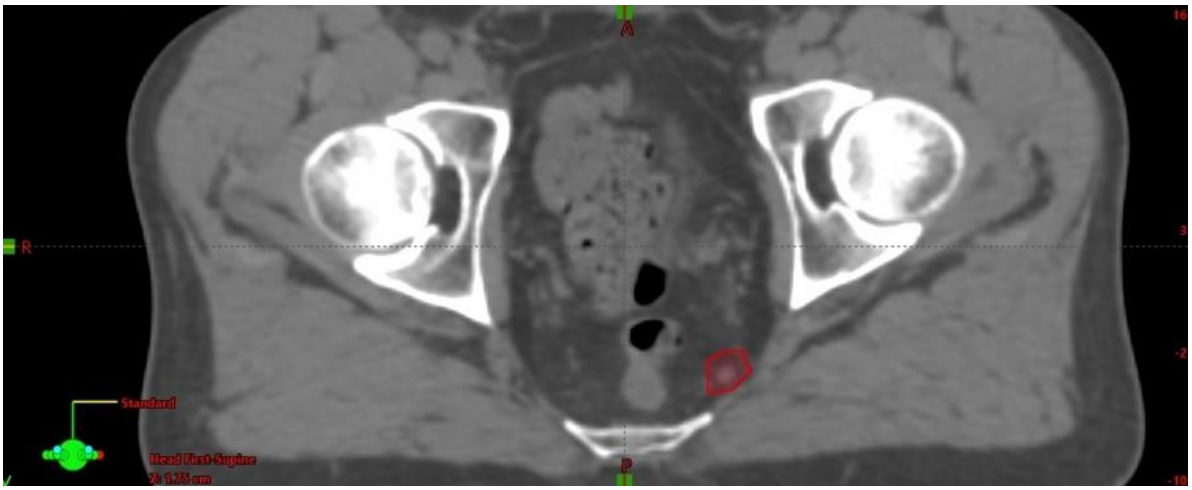

Figure 2. Metabolic image defining the site of failure in the mesorectum.

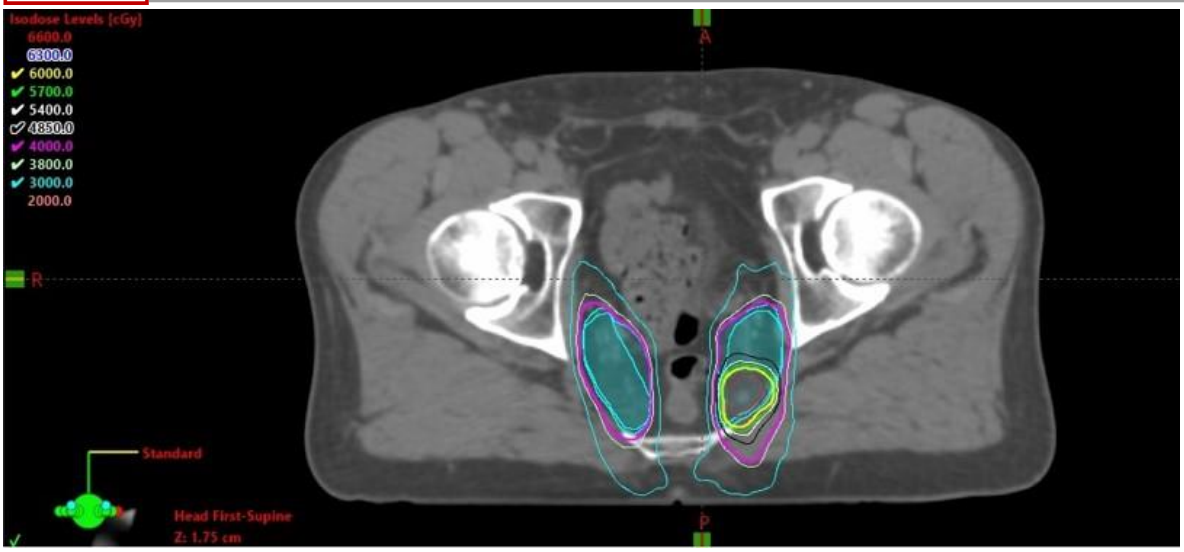

Figure 3. Fields of treatment for supplemental radiation therapy.

Discussion

Adjuvant radiotherapy to positive lymph nodes remains the standard of care in the treatment of metastatic prostate cancer, which was the case for this patient.[2-5] A systemic review of retrospective studies using IMRT/VMAT as adjuvant therapy for positive lymph nodes prostate cancer suggested a target dose of 45-60 Gy with boost dose as high as 70 Gy to high-risk areas.[6] The treatment plan for the lymph nodes in this patient was consistent with the plans used in atlas definition and other published studies.

The decision to preemptively treat negative lymph nodes at risk for failure should be considered with patient functional status and goals of care in mind. Prophylactic radiation to pelvic lymph nodes is known to increase dose to the intestine, rectum, femoral heads, bladder, and pelvis, especially in patients with previous pelvic surgery. The effects of treating pelvic organs can adversely affect patient quality of life and functional status, which may already be compromised following prostatectomy. Prior to initiating adjuvant radiotherapy, the patient in this case report had recuperated from radical prostatectomy and was continuing androgen suppressive therapy. Despite treatment targeting positive lymph nodes and prophylactic sentinel lymph node coverage, the patient developed recurrence in the left meso-rectal lymph node, which was not covered by this treatment plan. This failure could possibly be explained by disruption of the fascial plane between the prostate and the meso rectum. Nicosia et al. report that the majority of lymph node recurrences following adjuvant radiotherapy occur outside of treated fields recognizing diversity among radiation oncologists defining target volumes at risk and that many radiation oncologists do not intentionally treat expanded lymph node targets in patients considered low risk for failure.[7] Furthermore, for patients who had their iliac lymph nodes treated, recurrences were more likely to occur in the retroperitoneal lymph node stations.[8] While this could simply be due to coverage of neighboring iliac nodal stations from targeted treatment of positive iliac nodes, it does not rule out independent metastatic spread from the retroperitoneal lymphatic system. Elective radiotherapy of a wider range of lymph nodes in the pelvis may help eliminate microscopic disease that would not normally be covered by focused, radiotherapy of positive lymph nodes and surrounding lymph node groups. Thus, this case study raises the question of whether elective coverage of additional lymph node stations in the pelvis could benefit these prostate cancer patients, especially in patients who are node positive at presentation. This also could create an argument for additional anatomic or metabolic imaging validation of target prior to initiating radiation therapy. The value of imaging in the post prostatectomy setting is increasing and a broader use of imaging to define target volumes at risk has the potential of improving patient care. In earlier iterations of post prostatectomy target definition, radiation oncologists assigned target volume at risk based on clinical experience and the choices in retrospect could be considered both reasonable and arbitrary. Using advanced technology imaging pre therapy and fusing these objects into radiation oncology planning images may alter the standard of care and improve patient outcome.

The benefits of prophylactic radiotherapy to additional pelvic lymph node groups remain under

investigation. Tran et al. report that for prophylactic treatment of negative nodes the 5-year disease-free and distant progression-free survival were 43% and 58%, respectively.[9] A recent phase III randomized trial is currently investigating if whole pelvic irradiation with ADT provides an overall survival benefit to patients with unfavorable intermediate or favorable high risk prostate cancer (RTOG-0924). Further analysis, including looking into quality-of-life metrics, will provide invaluable information regarding the roles of prophylactic irradiation of negative lymph nodes in the treatment of prostate cancer. Assuming advanced technology imaging improves and optimizes radiation therapy target definition, the role and duration of hormone therapy can be re-visited and potentially titrated with improved guidelines established for risk of failure based on location of disease recurrence and volume of disease.

Conclusions

This case reports presents a prostate cancer patient with regional, nodal metastases who was treated with ADT, radical prostatectomy, and adjuvant radiotherapy who developed mesorectal nodal recurrence. He was treated with salvage radiotherapy and is currently doing well. His experience is an example of the importance of better understanding the role of prophylactic treatment of regional lymph nodes in prostate cancer and the potential role of imaging to validate target definition. While additional studies are needed to draw meaningful conclusions, this case report may help catalyze additional interest in investigating this issue.

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