

Radiation treatment of bladder squamous cell carcinoma in a patient with spina bifida: A case report

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Abstract

Bladder cancer is the sixth most common cancer in Canada. While most patients present with transitional cell carcinoma, few present with squamous cell carcinoma (SCC). Risk factors for SCC include a history of chronic urinary tract infection, urothelial inflammation and indwelling catheters. We present the management of a patient with locally advanced SCC of the bladder.

Introduction

By the end of 2010, it is estimated that 7100 Canadians will have been diagnosed with bladder cancer, making it the sixth most common cancer in Canada.¹ Most presentations are transitional cell carcinoma (TCC). Because of the rarity of squamous cell carcinoma (SCC) of the bladder, there is no clear consensus on management. Treatment options are similar to TCC of the bladder.

An interesting subset of bladder SCC lies in patients having the neural tube defect spina bifida. It has been suggested that the link between spina bifida and bladder cancer lies with the neurogenic bladder, where associated factors, such as chronic urinary tract infections, urothelial inflammation, indwelling catheters and a history of calculi, lead to an increased risk of bladder oncogenesis.²⁻⁵ Of note, these associated risk factors are also observed in patients having spinal cord injuries; a 10% increased incidence of bladder cancer is seen with such patients having an indwelling catheter for more than 10 years.^{2,6} Patients with spina bifida and bladder cancer typically present at a younger age, have varied tumour histology, are advanced in stage and ultimately have poor survival.⁵ We present a patient with spina bifida and bladder cancer; this case highlights the radiation therapy aspect of combined chemo-radiation management.

Case report

History and staging

A 52-year-old woman was referred for management of her locally advanced, invasive SCC of the bladder. Her medical history is significant for spina bifida that left her wheel-chair bound; she also had Harrington spinal stabilizing rods inserted at age 14. She is a non-smoker and her family history includes her mother having ovarian cancer, her mother's twin sister having an unknown cancer and another maternal aunt having gastric cancer.

Her history of present illness involves recurrent urinary tract infections that started in March 2010 and were treated with antibiotics. Never requiring self-catheterization, she then developed hematuria and gradual loss of urinary function which prompted an ultrasound of the bladder. This revealed a focal 36-mm irregular thickening in the base of the right side of the bladder. Further investigation with cystoscopy showed a 3 to 4-cm sessile mass obstructing the right ureteric orifice. A computed tomography (CT) scan of the abdomen and pelvis further showed the following: thickening in the right posterior basal bladder wall close to the right ureterovesical junction measuring 7 × 5 cm, with no observed extravesical extension; right ureteral dilation to the bladder; moderate-to-severe right hydronephrosis; and mild left-sided hydronephrosis. Several bilateral sub-centimetre iliac and groin lymph nodes were noted, but there was no retroperitoneal lymphadenopathy. A Transurethral resection of bladder tumour (TURBT) was performed in April 2010, showing moderately differentiated invasive SCC and a bone scan was negative.

Surgical intervention

The patient would later have an attempted radical cystectomy with ileal conduit in early April 2010. However, upon laparotomy, the bladder cancer was much more locally

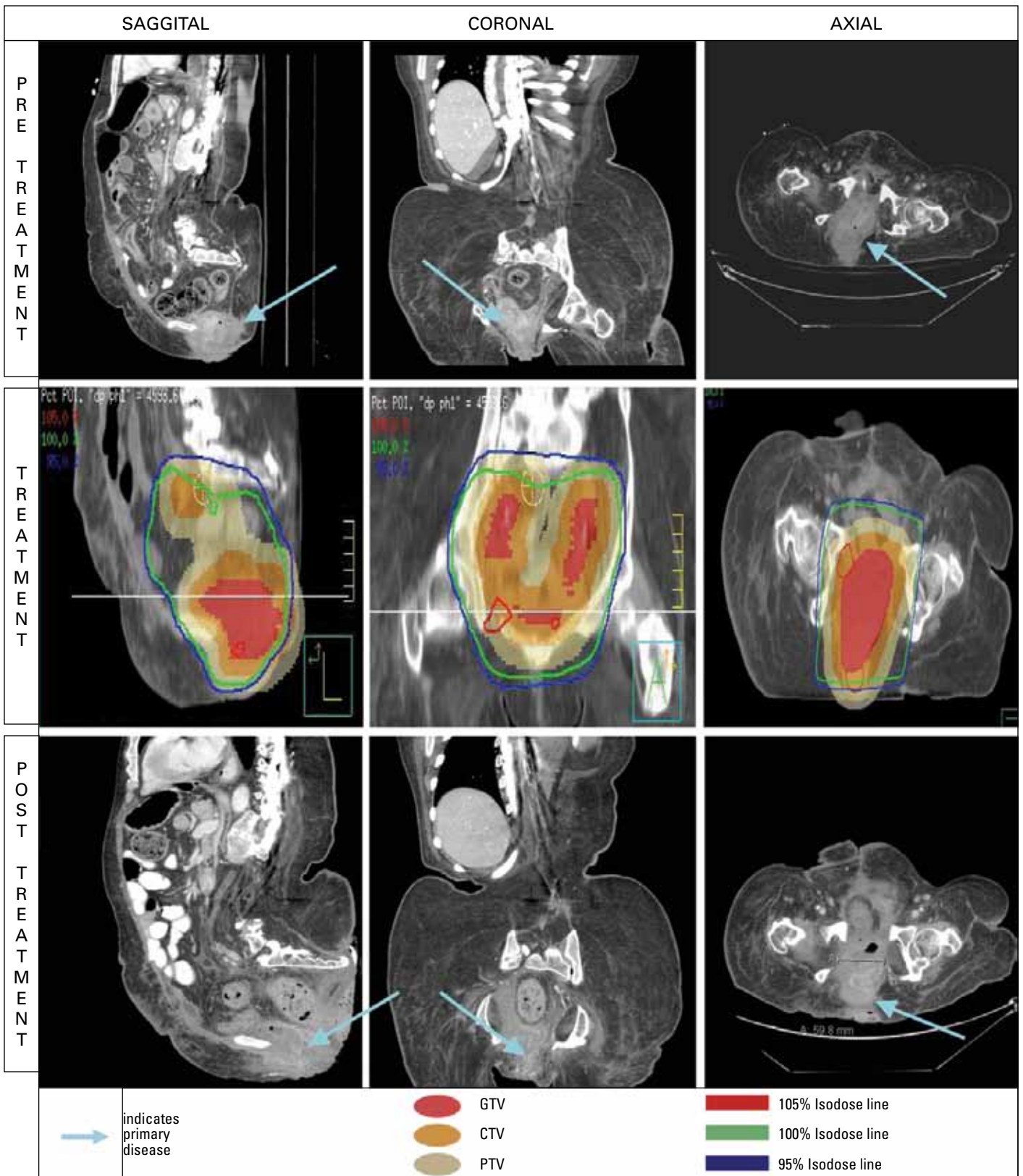


Fig. 1. Pre- and post-treatment diagnostic computed tomography scans and radiation therapy treatment plan.

advanced than initially anticipated. Thus, radical surgery was aborted and, instead, the patient had a debulking resection and ileoconduit leaving residual tumour fixed to the lateral rectum and pelvic sidewalls. She required 5 units of packed red blood cells intra-operatively and 1 unit postoperatively. She also required transfusion of 2 units of fresh frozen plasma. She was discharged 5 weeks later.

The pathology was centrally reviewed and showed the following: moderately differentiated SCC of the bladder and extending into the vagina and pelvic side wall (pathologic stage T4N0); tumour extension into perivesical fat; multiple positive margins, including the bladder and vagina; lymphovascular invasion, in which none of the 11 dissected lymph nodes were involved.

Referral to tertiary cancer centre

She was referred by her community urologist to our cancer centre for further management. When she was initially seen in mid-May 2010, she had mostly recovered from the surgery and only described pelvic pain requiring opioids. Her performance status was 1. The physical examination was unremarkable. Her blood work showed a hemoglobin of 88, with the remainder normal.

Her case was discussed at our institution's genitourinary oncology tumour board, where recommendations were made for a magnetic resonance imaging (MRI) and the examination under anesthesia (EUA) to help differentiate disease from normal tissue on the postoperative CT scan (Fig. 1).

On EUA, the tumour extended inferiorly to just proximal of the vaginal introitus. The tumour extended from the 4 to 7 o'clock position in the vagina, and was fixed. There was no involvement of the rectum. Unfortunately, on the way home after the EUA, the patient was involved in a motor vehicle accident with a small bowel perforation that required a resection. Therefore, her treatment for the bladder cancer was delayed.

On MRI, there was disease in the pelvis involving sidewalls, perineum and vagina. Pelvic lymphadenopathy was also seen.

The final treatment recommendation was to manage her bladder cancer with concurrent chemotherapy and radiotherapy.

Chemotherapy

Due to concerns about the patient's ability to tolerate chemotherapy, the medical oncologist treated her with weekly cisplatin.

Radiation treatment

She was placed in the supine position for simulation and a vaclock was used to provide immobilization and support for her legs. The Phase I Gross Tumour Volume (GTV₁) encompassed visible disease in the vagina, pelvic side walls, pelvic lymph nodes and residual bladder based on imaging and EUA. The Phase I Clinical Tumour Volume (CTV₁), defined as microscopic disease extension beyond the GTV₁, was a 1-cm expansion from the GTV₁. The Phase I Planning Target Volume (PTV₁), defined as a margin added to account for planning uncertainties, CTV motion, patient movement and day-to-day set-up variation, was a 1-cm expansion around CTV₁.

The Phase II Gross Tumour Volume (GTV₂) encompassed the residual bladder mass to limit toxicities. The Phase II Clinical Tumour Volume (CTV₂) was a 1-cm expansion from GTV₂ and the Phase II Planning Target Volume (PTV₂) was a 1-cm expansion around CTV₂. In effect, the superior and anterior borders were reduced by 2.5 cm and 2 cm, respectively, for Phase II.

Her radiation therapy was planned for 60 Gray (Gy) in 30 daily fractions, with an energy of 18 MV and given in two phases: (1) Phase I (PTV₁) using a four-field box technique and delivering 46 Gy in 2 Gy daily fractions, prescribed to the 98% isodose line with a clinical maximum of 48.7 Gy; 2); and (2) Phase II (PTV₂) using the same Phase I technique, but with reduced fields to the residual bladder mass, delivering 14 cGy in 2 Gy daily fraction, prescribed to the 99% isodose line with a clinical maximum of 14.3 Gy. Organs at risk included the stoma (which received low dose) and the rectum, which received full dose (Fig. 1).

Treatment delivery was preceded by a cone-beam CT to correct for any day-to-day set-up variation and organ motion. Linear accelerator gantry angles were rotated clockwise from standard four field box angles (i.e., 0°, 270°, 180°, 90°) to reduce scatter radiation from her Harrington rods as follows: the anterior beam by 15°; the posterior beam by 10°; and the right and left lateral beams by 5°.

Treatment course

On first day set-up, she was found to have lost significant weight in two weeks and therefore required a re-simulation planning CT. As a result, her radiotherapy was delayed for 2 days.

Once started, she had a difficult time with the chemoradiation. She only received 2 cycles of chemotherapy because of anemia requiring transfusion and acute renal failure from the cisplatin. Moreover, she received only 56 Gy out of a planned 60 Gy after being admitted with significant dehydration, electrolyte imbalance, diarrhea and a sacral ulcer.

Post-chemoradiation

Discharged nine days later, she had daily nursing care for her sacral ulcers. Upon follow-up, her improvements included normal bowel function, no hematuria, no pain and improved appetite with some weight gain. Her post-treatment CT scan showed a locally invasive and necrotic pelvis mass with fistulization to the mid-sigmoid. She also had a MRI, which essentially confirmed the CT results.

She was reviewed again at our tumour board. With the presence of necrotic tumour seen on the CT and MRI, the group was encouraged that she was having a response to the treatment. However, it remained difficult to differentiate tumour from inflammation. The recommendation was to repeat scans in three months.

However, a month after the tumour board she presented with bilateral lower leg swelling, constipation, swelling of her vulva and lower pelvic discomfort. She then developed an acute abdomen, fever and was admitted to hospital. An urgent abdomen CT revealed bilateral moderate to severe hydronephrosis, an obstructed right distal ureter and increased pelvis collections secondary to the fistulous connection in the sigmoid. It was determined that surgery was not an option and she was put on best supportive care. She died three days after admission.

Discussion

As noted earlier, spina bifida patients with bladder cancer typically have poor outcomes and presentation often includes advanced disease and an aggressive cell type (e.g., squamous cell or adenocarcinoma).⁵ Furthermore, there is a paucity of literature and little consensus on the management of SCC of the bladder. Thus, from the outset, optimal management is unclear and becomes even more difficult given unique patient circumstances, such as this case with spina bifida. While there are reports on spina bifida and bladder cancer (e.g., age and sex, pathological findings, treatment,

survival),⁵ to our knowledge no case report focuses specifically on the details of radiation treatment.

Conclusion

The treatment of spina bifida patients with SCC of the bladder is challenging. Though our patient ultimately died, she experienced health setbacks along the way. This time gave us the opportunity to explore different management options. One of those options was radiation therapy, which was emphasized in this case in terms of the dose, fractionation, two-phase approach, dosimetry and daily image guidance regimen. This can be used to guide other radiation oncologists facing similar situations.

Competing interests: None declared.

This paper has been peer-reviewed.

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