Structural Vulnerability of J-J Stents to Radiotherapy in Cervical Cancer Patients: Implications for Treatment Planning

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Abstract:

Introduction: Cervical cancer multimodal treatment causes 75% urethral complications. Application of surgery or radiotherapy can induce free radicals and vascular damage of the ureters. J-J stent placement, due to renal function preservation, increase infection, encrustation and obstruction risk. **Methodlogy:** A 38 year old patient with International Federation of Gynecology and Obstetrics (FIGO) Ib3 cervical cancer, was treated with radical hysterectomy. Bilateral J-J stents were placed due to bilateral renal calculus immediately after. Treatment continued with adjuvant radiotherapy. Following 10 radiotherapy fractions, patient presented with fatigue, fewer, diarrhea, and sepsis signs and symptoms, in absence of apparent infection (negative urine/blood cultures, stent swabs, stool samples, additional imaging procedures) and J-J stents were removed, accompanied by three weeks antibiotic course (quinolones, carbapenems and colistin), with general condition improved and postoperative radiotherapy continued. Upon finalizing the radiotherapy cycle, pelvic MR were conducted - without infection signs. Three weeks later, due to anuria and hydrouretheronephrosis grade 2, control multislice computed tomography (CT) showed distal ureter and bladder fibrosis. **Results:** Volumetric arc radiotherapy (VMAT) with 40 Gray (Gy)/20 fractions (fr) followed by three cycles brachytherapy (3x600cGy) was conducted, respecting recommendations for organs at risk. During the radiotherapy J-J stent mean dose was 41.71Gy on the left side, 42.49 Gy on the right side, respectively. Determining whether changing in stent structure was caused, under the same conditions J-J stent were irradiated, using 90 Gy/6fr. Stent density prior to radiation was 1884 HU, and after 2225 HU which may indicate a loss of stent elasticity, an increase in strength and a reduction in flexibility that can potentially lead to injury to the ureteral mucosa. **Conclusion.** All above mentioned factors can be contributing in urethral microenvironment, or J-J stent density alteration after

radiotherapy can potentially cause serious urethral damage in symbiosis with microbiota and altered local radiobiological effect.

Keywords: Cervical cancer, J-J stents, ureteral strictures, antibiotics, postoperative radiotherapy

1. Introduction

Ureteral strictures occur iatrogenically in 75% of cases as a complication of multimodal treatment of cervical cancer, either through direct injury during surgery or radiotherapy, indirectly due to free radical damage and impaired vascularization [1]. The placement of J-J stents to prevent hydronephrosis and preserve renal function increases the risk of infections, encrustations, and obstructions by 20% [1,2] . J-J stents are most often made of polyurethane, silicone, or special alloys such as nitinol, depending on the intended duration of use and clinical indication. In the presence of pelvic malignancies, stents made of nitinol (an alloy of nickel and titanium) are most often used [1]. There is no data in the available literature to date on whether it is possible for the structure of a J-J stent to change after exposure to ionizing radiation

The aim of this paper is to present a case of a patient with severe complications caused by the presence of bilateral nitinol J-J stents during adjuvant radiotherapy for early-stage cervical cancer.

2. Methodology

A 38-year-old female patient was diagnosed with stage IB3 FIGO cervical cancer and underwent a radical Wertheim–Meigs hysterectomy. Due to bilateral renal calculosis, bilateral ureteral J-J stents made of nickel-titanium alloys were placed immediately after surgery, and adjuvant radiotherapy was subsequently initiated. After the 10^{th} radiotherapy fraction, developed high-grade fewer and generalized weakness of the patient, leading to a treatment interruption and stent removal.

Laboratory analyses indicated sepsis without an identifiable infectious focus: urine cultures, blood cultures, swabs from the J-J stents, stool tests for Clostridium and Candida, and a chest CT scan were all negative. Reserve antibiotics were used in the therapy over 20 days (fluoroquinolones, carbapenems, colistimethate), resulting in clinical improvement and radiotherapy continued. On the final day of radiotherapy, a follow-up pelvic magnetic resonance imaging (MRI) was performed, revealing normal findings. Radiotherapy using the VMAT technique with TD 40 Gy in 20 fractions was performed with three brachytherapy applications with TD 600 cGy, respecting the limits for dose contribution to organs at risk (Figure 2). Twenty days after completion of radiotherapy, the patient developed anuria accompanied by grade two hydroureteronephrosis. A follow-up multi slice CT scan revealed fibrosis of the distal ureters and the superior wall of the urinary bladder, which coincides with the position of the radiotherapy field.

3. Results

During radiotherapy mean dose in the area of made of nickel-titanium alloy J-J stents on the left was 22.07 Gray (Gy) (max dose 42.49 Gy), on the right 22.74 Gy (max dose 41.71 Gy) (Figure 1). In order to determine the structural change afer radiation, stent from the same manufacturer were irradiated. The stent was placed on the linear accelerator table and irradiated with a dose of 90 Gy in 6 consecutive fractions with photons energy 6 megavolts (MV). The dose contribution for the J-J stent was calculated medical physics specialists after precise bilateral stents delineation by radiation oncologists. Results shown that after high-dose irradiation of J-J stents, it was observed that the density of the probe changed. The density of the probes before irradiation was 1884 HU, after irradiation 2225 HU, which may indicate a loss of stent elasticity, an increase in strength and a reduction in flexibility that can potentially lead to the ureteral mucosa injury.

4. Discussion

The presence of the J-J stent include stent migration, obstruction, or stone formation [2]. However, in the previous literature described that radiotherapy can be the cause of obstruction [1-4], but there is no data on the effect of radiotherapy on the ureter in which the J-J stent was placed. Although it was not possible to simulate how the structural change of the J-J stent affects the radiobiological effect of ionizing radiation locally in the ureters, this case report indicates for the first time that the structural change can potentially exert a bolus effect at the ureteral level. This effect causes an increase in the radiotherapy dose in the bolus environment, which can potentiate strong aseptic inflammation locally, strongly changing the microenvironment to that surrounded by the stent [3,4].

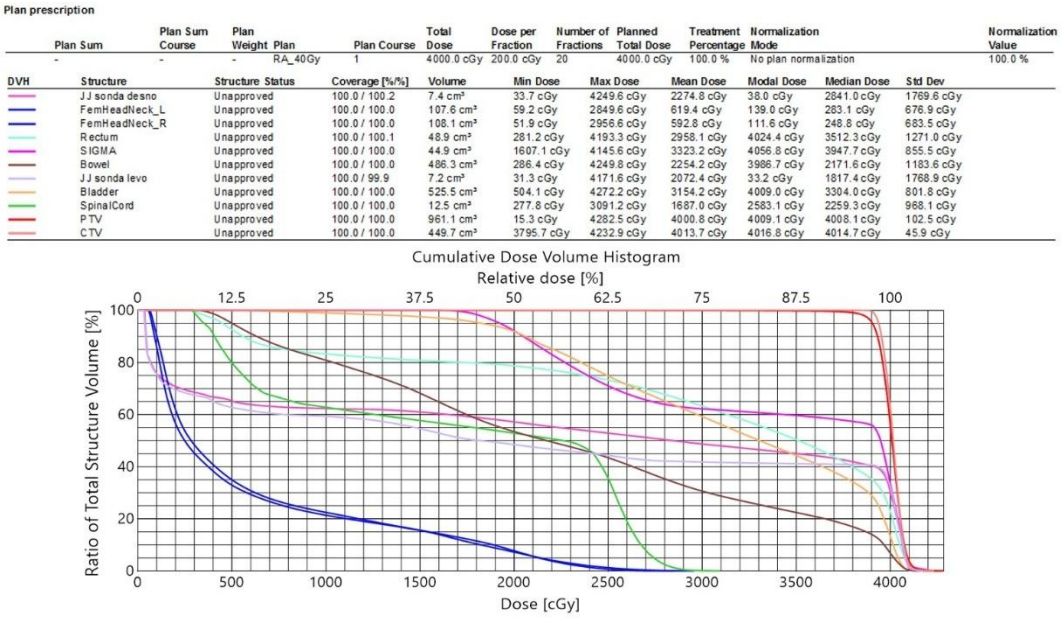

Figure 1. The dose-volume histogram shows the dose contribution to the target volumes and organs at risk when a dose prescription of 40 Gy was performed using the VMAT technique

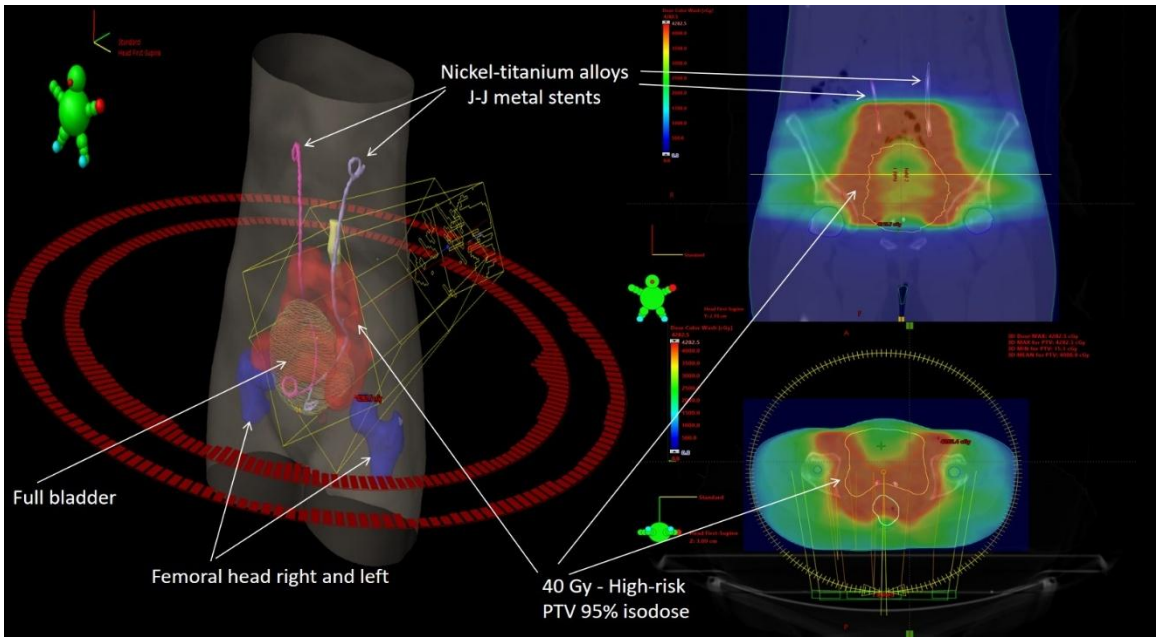

Figure 2. Position of J-J stents in relation to high risk planning target volume during VMAT

4. Conclusions

All above mentioned factors can be contributing in urethral microenvironment, or J-J stent density alteration after radiotherapy can potentially cause serious urethral damage in symbiosis with microbiota and altered local radiobiological effect. Additional research in this area is needed to precisely determine changes in the structure of materials under the influence of ionizing radiation in vivo and in vitro.

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