Gynecologic Oncology Reports 17 (2016) 89–92

Contents lists available at ScienceDirect

Gynecologic Oncology Reports

journal homepage: www.elsevier.com/locate/gynor

Case series

Treatment of early stage vaginal cancer with EBRT and MRI-based intracavitary brachytherapy: A retrospective case review

Shari Damast MD [a,*], Vinita Takiar MD, PhD [b], Shirley McCarthy MD, PhD [c], Susan A. Higgins MD, MS [a]

[a] Department of Therapeutic Radiology, Yale University School of Medicine, New Haven, CT, USA
[b] Department of Radiation Oncology, University of Cincinnati, Cincinnati, OH, USA
[c] Department of Diagnostic Radiology, Yale University School of Medicine, New Haven, CT, USA

ARTICLE INFO

Article history:
Received 29 June 2016
Accepted 2 August 2016
Available online 4 August 2016

Keywords:
Vaginal cancer
Intra-cavitary brachytherapy
MRI

ABSTRACT

This case series describes the use of pelvic radiotherapy (RT) and MRI-based intracavitary brachytherapy (ICBT) for patients with small volume, early-stage, primary vaginal cancer.

A customized pelvic MRI protocol with a vaginal cylinder in place (MRVC) was used to measure disease extent and tumor thickness (defined as distance from lateral/apical margin of tumor to cylinder surface) at time of diagnosis. Non-bulky tumors with initial (pre-RT) thickness ≤ 2 cm from the cylinder surface received pelvic RT followed by ICBT.

Ten patients with FIGO stage I–II primary vaginal cancer treated with pelvic RT +/− cisplatin and ICBT at our institution between 1998 and 2008 were included. Initial tumor thickness measured on MRVC ranged from 0 to 2 cm. Initial tumor volume ranged from 0 to 9.8 cm^3. Mean pelvic RT dose was 45 Gy. At the time of ICBT, 60% of patients had a complete response (cR) and 40% had a partial response (pR). No patients with a cR had a recurrence whereas one patient with a pR had a local recurrence following ICBT. For the entire cohort, the median follow-up time was 59.9 months (range: 15–153). The estimated 5-year overall survival, disease-specific survival, and local failure-free survival were 67%, 80%, and 90%, respectively. Among survivors, there were no late grade 3–4 toxicities.

In this series of patients with small primary early-stage vaginal tumors, long term clinical outcomes were acceptable following RT and MRI-based ICBT, especially among those with a cR at time of brachytherapy.

1. Introduction

Vaginal cancer is rare, comprising approximately 1–3% of all gynecologic cancers. The American Cancer Society estimates that in 2015 approximately 4070 new cases of vaginal cancer will be diagnosed, and 910 women will die from this disease (http://www.cancer.org/cancer/vaginalcancer/detailedguide/vaginal-cancer-key-statistics). Multiple single-institution studies have shown that excellent disease-specific survival and pelvic disease control can be obtained in patients with early-stage disease (Frank et al., 2005; Perez et al., 1999; Chyle et al., 1996). Brachytherapy is an integral component of treatment and must be carefully tailored to the size and extent of the tumor (Beriwal et al., 2012a; Lee et al., 2013).

The type of brachytherapy used in vaginal cancer is highly individualized, and decisions about brachytherapy boost modality may be based on size, location, and thickness of vaginal tumor as detailed on a pelvic MRI (Elsayes et al., 2007; Taylor et al., 2007; Gardner et al., 2015). However, due to the extreme rarity of vaginal cancer, studies analyzing how MRI information guides brachytherapy technique in vaginal cancer have been scarce (Dimopoulos et al., 2012; Vargo et al., 2015; Beriwal et al., 2012b).

At our in ≤ stitution, in the late 1990s, we developed an MRI protocol with a vaginal cylinder in place (MRVC) for the assessment of pelvic tumors. The information provided by the MRVC was used to document initial tumor extent and thickness and to select the appropriate brachytherapy boost modality. Patients with small primary vaginal tumors with an initial thickness ≤ 2 cm were considered for external beam radiotherapy (EBRT) followed by intra-cavitary brachytherapy (ICBT). The present case series seeks to describe the long-term outcomes of patients with early stage vaginal cancer who were treated definitively at our institution with EBRT and ICBT, using MRVC.

2. Material and methods

2.1. Patient population

This study was approved by the Institutional Human Investigations Committee. We performed a retrospective review of patients with

* Corresponding author at: Department of Therapeutic Radiology, Smilow Cancer Hospital, LL 515, PO Box 208040, New Haven, CT 06520-8040, USA.
E-mail address: shari.damast@yale.edu (S. Damast).

http://dx.doi.org/10.1016/j.gore.2016.08.002

FIGO I–II primary carcinoma of the vagina treated with radiation therapy (RT) with curative intent in our department over a 10-year period (1998–2008). Patients with a previous history of invasive carcinoma of the female genital tract and those treated with palliative intent were excluded. Initial search results yielded 16 patients with stage I-II primary vaginal carcinoma. Additional exclusions were: bulky early stage cases treated with interstitial or EBRT boost (n = 2), early stage ICBT cases which lacked pre-treatment MRI imaging (n = 3), and one patient from an outside institution with no follow-up records accessible (n = 1).

The final study population of 10 patients received MRI-based ICBT following EBRT. Pre-treatment evaluation included an examination under anesthesia for documentation of disease extent in clinical diagrams, a CT scan of the chest, abdomen, and pelvis, and an MRI of the pelvis with the MRVC protocol, as described below.

2.2. MRI imaging protocol

All patients underwent customized pelvic MRI imaging with a vaginal cylinder (MRVC) prior to RT. Prior to the date of imaging, patients were fitted with the appropriate size vaginal cylinder in the clinic. The single-channel cylinders utilized at our institution are made of Lucite, and fabricated in our department. Cylinders measure 14 cm in length and are available in diameters of 2.0, 2.3, 2.6 or 3.0 cm. At the time of imaging, the radiation oncologist placed the appropriate sized Lucite cylinder into the vaginal canal. MRI was performed on a 1.5 T magnet (General Electric Medical Systems, Milwaukee, WI, USA) using a phased array coil with the axial sequences performed perpendicular to the long axis of the cylinder and the sagittal and coronal planes performed parallel to the cylinder's long axis. A FOV (field of view) typically of 24 cm, and a 256 × 256 matrix centered on the tip of the cylinder was utilized; T2 and T1 weighted scans, 4 mm thick (skip 4.8 mm), were obtained. Subtracted volumetric 1 mm pre and post iv contrast enhanced, fat suppressed gradient echo with gadodiamide (Omiscan; Amersham, Princeton, NJ, 20 ml) were acquired in the axial plane. Larger FOV sagittal 3D T2 and fat saturated T2 weighted scans of the pelvis were obtained as well as a post enhanced scan of the pelvis to include the aortic bifurcation and inguinal regions to assess for any adenopathy.

2.3. External beam radiotherapy

All patients received pelvic EBRT with a prescribed dose of 4500–4600 cGy in 23–25 fractions. For tumors involving the upper vagina, the targets included the entire vagina/paravaginal region, pelvic sidewalls and the bilateral pelvic lymph nodes with a 4-field box technique. The inguinal lymph nodes were also treated in cases where there was involvement of the lower third of the vagina. Concomitant cisplatin chemotherapy (40 mg/m^2) was considered for patients with stage II disease during this time period.

2.4. Intra-cavitary brachytherapy

All patients received either high-dose-rate (HDR) or low-dose-rate (LDR) ICBT, depending on the year of treatment. For those treated with HDR, treatments were delivered on an outpatient weekly basis, with an Iridium-192 afterloader. The total doses of brachytherapy ranged from 18 to 21 Gy, in 3–5 fractions, prescribed to 5-10 mm depth, depending on disease extent. The same size single lumen vaginal cylinder utilized for the MRVC was also used for treatment. Treatment plans were customized for each patient, specifying the prescription depth as well as the length of vagina to be treated, based on the location and extent of disease evident on physical examination and imaging, and marked out on the cylinders. Dose was optimized on a phantom, and 3D planning was not utilized. In general, the entire vagina was treated to a minimum EQD2 dose of approximately 60Gy with additional dose given to boost the tumor bed and areas of higher risk to approximately 75 Gy. In select cases, partially shielded cylinders were used for one or more brachytherapy fractions in order to reduce the dose to uninvolved regions of the vagina and the adjacent critical structures.

2.5. Patient follow-up and outcomes assessment

All patients had clinical examination every 2–3 months for the first 2 years, and every 3–4 months until 5 years, and then at least every 6–12 months thereafter. Vaginal cytology was obtained every 3 months. For patients with an incomplete or uncertain response, serial MRVC studies were performed to document radiographic regression.

Follow-up time was calculated from the date of diagnosis to the date of the last gynecologic examination. Actuarial rates of local recurrence, disease-specific, and overall survival were estimated by the Kaplan-Meier method. Toxicity was recorded in clinic notes and retrospectively graded according to the Common Terminology Criteria for Adverse Events (CTCAE v4.0).

3. Results

A total of 10 patients with early stage primary vaginal cancer were included with characteristics shown in Table 1. Four patients were FIGO stage I and six patients were FIGO stage II. All patients were node-negative. The mean age was 69.6 years (range: 54–88). Histologic subtypes included: squamous cell carcinoma (n = 6), adenocarcinoma (n = 3), and neuroendocrine carcinoma (n = 1). Tumor location was distal (n = 4), mid (n = 1), or upper (n = 5). Following EBRT, seven patients received HDR ICBT and three received LDR ICBT. Cumulative equivalent dose delivered to tumor (EBRT + ICBT) for each patient is shown in Table 1. On average, higher doses (EQD2) were prescribed for apical tumors (~75–80 Gy) as compared to tumors in mid- or distal vaginal locations (~70–75 Gy).

In terms of imaging assessment of tumor extent, as shown in Table 2, the mean initial ellipsoid tumor volume in cubic centimeters (volume = height × width × thickness × pi / 6) (Mayr et al., 2002) was 3.3 cm cubed (range: 1.3–9.8 cm^3). Initial tumor thickness prior to EBRT as measured on the customized MRVC ranged from 0 to 20 mm from the cylinder surface, with a mean pre-EBRT thickness of 13 mm. At the time of ICBT, 60% of patients had a clinical complete response (cR). Four patients (40%) had a partial or uncertain response (pR). All patients achieved an eventual cR documented in subsequent followup visits. Fig. 1A–F illustrates serial MRVC imaging performed every few months until complete regression for one patient with a pR at time of ICBT (patient #7, Tables 1–2).

The median followup time was 59.9 months (range: 15–153). The estimated 5-year overall survival, disease-specific survival, and local failure-free survival were 67%, 80%, and 90%, respectively. There was one local recurrence and one distant failure. The local recurrence occurred in a patient with stage II SCC of the distal vagina/peri-urethral region. Her initial tumor thickness was 15 mm as documented on MRVC prior to EBRT. She had only a pR at time of ICBT, with residual thickness of 5 mm on MRVC at time of ICBT. She had a cR at 6 weeks with negative cytology. However, she developed a local recurrence 4 months post ICBT. Following PET/CT imaging and histologic confirmation, she required a pelvic exenteration.

As shown in Table 2, of the 8 patients with long-term followup who remained disease-free, there were no late grade 3–4 toxicities (Table 2).

4. Discussion

The patie ≤nts in this series had early stage primary vaginal cancer (FIGO I–II) with non-bulky (mean tumor volume 3.3 cm^3, range: 1.3–9.8 cm^3) vaginal tumors with initial thickness ≤ 2 cm, as measured from the cylinder surface to the lateral/apical margin of the tumor on MRVC prior to any treatment. MRVC provided valuable information with respect to the dimensions of the tumor, which complimented the