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Case Report

Management of Bartholin's gland carcinoma using high-dose-rate interstitial brachytherapy boost

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ABSTRACT

PURPOSE: To describe the patterns of use, clinical outcomes, and dose–volume histogram parameters of high-dose-rate interstitial brachytherapy (HDR-ISBT) in the management of Bartholin's gland cancer.

METHODS AND MATERIALS: Five patients with Stage II–III Bartholin's gland carcinoma treated with CT-based HDR-ISBT boost were reviewed. Plans were generated using an inverse planning simulated annealing algorithm. Dose–volume histogram parameters were assessed. The total doses of HDR-ISBT and EBRT were converted to total equivalent dose in 2 Gy (EQD_2).

RESULTS: All 5 patients received HDR-ISBT as a boost (median dose, 30 Gy) after EBRT (median dose, 45 Gy). Three patients received postoperative irradiation for gross residual tumor or positive surgical margins and 2 patients were treated by primary chemoradiotherapy. The median V_{100}, D_{90}, and D_{100} for the CTV were 98.3%, 89 Gy_{10}, and 64 Gy_{10} (EQD_2), respectively. A complete response was observed in all patients. No local recurrence occurred. All patients remain alive and free of disease (median followup, 78 months; range, 8–93). Severe vaginal toxicities were observed, including vaginal necrosis that resolved with hyperbaric oxygen therapy.

CONCLUSIONS: HDR-ISBT boost after EBRT offers excellent long-term local control in patients with Bartholin's gland carcinoma. HDR-ISBT should be considered for positive surgical margins or residual tumor after surgery and for locally advanced malignancies treated by primary chemoradiotherapy.

Keywords: Bartholin's gland carcinoma; Interstitial brachytherapy; High-dose rate; IPSA

Introduction

Carcinoma of the Bartholin's gland is a rare disease, occurring in less than 7% of all vulvar malignancies. It is considered by some as part of the spectrum of vulvar cancers and by others as a distinct entity. It has traditionally been treated with surgery with or without postoperative external beam radiation therapy (EBRT). Data concerning the role of brachytherapy is sparse. Currently, there is no definitive consensus on treatment or evidence to suggest Bartholin's gland carcinoma should be managed differently from other vulvar squamous cell cancers. However, because of the deep location of the Bartholin's glands in the posterior labia, to the left and right of the opening of the vagina, extensive deep excision is necessary to achieve negative margins. Deep dissection into the ischiorectal fossa is often performed, sometimes requiring partial resection of distal vagina or levator ani muscle (1, 2). It is more difficult to obtain adequate surgical margins, and the risk of local recurrence is high with surgery alone in patients with Bartholin's gland carcinoma (1, 3). Copeland *et al.* (1) at MD

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Anderson Hospital and Tumor Institute reported a local recurrence rate of 27% with surgery alone compared with 7% with the addition of adjuvant radiotherapy. Therefore, it is common to use adjuvant EBRT (4, 5). The role of definitive radiotherapy and chemoradiation therapy has been explored in recent case series, showing encouraging results (3).

Because local recurrence is the major pattern of failure (2), a rationale exists for the use of brachytherapy. This study reports our clinical experience with CT-based inverse-planned high-dose-rate interstitial brachytherapy (HDR-ISBT) boost for Bartholin's gland carcinoma. The primary objective was to review the patterns of use of HDR-ISBT in our center and tumor local control rates. The secondary objective was to evaluate toxicity, overall survival, and dose–volume histogram (DVH) parameters.

Methods and materials

Study population

Between 2001 and 2010, 5 patients with primary carcinoma of the Bartholin's gland received HDR-ISBT boost at L'Hôtel-Dieu de Québec. Diagnostic criteria for primary cancer of the Bartholin's gland included all the following (1): (*1*) tumor arising at the site of a Bartholin's gland, (*2*) histology consistent with a primary Bartholin's gland origin, and (*3*) no evidence of a distant primary tumor of similar histology elsewhere. A complete workup was mandatory before treatment, and Karnofsky performance status scores had to be at least 70. Staging was defined according to the International Federation of Gynecology and Obstetrics classification in use before 2009. For all patients, the same experienced radiation oncologist performed the brachytherapy implant, followup care, and surveillance. These cases were retrospectively reviewed.

Brachytherapy treatment procedure and planning

The implantation procedure was performed with the patient in the lithotomy position under general anesthesia. Gold markers were first implanted for target localization. This was followed by intrauterine tandem insertion (if the uterus was intact), vaginal cylinder, and perineal template installation (Syed–Neblett gynecologic template; Best Medical International, Inc., Springfield, VA). Interstitial needles were inserted along the grooves on the surface of the vaginal cylinder and were placed through the Syed–Neblett template, arranged in arcs or circles, with a spacing of 1 cm. The number and positioning of the implanted catheters was determined by the extent of the clinical target volume (CTV), based on radiological findings and on the clinical examination (visualization and palpation) performed immediately before the implant and reassessed during the procedure. Patients underwent postimplant flexible cystoscopy.

A CT scan was done to verify proper placement of the catheters and for image-based treatment planning. CTV and organs at risk (bladder, urethra, and rectum) were delineated, using the PLATO planning system (Nucletron, Veenendaal, The Netherlands). The CTV was defined as the residual tumor at the time of brachytherapy. Palpable suspicious indurations and the macroscopic disease on CT were included in the CTV, taking into account tumor spread at diagnosis, on a case-by-case basis, to ensure adequate coverage. The planning target volume was equal to the CTV. As in most brachytherapy treatment planning systems, there was no dose correction for tissue heterogeneity in the PLATO planning system.

Dosimetric optimization was performed using the anatomy-based inverse planning simulated annealing (IPSA) algorithm (6). Only dwell positions inside the CTV plus a 2-mm margin were activated. Dose objectives for dwell time optimization used in our department for gynecologic implant were previously described in detail, for the CTV, rectum, bladder, and urethra (7). After the IPSA dose plan was generated, manual adjustments of the dwell times to some of the source positions could be used at the discretion of the treating physician, to improve the target coverage while minimizing the dose to organs at risk. An example of an HDR-ISBT dose distribution is presented in Fig. 1.

The first treatment was delivered the same day, using an HDR microSelectron remote afterloading system (Nucletron), with an ^{192}Ir source. Subsequent fractions were given twice a day, with a minimum interval of 6 h between fractions. Before each treatment, visual inspection of the catheter and verification of the catheter depth were mandatory. CT scans were repeated when significant catheter displacement was identified to allow appropriate corrections to be made.

Dosimetric analysis and EBRT

The DVH were generated based on 100,000 sampling points. The DVH parameters for CTV and organs at risk were reported according to the Gynecologic Groupe Européen de Curiethérapie-European Society for Radiotherapy and Oncology (GEC-ESTRO) recommendations for image-based cervical intracavitary brachytherapy (8). Dose parameters were normalized to biologically equivalent dose in 2-Gy fractions (EQD_2) using the linear–quadratic model. As proposed by the Gynecologic GEC-ESTRO, we used an α/β ratio of 10 Gy for tumor and an α/β ratio of 3 Gy for normal tissue late effects. In addition to HDR-ISBT, all patients received EBRT. Total doses in EQD_2 were calculated, combining HDR-ISBT and EBRT contributions (8). All dose parameters were reported in total EQD_2.

All patients in this study received pelvic EBRT because of the risk of pelvic lymph node metastasis in locally advanced cancer, according to the lymphatic drainage along the internal pudendal vessels (5). Irradiation of unilateral or