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Case series

Using advanced wound care and hyperbaric oxygen to manage wound complications following treatment of vulvovaginal carcinoma

C. Griffiths[a,b], R.S. Howell[a,b], H. Boinpally[a,b], E. Jimenez[a,b], E. Chalas[a,b], F. Musa[a,b], S. Gorenstein[a,b,*]

[a] Department of Gynecologic Oncology, NYU Winthrop Hospital, Mineola, NY, USA
[b] Department of Surgery, NYU Winthrop Hospital, Mineola, NY, USA

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ABSTRACT

Postoperative management of patients with vulvar cancer is associated with a high incidence of poor wound healing and radiation -induced late tissue necrosis. This case series demonstrates the impact on wound healing with the use of hyperbaric oxygen therapy and advanced wound care following radical vulvectomy and/or radiation therapy.

A retrospective case series was performed of all patients from 2016 to 2017 with lower genital cancer who underwent radical surgery with or without chemoradiation treatment, experienced wound dehiscence or late tissue radionecrosis, and were treated with advanced wound care, including hyperbaric oxygen therapy (HBO).

Five patients were included with a mean age of 63; four had squamous cell carcinoma and one patient had vaginal adenocarcinoma secondary to prior diethylstilbestrol exposure. Three patients underwent radical vulvectomy. All received pelvic radiation therapy, subsequently experienced wound complications, and were managed with advanced wound care and HBO. The mean reduction in wound area at the final wound follow up visit after completion of HBO therapy was found to be 76%, ranging 42–95%, with an average follow up of five months. The mean number of HBO sessions per patient was 58. Complete tissue granulation or significant improvement in tissue radionecrosis was present in all patients.

Advanced wound care and hyperbaric oxygen therapy are beneficial in the management of postoperative wound complications. Prospective studies are needed to identify the optimal use of perioperative hyperbaric oxygen and appropriate wound care for patients with gynecologic malignancies.

1. Introduction

Vulvar carcinoma is diagnosed in approximately 6000 women annually in the United States, with a 5-year survival rate of 72% (Vulvar Cancer - Cancer Stat Facts, n.d.). The high morbidity of radical procedures is a major challenge in treatment planning. Prognosis is strongly correlated to inguinal lymph node metastasis and the disease stage at the time of diagnosis (Sharma, 2012). Although the current “three incision” technique is associated with decreased postoperative morbidity compared to historical “en bloc” resection, including significant wound dehiscence (Hopkins et al., 1993), wound complications remain one of the biggest challenges of vulvar cancer management.

Radiation therapy has been utilized as a definitive treatment option for nonsurgical candidates, for both prevention of locoregional recurrence and palliation. Late tissue necrosis from prior radiation affects 5–15% of long-term survivors, with a prevalence of 2–4% for patients who have received prior pelvic radiotherapy for a gynecologic malignancy (Craighead et al., 2009). Therefore, alternative approaches must be considered to decrease the incidence of postoperative complications and effects of radiation tissue necrosis, while aiming to maintain optimal disease-free intervals. These include biologic growth factors, extracellular matrixes, skin substitutes, and biophysical approaches such as hyperbaric oxygen (HBO) and negative pressure wound therapy. Specifically, HBO has been shown to improve tissue damaged from prior radiation by promoting angiogenesis and improving local tissue hypoxia (Craighead et al., 2009). Physiologic effects of HBO include increasing arterial partial pressure of oxygen to > 1000 mmHg and facilitation of oxygen delivery to hypoxic tissue, stimulating a wound-healing cascade (Johnston et al., 2016).

This retrospective case series aims to demonstrate the positive impact of HBO and advanced wound care on healing of post-treatment vulvar wound complications.

* Corresponding author at: 259 1st Street, Mineola, NY 11501, USA.
E-mail address: sgorenstein@nyuwinthrop.org (S. Gorenstein).

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2. Methods

This was an IRB-approved retrospective case series of patients diagnosed with vulvar and vaginal cancer in 2016 and 2017 at a single institution with informed consent obtained. Patient population included those who underwent either radical vulvectomy and/or chemoradiation treatment of lower genital malignancy, subsequently experienced wound breakdown or late tissue radionecrosis, and were treated with advanced wound care, including HBO. Patients who experienced a failed flap or tissue necrosis from delayed radiation effects were eligible for HBO therapy. Those with a diagnosis of vulvar intraepithelial neoplasia or lichen sclerosis were excluded. The institutional HBO protocol included daily sessions of 100% oxygen at 2.0 to 2.5 atm absolute (ATA) for 90 min. The number of sessions was determined by the severity of the tissue necrosis and/or failed flap and serial examinations by the wound care and gynecologic providers caring for the patient.

3. Case presentations

3.1. Case 1

68-year-old had well-differentiated invasive squamous cell carcinoma which extended within one cm of the anus. She underwent chemoradiation with weekly Cisplatin and pelvic radiation therapy (4500 cGy) with residual disease noted on right vulva. Partial right radical vulvectomy with rotational rhombic flap reconstruction was performed four months after completion of chemoradiation. Pathology revealed residual moderately-differentiated, keratinizing SCC with 6 mm of invasion and negative margins. Surgical wound dehiscence occurred on postoperative day (POD) 28 and was treated with 60 consecutive HBO sessions at 2.5 ATA for 90 min each. Initial wound area was measured to be 120 cm^2. Successive wound measurements were unable to be located due to conversion to a new electronic medical record system; however, complete wound healing was noted at the last office visit approximately 112 days following initiation of hyperbaric treatment. No evidence of recurrent disease was noted on the most recent PET CT scan. Fig. S1 demonstrates the pre- and post-HBO wound appearances.

3.2. Case 2

77-year-old with invasive SCC of the vulva underwent neoadjuvant chemoradiation with Cisplatin and pelvic radiation therapy (4320 cGy with a vulvar boost 1440 cGy) for one month with residual disease noted bilaterally, abutting the urethra. The patient underwent a total radical vulvectomy and bilateral V—Y fasciocutaneous flaps six months later. Pathology confirmed moderately differentiated SCC with 2 mm depth of invasion. Wound breakdown occurred on POD 24. She received 58 sessions of HBO at 2.5 ATA for 90 min, followed by weekly debridement in the operating theater and sequential applications of advanced wound dressings (six antimicrobial-coated collagen bilayer matrixes and one porcine small intestine submucosal extracellular matrix scaffold). A 26% decrease in wound area was noted at the completion of HBO and 92% decrease at the final wound follow up visit. This near complete wound recovery was achieved approximately 280 days following initial HBO treatment. Approximately 76–100% granulation tissue was noted at her 8-month follow up visit compared to 0% at the initial visit. To date, the patient has had no evidence of recurrent disease. Fig. 1 illustrates the pre- and post-HBO wound appearances.

3.3. Case 3

68-year-old with ulcerating vulvar SCC metastatic to the left groin lymph nodes underwent weekly Cisplatin and pelvic RT (4500 cGy with boost of 1260 cGy), followed by 30 sessions of HBO at 2.5 ATA for 90 min. An 84% reduction in wound area with 50% increase in granulation tissue was recorded (Fig. 2). Additional therapy included wound debridement in the operating theater, fat grafting, 40 additional sessions of HBO and ten weekly applications of antimicrobial-coated collagen bilayer matrixes followed by an epidermal harvest graft for a further 95% reduction in wound area and an increase to 51–75% granulation tissue noted at her three-month follow up visit. Near complete wound healing was noted approximately 252 days following initiation of treatment. No clinical evidence of recurrent disease was identified at her most recent office visit.

3.4. Case 4

62-year-old with a history of vaginal adenocarcinoma underwent radiation therapy 30 years prior with a non-healing perineal lesion due to delayed radiation effects. She was referred to the Wound Care center where received 30 sessions of HBO at 2.0 ATA for 90 min along with silver alginate. A 42% reduction in wound area was noted at her 5-month follow up visit with 76–100% granulation tissue (Fig. 3), approximately 140 days following initiation of HBO. No evidence of recurrence was noted at her last documented visit.

3.5. Case 5

41-year-old with a diagnosis of vulvar SCC after biopsies of granulation tissue from a prior perineal laceration were obtained, underwent radical vulvectomy and bilateral inguinal node dissection followed by chemoradiation for 6 cycles. She presented with a three-month old non-healing wound and received 44 treatments of HBO at 2.5 ATA for 90 min for soft tissue radionecrosis. Silver sulfadiazene was applied at follow up visits. At the four-month follow up visit, 76–100% epithelialization of post radiation vulvovaginitis was noted (Fig. S2), approximately 168 days following initiation of HBO treatment. She was noted to have no evidence of disease at this same visit.

4. Results

Five patients were identified and included in this series. All patients were referred to the Wound Care Center for wound complications and received advanced wound care therapy, including HBO (Table 1). Objective documentation was recorded by wound photographs and measurements obtained at interval wound care visits and at completion of HBO. The mean reduction in wound area at the final wound visit after completion of HBO therapy was found to be 76%, (42–95%) with a mean follow up of five months. Patients were treated for an average of 58 HBO sessions (range 44–100).

5. Discussion

Historically, "en bloc" radical surgery was associated with high morbidity. A subsequent three-incision technique for stage I disease significantly lowered morbidity and improved 5-year survival up to 97% Higgins et al., n.d.; Marsden and Hacker, 2001). Risk of wound breakdown of en bloc resection and three separate incision techniques was reported to be 64 vs 38% respectively, wound cellulitis of 21 vs 14% and lymphocyst of 28 vs 14% (Hopkins et al., 1993).

Surgical complications are associated with adverse psychosocial, sexual, self-image, and quality of life effects. Advanced treatment modalities for wound breakdown include bioengineered skin and tissue equivalents, HBO, and negative pressure wound therapy (Wu et al., 2010). HBO specifically has been commonly used for failed grafts/flaps (Thom, 2011). During HBO, patients are placed into a hyperbaric chamber and breathe 100% oxygen at 2.0 to 2.5 ATA for 1 to 2 h. Failed grafts or flaps within radiated fields benefit from such enhanced healing processes (Francis and Baynosa, 2017). HBO improves survival of

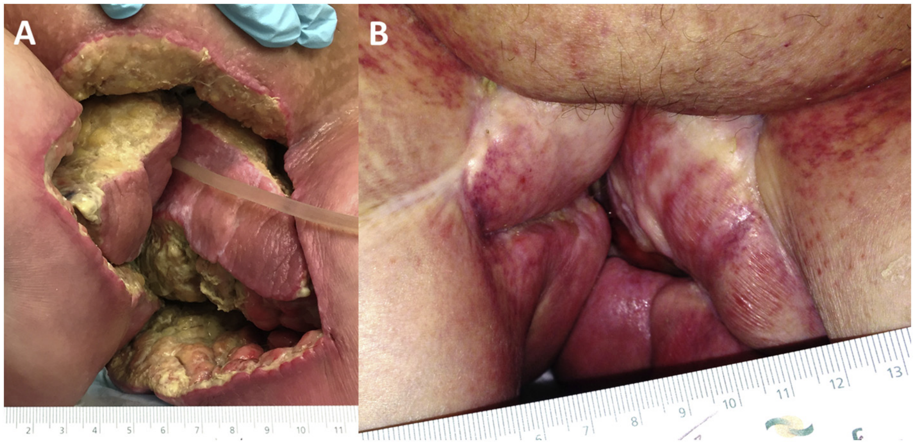

Fig. 1. Case 2 prior to (A) and following completion of hyperbaric treatment (B).

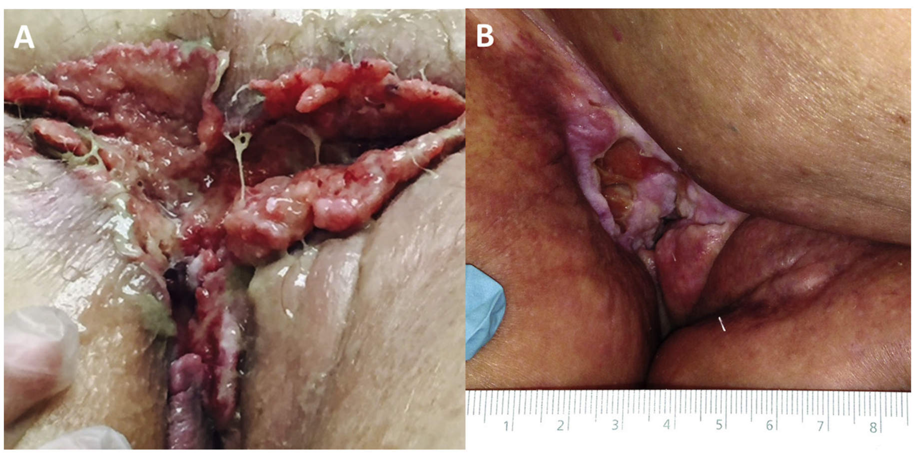

Fig. 2. Case 3 prior to (A) and following completion of hyperbaric treatment (B).

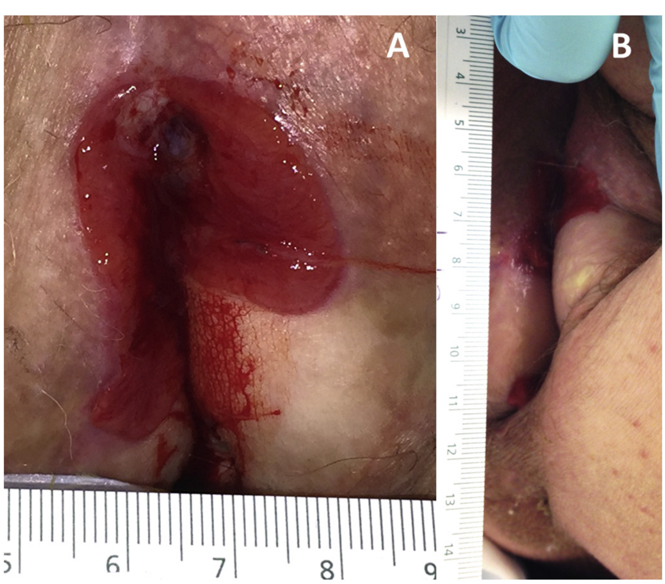

Fig. 3. Case 4 prior to (A) and following completion of hyperbaric treatment (B).

compromised grafts by reversal of tissue hypoxia and initiation of vasoconstriction, thereby decreasing local tissue edema, promoting angiogenesis and increasing stem cell mobilization by activation of nitric oxide synthase type 3 (NOS-3) in bone marrow, and enhances engraftment and differentiation of several progenitor cell types. These mobilized progenitor stem cells promote angiogenesis and improve wound healing (Heyboer et al., 2014).

HBO has been shown to be an effective therapy for non-healing wounds. A randomized controlled trial was conducted including 30 patients with non-healing ulcers receiving HBO plus standard wound care versus standard wound care alone (Kaur et al., 2012). The HBO group had 59% reduction in wound area compared to 26% in the control group, with complete healing in three patients in the HBO group and none in the control group. A recent Cochrane review confirmed HBO efficacy for delayed radiation injury to pelvic tissue, particularly for symptomatic relief and reduction of postoperative complications (Bennett et al., 2016). A prospective study examined the effects of HBO on radiation-induced soft tissue necrosis (Williams et al., 1992). Fourteen patients were included and underwent 15 sessions of HBO therapy. Thirteen patients (93%) exhibited complete resolution of tissue necrosis.

The effect of postoperative HBO on wound breakdown following radical vulvectomy was prospectively studied in eight patients. Breakdown occurred in only one patient and decreased length of stay in all patients (Reedy et al., 1994). However, HBO therapy was initiated during the immediate postoperative period in contrast to the patients in this case series. The limited information on utilization of HBO in gynecologic literature suggests that additional studies are needed to further delineate its efficacy, determine optimal treatment timing and develop evidence-based regimen for lower genital malignancies. As seen in many centers, treatment for the late effects of radiation traditionally occurs approximately 6 months or later following conventional

Table 1
Demographic variables associated with patient selection.a, b

Case number	Age	Histology	Initial treatment	Complication	Initial wound area (cm^2)	Final visit wound area (cm^2)	Length of time to wound response (days)
1	68	SCC[a]	Chemoradiation with Cisplatin and pelvic RT followed by partial right radical vulvectomy	Wound dehiscence (POD#28)[b]	120	–	112
2	77	SCC	Total radical vulvectomy and bilateral V–Y fasciocutaneous flaps following chemoradiation with Cisplatin and pelvic RT	Wound dehiscence (POD#24)	118.8	10	280
3	68	SCC	No surgery; chemoradiation therapy with Cisplatin and pelvic RT; wound debridement	Radiation effects	114.7	5.8	252
4	62	Vaginal adenocarcinoma	Hysterectomy (1980s) and adjuvant radiation therapy	Non-healing wound and late tissue necrosis from prior radiation	7.4	4.3	140
5	41	SCC	Partial radical vulvectomy and bilateral inguinal LN dissection followed by chemoradiation therapy with Cisplatin and pelvic RT	Soft tissue radionecrosis	–	–	168

[a] SCC: Squamous Cell Carcinoma.
[b] POD: post-operative day.

radiation therapy, however there is insufficient data to comment on clear cut guidelines. Our case series demonstrates positive outcomes with the use of HBO at a shorter time interval from adjuvant therapy and we aim to demonstrate promising results with the use of perioperative HBO in future prospective studies. These studies should also include assessment of fiscal impact. The economic feasibility of HBO treatment in the setting of wound breakdown and tissue necrosis is currently not well understood. A Canadian study devised an economic model analyzing the use of adjunctive HBO therapy for the treatment of diabetic foot ulcers. This study deemed HBO treatment to be cost-effective when compared with standard care and demonstrated overall cost savings to the healthcare system (Chuck et al., 2008).

6. Conclusion

Treatment of lower genital tract malignancies is associated with poor wound healing. This retrospective case series demonstrates the efficacy of advanced wound care and HBO in the management of hypoxemic wounds. Additional prospective studies are needed to identify the optimal use and regimen of perioperative HBO.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.gore.2018.04.002.

Conflict of interest

All potential conflicts have been disclosed by the authors.

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