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Treatment of late morbidity

Treatment of radiation proctitis with hyperbaric oxygen

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Abstract

***Background and purpose*: Radiation proctitis is a potential complication following pelvic radiation therapy. There are no standard treatments and treatment outcomes are unpredictable. We report our experience with the use of hyperbaric oxygen treatment (HBOT) for radiation proctitis cases refractory to standard medical or laser therapy.**

***Patients and methods*: During the period 2000–2004, 10 patients with radiation proctitis were treated with HBOT (three males and seven females; mean age of 65). The median follow-up period was 25 months (range 6–43 months). Patient symptoms were retrospectively scored prior to, and following HBOT, based on the LENT-SOMA scale.**

***Results*: Prior to treatment, three patients had Grade 3 toxicity (i.e. requiring blood transfusions) and seven had Grade 2 toxicity with dominant symptoms of rectal pain and/or diarrhoea. HBOT was well tolerated and 9 of the 10 patients completed a full HBOT treatment program. Rectal bleeding completely stopped in four of nine symptomatic patients and improved in three others. Rectal pain completely remitted in three of five symptomatic patients. Diarrhea remitted completely in one of five patients and improved in three others. Of the 10 patients treated, only two did not respond to HBOT.**

***Conclusions*: Significant improvement of rectal bleeding, diarrhea and rectal pain is possible using HBOT. HBOT should be offered to patients who fail conventional treatments for radiation proctitis.**
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Keywords: Proctitis; Hyperbaric oxygen; Complications; Radiotherapy; Rectal bleeding

Pelvic radiotherapy may be complicated by radiation proctitis. This is a distinct pathological process confined to the lower 25 cm of the large intestine caused by damage to the rectal mucosa. Acute radiation proctitis can develop during or shortly after a course of radiation therapy. It presents as diarrhoea and tenesmus and is usually short-lived. Chronic radiation proctitis (CRP) occurs after 3 months post radiotherapy and is characterized by the painless passage of blood per rectum (clots or streaking of the stool), mucous rectal discharge, frequent bowel movements and rectal pain. Less commonly, bowel obstruction, fistulae, bowel perforation, and severe rectal bleeding can occur requiring blood transfusions.

Acute radiation injury results from the death of mitotically active intestinal crypt cells, whereas chronic radiation injury is the result of progressive endarteritis leading to hypovascular, hypocellular and hypoxic tissue [17]. CRP is associated with prominent structural changes including mucosal atrophy, intestinal wall fibrosis and vascular sclerosis [16]. CRP can develop either as a consequence of non-healed acute rectal injury or after a latent period of at least 90 days [16]. Denham et al. reported that patients who experienced acute proctitis were at least twice as likely to develop more severe late RTOG/EORTC grades than patients who did not [9,19].

About 85% of cases present within the first 2 years after RT. Although the true incidence is unknown, estimates from retrospective data suggest that between 2 and 20% of patients who receive radical pelvic irradiation may be at risk of developing CRP [27]. This risk will be influenced by both treatment (e.g. dose per fraction, total dose and technique) and patient factors (e.g. diabetes mellitus, inflammatory bowel disease, hypertension or peripheral vascular disease) [23].

Treatments for CRP are not universally successful. Current modalities include pharmacological agents such as oral and rectally administered steroids, 5-amino salicylates, sucralfate, short chain fatty acid enemas, oral metranidazole, oral vitamins E and C [3–5,8,15,17,18,21,24,25]. Local haemostatic treatments include topical formalin,

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yttrium–aluminum–garnet (YAG) laser and surgical intervention includes the use of a defunctioning colostomy for severe cases [14,28]. Hyperbaric oxygen therapy (HBOT) has previously been described as a non-invasive therapeutic option for the treatment of radiation proctitis [2,29,30]. The European Committee for Hyperbaric Medicine and EORTC consensus conference in 2001 and systemic reviews by Feldmeier et al. and Pasquier et al. recommended the use of HBOT in the management of radiation proctitis and enteritis [2,13,22]. We describe our experience with the use of HBOT for patients with CRP who were resistant to conventional oral or topical treatments.

Materials and methods

During the period August 2000 to early 2004, 10 patients with CRP, who failed to respond to oral or topical conventional treatments, were referred to the Adult Radiation Late Effects Clinic (ARLEC) at the Princess Margaret Hospital (UHN). The clinical data were extracted from the medical records and by telephoning the patients for updated information.

The characteristics of the patient cohort are shown in Table 1. None of the patients had associated conditions of diabetes mellitus, inflammatory bowel disease, hypertension or peripheral vascular disease. All patients had received radical radiation treatment. Two patients had undergone surgery before radiation (abdomino-perineal resection for rectal cancer and total abdominal hysterectomy and bilateral salpingo-oophorectomy for uterine cancer). The four patients with cervical cancer had received concomitant weekly cisplatin infusions with the external beam radiation therapy (EBRT) followed by intracavitary brachytherapy. The patient with rectal cancer had received concurrent EBRT, 5-FU and folinic acid.

Table 1
Characteristics of patients with CRP

Age, mean (years)	65 (range: 39–79)
	(*n*)
Sex	
Male	3
Female	7
Primary diagnosis	
Prostate Cancer	3
Cervical cancer	4
Uterine cancer	1
Rectal cancer	1
Vaginal cancer	1
Toxicity	
LENT SOMA	7
Grade 2	
Grade 3	3
Primary symptoms	
Rectal bleeding	9
Diarrhoea	1
Secondary symptoms	
Rectal pain	5
Diarrhoea	4
Bladder symptoms	3
Onset of symptoms following radiotherapy	
<24 months	8
>24 months	2
Hyperbaric oxygen therapy	
Interval between onset of symptoms and HBOT:	20 months (range: 4–60)
Maximum number of treatments per patient:	40 (range: 36–41)

n, number of patients.

All patients had been treated with various medical therapies before referral. Failed treatments included: loperamide, lomotil (diphenoxylate and atropine), psyllium fiber, steroid enemas, mesalazine/5-ASA suppositories, a variety of analgesics and YAG-laser treatments. These were used for a median duration of 12 months (range 3–60 months). Two patients had additionally failed laser coagulation. All patients had endoscopic assessments and histological confirmation of radiation proctitis prior to HBOT. Routine HBOT pre-screening included a chest X-ray, spirometry, ophthalmological assessment and audiography. Patients breathed 100% oxygen in the hyperbaric chamber at pressures of between 2 and 2.5 (average: 2.4) atmospheres absolute for 90 min, 5 days a week for 40 treatments (range: 36–41). Mean time between the onset of proctitis and starting HBOT was 20 months (range: 4–60 months). Symptoms prior to, and following HBOT, were retrospectively graded based on a LENT-SOMA Scale for rectal injury [19].

Results

Four of the ten patients developed proctitis within 6 months of completion of radiotherapy; another four of the patients developed their symptoms between 7 and 24 months following treatment and the other two patients developed symptoms at 2 years following treatment. Nine of the ten patients presented with rectal bleeding and one presented with severe diarrhea. The associated secondary symptoms were diarrhea (four patients), rectal discomfort or pain (five patients) or bladder symptoms (three patients). Three patients required multiple blood transfusions. Using the LENT-SOMA scale, seven patients had Grade 2 proctitis and three patients had Grade 3 proctitis.

HBOT was well tolerated by all the patients. Nine patients completed the planned course of hyperbaric oxygen treatment. One patient had the treatment course curtailed due to extended closure of the HBOT unit for SARS infectious precautions. Five patients developed side effects related to HBOT: minor otic barotrauma occurred in four patients and there was exacerbation of amiodarone-induced pulmonary fibrosis in one patient. After completion of HBOT, these side effects completely resolved with supportive measures alone.

Patients were regularly followed after completion of HBOT. The median follow-up period from completion of HBOT was 25 months with a range of 6–43 months. The outcome of treatment was clinically assessed and is described in Table 2. Of the nine patients who completed an entire course of HBOT, four experienced complete resolution of rectal bleeding and three experienced reduction in frequency and severity of rectal bleeding.