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Hyperbaric oxygen therapy in hemorrhagic radiation cystitis: a report of 20 cases

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Lee HC, Liu CS, Chiao C, Lin SN. Hyperbaric oxygen therapy in hemorrhagic radiation cystitis: a report of 20 cases. Undersea Hyperbaric Med 1994; 21(3):321–327.—Radiation cystitis with macroscopic hematuria has been a frustrating clinical problem for urologists. Since 1985 hyperbaric oxygen (HBO) has been used to treat this disease, showing favorable results. Between November 1989 and October 1992, 20 female patients with hemorrhagic radiation cystitis were treated with HBO at a pressure of 2.5 atm abs, breathing 100% O_2 for 100 min in our multiplace hyperbaric chamber. After an average of 44 HBO sessions, macroscopic hematuria was completely halted in 16 patients (80%) and markedly decreased in 2 patients (10%). Comparison of the cystoscopic findings before and after HBO showed a significant decrease in hemorrhagic sites and telangiectasis of the bladder mucosa. One patient had urinary frequency and urgency without hematuria during her hospital stay. After 30 sessions of HBO therapy, her symptoms subsided, and the cystoscopic findings were much improved. Only one patient failed to respond to HBO and underwent ileal conduit diversion. The mean follow-up period was 14 mo. (5–41 mo.). From our clinical results and cystoscopic findings, we suggest that HBO is an effective and safe treatment for hemorrhagic radiation cystitis.

hyperbaric oxygen, radiation cystitis

Radiation therapy has been used to treat pelvic malignancies such as carcinoma of the prostate, urinary bladder, and uterine cervix. Five to 20% of the patients treated with radiation develop urologic complications such as hemorrhagic cystitis, ureteral stricture, incontinence, bladder ulcer, and fistula (1–3). Among these complications, hemorrhagic radiation cystitis remains perhaps the most frustrating clinical problem. Several methods of palliating radiation cystitis have been reported, including bilateral hypogastric artery occlusion; hydrostatic bladder dilatation (4); intravesical instillation of formalin (5), silver nitrate (6), or alum (7); and urinary diversion with cystectomy. Nevertheless, a number of disadvantages are seen in the above-mentioned measures: a) lack of efficacy in controlling hematuria, b) decrease in bladder capacity, c) painful and only temporary cauterization, d) failure to heal

ischemic mucosa, and e) unacceptable hazards in older patients. Since 1985, when Weiss et al. (8, 9) used hyperbaric oxygen (HBO) to resolve hematuria in three cases of radiation cystitis, many other investigators have reported a similar favorable response to HBO (10–13). This paper describes our clinical experience in treating 20 cases of hemorrhagic radiation cystitis with HBO.

METHODS

Between November 1989 and October 1992, 20 patients with hemorrhagic radiation cystitis were referred for HBO therapy at our hyperbaric facility. All were females with a mean age of 63 yr (42–79 yr). They had previously been treated with radiotherapy averaging 6,200 cGy for carcinoma of the uterine cervix in 19 cases and, in 1 case, carcinoma of the urinary bladder. Gross hematuria appeared an average of 9.5 yr after radiotherapy. In all patients, intravesical irrigation, antibiotics, and tranexamic acid had been tried and failed in an effort to stop hematuria. The clinical symptoms were acute hematuria, dysuria, and urgency and frequency of urination.

Before HBO therapy each patient had routine blood work which included bleeding and coagulation times to exclude clotting disorders, routine urine and bacterial cultures for secondary infections, a pap smear, a pelvic examination, an ultrasonogram of the abdomen to rule out possible metastasis or recurrence of carcinoma, and cystoscopic examination to confirm the diagnosis and evaluate the severity of the radiation cystitis. Initially, a Foley catheter was inserted for intravesical irrigation with cold normal saline to manage obstruction secondary to blood clots. Blood transfusions were also administered if necessary. Parenteral antibiotics were used to prevent secondary infection of the urinary tract. HBO therapy was carried out in a multiplace hyperbaric chamber at 2.5 atm abs with 100% oxygen by double-seal oronasal mask for 100 min once a day, 6 days per wk (Fig. 1). No other methods were used to control hematuria except for emergent laser fulguration to check acute massive bleeding in one patient. After completion of HBO therapy, cystoscopic examination was repeated for comparison with the previous exam.

RESULTS

After an average of 44 HBO sessions (range, 10–87 sessions), macroscopic hematuria stopped completely in 16 patients (80%) and was markedly decreased in 2 patients (10%). One patient who only complained of urinary frequency and urgency, without hematuria, had relief of those symptoms. One patient with diabetes mellitus (DM) and cirrhosis of the liver failed to respond to HBO therapy and finally underwent ileal conduit diversion. After HBO, the cystoscopic findings showed a significant decrease of hemorrhagic sites and telangiectasis (Fig. 2). Twenty cases of radiation cystitis treated with HBO are summarized in Table 1.

For five examples of radiation cystitis, there was much improvement in hemoglobin (Hb) levels, hematocrits (Hct), and routine urinalysis after HBO in patients 1, 2, 3, and 5 (Table 2). Patient 1 had a past history of DM which was poorly controlled. She received 22,500 ml of blood because of sudden onset of massive hematuria, which was emergently controlled by laser fulguration. Although patient 3 was found to have recurrent carcinoma of the uterus, she still received 10 sessions of HBO

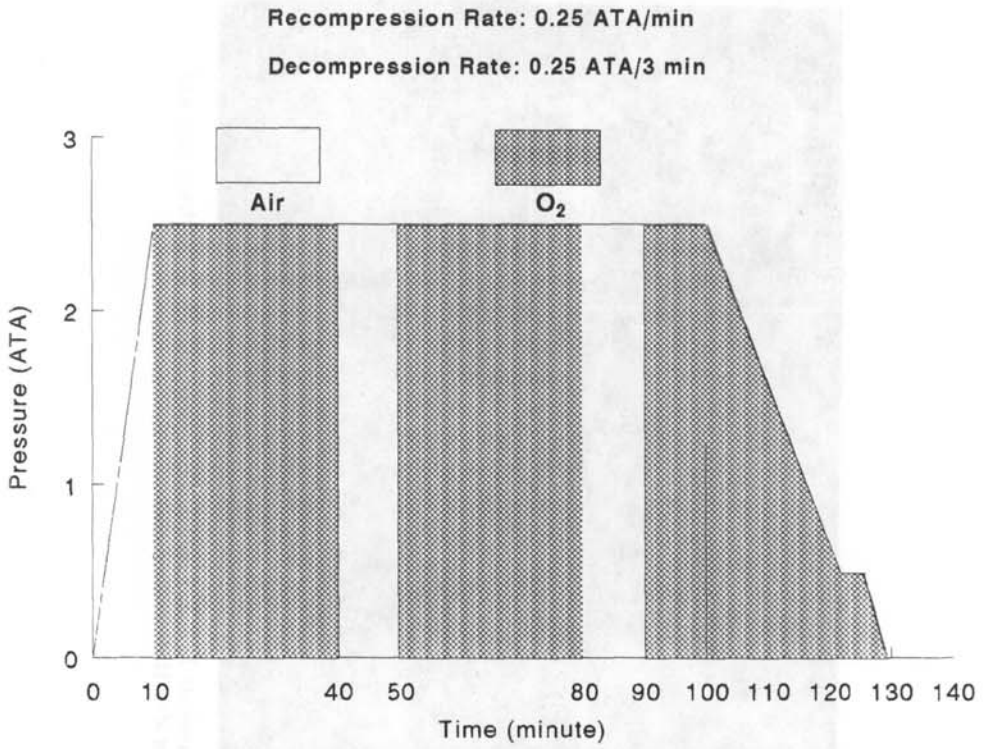

FIG. 1—Treatment profile (pressure/time) of each HBO therapy for hemorrhagic radiation cystitis. The decompression stop at 0.5 atm abs for 3 min is to prevent the occurrence of decompression sickness in the inside attendant.

therapy. After cessation of hematuria she was referred for further management of recurrent tumor. Patient 4 had no hematuria on admission or during HBO therapy, but had experienced occasional hematuria before admission. Interestingly, the cystoscopic findings after 30 sessions of HBO therapy revealed much improvement of the bladder mucosa. The oblique view in patient 4 (Fig. 2) demonstrates clearly the edema and telangiectasia of the bladder mucosa before HBO. In all patients, the mean follow-up period was 14 mo. with a range of 5 to 41 mo. Neither oxygen toxicity nor barotrauma was encountered.

DISCUSSION

From our experience in these 20 patients, hemorrhagic radiation cystitis seems to respond well to HBO with control of hematuria in 90% of cases. We think this result is explainable by the known mechanisms of action of HBO. In patients who have complications after radiotherapy of the pelvis, a progressive obliterative endarteritis develops in small blood vessels of the urinary bladder and finally creates a hypovascular, hypocellular, hypoxic tissue. Subsequent tissue breakdown may take place spontaneously or may be induced by trauma, and then leads to bleeding. Secondary infection may further compromise the tissue with resultant bleeding. HBO has three

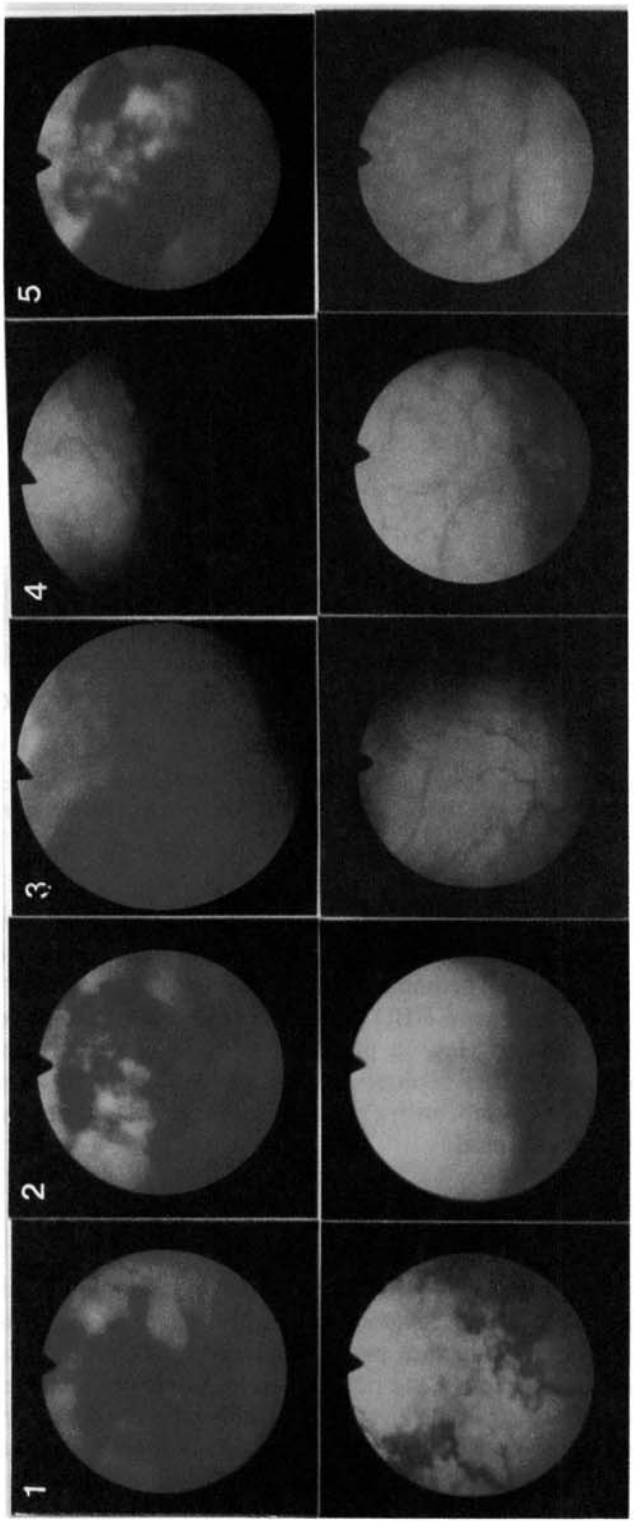

FIG. 2—Comparisons of cystoscopic findings before HBO and after HBO in patients 1, 2, 3, 4, and 5. There were multiple hemorrhagic sites and telangiectasias of bladder mucosa before HBO (*top row*) and much improvement after HBO (*bottom row*).

Table 1: Clinical Results of HBO of 20 Cases of Hemorrhagic Radiation Cystitis Treated With HBO[a]

Case No.	Age yr	Duration After Radiation Therapy, yr (cGy)	HBO Sessions	Clinical Results After HBO	Follow-up, mo.
1	58	20 (7,275)	40	no hematuria	22
2	59	6 (9,000)	20	no hematuria	26
3	42	5 (6,000)	10	no hematuria	20
4	79	7 (6,000)	30	improved bladder mucosa	11
5	51	4 (6,000)	30	no hematuria	13
6	62	7 (9,000)	30	no hematuria	41
7	54	6 (6,500)	60	no hematuria	20
8	66	7 (5,000)	30	no hematuria	9
9	66	8 (5,500)	60	no hematuria	15
10	69	26 (6,000)	30	no hematuria	9
11[b]	63	18 (6,000)	52	no hematuria	8
12	76	13 (5,500)	77	no hematuria	18
13	47	2 (6,000)	30	no hematuria	11
14	72	9 (6,000)	30	less hematuria	9
15	71	2 (7,000)	87	no hematuria	9
16	65	8 (5,000)	60	less hematuria	8
17	75	10 (6,000)	30	no hematuria	10
18	60	7 (5,000)	52	no hematuria	6
19	65	5 (5,200)	64	no hematuria	5
20	60	20 (6,000)	58	ileal conduit diversion	19

[a]All cases were carcinoma of the uterine cervix. [b]Carcinoma of urinary bladder.

Table 2: Laboratory Data of Five Examples of Hemorrhagic Radiation Cystitis Treated With HBO

Case No.	Hb, g/dl (Hct, %)			Urine Routine (/HPF)			Total Blood Transfusion, ml
	Pre-HBO	During HBO	Post-HBO	Pre-HBO	During HBO	Post-HBO	
1	7.8 (22.0)	8.4 (23.2)	10.2 (32.1)	TNTC[a]	50–60	2–3	22,500
2	7.9 (23.1)	9.1 (26.8)	10.4 (32.4)	TNTC	45–50	2–3	1,500
3	6.0 (18.2)	7.8 (22.2)	10.4 (33.0)	TNTC	45–50	1–2	4,250
4	12.0 (35.2)	12.5 (37.2)	12.7 (37.5)	1–2	0–1	0–1	nil
5	8.2 (23.2)	9.3 (27.4)	10.1 (31.3)	45–50	5–10	1–2	1,500

[a]TNTC: Too numerous to count. Some data of the remaining 15 cases are incomplete and not included in this table.

beneficial effects which tend to resolve these problems: a) increase of blood and tissue oxygen tensions to improve the hypoxic tissue (14); b) enhancement of wound healing by promoting fibroplasia and angiogenesis which seems to be the dominant mechanism in the repair of radiation-damaged tissue (15); and c) enhancement of leukocyte bacterial killing through production of a group of highly reactive microbicidal agents secondary to the reduction of molecular oxygen (16).

It is very difficult to document the actual amount of blood loss, particularly in hematuria. The only parameters for estimating blood loss are the Hb and Hct levels, routine urinalysis, and the total amount of blood transfused to maintain the level of Hb above 10.0 g/dl. From our data before, during, and after HBO therapy (Table 2), we think HBO therapy contributes to the control of hematuria in radiation cystitis by gradual healing of mucosal wounds of the urinary bladder. The improvement in cystoscopic findings (Fig. 2) also confirms these results. Whether HBO may enhance vesicourethral compliance to improve urinary frequency needs further study of the urodynamic changes that follow HBO. Only one patient had a poor outcome and that was probably due to the underlying DM and cirrhosis of the liver, which compromised wound healing.

Considerable interest has been voiced within the medical community as to the relationship between HBO and malignant tumor. Several reports (17–20) suggest that HBO has no significant effect on promoting tumor growth. We conclude that HBO therapy should be considered an effective and safe treatment for hemorrhagic radiation cystitis.

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