



The Impact of Hyperbaric Oxygen Therapy on Pain Management in Cervical Squamous Cell Carcinoma

Shahram Ghayomi ¹, Reza Eslami ¹, Mohamad Karim Heravi Bujabadi ¹, Mahboubeh Alidoost ², Pedram Neshati ¹, Mehrzad MohsseniPour ^{3,*}

¹ Department of Hyperbaric Medicine, Besat Hospital, Tehran, Iran

² Department of Nursing and Midwifery, Islamic Azad University, Tehran, Iran

³ Department of Microbes, Infection and Microbiomes, University of Birmingham, Birmingham, United Kingdom

*Corresponding Author: Department of Microbes, Infection and Microbiomes, School of Infection, Inflammation and Immunity, College of Medicine and Health, University of Birmingham, Birmingham, United Kingdom. Email: mohsenipour_mehrzad@yahoo.com

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Abstract

Introduction: Radiation therapy is an established treatment for gynecological cancers but may cause delayed radiation injuries, including pelvic soft-tissue necrosis and severe pain. Pelvic radiation-related genitourinary complications occur in 17%–40% of women with cervical cancer. Hyperbaric oxygen therapy (HBOT) is used to treat delayed radiation injuries by improving tissue oxygenation and blood supply; however, its potential role in reducing severe pelvic radiation-associated pain is less well characterized.

Case Presentation: A 51-year-old woman with cervical squamous cell carcinoma developed extensive pelvic radiation-associated necrosis, fistulization, and debilitating pelvic pain 25 months after radiotherapy. Her pain was rated 9/10 on the Numerical Rating Scale (NRS), was associated with substantial functional impairment and 2 previous suicide attempts, and required treatment with oral oxycodone. She underwent 30 HBOT sessions, administered once daily at 2.5 - 2.8 atmospheres absolute for 60 - 75 minutes per session. By the 15th session, her pain had decreased to an NRS score of 5/10, allowing her to resume daily activities and discontinue oral oxycodone. By the 30th session, her pain had further decreased to an NRS score of 3 - 4/10. Gynecological examination showed resolution of the previously observed necrotic tissue, except for a small mucosal area that had not yet been replaced by normal tissue.

Conclusions: This case highlights the potential value of HBOT in promoting healing of radiation-associated pelvic tissue injury and reducing severe pain and its associated functional and psychosocial burden. Further studies are needed to determine whether this analgesic benefit is reproducible in patients with radiation-associated pelvic pain.

Keywords: Cancer Pain Control, Hyperbaric Oxygen Therapy, Case Report

1. Introduction

Cervical cancer is among the most prevalent cancers in women, accounting for approximately 600,000 new cases worldwide annually (1). Radiation therapy is a well-established treatment modality for gynecological cancers; however, radiation-related complications, including delayed radiation injuries, may occur (2). Key consequences of radiation therapy include cellular hypoxia, hypocellularity, and hypovascularity (3). Vascular damage is primarily characterized by obliterative endarteritis (4). The fibroatrophic effect is another

important mechanism of injury in severely damaged irradiated tissues; together with vascular damage, it can lead to diffuse tissue necrosis (5).

Hyperbaric oxygen therapy (HBOT) is widely recommended for delayed radiation injuries, including osteoradionecrosis, because it enhances blood supply and mitigates tissue hypoxia (6). Marx et al. advocated the use of HBOT in severely irradiated tissues to promote neovascularization and increase vascularity and cellularity in hypoxic tissues (7). Although most reports of HBOT for late radiation tissue injury have focused on tissue healing and resolution of radiation-associated complications,

symptomatic outcomes are also clinically important. Cancer- and treatment-related pain is a multidimensional condition involving nociceptive, neuropathic, inflammatory, and central mechanisms, and persistent severe pain can substantially impair physical function and psychological well-being (8). In this case, severe pelvic pain was the dominant clinical problem, substantially limiting daily activities, necessitating opioid treatment, and occurring in the context of 2 suicide attempts. This case is therefore significant not only for the improvement in radiation-associated necrosis but also for the objectively documented reduction in pain and the discontinuation of opioid therapy during HBOT. We present a case of successful HBOT treatment in a 51-year-old woman with cervical squamous cell carcinoma and a history of radiation therapy, focusing on its role in alleviating her pain.

2. Case Presentation

A 51-year-old woman with a history of cervical squamous cell carcinoma was referred to our clinic for treatment of radiation-associated tissue necrosis and severe pelvic pain. Three years earlier, she had reported vaginal discharge followed by vaginal bleeding during intercourse. She consulted a gynecologist, and colposcopic examination revealed necro-inflammatory tissue. Subsequent abdominopelvic ultrasonography showed a 20 × 30 mm heterogeneously enhanced echogenic lesion on the anterior cervical wall, adherent to the bladder. Pelvic magnetic resonance imaging (MRI) confirmed these findings, demonstrating a heterogeneously enhancing cervical mass with craniocaudal, transverse, and anteroposterior diameters of 36, 45, and 35 mm, respectively, necrotic changes, and suspected right-sided parametrial invasion.

A biopsy was performed, and pathology confirmed moderately differentiated squamous cell carcinoma, stage IIB. The patient underwent high-dose-rate external beam radiation therapy (EBRT) combined with brachytherapy (BT), with a total dose of 90 Gray (Gy), including 50 Gy EBRT and 30 Gy BT, delivered in five 6 Gy sessions.

Twenty-five months after radiotherapy, the patient presented with severe pelvic pain and anuria. The pain was debilitating and had led to 2 suicide attempts. She was initially treated with nonsteroidal anti-inflammatory drugs (NSAIDs). Because of the severity of her pain, treatment was escalated to oral oxycodone at 60 mg/day. Imaging revealed a fistula between the bladder and cervix on the anterior cervical wall. Repeat MRI showed a residual mass with central necrosis, and biopsy revealed necro-inflammatory tissue without malignant cells, confirming radiation-associated tissue necrosis. Following a urological

consultation, surgery was ruled out at this stage, and the patient was referred for HBOT.

She underwent 30 HBOT sessions, administered once daily at 2.5 - 2.8 atmospheres absolute (ATA) for 60 - 75 minutes per session. After the fifth session, she developed hemorrhage requiring emergency care and transfusion of 2 units of packed red blood cells, which increased her hemoglobin level from 7 to 9.5 g/dL. Treatment resumed after this interruption. At presentation for HBOT, she reported severe pelvic pain rated 9/10 on the Numerical Rating Scale (NRS). The pain substantially impaired her daily activities and had been associated with 2 suicide attempts. Initial NSAID therapy had been insufficient, and oral oxycodone had subsequently been required. Her pain progressively improved during HBOT. By the 15th session, the NRS score had decreased to 5/10, with sufficient functional improvement to allow her to resume daily activities, and oral oxycodone was discontinued. By completion of 30 sessions, the NRS score had further decreased to 3 - 4/10. Although the pain had not completely resolved, this reduction represented a substantial improvement from baseline. Gynecological examination also showed resolution of the necrotic tissue, except for a small mucosal area that had not yet been replaced by normal tissue. The clinical course and changes in pain intensity during HBOT are summarized chronologically in [Table 1](#).

3. Discussion

Cancer pain is a complex condition involving nociceptive, neuropathic, inflammatory, and central mechanisms (8). Opioids remain the mainstay of therapy for moderate to severe cancer pain (9), whereas refractory cancer pain may require multidisciplinary and interventional approaches (10). Recent evidence also highlights an association between inadequately managed pain and suicidal thoughts in patients with cancer (11). In patients with late radiation tissue injury, HBOT has demonstrated benefits for several gynecological radiation-related complications; however, the quality of the available evidence remains limited, and detailed pain outcomes are inconsistently reported (12).

Radiation therapy is a cornerstone of treatment for various gynecological cancers; however, it is associated with complications, including radiation injury (13). These injuries are classified as acute, subacute, and delayed complications (14). The mechanisms underlying delayed radiation injuries remain incompletely understood, but proposed factors include vascular damage, leakage of bioactive substances such as fibrogenic cytokines, and the fibroatrophic effect (5).

Table 1. Chronological Timeline of the Patient's Clinical Course, Pain Intensity, and Response to Hyperbaric Oxygen Therapy ^a

Time/Event	Clinical Course
Diagnosis	51-year-old woman diagnosed with moderately differentiated cervical squamous cell carcinoma, stage IIB.
Radiotherapy	EBRT plus brachytherapy.
Approximately 25 months after radiotherapy	Severe pelvic pain and anuria developed. Imaging demonstrated a bladder-cervical fistula and residual necrotic tissue. Biopsy showed necro-inflammatory tissue without malignant cells.
Pain burden	NRS 9/10; severe functional impairment and 2 suicide attempts. NSAIDs were insufficient, and oral oxycodone was initiated.
HBOT initiated	30 sessions, administered once daily at 2.5 - 2.8 ATA for 60 - 75 minutes.
HBOT session 5	Hemorrhage requiring emergency management and transfusion of 2 units of PRBCs; treatment subsequently resumed.
HBOT session 15	NRS decreased to 5/10; the patient was able to resume daily activities; oral oxycodone was discontinued.
HBOT session 30	NRS 3 - 4/10; gynecological examination showed resolution of necrotic tissue except for a small mucosal area that had not yet been replaced by normal tissue.
Discharge/follow-up	Discharged after treatment. The long-term durability of pain improvement could not be assessed because follow-up at the treating center was discontinued.

^a Abbreviations: ATA, atmospheres absolute; EBRT, external beam radiation therapy; HBOT, hyperbaric oxygen therapy; NRS, Numerical Rating Scale; NSAIDs, nonsteroidal anti-inflammatory drugs; PRBCs, packed red blood cells.

Hyperbaric oxygen therapy has recently emerged as a valuable adjunctive treatment for managing late complications of radiation therapy (15). It involves breathing pure oxygen under elevated atmospheric pressure, above 1.4 ATA, within a specialized chamber (16). A key mechanism is the induction of neovascularization in hypoxic tissues. Goldstein et al. demonstrated that HBOT stimulates stem cell mobilization through the nitric oxide pathway, with histological evidence of increased cellular density in patients with mandibular osteoradionecrosis treated with HBOT (17).

Pelvic radiation therapy for cervical cancer is associated with genitourinary complications in approximately 17% - 40% of cases (18). Tissue necrosis is an important late complication of radiation therapy (19). Studies support HBOT as a treatment for delayed radiation injuries, particularly radiation-associated necrosis, with level B evidence for its efficacy (20). Recent evidence supports the use of HBOT to alleviate late radiation tissue injuries, highlighting its potential as a complementary treatment in carefully selected patients (21). Although mandibular osteoradionecrosis is a well-documented indication for HBOT, with substantial evidence supporting its effectiveness (22, 23), comparatively fewer studies have evaluated its use in pelvic radiation-associated necrosis (24). Hyperbaric oxygen therapy has shown promise in managing delayed radiation-induced necrosis by mitigating disease progression and reducing the need for additional interventions (25).

3.1. Pain Relief and Opioid Discontinuation

During HBOT, the patient experienced a substantial improvement in severe pelvic pain. Her initial NRS score was 9/10 despite analgesic treatment with oral oxycodone.

By the 15th session, the score had decreased to 5/10, and she was able to resume daily activities. Oral oxycodone was discontinued at that point. After 30 sessions, the NRS score had further improved to 3 - 4/10, representing a reduction of 5 - 6 points from baseline, although pain was not eliminated. This reduction was particularly important because severe pelvic pain was associated with substantial functional impairment and 2 previous suicide attempts. Opioids remain an established treatment for moderate to severe cancer pain, but patients with complex or refractory pain may require additional or alternative approaches for adequate symptom control (9). In this case, discontinuation of oxycodone following improvement in the underlying pelvic condition was an important clinical outcome in addition to the observed tissue healing. However, this observation should be interpreted cautiously. As this is a single case report, the observed pain reduction cannot establish that HBOT directly caused the analgesic effect. Several factors could have contributed, including resolution of the underlying radiation-associated tissue injury, concurrent supportive care, and the natural course of the condition. The close temporal association between HBOT and pain improvement, together with functional improvement and opioid discontinuation, provides a rationale for further investigation of pain outcomes in patients receiving HBOT for pelvic radiation tissue injury.

3.2. Psychosocial Significance

The psychosocial aspect of this case is important. Before HBOT, severe pelvic pain contributed to substantial functional impairment and was temporally associated with 2 suicide attempts. Pain in patients with cancer is not solely a physical symptom but may interact with psychological

distress, anxiety, depression, and suicidal thoughts. Recent evidence suggests an association between inadequately managed cancer pain and suicidal thoughts, emphasizing the importance of pain assessment and psychosocial support in oncology care (11). For patients with such debilitating pain, substantial pain reduction may provide benefits beyond analgesia by restoring function and reducing an important contributor to psychological distress. Hyperbaric oxygen therapy should not, however, be interpreted as a psychiatric or suicide-prevention intervention in this case. Its indication was the treatment of delayed radiation-associated tissue injury. The psychosocial significance of the observed outcome lies in the indirect benefit that substantial pain reduction and improved function may provide in a patient with previous pain-associated suicidal behavior.

In this report, we successfully managed the late adverse effects of radiation therapy in a patient with cervical squamous cell carcinoma and extensive tissue necrosis using HBOT. During treatment, the patient experienced minor side effects, including mild ear pain. She also experienced significant blood loss, although whether the hemorrhage was directly related to HBOT remains unclear.

Given the high rate of complications, particularly late adverse effects of radiation therapy, further studies are warranted to better define the efficacy of HBOT in controlling pain and reducing tissue necrosis in these patients.

Footnotes

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