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Case Report

A Case of Radiation-Induced Lumbosacral Radiculoplexy Responding to Hyperbaric Oxygen Therapy

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Abstract

With modern radiation delivery techniques and dosing, radiation-induced peripheral neuropathy is an uncommon side effect of radiation therapy. Occurring most often as brachial plexus injury in women receiving adjuvant treatment for breast cancer, the annual incidence is less than 1%. Greenfield and Stark first reported on radiation-induced neuropathy of the lower limb in 1948, describing a case series of three patients treated with retroperitoneal external beam radiation after radical orchiectomy and retroperitoneal lymph node dissection for testicular non-seminomatous germ cell tumors. This case report discusses a patient who developed radiation-induced lumbosacral radiculoplexy after adjuvant treatment for stage 1S testicular seminoma, then experienced clinical and myogram-proven symptom improvement after a series of thirty treatments with hyperbaric oxygen therapy. Few prospective trials have been conducted examining the use of hyperbaric oxygen for late neurologic side effects of radiotherapy, and it is generally used in concert with other treatments or when the neuropathy has proven resistant to other available treatment strategies.

Keywords: Radiation-Induced Peripheral Neuropathy; Hyperbaric Oxygen Therapy; Lumbosacral Radiculoplexy

Introduction

Radiation-induced peripheral neuropathy of the lower limb was first described in 1948 by Greenfield and Stark, with a report of three patients with testicular non-seminomatous germ cell tumors treated with adjuvant retroperitoneal external beam radiation after radical orchiectomy and retroperitoneal lymph node dissection [1]. The pathophysiology for radia-

tion-induced nerve injury is not fully known but likely related to a stepwise progression from chronic inflammation and tissue hypoxia to active fibrosis, finally progressing to fibroatrophy and necrosis. While modern radiation therapy methods and doses minimize damage to nerve roots, patient-related risk factors include very young or advanced age, obesity, high blood pressure, diabetes mellitus, preexisting peripheral neuropathy, arteritis, or collagen vascular disease, dyslipidemia, smoking, and alcohol use [2].

Treatment strategies for radiation-induced peripheral neuropathy have included managing symptoms, controlling comorbid conditions (diabetes, hypertension), ceasing aggravating activities (smoking, alcohol use), hyperbaric oxygen therapy, and the use of medications such as clondronate, corticosteroids, and pentoxifyllin-tocopherol [2-4]. There are few prospective trials examining the use of hyperbaric oxygen therapy for late neurologic side effects of radiation therapy, and results of these have been equivocal [2, 3, 5]. In general, hyperbaric oxygen therapy is used in concert with other treatments or when the neuropathy has proven resistant to other treatments.

Herein, we report a case of radiation-induced lumbosacral radiculoplexy occurring after adjuvant treatment for stage 1S testicular seminoma, with clinical and myogram-proven improvement after a series of treatments with hyperbaric oxygen therapy.

Case Report

The patient is a 33 year old Caucasian male who originally presented in December 2007 after noticing a non-tender mass in his right testicle. A testicular ultrasound was ordered and concerning for a solid tumor. Serum beta human chorionic gonadotropin (beta-hCG) and alpha fetoprotein (AFP) were within normal limits, however serum lactate dehydrogenase (LDH) was elevated approximately four times the upper limit of normal at 801 international units per liter (IU/L). Preoperative imaging (chest radiograph, computed tomography of the abdomen/pelvis) were unremarkable except for slightly enlarged paracaval and aortocaval lymph nodes measuring 8-11 millimeters (mm) in size.

He underwent radical right orchiectomy in January 2008. Pathology revealed a tumor almost 9 centimeters (cm) in size exhibiting pure seminoma histology. Surgical margins were negative and there was no capsular invasion. Post-operatively, serum beta-hCG and AFP remained normal, and LDH decreased to 261 IU/L after 10 days. By 15 days after surgery, serum LDH had normalized to 132 IU/L. Final pathologic staging was stage 1S, T1N0M0S2 testicular seminoma.

The patient was originally seen by radiation oncology in February 2008 to discuss adjuvant external beam radiation therapy. By computed tomography (CT) imaging he did have a slightly enlarged para-aortic lymph node, however it was not technically pathologic in size or appearance. In addition, the patient's serum LDH returned to normal after orchiectomy, suggesting resection of all gross disease. Though treatment options for early stage seminoma include observation or adjuvant treatment with either radiation or chemotherapy, with adjuvant treatment the relapse free and overall survival for early stage seminoma approaches 100% [6-8]. Given the 10-25% incidence of occult para-aortic lymph node involvement in testicular seminoma at the time of diagnosis, the decision was made to treat the patient conservatively as a stage IIA with the expectation of a high cure rate. In addition, the large size of the primary tumor (9.0 cm) served as a negative prognostic factor for future recurrence [9].

The risks, benefits, and alternatives to adjuvant radiation therapy in this context were discussed in detail with the patient and informed consent was obtained. He returned for CT simulation in March 2008 after completion of elective sperm banking. The radiation fields included the pelvic and para-aortic lymph nodes with appropriate margin to cover patient motion and daily set up error, with daily 150 centigray (cGy) fractions to a total dose of 2,550 cGy. Given the potential benefit of recurrence prevention and low mortality, an additional three fractions of 150 cGy/fraction were delivered to the enlarged para-aortic node, for a total dose of 3,000 cGy.

Radiation therapy was delivered via linear accelerator using 10 MV photons and ventrodorsal opposing fields. He completed treatment as planned with no breaks required and experienced only mild fatigue, nausea, loose stools and anxiety intermittently during treatment. However, at a follow-up appointment nine months after the completion of radiation therapy, he reported about three weeks of low back pain as well as an additional two-month history of lower extremity weakness and paresthesias. Physical exam was significant for mild tenderness to palpation over the spinous processes in the L3-4 region. He was unable to stand on his toes on either foot due to weakness, and strength was rated 5/5 in the other muscle groups of the bilateral lower extremities. Imaging and lab studies were negative for any recurrence of primary disease.

The patient was evaluated by neurology with history and physical exam, magnetic resonance imaging (MRI), and electromyogram and nerve conduction studies (EMG/NCS). MRI of the lumbosacral spine was normal and EMG/NCS was consistent with a chronic lumbosacral polyradiculopathy with probable plexopathy. There was no myokymia. The patient was ultimately diagnosed with radiation-induced radiculoplexopathy. Though he had some improvement in symptoms with physical therapy, he was referred for multiple treatments with hyperbaric oxygen from June to July 2009, completing 30 sessions of 90 minutes each at 2.5 atmospheric pressure (atm) and

100% oxygen. At follow up in July 2009, he noted substantial improvement in his back pain and lower extremity weakness. Repeat EMG/NCS in November 2009 showed some improvement in the sensory changes with evidence of reinervation, but motor studies remained largely unchanged. At last follow up, five years after the completion of radiation therapy, there was no evidence of disease recurrence, with stabilized neurological function.

Discussion

Radiation-induced plexopathy is a rare occurrence and most often associated with injury to the brachial plexus in women receiving adjuvant radiation in breast cancer treatment, with an annual incidence of < 1% using modern radiation techniques. Lower limb radiation-induced peripheral neuropathy is more rare, and first described in 1948 in a series of three patients treated with testicular irradiation [1]. Maier and colleagues published a larger case series in 1969, in which 15 cases of radiation myelitis were described in patients treated for testicular tumors [10]. A Norwegian retrospective study from 2007 examined 346 patients diagnosed with stage I or IIA seminoma who received adjuvant radiation therapy as their only treatment after orchiectomy. Of these, only 11 patients (3.2%) had neurological symptoms related to radiotherapy. Retrospective analysis concluded that motor impairment was related to higher radiation doses (p=0.02), as four men who received doses of 36-40 Gray (Gy) had motor symptoms lasting at least one year whereas seven men treated with lower doses of 25.2 – 36 Gy had sensory symptoms which resolved after 1-3 months [11]. More recently, in 2012, Delanian and colleagues published a review of 75 previously published cases of lower limb radiation-induced neuropathy. Fifty-four patients had been treated for testicular cancer, with total doses ranging from 30 – 59 Gy. Neurologic symptoms occurred anywhere from 0.4 – 25 years after completion of radiation therapy [2].

A literature review identified only one randomized study regarding the use of hyperbaric oxygen in the treatment of radiation-induced plexopathy. In 2001, Pritchard et al conducted a phase II, double-blinded randomized study examining the effect of hyperbaric oxygen therapy in 34 patients with radiation-induced brachial plexopathy. At the end of the trial, there was no evidence to suggest hyperbaric oxygen therapy slowed or reversed radiation-induced brachial plexopathy, although in two individuals, neurophysiological testing suggested an improvement in warm sensory threshold [3].

Also in 2001, Carl et al prospectively examined the effects of radiation therapy on 32 patients with symptomatic breast edema following lumpectomy and radiation, as compared to 12 control patients. Their results found that hyperbaric oxygen therapy significantly reduced pain, edema, and erythema scores as compared to untreated controls (p < 0.001), with no effect on fibrosis or telangiectasia. However, other than pain, these women were not experiencing any other neurological complaints [5].

Bui et al conducted a retrospective analysis of 45 patients with late side effects due to radiation therapy. Thirty-seven of these patients had symptoms that had failed previous therapies. Their data found a high response rate to hyperbaric oxygen therapy for patients with osteoradionecrosis (81%), cystitis, and proctitis (83%), however low response rates for patients with salivary (11%), neurologic (17%), laryngeal (17%), and upper gastrointestinal symptoms (22%) [12]. However, patients with neurologic symptoms made up only a small part of the population analyzed (n = 6), and the nature of the neurological symptoms was not detailed.

In 2002, Feldmeier et al conducted a systematic literature review examining the evidence for hyperbaric oxygen therapy in the treatment of radiation-induced injuries. Fourteen publications were examined for the use of hyperbaric oxygen therapy for patients with neurologic symptoms, including radiation myelitis of the spinal cord, radiation necrosis of the brain, optic nerve injury, and brachial plexopathy [13]. For patients with brachial plexopathy, this paper only included findings from the 2001 Pritchard study, and the level of evidence for use of hyperbaric oxygen therapy for brachial plexopathy was designated “indeterminate”.

In conclusion, this patient was treated successfully with adjuvant radiation therapy for stage 1S testicular seminoma, however developed lumbosacral radiculoplexy approximately seven months after treatment. As no randomized trials have been conducted examining the effect of hyperbaric oxygen therapy on radiation-induced lumbosacral radiculoplexy, and since no clear morbidity has been shown to occur following hyperbaric oxygen therapy in the treatment of plexopathy, this treatment modality was explored in this patient’s care. He clinically responded to multiple hyperbaric oxygen treatments, and had evidence of improvement on EMG/NCS. At last follow-up five years after completion of therapy, there was no clinical or radiographic evidence of either local recurrence or distant metastasis, and his neurological symptoms had continued to improve.

Ideally, further randomized, blinded, prospective trials examining the benefits of hyperbaric oxygen therapy in the treatment of radiation-induced neurologic side effects would be conducted to help guide treatment recommendations in those patients unfortunate enough to develop this rare side effect. Due to the low incidence of radiation-induced peripheral neuropathy and plexopathy, adequate patient enrollment would prove challenging. In addition, the equivocal results of the sole randomized study examining this question, and indeterminate and negative results of other reviews, could make research

funding for this topic limited. Until more data emerges, use of hyperbaric oxygen therapy as a treatment modality for radiation-induced neurologic sequelae will likely remain as it is today, either as part of a multi-modality approach or as an option for those with symptoms resistant to other known therapies.

Conflicts of Interest Notification: None

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