

toma, unlike solitary myeloma, advances to multiple myeloma only in a minority of cases.³ There are six cases of primary pulmonary plasmacytoma in which the M-protein spike was present. The M-protein level is directly related to tumor burden and clinical course.⁴ The M-protein component usually consists of Ig G κ chains.² This case is the third in which the patient's M-protein level returned to normal after resection. Diagnosis is usually made after the resection of the tumor.³ After resection, immunohistochemical markers are essential to identify monoclonal plasma cells. Negative results of a postoperative myeloma survey, and negative results of testing a bone marrow biopsy specimen are essential for ruling out multiple myeloma.

The treatment for primary pulmonary plasmacytoma is usually resection. Our patient, like the majority of other patients who have undergone resections (14 of 23 cases), was considered to be treated and is not receiving adjunctive chemotherapy or radiation.^{2,3} Two patients have received surgery and radiation therapy. One patient has received surgery and chemotherapy. Three patients received radiation therapy and chemotherapy. One patient received radiation therapy only. One patient received chemotherapy only. There is no difference in survival among any of these treatment modalities.¹ The 2-year and 5-year survival rates are 66% and 40%, respectively.² Two patients have been reported to survive for 9 years, and two patients have been reported to survive for > 20 years.²

This case is unique in the presentation of renal failure with monoclonal gammopathy, and a negative result for the initial multiple myeloma investigation.

REFERENCES

- 1 Wiltshaw E. The natural history of extramedullary plasmacytoma and its relation to solitary myeloma of bone and myelomatosis. *Medicine (Baltimore)* 1976; 55:217-238
- 2 Koss MN, Hochholzer L, Moran CA. Pulmonary plasmacytomas: a clinicopathologic and immunohistochemical study of five cases. *Ann Diagn Pathol* 1998; 2:1-11
- 3 Joseph G, Pandit M, Korfhage L Primary pulmonary plasmacytoma. *Cancer* 1993; 71:721-724
- 4 Salmon SE. Immunoglobulin synthesis and tumor kinetics of multiple myeloma. *Semin Hematol* 1973; 10:135-147

Pulmonary Edema Associated With Hyperbaric Oxygen Therapy*

Lindell K. Weaver, MD, FCCP; and Sue Churchill, APRN-NP

We report three cases of pulmonary edema associated with hyperbaric oxygen therapy, including one fatality. All three patients had cardiac disease and reduced left ventricular (LV) ejection fractions (EFs). Two patients had diabetes, and one patient had severe aortic stenosis. Hyperbaric oxygen therapy may contribute to pulmonary edema by increas-

ing LV afterload, increasing LV filling pressures, increasing oxidative myocardial stress, decreasing LV compliance by oxygen radical-mediated reduction in nitric oxide, altering cardiac output between the right and left hearts, inducing bradycardia with concomitant LV dysfunction, increasing pulmonary capillary permeability, or by causing pulmonary oxygen toxicity. We advise caution in the use of hyperbaric oxygen therapy in patients with heart failure or in patients with reduced cardiac EFs.

(*CHEST* 2001; 120:1407-1409)

Key words: adverse effects; heart failure; hyperbaric oxygen; pulmonary edema; risk

Abbreviations: AMI = acute myocardial infarction; atm abs = atmospheres absolute; EF = ejection fraction; HR = heart rate; LV = left ventricular; RR = respiratory rate

Pulmonary edema is a rare complication of hyperbaric oxygen therapy.^{1,2} Abel et al¹ estimate the incidence of pulmonary edema associated with hyperbaric oxygen therapy at 1 in 1,000, and Riddick² suggested that patients with reduced cardiac ejection fractions (EFs; < 40%) should not receive hyperbaric oxygen therapy because of the risk of acute pulmonary edema. Details of these cases were not presented.^{1,2} We have observed three cases of pulmonary edema associated with hyperbaric oxygen therapy in 1,028 patients, who collectively represent 13,658 hyperbaric oxygen exposures. The etiology of pulmonary edema in patients treated with hyperbaric oxygen is unknown. The purpose of this report is to present information about these three cases, to raise awareness that selected patients treated with hyperbaric oxygen may be at risk for acute pulmonary edema, and to explore possible pathophysiologic mechanisms.

CASE REPORTS

Case 1

A 52-year-old woman with insulin-dependent diabetes mellitus for 20 years, renal insufficiency, a history of acute myocardial infarction (AMI) requiring coronary artery bypass grafting 14 years previously, and a history of acute pulmonary edema had a nonhealing ischemic plantar wound. One year earlier, her EF was 0.45 with mild-to-moderate global hypokinesia. Her pre-hyperbaric oxygen therapy heart rate (HR) was 78 beats/min, BP was 130/80 mm Hg, and respiratory rate (RR) was 18 breaths/min. After 24 min at 2.0 atmospheres absolute (atm abs), 100% oxygen, she complained of feeling hot and short of breath and was decompressed. As the patient exited the chamber, she had breathlessness and tachypnea with bibasilar inspiratory and expi-

*From the Department of Hyperbaric Medicine, LDS Hospital, Salt Lake City, UT.

Presented as an abstract at the Annual Scientific Meeting of the Undersea and Hyperbaric Medical Society, Boston, MA, June 26-29, 1999.

Manuscript received December 12, 2000; revision accepted April 4, 2001.

Correspondence to: Lindell K. Weaver, MD, FCCP, Department of Hyperbaric Medicine, LDS Hospital, 8th Ave, C St, Salt Lake City, UT 84143; e-mail: lweaver@ihc.com

ratory crackles. She was admitted to the ICU and treated with supplemental oxygen and furosemide. Her chest radiograph showed an enlarged azygous vein, interstitial edema, and alveolar infiltrates. She did not have an AMI based on the ECG and creatinine kinase levels. Within 2 days, she felt asymptomatic and was discharged home. She was not treated further with hyperbaric oxygen therapy and ultimately required an above-the-knee amputation.

Case 2

A 75-year-old woman with noninsulin-dependent diabetes mellitus for 10 years, anterior wall AMI 3 weeks prior, and an EF of 0.34 without orthopnea or paroxysmal nocturnal dyspnea was treated uneventfully with hyperbaric oxygen therapy for a plantar full-thickness wound and cellulitis until her 14th hyperbaric oxygen treatment. Prior to this hyperbaric oxygen treatment, her HR was 104 beats/min, BP was 96/54 mm Hg, and RR was 14 breaths/min. After 40 min of breathing 100% oxygen at 2.4 atm abs, she developed shortness of breath, cough, tachypnea, tachycardia, ashen color, and diaphoresis. After hyperbaric oxygen therapy, her HR was 140 beats/min, BP was 126/80 mm Hg, RR was 25 breaths/min, and she had bilateral rhonchi. When breathing room air, her arterial blood gas values were as follows: pH, 7.40; PaCO₂, 38 mm Hg; PaO₂, 37 mm Hg; and arterial oxygen saturation, 0.67. Upright posture, supplemental oxygen (15 L/min via nonrebreather face mask), and sublingual nitroglycerine treatment improved her symptoms. She was admitted to the ICU. Chest radiography showed bilateral alveolar and perivascular infiltrates. Her EF was 0.30, with an anterolateral infarct and apical aneurysm, although she did not have an AMI based on results of ECG and creatinine kinase criteria. She excreted 2 L of urine and improved. Her foot wound healed without additional hyperbaric oxygen therapy.

Case 3

A 77-year-old woman who had an AMI 7 years previously was treated with hyperbaric oxygen for chronic chest wounds following chest radiotherapy for breast carcinoma. She was ambulatory, walking approximately 2 miles per day, including up stairs, without dyspnea. She had no clinical manifestations of heart failure. During her third hyperbaric oxygen treatment (2.4 atm abs for 90 min), she complained of feeling hot, developed a nonproductive cough 10 min prior to the scheduled treatment conclusion, and required urgent decompression. On removal from the chamber, her HR was 112 beats/min, BP was 138/82 mm Hg, RR was 38 breaths/min, and arterial oxygen saturation was 0.80, which increased to > 0.90 with supplemental oxygen. Over the next 2 h, she improved and was discharged home. She was referred subsequently to a cardiologist, who diagnosed severe calcific aortic stenosis (transaortic gradient, 36 mm Hg; aortic valve area, 0.58 cm²). Her EF was 0.50, and she was advised to have aortic valve replacement surgery, but only after resolution of her chest wounds, which required a preoperative course of hyperbaric oxygen therapy. Hyperbaric oxygen treatment was resumed 1 month after her initial three treatments. The patient remained functional, ambulating as before, and was able to sleep and rest in the supine position. Her HR was 104 beats/min, BP was 130/90 mm Hg, and RR was 24 breaths/min. The first treatment of the second course was decreased from 2.4 to 2.0 atm abs. Immediately following a routine decompression from her second (of the second course) hyperbaric oxygen treatment (2.0 atm abs for 90 min), she developed tachypnea, dyspnea, and cough. Chest examination revealed rales and respiratory distress. She was administered 30 mg of furosemide IV immediately and

supplemental oxygen. Despite intervention, she became bradycardic and lost consciousness, necessitating emergent intubation and advanced cardiac life support protocol. An emergent echocardiogram showed no pericardial effusion and no myocardial activity, at which point advanced cardiac life support was terminated and the patient was declared dead. The family declined autopsy.

DISCUSSION

Acute pulmonary edema associated with hyperbaric oxygen therapy is rare. Although others have commented about hyperbaric oxygen precipitating pulmonary edema,^{1,2} heart failure is generally not considered a risk factor in hyperbaric oxygen treatment.³ Our three cases suggest that acute pulmonary edema may complicate hyperbaric oxygen therapy.

Unfortunately, our cases do not elucidate the mechanism(s) leading to pulmonary edema during hyperbaric oxygen, and we have insufficient numbers of cases to prove causality. Noncardiac pulmonary edema is unlikely, or we would expect to observe pulmonary edema in patients without cardiac histories. AMI, drugs that are known to cause pulmonary edema, and iatrogenic fluid overload were excluded as causes of acute pulmonary edema.

Possible mechanisms for hyperbaric oxygen exposure causing pulmonary edema include the following: hyperbaric oxygen exposures cause an increase in systemic vascular resistance⁴ and a reduction in cardiac output⁴; both effects could contribute to pulmonary edema in a patient with compromised cardiac function. Increases in the pulmonary capillary wedge pressure occur with inhalation of high concentrations of normobaric oxygen in New York Heart Association class III or class IV heart failure patients (EF of 15 to 20%).⁵ We assume that the partial pressures of oxygen that patients breathe during hyperbaric oxygen therapy might exaggerate increases in wedge pressure compared to breathing normobaric 100% oxygen, which could result in pulmonary edema. Oxygen radicals could damage the myocardium or interfere with myocyte calcium homeostasis.⁶ Also, oxygen radicals can consume endothelial-derived nitric oxide,⁷ which would decrease diastolic left ventricular (LV) distensibility.⁸ An imbalance in cardiac output between the right and left heart during hyperbaric oxygen therapy mediated by differential sympathetic tone could explain acute pulmonary edema if the right-sided cardiac output exceeded that of the left.¹ However, Haque et al⁵ measured sympathetic tone in muscles and found no change with inhalation of normobaric oxygen.⁵ Nevertheless, it is possible that cardiac sympathetic tone could be affected by hyperbaric oxygen, but not by 100% normobaric oxygen breathing. Hyperbaric oxygen therapy can cause pulmonary oxygen toxicity,⁹ resulting in increased sympathetic tone leading to a decrease in LV compliance while increasing afterload, leading to pulmonary edema. However, pulmonary oxygen toxicity at the hyperbaric oxygen pressures and durations used clinically is not expected.⁹ It is unlikely that hyperbaric oxygen-associated pulmonary edema is caused by similar mechanisms as the development of high altitude-

induced pulmonary edema, which may be caused by hypoxic-induced pulmonary venous constriction and cytokine activation. Echocardiography and/or measurements of cardiac output and intravascular filling pressures in heart failure patients during hyperbaric oxygen treatment might be informative regarding the etiology of pulmonary edema.

These patients were all treated in the single-person, monoplace oxygen-filled hyperbaric chamber (Sechrist; Anaheim, CA), necessitating the patient to be in a supine position, which might increase the risk of pulmonary edema. A difference in the incidence of pulmonary edema associated with hyperbaric oxygen therapy in supine patients vs upright patients is unknown.

Fluid overload could contribute to pulmonary edema associated with hyperbaric oxygen therapy. Death due to postoperative pulmonary edema following excess fluid retention has been reported¹⁰; the authors concluded that careful attention to fluid balance was imperative. Our cases occurred in outpatients who were functional. None of these patients had recent surgery or overt manifestations of heart failure. Nevertheless, if the hyperbaric service recommends hyperbaric oxygen therapy in patients with compromised LV function, careful attention to fluid balance during their course of therapy is advised.

In case 3, it is possible that the patient's history of radiation therapy made her disease process more complicated than just ischemic coronary disease and aortic stenosis. Radiation therapy causes tissues to become hypovascular, hypocellular, and hypoxic.¹¹ This scarred fibrotic tissue might have altered her pericardium or her cardiac function. Furthermore, her aortic stenosis may have contributed to increased afterload to a marginal left ventricle. It is interesting and of concern that this patient had no symptoms compatible with congestive heart failure and had good exercise tolerance.

Acute pulmonary edema is not expected in patients treated with hyperbaric oxygen therapy, yet pulmonary edema may occur in certain patients with heart failure. Most patients treated with hyperbaric oxygen have hypoxic wounds, which often occur in patients with ischemic cardiovascular disease who may be at risk for acute pulmonary edema during hyperbaric oxygen therapy. Unfortunately, we cannot identify in whom or when acute pulmonary edema may develop. Caution is recommended in treating heart failure patients with hyperbaric oxygen.

ACKNOWLEDGMENT: We thank Laura Ogaard for manuscript preparation. We also thank Drs. C. Gregory Elliott, Terry P. Clemmer, and Brent Muhlstein for thoughtful reviews.

REFERENCES

- 1 Abel FL, McNamee JE, Cone DL, et al. Effects of hyperbaric oxygen on ventricular performance, pulmonary blood volume, and systemic and pulmonary vascular resistance. *Undersea Hyperb Med* 2000; 27:67-73
- 2 Riddick MF. Sternal wound infections, dehiscence, and sternal osteomyelitis: the role of hyperbaric oxygen therapy. In: Kindwall EP, Whelan HT, eds. *Hyperbaric medicine practice*. 2nd ed. Flagstaff, AZ: Best Publishing, 1999; 617-640

- 3 Side effects. In: Hampson NB, ed. *Hyperbaric oxygen therapy: 1999 committee report*. Kensington, MD: Undersea and Hyperbaric Medical Society, 1999; 73-75
- 4 Whalen RE, Saltzman HA, Holloway DH Jr, et al. Cardiovascular and blood gas responses to hyperbaric oxygenation. *Am J Cardiol* 1965; 15:638-646
- 5 Haque WA, Boehmer J, Clemson BS, et al. Hemodynamic effects of supplemental oxygen administration in congestive heart failure. *J Am Coll Cardiol* 1996; 27:353-357
- 6 Kaneko M, Beamish RE, Dhalla NS. Depression of heart sarcolemmal Ca²⁺-pump activity by oxygen free radicals. *Am J Physiol* 1989; 255:H368-H374
- 7 Rubanyi GM, Vanhoutte PM. Superoxide anions and hyperoxia inactivate endothelium-derived relaxing factor. *Am J Physiol* 1986; 250:H822-H827
- 8 Paulus WJ, Vantrimpont PJ, Shah AM. Acute effects of nitric oxide on left ventricular relaxation and diastolic dispensability in humans: assessment by bicoronary sodium nitroprusside infusion. *Circulation* 1994; 89:2070-2078
- 9 Clark J, Whelan H. Oxygen toxicity. In: Kindwall EP, Whelan HT, eds. *Hyperbaric medicine practice*. 2nd ed. Flagstaff, AZ: Best Publishing, 1999; 69-82
- 10 Arieff AI. Fatal postoperative pulmonary edema. *Chest* 1999; 115:1371-1377
- 11 Marx RE, Johnson RP. Studies on the radiobiology of osteoradionecrosis and their clinical significance. *Oral Surg* 1987; 64:379-390

Stress Thallium-201 Myocardial Scintigraphy in Patients With Complete Occlusion of the Left Main Coronary Artery*

Takashi Hatori, MD; Takuji Toyama, MD; Tomoyuki Yokoyama, MD; Masashi Arai, MD; Masahiko Kurabayashi, MD; Tsugiyasu Kanda, MD; and Shigeru Oshima, MD

Complete occlusion (CO) of the left main coronary artery (LMCA) is a rare but often fatal condition. The diagnosis is frequently missed because the signs and symptoms are often obscure and diverse. We describe three patients with CO-LMCA who showed unusual myocardial scintigraphic findings. The patients had extensive right-to-left collateral channels and decreased uptake and washout rates at the basal anterior and anterolateral portions of the heart wall during stress thallium-201 scintigraphy. The basal anterior to anterolateral portion of the heart wall is the most distant from the collateral artery and should be the most ischemic area shown during exercise, resulting in this scintigraphic pattern. This scintigraphic finding may be useful for the noninvasive diagnosis of CO-LMCA.

(*CHEST* 2001; 120:1409-1412)

Key words: complete occlusion; left main coronary artery; stress ²⁰¹Tl myocardial single photon emission CT; washout rate

Abbreviations: CO = complete occlusion; EF = ejection fraction; LAD = left anterior descending artery; LCX = left circum-