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Hyperbaric Oxygen Therapy for Severe Ulcerative Colitis

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Abstract
Hyperbaric oxygen therapy has been used to successfully treat perineal Crohn's disease. We describe the first successful use of hyperbaric oxygen therapy in the treatment of ulcerative colitis, refractory to conventional therapies. Therapy consisted of 30 courses of 100% oxygen at a pressure of 2.0 atm absolute. Clinical remission was achieved on the basis of the Truelove–Witts and disease activity index scores. Corticosteroids were successfully tapered off once remission was achieved.
Key Words: Hyperbaric oxygen therapy—Ulcerative colitis—Crohn's disease.

Ulcerative colitis is a chronic disease, characterized by intermittent periods of relapse and remission, which causes ulceration of the colon. Complications include colonic perforation, hemorrhage, pain, and extraintestinal manifestations (e.g., arthritis, skin lesions, and liver disease). Treatment consists of 5-aminosalicylic preparations (oral, topical, or both) for mild to moderate disease and prednisone for more severe disease. Those patients who do not respond to prednisone may require hospitalization or treatment with cyclosporin, methotrexate, or colectomy. Preliminary data suggest that the anticoagulant heparin may have efficacy in the treatment of active ulcerative colitis.[1–4] Although the mechanism for heparin's effect in ulcerative colitis is unknown, it may relate to the increase in the availability of blood and oxygen flow by the prevention of capillary microthrombi.[5–7] Decreased rectal blood flow has been reported in ulcerative colitis.[8]

Several reports have described the use of hyperbaric oxygen therapy in the healing of perineal Crohn's disease involving the colorectum.[9–12] This therapy has been shown to increase the dissolved oxygen content of plasma from 0.32 to 6.8 vol%.[13] This increase in oxygen delivery may be important for the treatment of ischemic disease related to microvessel hypoperfusion. Recent data from both the acetic acid and trinitrobenzesulphonic models of colitis in rats indicated that disease severity could be limited with hyperbaric oxygen treatment (HBOT).[14]

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CASE REPORT

The patient was a 24-year-old man diagnosed with pan-colonic ulcerative colitis at the age of 17 years when he presented with bloody diarrhea. He had two previous hospitalizations for exacerbations of his disease, the most recent of which was 4 years prior. His current exacerbation was of 22 months' duration, and he had remained corticosteroid-refractory over that time period. He had 4 to 10 bowel movements daily and, occasionally, up to 15 daily, approximately 50% with blood. He had significant fatigue, but no fever or arthralgias. He had lost 20 lb over the past 6 months. Abdominal pain was minimal and was more centered in the lower portion. The patient had been taking 20 to 60 mg/d of prednisone over the previous 22 months, with inability to taper; he had taken 40 mg/d for the 3 weeks before hyperbaric therapy, which was continued during treatment. The patient had taken azathioprine (maximum dosage, 100 mg/d) for 3 years, but this was discontinued for unclear reasons 18 months before. 6-Mercaptupurine (100 mg/d) was started 14 weeks before hyperbaric oxygen therapy. The patient had taken mesalamine (4 g/d) for several months as well, and tetracycline (250 mg four times daily for 3 weeks) for corticosteroid-associated acne before hyperbaric oxygen therapy. The patient was afebrile, his height was 180 cm, and his weight was 82 kg. On physical examination there was minimal lower abdominal tenderness and brown, heme-positive stool. The examination was otherwise unremarkable. The Truelove–Witts score was 15,[15] the disease activity index was 9,[16] and the inflammatory bowel disease questionnaire score was 126.[17] Laboratory data included a hemoglobin level of 12.7 g/dL; mean corpuscular volume, 99.1 Fl; white blood cell count, 4.3/mm^3; and erythrocyte sedimentation rate, 17 mm/h. Blood chemistries were normal except for a serum potassium concentration of 3.4 mEq/L (normal, >3.5 mEq/L). Colonoscopy showed endoscopic grade 3–4 (Truelove scale[18]) colitis in the rectum and sigmoid colon with pseudopolyposis, with decreasing severity on a distal-to-proximal gradient. The ascending colon and cecum were endoscopically normal. Multiple biopsies from throughout the colon showed marked distortion of glandular architecture, prominent lamina propria lymphoplasmacytic infiltrates, Paneth cell metaplasia, and numerous multifocal mucosal neutrophilic infiltrates forming numerous crypt abscesses (Figs. 1

and 2, Grade 5 by the Floren criteria[19]). There was extensive mucosal ulceration.

The patient was given 30 courses (2-hour duration) of HBOT on a 5-day per week basis. This consisted of 100% oxygen at a pressure of 2.0 atm absolute delivered in a multiplace hyperbaric chamber (Hyperbaric Oxygen Therapy Systems, National City, CA, U.S.A.). After 20 treatments, the inflammatory bowel disease questionnaire score was 157. Subjectively, the patient noted significant improvement. At the conclusion of HBOT, the patient had achieved two normal bowel movements daily and his Truelove–Witts score was 4, the disease activity index score was 2, and the inflammatory bowel disease questionnaire score was 180. A decrease in the Truelove–Witts score indicates clinical improvement, and an increase in the inflammatory bowel disease questionnaire score indicates quality of life improvement. A flexible sigmoidoscopy showed mild-to-moderate ulcerative colitis (grade 1–2). Histologic examination of biopsy specimens obtained from the rectum was difficult to compare with the baseline specimens because they were small and were artifactually distorted, but subjective comparison with the baseline biopsies indicated a less robust inflammatory response. The hemoglobin level was 13.0 g/dL; mean corpuscular volume, 103.5 Fl; white blood cell count, 4.3/mm^3; and erythrocyte sedimentation rate, 11 mm/h. Corticosteroid (prednisone) weaning was begun immediately after the final hyperbaric treatment by 5-mg weekly increments (2.5-mg weekly increments once 20 mg/d was reached) and the patient remained in clinical remission and devoid of corticosteroids for 2 months until mild diarrhea and associated mild abdominal cramping returned.

DISCUSSION

This case illustrates the potential utility of HBOT in ulcerative colitis, refractory to conventional therapies. Successful treatment with HBOT also suggests a potential role for ischemia/reperfusion injury in the pathogenesis of ulcerative colitis, although the potential immunosuppressive effects of HBOT may also have played an important role. Some investigations in animal models have indicated that HBOT may result in a reduction of B and T lymphocyte populations in lymphoid tissues, which is suggestive of an immunosuppressive effect,[20] although studies have shown the opposite effect.[21] Some investigations have shown that HBOT is associated with an increase in the macrophage release of some inflammatory cytokines,[22] but other have shown decreases.[23] Studies in humans have shown no affect on T lymphocytes or immunoglobulin production, although cytokine production has not been evaluated.[24] Therefore, the effects of HBOT on the immune system remain unclear. A larger case series study is underway.

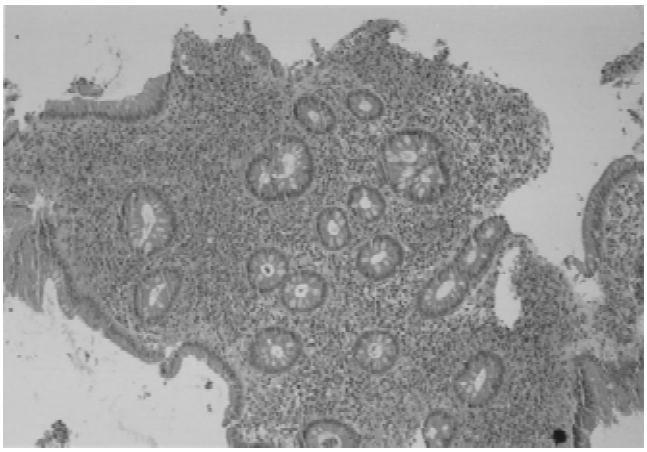

FIG. 1. Low power photomicrograph (original magnification, ×4) of colonic mucosa showing marked glandular distortion and lamina propria and lymphoplasmacytic infiltrates with overlying ulceration.

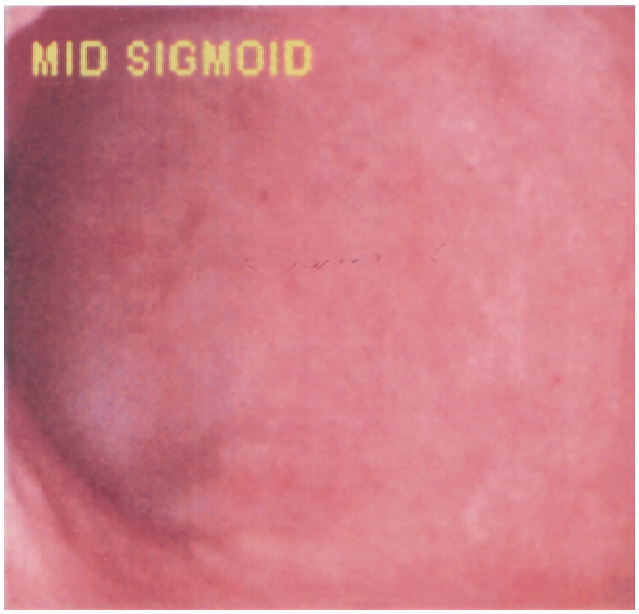

FIG. 2. Endoscopic photograph showing grade 1–2 colitis in the midsigmoid colon (posttreatment).

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