

# Ulcerative Colitis and Sarcoidosis

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## Abstract

A 38-year-old woman with ulcerative colitis subsequently developed sarcoidosis. After ten years of recurrent episodes of colitis, she had presented with respiratory symptoms. The diagnosis of sarcoidosis was confirmed by mediastinal lymph node biopsy. Her respiratory symptoms gradually resolved without any specific treatment. Within the remission period of sarcoidosis, she underwent uneventful subtotal colectomy due to refractory colitis. Alterations in immune function and genetic susceptibility have been suggested to be present in both ulcerative colitis and sarcoidosis. However, the occurrence of both in the same patient has been rare. This is only the nineteenth case reported in the literature.

**Key Words:** Ulcerative colitis, sarcoidosis, autoimmune, human leukocyte antigen.

## Introduction

THE ASSOCIATION of ulcerative colitis and sarcoidosis has been reported in the literature in only eighteen patients (1–9). The authors report another patient who was diagnosed with both conditions. While the sarcoidosis was in remission, she presented with a severe relapse of ulcerative colitis refractory to medical treatment; it subsequently required subtotal colectomy. The relationship between these two diseases is still unclear, but cellular immunity as well as genetic susceptibility may share an important role in the development of both. The course of each disease seems to be independent and unpredictable. Human leukocyte antigen (HLA) analyses were performed to evaluate a possible genetic correlation of both diseases. The results of this evaluation indicated that the patient's genetic patterns differed from those reported previously for other patients with both conditions.

## Case Report

A 38-year-old Caucasian woman, a non-smoker, had a fourteen-year history of ulcerative colitis. At the age of 24, she had first noted abdominal cramps and bloody diarrhea; sigmoidoscopy and biopsy were consistent with the diagnosis of ulcerative colitis. After three months of sulfasalazine and corticosteroid enemas, her

colitic symptoms began to improve. Despite the maintenance dose of sulfasalazine, she continued to experience at least one or two exacerbations per year, which were controlled by increasing the dose of sulfasalazine. She has no familial history of inflammatory bowel disease.

At the age of 34, she developed a chronic productive cough, low-grade fever, and shortness of breath along with her active colitic symptoms. She also experienced a 10 kg weight loss. She had no family history of pulmonary disease or exposure to occupational toxins. Complete blood count and liver function tests were within normal limits. Erythrocyte sedimentation rate was elevated. Sequential chest x-rays revealed an infiltration in the right middle and lower lobes, which progressed to multiple bilateral nodular infiltration, despite treatment with antibiotics for one month. The purified protein derivative (PPD) skin test and serum anti-nuclear antibodies (ANA) were both negative. Liver enzymes which had been elevated returned to normal after 6-mercaptopurine was discontinued. Chest CT scan revealed a slightly enlarged subcarinal lymph node and multiple bilateral pulmonary nodules, the largest of which was in the left mid-lung field and demonstrated an air-bronchogram and a cavitory lesion. Bronchoscopic examination was negative. CT-guided needle biopsy of the right lower lung revealed non-necrotizing granulomas, with numerous histiocytes and some multinucleated giant cells, which was compatible with sarcoidosis. Mediastinoscopic biopsy of the hilar lymph node revealed non-caseating granulomas with Schaumann bodies, also consistent with sarcoidosis. Malignant cells, acid-fast bacilli, and fungi were not seen and acid-

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fast bacilli, yeast, and fungi were not cultured from the tissue. The patient's respiratory symptoms and follow-up chest x-ray improved without specific treatment. Her concurrent, active ulcerative colitis responded to treatment with increased doses of sulfasalazine and corticosteroid enemas. These medications were then reduced to maintenance doses, but three months later she developed a severe exacerbation of her colitis, which required hospitalization and intravenous corticosteroid, cyclosporine and 6-mercaptopurine.

After several mild exacerbations, at age 36 she developed a severe relapse of colitis. Once the diagnosis of toxic colitis was made, high doses of steroids and cyclosporine were administered intravenously, but without a significant improvement. Subtotal colectomy and end ileostomy were performed. Pathology confirmed universal, fulminant, chronic ulcerative colitis with toxic dilatation. The patient recovered and was discharged on postoperative day 7 without complication.

HLA analyses revealed HLA-A2, A28, B44 and HLA-B27. HLA-B8 and DR3 were not found.

### Discussion

Unexplained bronchopulmonary disease associated with inflammatory bowel disease was reported by Kraft et al. (10) in 1976. They described six patients who developed severe, unexplainable bronchopulmonary disease from 3–13 years after the onset of nonspecific inflammatory bowel disease of the colon. Bronchiectasis was identified in four, obstructive disease in five, and chronic bronchitis in all six. Abnormal pulmonary function testing has been reported in patients with ulcerative colitis (11, 12); however, no definitive etiology has been elucidated. In one study, two patients with ulcerative colitis were shown to have nonspecific pulmonary vasculitis (13, 14). Other causes of pulmonary pathology in patients with ulcerative colitis include sulfasalazine-induced lung disease (15).

Sarcoidosis is seen in all races, with a slight female predominance. It is characterized by the presence of T lymphocytes and mononuclear phagocytes, noncaseating granulomas, and cervical lymphadenopathy. While the lung is most commonly affected, other organ systems also may be involved. Papadopoulos et al. (16) reported that there was a greater incidence of autoimmune diseases in patients with sarcoidosis.

These included the autoimmune thyroid disease and polyglandular autoimmune syndrome type 3 (16). They suggested that HLA-linked genetic susceptibility (HLA-B8/DR3) might predispose these patients to the development of autoimmune diseases. Yoshioka et al. reported a patient with ulcerative colitis who subsequently developed sarcoidosis and IDDM (insulin-dependent diabetes mellitus), which has been reported to be associated with HLA-DR2/DR4 (8).

Cox and McCrea (17) also reported a patient who had Sjögren's syndrome, sarcoidosis, and ulcerative colitis, in whom gastric autoantibodies were found. They suggested the more extensive acronym TOASSUC (thyroiditis, other autoimmunity, Sjögren's syndrome and ulcerative colitis).

Cohen and Sahn (18) reviewed five major clinicopathologic categories of respiratory involvement that have been described with ulcerative colitis: (a) airway disease, including subglottic stenosis, chronic bronchitis, chronic bronchial suppuration, bronchiectasis, and chronic bronchiolitis; (b) interstitial lung disease, including bronchiolitis obliterans with organizing pneumonia, unspecified interstitial lung disease, and pulmonary infiltrates and eosinophilia; (c) necrobiotic parenchymal nodules; (d) serositis with pleural or pericardial effusions; and (e) pulmonary vascular disease, including vasculitis and pulmonary embolism. Many patients (43–63%) with ulcerative colitis reported in the literature have had airway disease (19–23), with chronic bronchitis and bronchiectasis being the most common, 21% and 25%, respectively (24).

The association of ulcerative colitis and sarcoidosis has been reported in the literature. Each disease is believed to be mediated by an alteration in the body's immune function, but the definitive etiology still cannot be elucidated. Barr et al. (5) reported a higher frequency of the HLA-B8 and DR3 haplotypes in three of the eight patients (38%) who harbored both diseases. Cottone et al. (24) described the frequencies of these haplotypes in healthy persons to be 28%, while in patients with either ulcerative colitis or sarcoidosis alone it was 21% and 22% respectively. Rubinstein and Baum (6) reported three instances of ulcerative colitis and sarcoidosis appearing together and surmised that a number of immunologic factors may be present in one or both diseases. They speculated that the immunologic responses might be related to enhanced activity of circula-

tory killer and natural killer lymphocytes, an increased number of T helper lymphocytes in sites of disease, and the presence of circulating immune complexes and autoantibodies.

Our patient does not carry HLA-B8/DR3 as described in the previously mentioned reports; however, we have determined that our patient carries HLA-A2, A28, B44 and HLA-B27. The relationship of these findings to proven ulcerative colitis and sarcoidosis in this patient is uncertain. While the pathogenesis of both sarcoidosis and ulcerative colitis is unknown, both conditions may yet be shown to be mediated by some genetic susceptibility in immune responsiveness. Ulcerative colitis and sarcoidosis are sometimes seen in patients who have other autoimmune diseases such as Sjögren's syndrome and autoimmune thyroiditis. The occurrence of sarcoidosis and Crohn's colitis together has been reported as well (25). While increased cellular immunity, circulating immunocomplexes and autoantibodies may play a role in the pathogenesis of both diseases, each disease in our patient followed an independent course.

Our case brings to nineteen the total number of patients who have been reported to have both diseases. The adjusted prevalence rate of ulcerative colitis in Olmsted County, MN on January 1, 1991 was 229 cases per 100,000 (26) and the prevalence rate of sarcoidosis in the United States was 10–40 cases per 100,000 (27). The coexistence of both diseases in the same patient by chance can be calculated from these data to range from 2–9 cases per 10 million people. It would appear that the number of cases in which ulcerative colitis and sarcoidosis coexist in the same patient has not exceeded an association by chance. Such a conclusion necessarily depends on the reliability of the prevalence data in a given population. More data are certainly needed to establish an etiologic association between ulcerative colitis and sarcoidosis in the same patient.

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