Leukocytapheresis in the Treatment of Nasal Crohn’s Disease

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Extraintestinal manifestations of Crohn’s disease are recognized phenomena. Biopsy of intestinal tissue from Crohn’s disease patients may reveal edema of the lamina propria, perivascular inflammation with infiltrates, or noncaseating granulomas with multinucleated Langerhans-type giant cells. Nevertheless, evidence of nasal involvement, which is characterized by chronic mucosal inflammation, obstruction, bleeding, and, occasionally, septal perforation, is extremely rare. To date, only four cases of nasal Crohn’s disease have been reported in the literature. This case report discusses a patient with this extremely rare manifestation of Crohn’s disease and highlights the importance of its inclusion in the differential diagnosis of chronic sinusitis that is nonresponsive to standard therapy.

Case Report

A 54-year-old woman with a history of active Crohn’s colitis presented to her otolaryngologist with a complaint of nasal discharge. She had persistent cough and nasal congestion for several months that was not responsive to several nonprescription medications. She also noted pain, which was localized to the right nasal and infraorbital areas of her face and had increased in intensity over the previous 2–3 weeks, with small amounts of clear nasal discharge.

On physical examination, the patient was normotensive and afebrile, and no facial tenderness or purulent discharge was noted. Her serum chemistries and complete blood count were all within normal limits, and her nasal endoscopy was also normal. Nasal biopsies, however, revealed edema, giant cells, and multiple caseating (Figures 1 and 2) and noncaseating (Figures 3 and 4) granulomas in both the nasal septum and right maxillary sinus. The patient was resistant to treatment regimens of sulfasalazine and 6-mercaptopurine. Upon enrollment in a leukocytapheresis protocol, her congestive symptoms resolved.

Discussion

In a series of 498 patients reviewed by Greenstein and associates, 36% of patients with Crohn’s disease experienced extraintestinal manifestations of the disease.1 Nasal involvement is extremely rare and characterized by chronic mucosal inflammation, obstruction, or bleeding. The differential diagnosis includes Wegener granuloma-
tosis, sarcoidosis, tuberculosis, and sinonasal lymphoma. Biopsy may confirm the diagnosis, regardless of whether ulcerations, edema of the lamina propria, perivascular inflammation with infiltrates, or multinucleated Langerhans-type giant cells are observed. Granulomas may not necessarily be present.\(^2\) The treatment generally consists of oral or systemic steroids, with intervention to relieve obstruction when necessary.\(^3,5\)

To date, only four cases of nasal Crohn’s disease have been reported in the literature.\(^2,4\) All of the patients presented with symptoms consistent with nasal congestion or obstruction. Physical examination findings, however, differed in each case. The first reported case, published in 1985 by Kinnear and colleagues, noted chronic atrophic rhinitis with crusting in a patient with chronic nasal congestion. Biopsy revealed chronic fissuring and deep ulcerations with a chronic cell infiltration and granulomatous formation.\(^4\)

Ernst and coworkers found edema, polyposis, and sinusitis in a 17-year-old girl diagnosed with concurrent peritonsillitis.\(^5\) Although biopsy revealed ulcerations, granulomas were not detected. Similarly, Pochon and associates described rhinorrhea and epistaxis in a 38-year-old man. Although pathologic specimens revealed macrophages with lymphocytic infiltrates, a true granuloma was not visible.\(^3\) Nevertheless, both patients responded to oral steroids.

In 2000, Ulnick and Perkins reported a patient with epistaxis and recurrent nasal stenosis caused by bilateral edema of the nasal septum, with concurrent edema of the epiglottis and false vocal folds. The patient was treated with a combination of laser surgery and 6-mercaptopurine, as well as systemic and topical steroids. This combination therapy caused the remission of symptoms, though they ultimately returned. In this patient, as with the patients discussed previously, biopsy revealed submucosal microabscesses.\(^2\)

Our patient’s symptoms correlated with the previous descriptions of Crohn’s disease of the nasal passages. Nevertheless, physical examination and nasal endoscopy findings were completely normal. There was no evidence of obstruction, edema, or sinusitis, yet biopsies revealed true granulomatous disease.

This case study is the first report of leukocytapheresis in the treatment of nasal manifestations of Crohn’s disease. Leukocytapheresis is a treatment technique involv-
ing the extracorporeal filtration of blood through cellulose acetate beads (Adacolumn, Otsuka), which allows for the adsorption of targeted activated granulocytes, monocytes, and macrophages. Leukocytapheresis has been proposed as an alternative therapy in moderately severe and steroid-refractory ulcerative colitis, as well as Crohn's ileocolitis. Small-scale uncontrolled studies have demonstrated success rates ranging from 25% to 85%, primarily within the ulcerative colitis population. Large-scale studies are currently ongoing to fully assess the clinical effectiveness of the therapy.

**Conclusion**

Crohn's disease of the maxillary sinus is extremely rare. Findings of this condition despite benign physical and endoscopic examinations of the nasal passages suggest that it may be an underreported phenomenon. Leukocytapheresis may be an acceptable therapy for patients with inflammatory bowel disease, though further studies are necessary to elucidate the value of the therapy.

**References**


**Review**

**Nasal Crohn’s Disease/Apheresis**

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Extraintestinal manifestations of inflammatory bowel disease (IBD) are very common and are estimated to occur in 20–36% of patients with Crohn’s disease or ulcerative colitis. The most common sites for extraintestinal manifestations include the joints, skin, mouth, and eyes. As illustrated in the case study by Wiesen and colleagues, extraintestinal manifestations can affect any organ system and cause a tremendous negative impact on the life of a patient. Patients with colonic disease develop extraintestinal manifestations from their disease at an increased rate. In one large series, patients with colonic involvement of their IBD were almost twice as likely to have extraintestinal manifestations compared to patients with isolated small-bowel disease (42% vs 23%).

The exact pathogenesis of extraintestinal manifestations in IBD is unknown. One theory suggests that in genetically susceptible hosts the presentation of luminal antigens from a leaky bowel causes activation of the systemic immune system, resulting in inflammation outside of the bowel. The majority of extraintestinal manifestations such as peripheral arthritis, erythema nodosum, episcleritis, and aphthous stomatitis tends to parallel activity of the luminal disease and resolves once the underlying bowel inflammation improves. However, several extraintestinal manifestations, including axial arthritis, pyoderma gangrenosum, uveitis, and primary sclerosing cholangitis (PSC), can be active even with the remission of underlying IBD. Indeed, PSC can occur even after colectomy. In the patient discussed by Wiesen and associates, the nasal involvement of Crohn’s disease appears to fall into the latter category, as her luminal disease was quiescent at the time of her nasal symptoms.

Treatment for extraintestinal manifestations that are independent of bowel activity can be difficult, as the treating gastroenterologist needs to balance the severity of the underlying IBD and the effects of the extraintestinal manifestations on the patient’s quality of life with the side effects of the medications. Various agents have been utilized, including pain medication (eg, nonsteroidal anti-