Laryngeal Manifestations of Inflammatory Bowel Disease

***,†Elke Loos, *Peter Lemkens, †Vincent Vander Poorten, ‡Evelien Humblet, and *Griet Laureyns,** *‡*Genk and* †*Leuven, Belgium*

Summary: Background. Laryngeal involvement in inflammatory bowel disease is rare. Only 12 cases of laryngeal involvement in Crohn disease have been reported until now. Moreover, only one case of laryngeal manifestations in ulcerative colitis has been reported so far.

Materials and Methods. In this article, we present a patient with ulcerative colitis, who consulted our ear, nose, and throat (ENT) clinic with laryngeal complaints. Furthermore, a review of current literature was performed.

Results. A concise overview of this rare extraintestinal manifestation and other ENT manifestations of inflammatory bowel diseases is provided.

Conclusions. Laryngeal manifestations in inflammatory bowel disease are very rare, but these manifestations should be known by the otorhinolaryngologist.

Key Words: Inflammatory bowel disease–Crohn disease–Colitis, ulcerative–Larynx–Voice.

INTRODUCTION

Inflammatory bowel disease (IBD) is a group of chronic inflammatory disorders involving the gastrointestinal tract, of which the two major types are Crohn disease and ulcerative colitis. Besides the gastrointestinal symptoms, patients with IBD can present with a large variety of extraintestinal manifestations, such as uveitis, arthritis, pyoderma gangrenosum, erythema nodosum, episcleritis and sclerosing cholangitis. Sometimes the extraintestinal manifestations can even present before the onset of gastrointestinal symptoms.[1]

Laryngeal involvement in IBD is very rare. To date, only 12 cases of Crohn disease[2–12] and only one case of ulcerative colitis[13] have been reported. We present a patient with ulcerative colitis suffering from laryngeal manifestations of their disease. Furthermore, a concise literature review is provided to inform otorhinolaryngologists about the existence of this rare entity and other ear, nose, and throat (ENT) manifestations of IBD. To our knowledge, this is only the second case report about laryngeal manifestations in ulcerative colitis.

MATERIALS AND METHODS

A literature review of the PubMed, Cochrane, and EMBASE database was performed. Search terms included ulcerative colitis, Crohn, inflammatory bowel, IBD, Humira®, adalimumab, Imuran®, azathioprine, mesalazine, 5-ASA, larynx, hoarse, voice, Larynge*, Laryngi*, otorhinolaryngolog*, rhinosinusitis, dysphoni*, Aphoni*. The search retrieved 807 results.

All articles about patients with IBD who had laryngeal manifestations were included in this paper. Because of the lack of large case-control studies, we reviewed case reports, editorials, if they included a case report, and case series. Books and opinions were not included. After deduplication and applying the inclusion criteria, 12 articles were selected. Patient demographics, symptoms, clinical examination, histology, and treatment are presented in Table 1.

CASE REPORT

A 23-year-old woman presented at our ENT clinic with recurrent hoarseness, a lump sensation in her throat, a thickened left side of the tongue, and dysphagia for solids. She had no complaints of odynophagia or stridor. She had no relevant medical or family history, did not smoke, and drank two units of alcohol a day.

Clinical examination revealed a thick fibrotic epiglottis (Figure 1), edematous arytenoids, and vocal cord nodules. The patient was started on corticosteroids, but because there was no improvement, a magnetic resonance imaging (MRI) was performed. The MRI demonstrated a nonspecific inflammation of the aryepiglottic folds, epiglottis, and left side of the tongue, suggestive of a nonspecific inflammation or allergy (Figures 2 and 3). Subsequently, a biopsy was taken under general anesthesia. Anatomopathologic examination showed a nonspecific chronic inflammation with lymphocytes and macrophages, but without granulomas. Therefore, the patient was referred to a specialist in systemic diseases and rheumatology. When the patient presented at the rheumatologist, she mentioned that recently she started having bloody diarrhea. Hematologic examination and serology for autoimmune diseases and angiotensin-converting enzyme were normal. The patient was referred to a gastroenterologist for a colonoscopy. This examination revealed a chronic inflammation of the colon. The ileum was completely normal. Biopsies showed crypt abscesses, but no granulomas, suggestive of ulcerative colitis. The patient was started on mesalazine four times a day. Almost all the laryngeal and gastrointestinal complaints resolved with this treatment.

DISCUSSION

Patients with IBD present with a chronic inflammation of the gastrointestinal tract. The inflammation is caused by an excessive

Accepted for publication September 27, 2017.

From the *Department of Otorhinolaryngology—Head and Neck Surgery, Ziekenhuis Oost-Limburg, Genk, Belgium; †Department of Otorhinolaryngology—Head and Neck Surgery, KULeuven, Leuven, Belgium; and the ‡Department of Gastroenterology, Ziekenhuis Oost-Limburg, Genk, Belgium.

Address correspondence and reprint requests to Griet Laureyns, Department of Otorhinolaryngology—Head and Neck Surgery, Ziekenhuis Oost-Limburg, Schiepse Bos 6, 3600 Genk, Belgium. E-mail: Grietlaureyns@hotmail.com

Journal of Voice, Vol. 33, No. 1, pp. 1–6
0892-1997

https://doi.org/10.1016/j.jvoice.2017.09.021

TABLE 1.
Review of Previous Case Reports Demonstrating Patient Demographics, Symptoms, Clinical Examination, Histology, and Treatment

Article	IBD Type	Age	Gender	Symptoms	Clinical Findings	Histology	Treatment	Outcome
Croft et al (1972)	Crohn	27	M	Dysphagia, odynophagia, blood-tinged expectorate	Generalized edema, ulcerations, erythema, and granulation tissue with normal-appearing false vocal folds	/	Systemic corticosteroids	Improvement
Kelly et al (1979)	Crohn	1)22 2)25	(1) F (2) M	(1) Dysphagia, odynophagia, hoarseness (2) Stridor, dyspnea	(1) Cricoarytenoid joint: inflammatory process (2) Extensive edema of the upper airway due to submucosal involvement of the disease	/	(1) Oral steroids (2) Oral steroids	(1) Improvement, but tracheotomy (2) Improvement
Wilder et al (1980)	Crohn	23	F	Sore throat and difficulty in breathing	Chronic inflammatory changes of the epiglottis and aryepiglottic folds	Chronic granulomatous reaction	Corticosteroids, sulfasalazine, Flagyl, regular diet	Only after dietary changes improvement
Lemann et al (1987)	Crohn	24	F	Dysphagia, cough, and mild dyspnea	Marked edema of the nasopharynx, epiglottis, arytenoids, and true vocal cords	Chorionic mononuclear infiltrate with a few tuberculoid granulomas made of epithelioid cells	Oral prednisolone	Improvement without recurrence
Gianoli and Miller (1994)	Crohn	44	F	Odynophagia and hoarseness	Normal vocal fold mobility, marked edema of the posterior commissure and arytenoid area, ulcerations on the right mid true vocal fold and posterior part of the left true vocal fold, ulcerated epiglottis with cobblestone appearance	Nonspecific inflammation	Prednisolone	Improvement after 2 d
Ulrich et al (2000)	Crohn	41	M	Progressive dyspnea, sore throat, rhinorrhea, raspy voice, moderate inspiratory stridor	Hypopharynx filled with inflammatory lymphoid tissue, deformed, cicatrized epiglottis with inspiratory collapse. Edematous false cords.	/	Humidified oxygen as well as i.v. Decadron 8 mg, and ceftriaxone 1 g.	Improvement

(*Continued*)

TABLE 1.
(continued)

Article	IBD Type	Age	Gender	Symptoms	Clinical Findings	Histology	Treatment	Outcome
Ulnick and Perkins (2001)	Crohn	45	M	Hoarseness	Supraglottic edema with granulation involving epiglottis and false vocal cords	"Consistent with Crohn disease"	6-Mercaptopurine	Stabilization but no improvement
Yang et al (2002)	Crohn	49	F	Mild "tickling" sensation on the left side of her throat, dysphagia, frequent throat clearing, morning throat soreness, nocturnal cough	Large submucosal mass primarily involving the left arytenoid, approximately 2–3 cm in diameter, prolapsed over the laryngeal inlet making visualization of the true vocal folds difficult. Right arytenoid also full, but to a much lesser degree. The vocal folds mobile bilaterally.	Benign squamous mucosa and lymphoid tissue with follicular hyperplasia and occasional small, non-necrotizing granulomas	Steroids + infliximab	Improvement of the arytenoid edema. Arytenoid edema persisted.
Ottaviani et al (2003)	Crohn	50	M	Severe odynophagia and dysphagia.	Marked edema of the epiglottis and arytenoid area, with multiple ulcerated lesions of the epiglottis and laryngeal vestibule. The epiglottis had a cobblestone appearance. The vocal fold mobility was normal.	No biopsy of larynx	(1) Prednisone (2) Infliximab	(1) Worse (2) Resolved lesions
Hasegawa et al (2009)	Crohn	31	F	Recurrent hoarseness	Ulceration of the left vocal fold extending to the false vocal fold	Chronic inflammatory process suggestive of Crohn disease. Plasmacytes, although markedly intestinal manifestations such as granulomas, were not found	Antibiotics and oral, steroids (prednisone 30 mg/d) for 5 d	Improvement, but recurrence after 6 mo, resolved after corticoid spray was initialized

(*Continued*)

TABLE 1.
(continued)

Article	IBD Type	Age	Gender	Symptoms	Clinical Findings	Histology	Treatment	Outcome
Price et al (2013)	Crohn	15	M	Continuous sensation of airway restriction	Abnormal appearance of the supraglottis with a swollen and infantile-looking epiglottis and marked prolapse of the aryepiglottic folds over the glottic inlet. The underlying vocal cords appeared normal.	Chronic inflammation and ill-defined granulomas	Infliximab	Improvement
Rickli et al (1994)	Ulcerative colitis	23	F	Hoarseness, exertional dyspnoea, nonproductive cough and dysphagia	Symmetrical, pseudotumoral, flesh-colored swellings in the glottic or subglottic area, the vocal cords appearing as narrow, white lines. Phonation produced no movement of the vocal cords. The rima glottidis was rigid and too narrow to allow passage of a 5-mm-diameter fiber-optic bronchoscope. The subglottic cavity appeared as a long, narrow, and rigid channel.	Respiratory epithelium with severe lymphoplasmacytic inflammation, mild proliferation of granulocytes, including eosinophils, and isolated histiocytic collections	Systemic corticosteroids (initially 1 $mg \cdot kg^{-1}$ prednisone daily) and topical budesonide	Improvement, although mild laryngotracheobronchial swelling persisted, along with a tendency to vocal fatigue and hoarseness
Current study	Ulcerative colitis	23	F	Hoarseness, a lump sensation in the throat, a thickened left side of the tongue, and dysphagia for solids	Thickened, fibrotic left side of the tongue, fibrotic epiglottis, edematous arytenoids and vocal cord nodules	Nonspecific chronic inflammation with lymphocytes and macrophages, but without granulomas	Mesalazine	Improvement

Abbreviation: IBD, inflammatory bowel disease; i.v., intravenous.

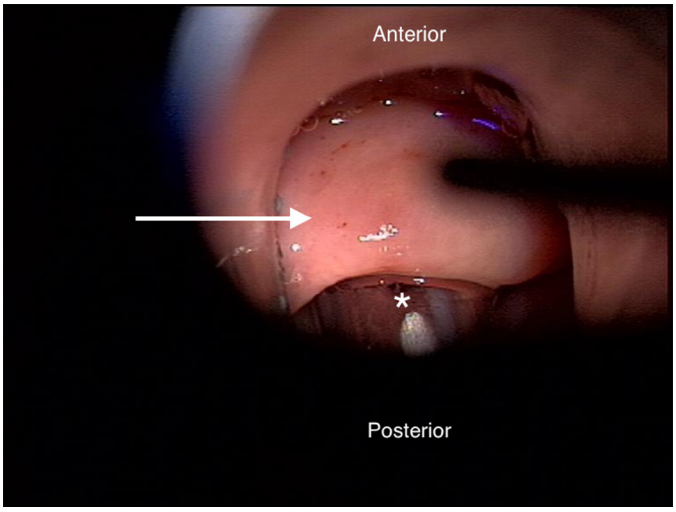

FIGURE 1. Fibrolaryngoscopy demonstrating a thick fibrotic epiglottis (white arrow), intubation tube (*).

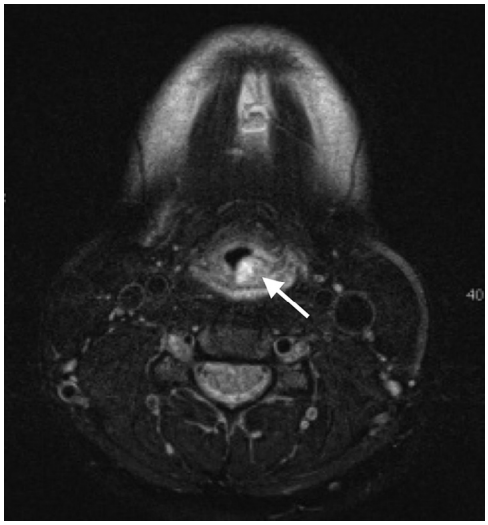

FIGURE 2. Axial T2-weighted magnetic resonance imaging. Thickened, edematous left aryepiglottic fold (white arrow).

activation of the gastrointestinal mucosal T cells of unknown etiology. Crohn disease is characterized by noncontiguous transmural chronic inflammation with noncaseating granuloma formation. It can involve any portion of the alimentary tract. Ulcerative colitis differs from Crohn disease because it is characterized by contiguous chronic inflammation without transmural involvement. Furthermore, in ulcerative colitis, the disease is more frequently limited to the colorectal area.[14]

In IBD, extraintestinal manifestations are seen in 25%–40% of patients with IBD, but laryngeal manifestations are fairly rare. Laryngeal manifestations include edema of the epiglottis and arytenoid area, multiple ulcerative lesions of the epiglottis and laryngeal vestibule, and inflammation of the vocal cords.[9,15] Patients present with dysphonia, chronic cough, odynophagia, or difficulty breathing. A review of all laryngeal manifestations described in the literature is presented in Table 1.

FIGURE 3. Coronal T2-weighted magnetic resonance imaging. Hyperintense, edematous left base of tongue (white arrow).

Histological findings vary from nonspecific inflammatory changes to chronic inflammation with granuloma formation (Table 1). The differential diagnosis of laryngeal lesions in IBD is challenging, especially if the diagnosis of IBD has not already been suggested, because of gastrointestinal symptoms. The definite diagnosis can only be made after exclusion of other laryngeal diseases with similar manifestations such as sarcoidosis, tuberculosis, Behçet disease, fungal infection, bacterial infection, hereditary angioneurotic edema, granulomatosis with polyangiitis, and gastroesophageal reflux disease.[10,11]

Besides laryngeal manifestations, other ENT manifestations are also uncommon. The most frequent ENT manifestations are oral lesions. Intraoral Crohn disease is observed in 9% of the diagnosed Crohn cases.[11] The most common lesions are oral aphthous ulcers of the tongue, buccal mucosa, and palate. Other symptoms include a cobblestoned appearance of the buccal mucosa, angular cheilitis, thickening and edema of the lips, gingiva and buccal mucosa, and gingivitis. There may also be scarring of the mucosa after ulcers have healed.[16] Oral lesions are less common in ulcerative colitis.[1,16]

Respiratory manifestations include tracheobronchitis, tracheal stenosis, bronchiectasis, granulomatous bronchiolitis, diffuse or localized interstitial fibrosis, and pneumonitis.[17] These manifestations are also rare. Pulmonary involvement is most often subclinical and only presents with an increased lymphocyte count in the bronchoalveolar lavage fluid or lung function test abnormalities.[18]

Patients with IBD can also present with nasal manifestations. Sinonasal disease is more frequent in patients with Crohn disease than in patients with ulcerative colitis.[14] Symptoms include inflammation of the nasal mucosa with erosion, ulcerations, necrosis, and bleeding upon contact. Patients may complain of nasal obstruction, epistaxis, impairment of smell, purulent rhinorrhea,

crusting, acute or chronic sinusitis, and deformity of the nasal pyramid.[9,14]

Lastly, sensorineural hearing loss is described as an extraintestinal manifestation of IBD, especially in ulcerative colitis. The hearing loss can be sudden or progressive. Curiously, the hearing loss can also be unstable, with periods of exacerbation alternating with periods of partial or complete remission.[19] The exact pathophysiology of hearing loss in IBD remains largely unknown. It is hypothesized that the hearing loss could be caused by an immune response because corticosteroids and immunosuppressants lead to improvement.[20]

Most frequently, ENT manifestations will respond well to the treatment of the gastrointestinal symptoms. Additionally, topical corticosteroids can be useful. When topical corticosteroids fail or are not possible, oral corticosteroids become the main therapy. If there is no response to steroid therapy, then anti-TNF-alfa therapy may be effective.[11] Concerning laryngeal manifestations specifically, little is known about the best treatment modality. In the literature, most of the presented cases were treated with oral or systemic steroids. Mostly, steroids provided improvement of the laryngeal symptoms, although no long-term follow-up was described (Table 1).

CONCLUSIONS

Still, little is known about ENT manifestations of IBD. Laryngeal involvement in IBD is rare, but it should be recognized by otorhinolaryngologists.

Acknowledgments

We like to thank Dr. Monique Horvath, Head and Neck radiologist of Ziekenhuis Oost-Limburg, Genk, Belgium, for the reevaluation of the imaging and selection of figures.

REFERENCES

1. Levine JS, Burakoff R. Extra intestinal manifestations of inflammatory bowel disease. *Gastroenterol Hepatol (N Y)*. 2011;7:235–241.
2. Croft CB, Wilkinson AR. Ulceration of the mouth, pharynx, and larynx in Crohn's disease of the intestine. *Br J Surg*. 1972;59:249–252.
3. Kelly JH, Montgomery WW, Goodman ML, et al. Upper airway obstruction associated with regional enteritis. *Ann Otol Rhinol Laryngol*. 1979;88:95–99.
4. Wilder WM, Slagle GW, Hand AM, et al. Crohn's disease of the epiglottis, aryepiglottic folds, anus, and rectum. *J Clin Gastroenterol*. 1980;2:87–91.
5. Lemann M, Messing B, D'Agay F, et al. Crohn's disease with respiratory tract involvement. *Gut*. 1987;28:1669–1672.
6. Gianoli GJ, Miller RH. Crohn's disease of the larynx. *J Laryngol Otol*. 1994;108:596–598.
7. Ulrich R, Goldberg R, Line WS. Crohn's disease: a rare cause of upper airway obstruction. *J Emerg Med*. 2000;19:331–332.
8. Ulnick KM, Perkins J. Extraintestinal Crohn's disease: case report and review of the literature. *Ear Nose Throat J*. 2001;80:97–100.
9. Yang J, Maronian N, Reyes V, et al. Laryngeal and other otolaryngologic manifestations of Crohn's disease. *J Voice*. 2002;16:278–282.
10. Ottaviani F, Schindler A, Capaccio P, et al. New therapy for orolaryngeal manifestations of Crohn's disease. *Ann Otol Rhinol Laryngol*. 2003;112:37–39.
11. Hasegawa N, Ishimoto S, Takazoe M, et al. Recurrent hoarseness due to inflammatory vocal fold lesions in a patient with Crohn's disease. *Ann Otol Rhinol Laryngol*. 2009;118:532–535.
12. Price SE, Frampton SJ, Coelho T, et al. Crohn's supraglottitis—the presenting feature of otherwise asymptomatic systemic disease. *Int J Pediatr Otorhinolaryngol Extra*. 2013;8:131–136.
13. Rickli H, Fretz C, Hoffman M, et al. Severe inflammatory upper airway stenosis in ulcerative colitis. *Eur Respir J*. 1994;7:1899–1902.
14. Book DT, Smith TL, McNamar JP, et al. Chronic sinonasal disease in patients with inflammatory bowel disease. *Am J Rhinol*. 2003;17:87–90.
15. Bradley PJ, Ferlito A, Devaney KO, et al. Crohn's disease manifesting in the head and neck. *Acta Otolaryngol*. 2004;124:237–241.
16. Plauth M, Jenss H, Meyle J. Oral manifestations of Crohn's disease. An analysis of 79 cases. *J Clin Gastroenterol*. 1991;13:29–37.
17. Henry MT, Davidson LA, Cooke NJ. Tracheobronchial involvement with Crohn's disease. *Eur J Gastroenterol Hepatol*. 2001;13:1495–1497.
18. Kuźniar T, Sleiman C, Brugière O, et al. Severe tracheobronchial stenosis in a patient with Crohn's disease. *Eur Respir J*. 2000;15:209–212.
19. Casella G, Corbetta D, Zolezzi M, et al. Symptomatic sensorineural hearing loss in patients with ulcerative colitis. *Tech Coloproctol*. 2015;19:729–731.
20. Jachiet M, Lependu C, Fragny D, et al. Severe deafness associated with Crohn's disease and spondyloarthropathy: successful treatment with anti-TNF. *Rheumatology*. 2013;52:1145–1147.