Published in final edited form as:

Am J Gastroenterol. 2009 September ; 104(9): 2368–2370. doi:10.1038/ajg.2009.274.

Twenty-Year Follow-Up of Esophageal Involvement in Chronic Granulomatous Disease

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To the Editor

Chronic granulomatous disease (CGD) is an inherited disease that affects superoxide production by phagocytic cells and inhibits their ability to kill bacteria and fungi. CGD is most commonly X-linked recessive but can also be autosomal recessive and usually presents in childhood, leading to recurrent infection and granuloma formation. The granulomatous obstruction of hollow viscera is well described. Gastrointestinal involvement is common and varied (1-3). Hepatic involvement typically includes abscess, drug injury, and nodular regenerative hyperplasia. Gastrointestinal tract luminal involvement is typically an inflammatory bowel disease-like syndrome, including fistula formation and obstructive symptoms. Esophageal involvement is rare and the most-described cases have been in children. This report of esophageal involvement in an adult with CGD highlights the natural history of esophageal disease over 20 years.

The patient is a 48-year-old man who was diagnosed with CGD in 1988 at the age of 27 years, after his brother was diagnosed with CGD at autopsy. He has had intermittent dysphagia throughout his life. His initial presentation of dysphagia was at the age of 9 years, when he had esophageal strictures, which were treated with dilations. During his initial visit after the diagnosis of CGD, he was given antibiotics and prednisone for 2 months and his dysphagia symptoms were resolved for several months.

Since his initial diagnosis, he has been followed up at the National Institutes of Health on multiple medication regimens, including antibiotics and steroids. Throughout the years, the patient has had intermittent dysphagia that has been worse with solids than liquids. He reports that his dysphagia worsens when he is not taking steroids. In the 1990s, he had meat impactions requiring endoscopy several times a year. In 1989, 1992, and 2006, the patient

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Guarantor of the article: Theo Heller, MD.

Specific author contributions: Heather Laskey: wrote first draft and collected images. All remaining authors: editing, writing, intellectual input, and patient care.

CONFLICT OF INTEREST

Potential competing interests: None.

had esophograms (Figure 1), which showed “multiple sacculations.” The radiology report states that when the patient drank water after drinking barium it “looked like a toilet washing out the barium” and descended stepwise out of the esophagus. The patient has had multiple endoscopies, which are useful for comparison with the barium studies (Figure 2). The endoscopies have consistently shown diverticula, which contain undigested food and strictures throughout the esophagus. Endoscopic biopsy of the strictures showed reactive changes without granulomata.

Presently, his difficulty in swallowing solids is managed by sitting upright while eating. His dysphagia has worsened since becoming edentulous. In addition, he has had difficulty with dentures. Recent reflux and heartburn with occasional chest pain are relieved with over-the-counter antacids. He also complains of halitosis and a bad taste in his mouth that can last for several days at a time.

The descriptions of esophageal involvement in CGD consist of case reports with varying presentations, typically involving children. Esophageal involvement in CGD includes motility and structural abnormalities. However, there are no previous studies or case reports with long-term follow-up. Therefore, this 20-year follow-up of an adult patient with severe symptomatic CGD-related esophageal involvement is of potential value.

Two adults with CGD and dysphagia have been described (4,5). Golioto and O'Connor described a 27-year-old man with progressive dysphagia, a normal barium swallow, endoscopy, and pathology but manometry showing diffuse esophageal spasm. A chest computerized tomography scan also showed periesophageal adenopathy and thickening of the esophageal wall. The authors suggested that the motility disorder might have been secondary to mediastinal adenopathy. Renner *et al.* (5) described a 21-year-old man with progressive dysphagia. Their case is similar to ours in that he had strictures and pseudodiverticulosis. However, their patient was successfully treated with repeated dilations without using steroids.

Hiller *et al.* (6) and Renner *et al.* (5), respectively, described 5- and 14-year-old girls with esophageal strictures. Both patients had progressive dysphagia that responded to steroids, but symptoms recurred with withdrawal of steroids. The pathology in both was normal or non-specific. Markowitz *et al.* (7) presented the case of an 11-year-old boy with chest pain and vomiting. Esophogram showed a dilated esophagus with areas of narrowing and the “esophageal body was atonic.” Antibiotics, dilation, and atropine were unsuccessful. The patient eventually received a gastric tube for feeding. Chin *et al.* (8) described a 10-year-old boy with progressive dysphagia, whose barium swallow showed esophageal narrowing and thickened gastric mucosa. Antibiotics caused no improvement, nor did steroids followed by dilation. Higher-dose steroids resulted in symptom improvement and in the improvement in his barium swallow. Ruiz-Contreras *et al.* (9) described a 14-year-old boy with progressive dysphagia and weight loss, whose barium swallow showed a rigid, narrow esophagus with normal mucosa, and whose pathology was non-specific. He received antibiotics for 3 weeks and became asymptomatic for 2.5 months. Recurrence led to antibiotics and steroids. On barium examination, after the combination of antibiotics and steroids, there was an almost complete resolution of the stricture.

Our patient is unique because his dysphagia has been followed up since his diagnosis of CGD in 1988. Throughout follow-up, his symptoms have fluctuated, but the anatomy of his esophagus has not changed significantly. Although progression might have been expected, both his symptoms and anatomy have remained relatively stable. The patient has not had meat impaction for several years, raising the question of whether the strictures have enlarged over time to allow easy passage of meat. Some of the earlier cases have had only functional

dysmotility, whereas our patient has strictures, diverticula, and presumed dysmotility. It is interesting to note that despite long-term significant inflammation of the esophagus, there is no evidence of pre-malignant or malignant lesions in this patient.

As in the previous case reports, anatomical pathology has not given any clues as to why esophageal dysfunction occurs. It is suspected that granulomatous inflammation causes strictures, although this has not been shown. Alternatively, functional dysmotility may exist before anatomical changes. Because the patient in this case had anatomical changes upon presentation, the full evolution of his illness has been missed. As the management of CGD has improved and patients are living longer, non-infectious complications are becoming increasingly relevant. Esophageal involvement in CGD should be suspected in the appropriate clinical setting, worked up, and aggressively managed.

Acknowledgments

Financial support: This research was supported by the Intramural Research Programs of the NIDDK (Z01 DK075008-03 LDB) and NIAID, CC, and NIH.

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Figure 1. Barium esophagrams (**a**) from December 1992 showing multiple strictures and dilations and (**b**) from May 2006, showing a tortuous proximal esophagus with continued strictures and dilations.

Figure 2.

Endoscopic photographs from different time points. (a) Endoscopy in 1993. The beginning of a diverticulum (arrow) is shown. (b) Multiple tight strictures in July 2000. (c) June 2002 showing large diverticulum (arrow). (d) Most recent endoscopy from April 2008 showing multiple strictures, undigested food (*), and a diverticulum (arrow).