CASE REPORT
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Effect of Corticosteroid Therapy in Esophageal Stricture of a Child with Chronic Granulomatous Disease

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ABSTRACT

In chronic granulomatous disease (CGD) patients, esophageal stricture is a rare complication and the treatment of choice is still controversial. There are few reports of successful therapy with antibiotics, corticosteroids, multiple balloon dilatations or their combination.

We report a 3-three-year-old Iranian boy with recurrent esophageal obstruction due to CGD. The patient transiently responded to dilatation in one occasion and at another time to short term steroid therapy. We observed an excellent response when long term and high dose of corticosteroid was administered.

It showed that a long term and high dose steroid therapy is more effective than a short term in a patient with CGD and esophageal stricture.

Key words: Chronic granulomatous disease; Corticosteroid; Esophageal stricture

INTRODUCTION

Chronic granulomatous disease (CGD) is a primary immunodeficiency disorder affecting the oxidative mechanisms of phagocytic cells against certain microorganisms. In addition, obstructive lesions resulting from exaggerated immune responses and sometimes granuloma formation in hollow viscera (gastrointestinal tract, bladder), have been a source of morbidity in these patients.[1-3] Esophageal obstruction is rare and so far, only eight cases have been reported in literature.[3-8] We present a case with esophageal stricture due to CGD and the possible mechanisms of corticosteroid therapy in relief of this stenosis.

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CASE REPORT

A 3-year-old Iranian boy referred to Dena Hospital, Shiraz, Iran with a history of dysphagia, pain and a feeling of pressure on the mid-thoracic area immediately after ingesting of food materials which got relieved by drinking lots of fluid or by vomiting.

Six months prior to his admission, he had been referred to the hospital because of axillary lymphadenitis, fistulization at the site of BCG inoculation which had developed for 5 months, an ulcerative lesion over the right forearm which had not responded to broad spectrum antibiotics for one year, with hepatosplenomegaly, anemia and poor weight gain. Liver biopsy showed chronic granulomatous inflammation, ballooning degeneration, cell necrosis and intra-sinusoidal lymphocytes with multiple granulomas within and outside the portal tracts without any fibrosis. Acid fast staining of

the specimen was negative. Immunological studies revealed normal levels of IgG, IgM, IgA, C3, C4, CD^{+}_{19} (B-cell), CD^{+}_{3} (T-cell), CD^{+}_{4} (helper T-cell), CD^{+}_{8} (cytotoxic T-cell), CD^{+}_{16}/CD_{56}^{+} (natural killer cell) and CD_4+/CD_8+ ratio. Nitrotetrazolium blue test (NBT) was performed in three occasions which were zero in two occasions and less than 10% at another time.

With the impression of disseminated BCGitis syndrome on the basis of CGD, isoniazid (INH) and rifampin were commenced and the condition of the patient significantly improved. Forearm ulcer was healed and right axillary drainage stopped. However, 2 months prior to the present admission, he developed dysphagia, pain and feeling of pressure on mid-thoracic area after ingesting solid materials, which was relieved by vomiting of the food materials. His parents believed that the condition was due to a hard foreign body (apricot seed) ingested the day before. The patient was visited by a pediatric gastroenterologist and an upper endoscopy was performed revealing a ringed narrowing in one-third of the proximal part of the esophagus. The diameter of the narrowing was about 2 mm; therefore, an infant endoscope with the external diameter of 6 mm could not be passed through it. No foreign body or ulcer was detected. Unfortunately, biopsy was not done by the gasteroenterologist. According to the parents' report, symptoms were relieved temporarily for about 40-50 days after endoscopy, but reoccurred again. So, the patient was referred to our center.

On examination, his vital signs were normal. The abdomen was soft and non-tender, but the liver was palpable 3-4 cm and the spleen 2-3 cm bellow the costal margin. Scars of healed ulcers with dimensions of 5 × 2 cm on the right forearm, and 1 × 2 cm in the right axillary area were remarkable. No lymphadenopathy was detected. Laboratory investigation revealed WBC: 12.6 × $10^3/mm^3$, neutrophil: 52%, lymphocyte: 39%, monocyte: 4%, eosinophil: 5%, RBC: 6.22 × $10^6/mm^3$, Hb: 9.5 g/dL, MCV: 57 fl, MCH: 15.5 pg, MCHC: 26.5 pg/L, RDW: 20.3, Platelet: 363000/mm^3, reticulocyte: 2.7%, and ESR: 2 mm/1st hour. It also revealed negative direct and indirect coombs tests. The liver, kidney and thyroid function tests, calcium, phosphorus and alkaline phosphatase levels, urinalysis, bone marrow aspiration and biopsy, Hb-electrophoresis and stool examination were all within normal limits. Upper gastrointestinal and small bowel series revealed a short-segment, benign stricture at the level of the carina with preserved mucosal fold (Figure 1).

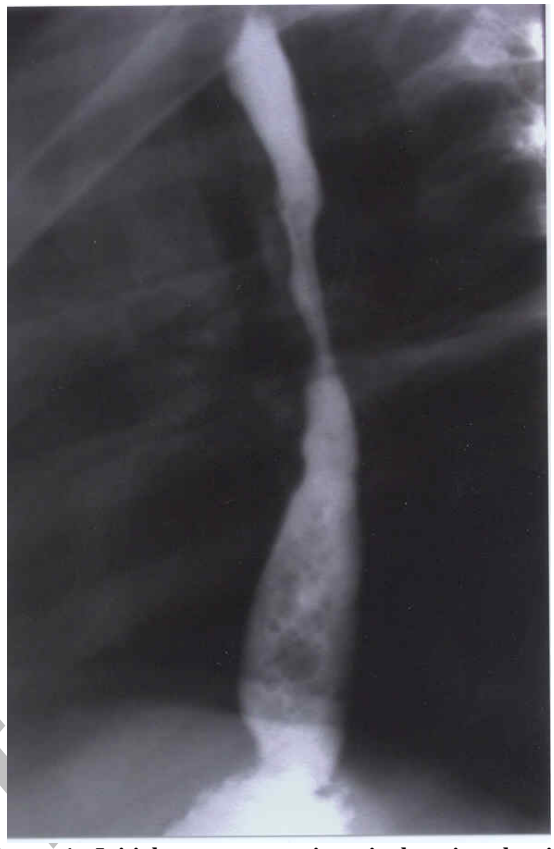

Figure 1. Initial upper gastrointestinal series showing midesophageal narrowing.

Based on previous reports on the positive effect of corticosteroids in relieving obstructive lesions in CGD, and our previous unreported experience of an excellent response in a 15-year-old CGD sufferer with esophageal stricture, prednisolone was commenced with a dose of 2 mg/Kg/day in 3 divided doses, and was continued for 2 weeks. Dramatic improvement in swallowing was achieved within 3-4 days, and prednisolone was tapered over a 10-day period after the completion of the 2-week course of the treatment.

Repeated barium swallows after the completion of therapy revealed no residual stricture at the site of the previous stenosis (Figure 2), but after 2 months, the patient developed gradual onset of dysphagia and difficulty in swallowing solid and then liquid materials. The upper GI series showed a smooth esophageal stenosis at the site of the previous stricture (Figure 3); therefore, prednisolone with the dose of 2 mg/Kg/day was started again, and was continued for 2 months. This time, the response was dramatic with an excellent follow-up after 7 months.

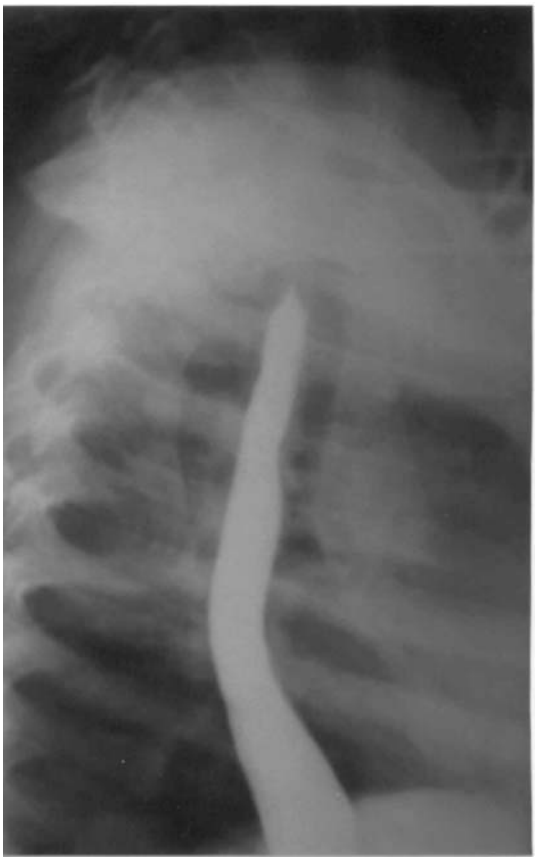

Figure 2. Upper gastrointestinal series one month after steroid therapy showing normal esophagus with disappearance of midesophageal narrowing.

Isoniazid and rifampin were continued during follow up. Cotrimoxazole and itraconazole as prophylaxis antimicrobials and interferon-γ injection were given after diagnosis of CGD.

DISCUSSION

In addition to recurrent life-threatening infections, CGD sufferers are at risk of developing chronic obstruction and inflammation of gastrointestinal and genitourinary tracts.[1-8] So far, only eight cases of esophageal stricture in CGD patients have been reported. [3-8]

Due to clinical presentation of the patient compatible with CGD and NBT results no further tests were performed for documentation of CGD in this case. According to the parents' report, the symptoms relieved transiently a few days after a diagnostic endoscopy. It is probable that instrumentation and the effort to pass the endoscope throughout the obstruction had produced some dilatation and caused a temporary relief. Based on our previous unpublished experience of a complete relief of esophageal obstruction in a 15-year-old CGD patient, and other papers on the subject, the patient was treated with prednisolone. Complete clinical and radiological cure were achieved by prednisolone for 1 month (Figure 2), but the stricture relapsed 2 months later at the previous site (Figure 3); therefore, prednisolone was started again for further two months producing an excellent response in the 7-month follow up. Experiences of other authors also suggest long course corticosteroid administration for completion of therapy.[4-8] The excellent response to steroid without adding antimicrobials, cotrimoxazole and itraconazole used as prophylaxis and isoniasid and rifampin given for treatment of disseminated BCG infection showed that an infectious process was not be the cause of stenosis in our patient.

The mechanism of these exaggerated inflammatory responses in CGD patients is not well understood. We believe that autoimmune processes most probably may be involved due to similarities of the disease with Crohns disease in terms of clinical, histological and white cell scanning aspects.[9-11]

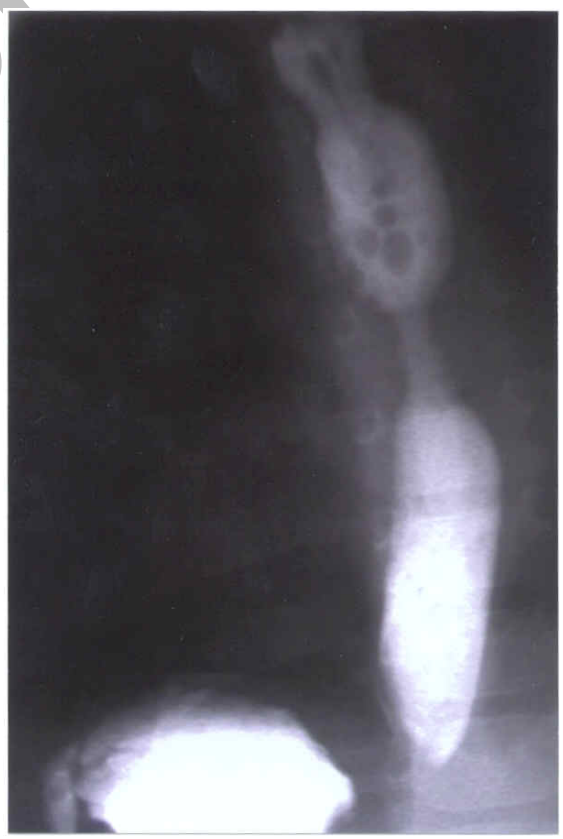

Figure 3. Upper gastrointestinal series two months after cessation of steroid therapy showing recurrence of midesophageal narrowing.

In Crohn's disease, chronic inflammatory responses to GI microflora are detected which are due to some defects in the innate immune system of GI mucosa.[12, 13]

Due to the probable role of autoimmune processes in CGD patients, long-term treatment with high-dose corticosteroids may be more effective than short-term therapy as in rheumatologic disorders. [14]

Our result showed that high dose and long term corticosteroid are highly effective treatment regimen in esophageal stricture in CGD patient.

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