Chronic inflammatory bowel disease in a patient with common variable immunodeficiency

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Common variable immunodeficiency (CVID) is a primary defect of the immune system involving an increased risk of respiratory and digestive tract infections and autoimmune diseases. Recently, it has been reported that chronic inflammatory bowel disease (CIBD) might occur with increased frequency (20%) in patients with CVID. A nine-year-old boy with CVID developed CIBD during follow-up and periodic intravenous immunoglobulin administration. Serum tumor necrosis factor-α concentration, which is suggested to show disease activity in CBD, was very high. The patient's radiological evaluation, both in active and remission periods, had characteristic features of CBD. We herewith present and discuss this case with both diseases, CVID and CIBD.

Key words: common variable immunodeficiency, chronic inflammatory bowel disease.

Common variable immunodeficiency (CVID) is a primary defect of the immune system involving an increased risk of respiratory and digestive tract infections[1]. Recurrent pyogenic infections usually appearing in late childhood, an increased incidence of autoimmune disease and total immunoglobulin levels below 300 mg/dl (with the IgG level below 250 mg/dl and normal B cell numbers) are the major immunological features of CVID[1-5]. Digestive tract infections are important due to frequent modifications of the intestinal bacteria which can give rise to severe malnutrition[6]. Many functional and anatomic irregularities of the gastrointestinal tract have been described during CVID, chiefly due to a defective immune response of the mucosal membranes[6]. Recently, it has been reported that chronic inflammatory bowel disease (CIBD) might occur with increased frequency in patients with CVID[7]. We present here a nine-year-old boy with CVID who developed CIBD during follow-up and periodic intravenous immunoglobulin (IVIG) administration.

Case Report

A nine-year-old boy with CVID has been followed-up for three years in the Pediatric Immunology Unit. On admission, he had mild growth retardation, recurrent upper and lower respiratory infections and mild diarrhea. After laboratory evaluation, he was diagnosed as CVID. Immunological findings were as follows: IgG: 207 mg/dl, IgM 24 mg/dl, IgA 6.6 mg/dl, IgG1 1.8 g/L, G2-G3-G4 undetectable, gamma globulin in protein electrophoresis 0.9%, CD3+ T lymphocytes 58%, CD19+ B cells 16%, CD4+ cells 22%, CD8+ cells 40%, and CD16+56+ cells 16%. Three years previously examinations for malabsorption, such as endoscopy of the gastrointestinal tract, duodenal biopsy, parasitic examinations and carbohydrate, protein and lipid malabsorption tests were all normal. The patient was on monthly administered IVIG treatment (500 mg/kg), and he was extremely well until one year ago.

A year ago, the patient began to admit to the hospital with severe diarrhea, nausea and vomiting which could not be explained with bacteriologic, fungal, viral (rotavirus), or parasitic examinations or malabsorption tests. The diarrhea was not bloody and presented over two months with remissions and exacerbations. Colonoscopy to the middle part of the transverse colon was performed and biopsies were obtained. In colonoscopy, the mucosa was hyperemic, edematous and friable. There was a

loss of vascular (submucosal vessels) pattern. Several acute and chronic ulcerations representing a more severe disease were the other endoscopic findings. Presence of mixed inflammatory cell infiltrates of the lamina propria, increased number of neutrophils in some mucosal glands, and destruction of mucosal surface epithelium were the biopsy features showing an inflammatory disease. An air-contrast barium enema was performed (Fig. 1). The roentgenograms showed involvement of the entire colon. There was a severe loss of haustration and many superficial ulcerations with 2-3 mm diameters. Terminal and distal ileum were normal. Based on these colonoscopic, histologic and X-ray features, the patient was diagnosed as chronic ulcerative colitis. Serum concentration of tumor necrosis factor-α (TNF-α) was measured for this patient by enzyme linked immunosorbent assay (ELISA) and was found to be very high (51.2 pg/ml).

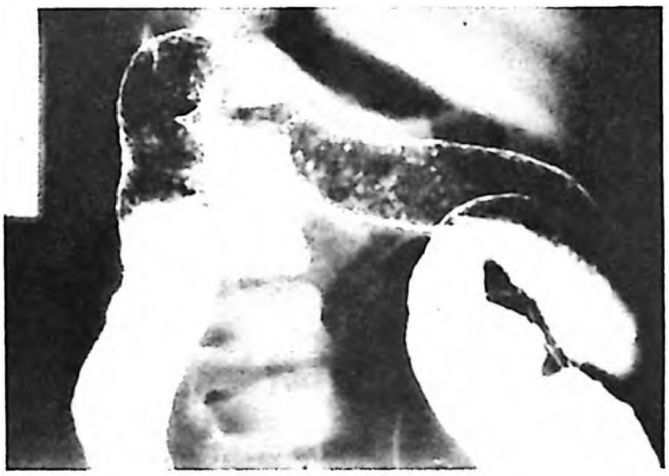

Fig. 1. Superficial ulcerations and severe loss of haustration in air-contrast barium enema.

Besides regular IVIG therapy, 1.5 mg/kg oral prednisolone and 1500 mg/day mesalazin (5-aminosalicylic acid) were given to the patient. In three weeks, all symptoms including diarrhea disappeared and the child had no pathologic symptoms. The dose of prednisolone was tapered gradually to 10 mg/day and then switched to alternate day therapy. Besides prednisolone, mesalasin was also tapered to 750 mg/day. Colonoscopy was performed every four months, and colonoscopic and histologic features resolved gradually. A year after the diagnosis, in the new air-contrast colon roentgenograms, the characteristic features such as complete disappearance of haustral markings, and shortening of the colon and uniform reduction in its caliber (lead pipe colon) were found (Fig. 2). These findings were expected in long-term management. However, the ulcerations observed previously had disappeared, and dilatation of the ileocecal valve and terminal ileum (backwash ileitis) was observed. Serum TNF-α concentration was 29.7 pg/ml in this period.

Fig. 2. After treatment: complete disappearance of haustral markings, shortening of the colon and uniform reduction in its caliber (lead pipe colon); disappearance of the ulcerations observed before; and a dilatation of the ileocecal valve and terminal ileum are seen.

The patient is still in follow-up and has had no complaints related to the gastrointestinal system except for mild abdominal distension.

Discussion

A consensus exists that the mucosal immune system is responsible for tissue damage in CIBD[8]. Two potential mechanisms for the involvement of the gut. associated lymphoid tissue in the pathogenesis of CIBD are postulated[8]. First, disordered immunoregulation leads to immune activation of the T cells, leading to nonspecific tissue injury, enhanced antibody production and chronic inflammation[8]. The activated T cells are postulated to cause tissue injury by the production of lymphokines and cytokines. Second, an autoimmune process

has been postulated by which specific immune response is directed against epithelial cell antigens[8]. On the other hand, it has been reported that patients with CVID were prone to a variety of autoimmune diseases[1,7]. Luzi[9] revealed that inflammation in the bowel, usually affecting the colon and ileum, occurs in at least 20 percent of CVID patients. Our patient also had the characteristic features of both diseases, CVID and CIBD.

Serum concentrations of TNF-α in childhood CIBD have been measured in several studies[10-12]. Serum TNF-α levels were found to be highly elevated in active disease state, and measurement of serum TNF-α levels has been accepted as a simple way of assessing disease activity in patients with CIBD[10,11]. In our patient, serum TNF-α concentrations were measured in the active and remission periods, and were found to be 51.2 pg/ml and 29.7 pg/ml, respectively. In another study, serum TNF-α concentrations were measured in healthy children and the mean ± standard deviation was 3.1 ± 2.2 pg/ml[13]. As seen, our patient's serum TNF-α level was extremely high in the active disease period, and then a decrease was observed after treatment. However, the serum TNF-α level was still high, suggesting the inflammatory process was continuing.

In conclusion, physicians should be aware that CIBD might occur in children with CVID. If a child with this humoral immunodeficiency presents with symptoms of chronic diarrhea, abdominal pain, nausea, vomiting, weight loss and growth retardation, the physician has to suggest and examine CIBD.

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