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Common variable immunodeficiency (CVID) presenting with malabsorption due to giardiasis

Giardiazise bağlı malabsorbsiyon tablosu ile prezente olan sık değişken immün yetmezlik

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Common variable immunodeficiency is characterized with B-cell and T-cell dysfunction and hypogammaglobulinemia. Recurrent bacterial infections, such as otitis media, chronic sinusitis and recurrent pneumonia due to diminished immunoglobulin (Ig) levels and impaired antibody production are frequently observed in common variable immunodeficiency. Almost half of the patients with common variable immunodeficiency have problems related to the gastrointestinal system. A 39-year-old woman was referred to our department with the complaint of chronic diarrhea. She had experienced diarrhea without mucus or blood in the last year and had lost 30 kg. In her medical history, she had suffered from recurrent upper and lower respiratory infections like sinusitis, otitis media and pneumonia since childhood. Serum immunoglobulin levels were low. There were no parasites or ova in her stool examinations. Esophagogastroduodenoscopy detected widespread macroscopic nodular appearance on duodenum, and biopsies from the duodenum revealed giardiasis invading the tissue. She was diagnosed as common variable immunodeficiency. After metronidazole therapy and intravenous immunoglobulin infusion was started, her diarrhea attacks ceased and she regained her normal weight. Common gastrointestinal system problems in patients with common variable immunodeficiency are lactose intolerance, lymphoid hyperplasia/diffuse lymphoid infiltration, loss of villi and infection, especially with Giardia lamblia. Giardiasis may lead to severe mucosal flattening and sometimes to lymphoid hyperplasia at the lamina propria of the duodenum. Medical history should be evaluated carefully regarding recurrent respiratory infections. In such cases with chronic diarrhea, common variable immunodeficiency should be kept in mind as a possible cause.

Key words: Common variable immunodeficiency, malabsorption, giardiasis

"Sık Değişken İmmün Yetmezliği", B-hücresi ve T-hücresi fonksiyon bozukluğu ve gamaglobulin azalması ile karakterizedir. Azalmış immunoglobulin seviyeleri ve bozulmuş antikor üretimine bağlı olarak tekrarlayıcı otitis media, kronik sinüzit ve tekrarlayıcı pnömoni ve bazen bronşektazidir sık gözlenir. Hastaların neredeyse yarısında gastrointestinal sistemde problemlerle karşılaşılır. 39-yaşındaki bayan, hastanemize kronik diare ile başvurdu. Kansız ve müküssüz ishali vardı ve çok iyi iştahı olmasına rağmen son bir yılda 30 kg zayıflamıştı. Öyküsünde çocukluğundan beri varolan tekrarlayıcı sinüzit, otitis media ve pnömoni gibi tekrarlayıcı üst ve alt solunum yolları enfeksiyonları tarif ediyordu. Serum immünoglobülin seviyeleri düşüktü. Gaitada parazit ve yumurtası gözlenmedi. Özofagogastroduodenoskopide duodenumda yaygın makroskopik nodüler bir görünüm mevcuttu ve biopsi sonucunda dokuya invazyon gösteren giardiazis saptandı. Metronidazol ve intravenöz immunglobulin infüzyonu ile diare atakları kesildi ve hasta normal ağırlığına ulaştı. Sık değişken immün yetmezliği hastalarındaki sık görülen gastrointestinal sistem problemleri laktoz intoleransı, lenfoid hiperplazi/diffüz lenfoid infiltrasyon, villus kaybı ve özellikle Giardia lamblia ile infestasyondur. Giardiazis ayrıca şiddetli mukozal düzleşmeye ve bazen duodenumun lamina propiasında lenfoid hiperplaziye yol açabilir. Uzun süreli metronidazol tedavisi ve düzenli intravenöz immunglobulin replasman tedavisi ile hem klinik hem de laboratuvar tablosunda düzelme gözlendi. Tekrarlayıcı solunum yolu enfeksiyonları olan olgularda medikal öykü dikkatli alınmalıdır. Kronik diaresi olan hastalarda sık değişken immün yetmezliği kronik diare sebebi olarak mutlaka akılda tutulmalıdır.

Anahtar kelimeler: CVID, sık değişken immün yetmezlik, malabsorbsiyon, giardiazis

INTRODUCTION

Common variable immunodeficiency (CVID), also called acquired hypogammaglobulinemia, adult-onset hypogammaglobulinemia, or dysgammaglobulinemia, is a heterogeneous group of disorders

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involving both B-cell and T-cell dysfunctions. As a result of these complex immunological dysfunctions, hypogammaglobulinemia occurs. CVID is characterized by recurrent sino-pulmonary bacterial infections due to decreased serum immunoglobulins and abnormal antibody responses. The most frequent infections of the respiratory tract are recurrent otitis media, chronic sinusitis and recurrent pneumonia often resulting in bronchiectasis. In approximately half of the patients with CVID, the gastrointestinal tract is affected, presenting with malabsorption or chronic diarrhea. Lactose intolerance, protein-losing enteropathy, or superimposed infection of the small bowel with Campylobacter or Yersinia species or parasite infestation with Giardia lamblia contributes to the gastrointestinal symptoms. Atrophic gastritis with achlorhydria may lead to pernicious anemia. Nodular lymphoid hyperplasia, diffuse lymphoid infiltration and loss of villi are frequently seen biopsy findings in patients with CVID. Hypertrophy of other lymphoid tissues, including peripheral lymph nodes, the spleen and occasionally the liver are frequently detected (1).

CASE REPORT

A 39-year-old woman was admitted to hospital with the complaint of chronic diarrhea and also recurrent upper and lower airway infections. The patient had a long childhood history of recurrent infectious sinusitis and otitis media. She had also experienced recurrent attacks of fever, productive cough and purulent sputum, treated with several antibiotics. After investigations, bilateral bronchiectasis had been established in 1998. The main problem of the patient was chronic diarrhea without blood or mucus for almost one year. She complained about unshaped, squishy stool, five to six times a day. Since last year she had lost approximately 30 kg despite her good appetite. She was diagnosed with different infectious diseases at different primary health care units and despite having received several antibiotics her complaints did not resolve. She was referred to a regional hospital and double contrast colon, small intestine and barium transit radiographs had been done. As the results of these radiographs were all reported to be normal, it was decided to consult our Department.

On admission at our hospital, her temperature was 37°C, pulse 84 beats/min/rhythmic, respiration rate 20 per minute and blood pressure 90/50 mmHg. Her height was 158 cm and weight 34 kg. On physical examination, a geographic tongue and bilateral crackles at the basal zones of the chest were detected. The liver was 3 cm palpable below the costal margin. Hb level was 9.5 g/dl, Hct 29.5%, white blood cells $9.0x10^9$/L (neutrophils 85%, lymphocytes 14%, monocytes 1%), and platelets $399x10^9$/L. Blood tests revealed slight elevation of liver enzymes (AST: 50 U/L, ALT: 30 IU/L, ALP: 303 U/L, GGT: 86 U/L). Erythrocyte sedimentation rate was 20 mm/h and C-reactive protein 0.5 mg/L. The values for urea nitrogen, creatinine, glucose and electrolytes were normal. Total protein was 3.3 g/dl, albumin 2.0 g/dl and globulin level 1.3 g/dl. Urinalysis was normal. 24-h urinary protein was 0.05 g. Chest radiograph revealed apical pleural thickening and a linear atelectatic band on the right basal region. Chest tomography was concomitant with bronchiectasis. Paranasal sinus tomography was concomitant with chronic bilateral maxillary sinusitis, and mucosal thickening in sphenoidal sinuses and in the right ethmoidal sinus. Electrocardiogram was normal. Microbiologic test results excluded some viral infections (hepatitis B, C and HIV). Repeated stool cultures, parasites and ova, and occult blood in the stool were all normal. Sputum culture was positive for hemophilus influenza. Standard autoantibody screen (ANA, antidsDNA, and ANCA) was negative. Concentrations of IgG (74 mg/dl), IgM (167 mg/dl) and IgA (9 mg/dl) were all decreased. Prothrombin time activated partial thrombin time was 13 and 27 seconds respectively. 24-h fecal fat excretion was 7.4 g/dl (N<5 g/dl).

In order to investigate the cause of chronic diarrhea, the patient underwent an upper gastrointes-

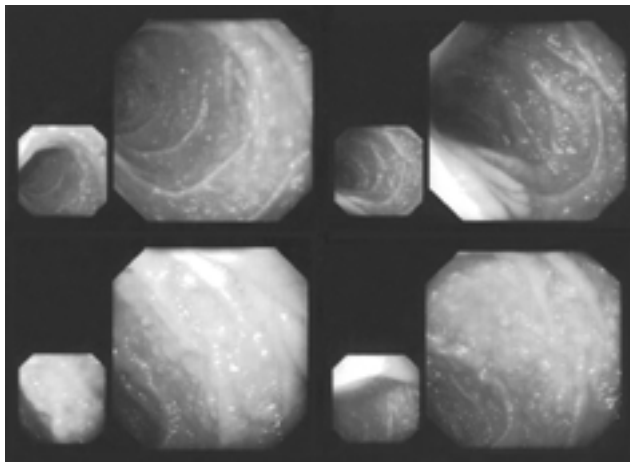

Figure 1. Nodular appearance on duodenum

tinal endoscope in our hospital. Endoscopy showed widespread macroscopic nodular appearance on duodenum, and biopsy specimens revealed giardiasis invading the tissue (Figure 1). According to these clinical and laboratory findings she was diagnosed as CVID. She began to receive replacement therapy with IVIG every three weeks (400 mg/kg every 3 weeks). At the same time, long-term oral metronidazole therapy (3x500 mg) was started. With these therapies, her diarrhea attacks ceased, blood albumin levels increased to normal and the patient regained her normal weight.

DISCUSSION

CVID patients are susceptible to bacterial infections, and this disease is characterized by defective antibody production and decreased serum immunoglobulins. CVID patients experience frequent bacterial infections of the respiratory and gastrointestinal tracts. An increased prevalence in malignancies and autoimmune diseases of the GI tract has been observed in these patients (1). CVID patients have a high prevalence of both intestinal metaplasia and p53 overexpression in the gastric mucosa. Chronic diarrhea, abdominal pain, celiac disease and inflammatory bowel diseases may be observed (2). An unknown increased tendency to Giardia lamblia infection had been reported in CVID patients. Giardiasis may lead to enterocyte damage, subtotal villous atrophy and to development of a nodular mucosal pattern. The sizes of these mucosal nodules vary, and may be up to 5mm in diameter. It has been thought that these nodules represent reactive hyperplasic lymphoid tissue as a result of faulty regulation of B-cell production. Nodular lymphoid hyperplasia is also an endoscopic manifestation of primary immunodeficiency disorders. Disappearance of this finding with therapy may suggest infection as the cause of the nodular pattern (3). Giardiasis in CVID patients is characterized by its difficult treatment, chronicity and frequent relapse. Metronidazole is the drug of choice for first-line therapy, but in resistant cases tinidazole, ornidazole and quinacrine are also reported to be useful (4). Giardia lamblia can produce serious diarrheal disease with intestinal malabsorption and cause marked weight loss (5). In our patient, diarrhea resolved after metronidazole therapy and IVIG replacement. On follow-up endoscopies the nodular appearance persisted, but despite this feature she returned to her previous weight after therapy. This led us to think that the infection more than the nodular lymphoid hyperplasia was the cause of her symptoms. Currently, she is receiving IVIG every three weeks and has experienced no additional problems.

REFERENCES

1. Ballow M. Primary immunodeficiency disorders: antibody deficiency. J Allergy Clin Immunol 2002; 109: 581-91.
2. Luzi G, Zullo A, Iebba F, et al. Duodenal pathology and clinical-immunological implications in common variable immunodeficiency patients. Am J Gastroenterol 2003; 98: 118-21.
3. Weerth A, Gocht A, Seewald S, et al. Duodenal nodular lymphoid hyperplasia caused by giardiasis infection in a patient who is immunodeficient. Gastrointest Endosc 2002; 55(4): 605-7.
4. Genel F, Erermiş S, Aksu G, et al. Quinacrine-induced psychiatric disturbances in a child with common variable immunodeficiency and chronic giardiasis. Hum Psychopharmacol 2002; 17: 357-9.
5. Ertan P, Yereli K, Kurt Ö, et al. Serological levels of zinc, copper and iron elements among Giardia lamblia infected children in Turkey. Pediatr Int 2002; 44: 286-8.