



## A COMMON VARIABLE IMMUNE DEFICIENCY (CVID) CASE WITH CHRONIC DIARRHEA : A CASE REPORT

### KRONİK İŞHAL İLE SEYREDEN BİR GENEL(YAYGIN) DEĞİŞKEN IMMUN YETMEZLİK OLGUSU: OLGU SUNUMU

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#### SUMMARY

*The patient with recurrent episodes of diarrhea and respiratory tract infections was analysed and determined to have immunoglobulin deficiency. The patient was diagnosed as Common Variable Immuno deficiency after flowcytometric assessment and immunoglobulin treatment was started. Giardiasis was found in the parasitologic analysis. During the 10 month follow-up after immunoglobulin replacement and the treatment of giardiasis, the diarrhea disappeared and the patient did not have respiratory tract infections.*

#### ÖZET

*Tekrarlayan diare ve solunum yolu enfeksiyonu nedeniyle tetkik edilen hastada serum immunglobulin eksikliği saptandı. Immune yetmezliği olan hastada flowstometrik değerlendirmeden sonra genel değişken immun yetersizlik tanısı kondu ve aylık intravenöz immunglobulin tedavisi başlandı. Parazitolojik analizde Giardiasis bulundu. On aylık izleme sırasında immunglobulin desteği ve giardiazis tedavisi sonrası diare geriledi ve hasta tekrar solunum yolu enfeksiyonu geçirmedi.*

#### INTRODUCTION

Data in the involvement of the immunologic factors are increasing rapidly in the etiology of the gastrointestinal system diseases. This is the result of the recognition of the acquired immune deficiency states in HIV patients and the recognition of the clinical manifestations in immune deficiencies that have been previously described (1). On the other hand, the better understanding of the basic immune principles and bringing out the functions of various immune cell subgroups and cytokines have also contributed to the development of information.

One of the most common forms of antibody deficiency is Common Variable Immune Deficiency (CVID) (2). The onset may be at any age but usually at early ages of the second decade, and both sexes are equally affected. Family cases have been reported and the relatives of CVID patients have a higher incidence of IgA deficiency than the normal population (3). It is a heterogeneous immune deficiency due to the defects in B cell activation and differentiation. T cell support. T cell suppression and macrophage functions. As a result, decreases in immunoglobulin levels and T cell functions occur (4). The pathogenesis of the disease is not known. In this article, CVID case is being presented.

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## CASE

26 years old, married male patient, born in Konya, had complained of diarrhea without blood or mucus that had started 3,5 months ago. He used to defecate 4-5 times a day some of which woke him up at nights. He had had similar complaints since childhood, which at most continued 15-20 days before disappearing. Since childhood, he had frequent upper and lower respiratory tract infections and many times he was admitted to the inpatient units of pediatric clinics with diagnosis of pneumonia. During the 3 month period before his diarrhea, he did not use any antibiotics. He was admitted to the Clinic Of Gastroenterology in Ege Medical Faculty for further evaluation and treatment.

Physical examination: Height 174 cm, weight 56.5 kg, Pulse 84/min rhythmic, BP 120/80 mmHg, temperature 36.5°C. There was no pathology detected in the examination of the abdomen except the palpation of the spleen just below costal margin. Rectal examination was assessed normal and the intestinal sounds were normoactive. Other system examinations were also unremarkable.

Laboratory Findings: Hemoglobin 12.5 g/dL, Htc % 35, leukocyte 10800/mm<sup>3</sup>, platelete 327000 /mm<sup>3</sup>, ESR 16mm/h, differential %74 neutrophil, %16 lymphocyte, % 5 monocyte, %1 eosinophil, %4 basophil were found. AST: 20U/L, ALT: 30U/L, alkaline phosphatase:166 U/L, GGT: 19U/L, T. Bilirubin 0.68 mg/dL, total protein 5.5 mg/dL, albumin 3.7g/dL, blood glucose 64 mg/dL, BUN 20 mg/dL, serum Na, K, Ca, Mg levels and amilase were detected normal. Protrombin time: 14 sec.,(INR:1.1), FreeT3 4.2 pg/dL , FreeT4 5 ng/dL, TSH 1.2 uU/mL were found to be normal. The results of Guthrie testing was found to be negative for 3 times. During the investigation of stool for parasite *Giardia intestinalis* trophozoite and cysts were found. Lactose tolerance test : Normal curve detected. Total fat in the stool was found to be 0.6 gr/24 h. The radiography of the gut was normal, rigid rectosigmoidoscopy findings were unremarkable was reported to be normal. The biopsy of the capsule of the gut was normal. In the paranasal frontal sinus graphy, the manifestations of possible frontal and maxillary sinusitis were found. PA lung radiogram was normal, thorax HRCT: was found to be consistent with bronchiectasis. Anti- gliadin antibody IgA (ELISA) and anti-endomysium antibody IgA tests were negative. The serum protein electrophoresis was (the values in the brackets are the normal values): albumin 68 % (52-65) alpha 1:2% (2.5-5) alpha 2:13.2 % (7-13) beta :12 % (8-14) gamma :3.5 % (12-22)

-IgG 35 mg/dL; (700-1600) IgA 1 mg/dL (70-400); IgM 64 mg/dL (40-230) serum protein electrophoresis :

-Anti-HIV (ELISA) (-); PPD (-)

-the investigation of the lymphocyte panel from the flow cytometry at 31.10.2001

CD3 (T cell) %69

CD19(Bcell)%4

CD4 (T helper/inducer) %20

CD8 (T supressor/cytotoxic)%45

CD3-/CD16+56(NK)%5

CD3 +/- HLA-DR+(activated T cell)%20

Evaluation : total B cell number decreased, CD4/CD8 ratio inverted, CD4 decreased, activated T cell number increased

Clinical progress, follow-up and discussion : Our case whom we investigated closely due to chronic diarrhea didn't have malabsorption. During the routine laboratory assessment, mild anemia and low total serum immunoglobulin levels were detected, this was followed by the protein electrophoresis at which the gammaglobulin levels were found to be significantly decreased. Therefore the immunoglobulins were assessed and found to be severely decreased. As the parasitology had reported giardia intestinalis infestation after the observation of the stool, a seven-day metronidazole therapy (250 mg tb. 2-3 times/day) was administered and the diarrhea disappeared. The patient was then discharged from the hospital and started to be followed by the immune deficiency clinic of the immunology department. The patient was administered the replacement therapy of 400 mg/kg IV immunoglobulin every 4 weeks and didn't have diarrhea for 10 months period.

The B cell immunodeficiencies can be classified according to the missing immunoglobulins and the time the clinic manifestations occur. These deficiencies include agamma- globulinemia, hyper-IgM syndrome, CVID, the transient hypogammaglobulinemia of the infant, IgG subgroup deficiencies, IgM deficiency and IgA deficiency. While the symptoms of the antibody deficiencies that exist at birth are usually appanent during the first year of life, the symptoms of CVID can be seen at any age. However they usually start after 18 months of age and make a "peak" in two periods of life ; 1 -5 years and 16-20 years of age. In agammaglobulinemias, there are either no B lymphocytes or a significant decrease in their number in the peripheral blood of the patients. The number and functions of T cells are normal. The patients having agammaglobulinemia usually have an IgG level less than 200 mg/dL and typically IgA and IgG levels less than 20 mg/dL. These patients have to have immunoglobulin replacement therapy starting in childhood, otherwise death is inevitable due to infections. Some clinical types of agamma-globulinemias are X-linked, therefore these type of diseases may arise in the male relatives of these patients.

Our case has a history of frequent upper and lower respiratory tract infections since childhood. These infections were treated by antibiotics and although he had frequent infections there was no growth retardation. This ruled out metabolic and genetic defects. The IgG, IgA and IgM levels were found to be 35 mg/dL, 1 mg/dL and 64 mg/dL respectively. The patient's IgM was above 20 mg/dL therefore it was not evaluated as agammaglobulinemia. Besides, by flow cytometry CD19 surface antigen which is a B lymphocyte marker, was found to be %4. In agammaglobulinemia B lymphocytes are either absent or below %2. In CVID patients, B cell number may be found either normal or decreased. IgG and IgA levels are decreased. IgM levels are found to be decreased in approximately half of the patients (6). With the help of these, our case was not thought to have agammaglobulinemia and was diagnosed as CVID.

Conclusion: Beside having a deficiency in immunoglobulins CVID patients also have a decline in T cell function. Our case was PPD (-). PPD reflects the delayed cell mediated functions. The (-) PPD in this patient indicates a defect in T cell function and therefore supports CVID diagnosis. HIV and EBV infections were ruled out by serologic assessment. Besides, chronic lymphocytic lymphoma, thymoma, non-Hodgkin

lymphoma and malignancies of B cells were ruled out either by physical examination or by laboratory findings.

*Giardia lamblia* is a frequent protozoon in the western world. This parasite infects by fecal-oral contamination. The symptoms include cramp-like abdominal pain, anorexia, nausea, abdominal swelling, weight loss and diarrhea (5). The stool is described to be foul-smelling and sticky. Rectosigmoidoscopy is useless for these patients. The diagnosis is made by the identification of the parasite in the stool and in the duodenal aspiration material. To detect the organism, especially in the doubtful cases, more than one stool sample may be needed. Usually the organisms that are detected in duodenal aspiration and biopsy are different. The patient who are thought to be infected are treated by empirical treatment instead of invasive and expensive techniques as empirical treatment is cheaper, morbidity is minimal and the treatment is effective. Metronidazole 250 mg tid PO for 7 days is the treatment of choice. In our case, the diarrhea of the patient disappeared after treatment of giardiasis and he started taking immunoglobulin therapy periodically from the immunology outpatient clinic because of his immunodeficiency. He didn't have diarrhea for the 10 month period of observation.

#### REFERENCES

1. Borre -Sinoussi F, Cherman JC, Rey F, et al. Isolation of a T lymphocytic retrovirus from a patient at risk for acquired immune deficiency syndrome(AIDS). *Science* 1983;220:868-871
2. Rosen FS, Cooper MD, Wedgwood RJP. The primary immunodeficiencies. *N Engl J Med* 1984;311:300-310
3. Hanson LA, Brandtzaeg P. The mucosal defense system. In: Stiehm RT, Fulginite V, eds. *Immunologic Disorders in infants and Children* 2nd Ed. Philadelphia: WB Saunders Company, 1980; pp 137-164.
4. Hermens PE, Diaz-Buxo JA, Stobo JD. Idiopathic late-onset immunoglobulin deficiency. *Am J Med* 1976;221-232
5. Moore GT, Cross WM, McGuire D, et al. Epidemic giardiasis at a ski resort. *N Engl J Med* 1969;281:402-407
6. *Pediatric Clinics of North America* Volume 47, Number 6, December 2000 Copyright © 2000 W.B. Saunders Company (1225-1252), 1355-1369)
7. Schmerin MJ, Jones TC, Klein H. Giardiasis: association with homosexuality. *Ann Intern Med* 1978;88:801-803