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Case Report

Efficacy of Ganciclovir on CMV Retinitis Complication of Common Variable Immunodeficiency

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Abstract

Common variable immunodeficiency (CVID) is a heterogeneous disease with different clinical phenotypes that is characterized by hypogammaglobulinemia, abnormal antibody response, and susceptibility to bacterial infections as well as severe viral infections and autoimmunity.

Here we report a case of CVID with autoimmune hemolytic anemia presenting with blurred vision and cytomegalovirus retinitis which improved after treatment with ganciclovir.

Keywords CVID, CMV retinitis, hypogammaglobinemia, ganciclovir

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Introduction

Common variable immunodeficiency (CVID) is a collection of primary immunodeficiency diseases characterized by hypogammaglobulinemia and impaired antibody response. The majority of CVID patients present between the ages of 20-40 years, but 20-50% are under the age of 20 years, according to population genetic studies (1). Delays in diagnosis and proper treatment lead to severe irreversible complications (2).

Factors such as consanguinity and early-onset disease can determine a subgroup of patients characterized with poor prognoses, more complications, and in need of aggressive treatment (3). In CVID patients, several conditions can occur, including recurrent bacterial/viral infection, autoimmunity, lymphocytic infiltration, and malignancy (4-8).

The pathophysiology of CVID is still unknown (9);

however, treatment universally commences with immunoglobulin replacement therapy and prophylactic antibiotic therapy. This treatment improved patient survival rates, but it cannot manage particular non-infectious complications of the disease (10-11).

Cytomegalovirus (CMV) is a DNA virus of the herpes viridian family. It causes severe infection in immunocompromised patients (12-13). Severe CMV infection is a rare condition in CVID patients usually with the coincidence of other non-infections complications (14). CMV infections in lymph node (lymphadenitis), lung (pneumonitis) and gastrointestinal tract (enteropathy) have been reported (14). Here we report a CVID patient with CMV retinitis associated with autoimmune hemolytic anemia.

Case report

Our patient is an 11-year-old boy with a history of chronic diarrhea, recurrent pneumonia, recurrent otitis media, and subcutaneous abscess. He is the second child of unrelated parents with no history of primary immunodeficiency in his family. He received vaccines without complications. He had a history of mastoiditis and surgical drainage in the third year of life. The first presentation was severe watery chronic diarrhea and failure to thrive (FTT) at 23 days after birth. He was healthy until the diagnosis of primary immunodeficiency in his second year of life. At his first immunological evaluation, a tentative diagnosis of selective IgA deficiency was made (IgA=5 mg/dl, IgM=54 mg/dl, IgE=33 IU/ml, IgG=2102 mg/dl).

At the age of 7 years, autoimmune hemolytic anemia, thrombocytopenia, and hepatosplenomegaly were added to his clinical picture. There was no evidence of anti-platelet antibody, and Coombs' test and all microbiological evaluations were negative. The patient was then treated with systemic corticosteroid. Recurrent pulmonary bacterial infection was the prominent clinical picture afterwards, leading to the boy's frequent hospitalization. Chest computed tomography (CT) scan revealed pulmonary bronchiectasis. Aspergillums grew in bronchoscopy and fungal cultures of bronchoalveolar lavage (BAL), and with the administration of an antifungal (amphotricin-B) the patient improved. In the second immunological evaluation, pan-hypogammaglobinemia was seen, and intravenous immunoglobulin therapy was initiated with a diagnosis of CVID. Specific antibody responses to tetanus and diphtheria toxin were impaired. Flow cytometry of the peripheral lymphocytes showed normal B cells and T cells (**Table 1**). Upon physical examination, the patient had a failure to thrive, huge hepatosplenomegaly, and diffuse wheezing and rales in both lungs. In the child's extremities, severe clubbing and acral cyanosis were observed, and diffuse flat warts on his trunk were also recorded.

At the age of 10 years, the child presented with blurred vision. In an ophthalmologic consultation, cotton-wool spot was reported, suggestive of CMV retinitis (**Figure 1**). To make a definite diagnosis, a virology investigation was performed which measured the CMV polymerase chain reaction (PCR) in a blood sample. The result was positive, and CMV

retinitis was confirmed. For treatment of this complication, intravenous ganciclovir was administered, after which, significant improvement was achieved without complications.

Table 1. Laboratory Data of the Patient at the Time of Diagnosis of CVID

Immunologic parameters	Results
IgA, mg/dl	5
IgM, mg/dl	24
IgG, mg/dl	452
IgE, IU/ml	11
Anti-tetanus Ab, IU/ml	<0.1
Anti-diphtheria Ab, IU/ml	<0.1
Anti-pneumococcal Ab, mg/L	<0.1
CD3+ T cells, in lymphocytes	56%
CD4+ helper T cells, in lymphocytes	30%
Regulatory CD4+ T cells, in T cells	2.2 %
CD8+ cytotoxic T cells, in lymphocytes	37%
CD16+ NK cells, in lymphocytes	5%
CD19+ B cells, in lymphocytes	3%
Switched memory B cells (CD19+CD27+IgD-, in total B-cells) 5	0.3%

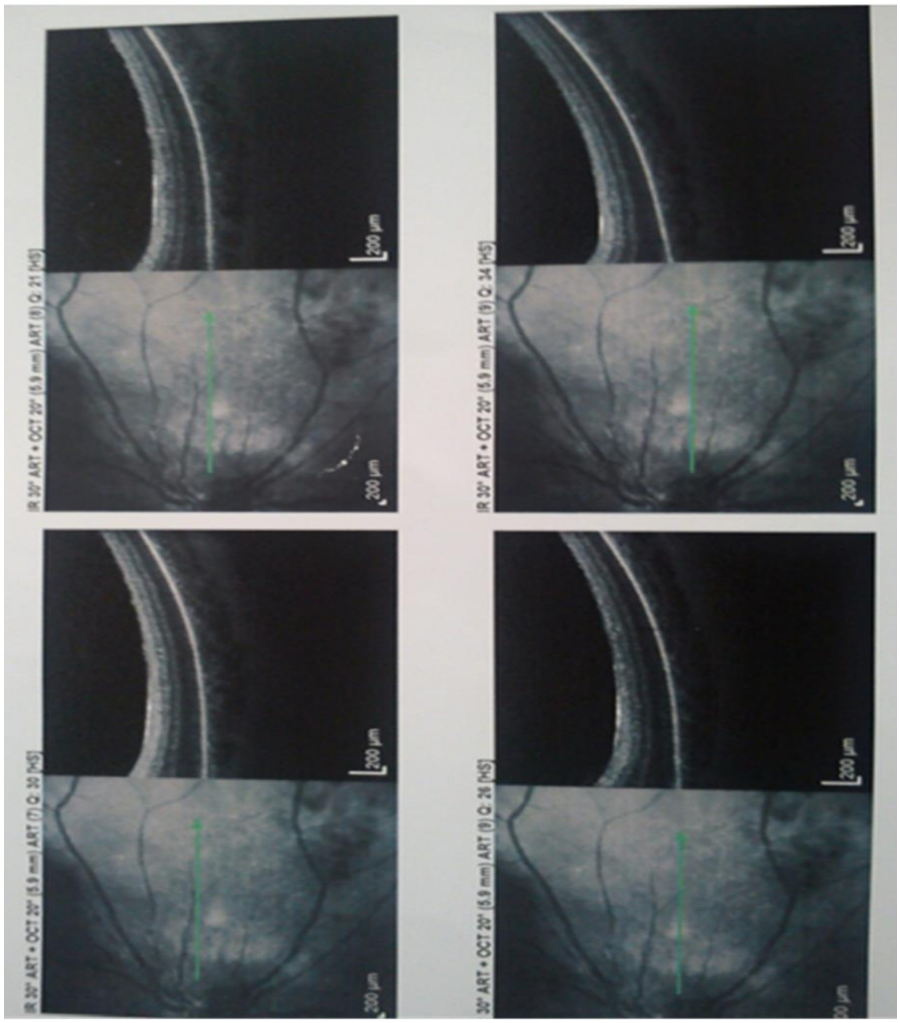

Figure 1. Optical Coherence Tomography in ophthalmologic evaluation revealed cotton-wool spot

Discussion

Common variable immunodeficiency is a heterogeneous disorder characterized by pan-hypogammaglobulinemia, abnormal antibody response, and profound susceptibility to bacterial infection (1). Diagnostic delay in CVID may result in severe irreversible complications; thus, early diagnosis and appropriate treatment can lead to a better prognostic outcome (2). Recurrent bacterial infections in the gastrointestinal and respiratory systems are major clinical pictures in CVID patients (15). Hematologic and ophthalmologic complications of CVM infection are seen in an estimated 8.6% and 5.5% of immunocompetent patients, respectively (15). There is no evidence that CMV infection is highly prevalent in CVID, but associations of reduced immunoglobulin production and herpes virus infection have been highlighted in patients with immune dysregulation syndromes (15-16).

Our patient presented with early onset CVID and a diagnosis of progressive antibody deficiency. His clinical presentations were chronic watery diarrhea, FTT, autoimmune hemolytic anemia, and recurrent bacterial infections which are typically recorded among other CVID patients. However, he was selective IgA deficient and progressed to CVID, which indicated a gradual increase in the severity of his condition usually associated with T-cell defects. The patient experienced blurred vision, and in an ophthalmologic evaluation, evidence confirmed CMV retinitis. Based on the patient's ophthalmologic consultation, intravenous ganciclovir was administered.

The authors have recently reported another case of CVID with macrophage activating syndrome and CMV retinitis associated with retinal detachment (15). Because of diagnostic delay, the patient in that case experienced retinal detachment and visual impairment despite appropriate treatment (15). In the current case, however, treatment was effective, indicating that treatment of retinitis due to CMV infection is individualized and the location of active retinitis and immune status are important factors in treatment (15). Current anti-CMV drugs available are ganciclovir, valganciclovir, foscarnet, cidofovir, fomivirsen, ganciclovir implants, and oral valganciclovir (15, 17). In our patient, CMV retinitis was significantly improved with intravenous ganciclovir without any visual impairment.

Conclusion

Early diagnosis of CVID and its complications, such as CMV retinitis, and appropriate treatment with intravenous ganciclovir can prevent irreversible changes in the retina.

Conflicts of interest The authors declare that they have no conflicts of interest.

References

1- Chapel H, Cunningham-Rundles C. Update in understanding common variable immunodeficiency disorders and the management of patients with these conditions. Br J Haematol. 2009;145:709–727.

2- Bazregari S, Azizi G, Tavakol M, et al. Evaluation of infectious and non-infectious complications in patients with primary immunodeficiency. Cent Eur J Immunol. 2017; 42(4): 336–341.

3- Aghamohammadi A, Abolhassani H, Moazzami K, et al. Correlation between common variable immunodeficiency clinical phenotypes and parental consanguinity in children and adults. J Investig Allergol Clin Immunol. 2010;20(5):372-9.

4- Azizi G, Bagheri Y, Tavakol M, et al. The Clinical and Immunological Features of Patients with Primary Antibody Deficiencies. Endocr Metab Immune Disord Drug Targets. 2018;18(5):537-545.

5- Aghamohammadi A, Farhoudi A, Moin M, et al.: Clinical and immunological features of 65 Iranian patients withcommon variable immunodeficiency. Clin Diagn Lab Immunol2005;12:825–832.

6- Aghamohammadi A, Parvaneh N, Tirgari F, et al. Lymphomaof mucosa-associated lymphoid tissue in common variableimmunodeficiency. Leuk Lymphoma. 2006;47:343–346.

7- Aghamohammadi A, Allahverdi A, Abolhassani H, et al. Comparison of pulmonary diseases in common variableimmunodeficiency and X-linked agammaglobulinaemia.Respirology. 2010;15:289–295.

8-Khodadad A, Aghamohammadi A, Parvaneh N, et al. Gastrointestinal manifestations in patients with common variable immunodeficiency. Dig Dis Sci. 2007;52:2977–2983.

9- Rezaei N, Aghamohammadi A, Kardar GA, et al. T helper 1 and 2 cytokine assay in patients with common variable immunodeficiency. J Investig Allergol Clin Immunol. 2008;18(6):449-53.

10- Abolhassani H, Aghamohammadi A, Abolhassani F, et al. Health policy for common variable immunodeficiency: burden of the disease. J Investig Allergol Clin Immunol. 2011;21:454–458.

11- Rezaei N, Abolhassani H, Aghamohammadi A, and OchsHD: Indications and safety of intravenous and subcutaneousimmunoglobulin therapy. Expert Rev ClinImmunol 2011;7:301–316.

12- Sissons JG, and Carmichael AJ. Clinical aspects and management of cytomegalovirus infection. J Infect. 2002;44:78–83.

13- Fallah S, Tabatabaei A, Pournasir Z, et al. Cutaneous cytomegalovirus infection in a child with hyper IgE and specific defects in antibody response to protein vaccines. Braz J Infect Dis 2011;15:484–485.

14-Stack E, Washington K, Avant GR, et al.: Cytomegalovirus enteritis in common variable immunodeficiency. South Med J 2004;97:96–101.

15- Aghamohammadi A, Abolhassani H, Hirbod-Mobarakeh A, et al. The uncommon combination of common variable immunodeficiency, macrophage activation syndrome, and cytomegalovirus retinitis. Viral Immunol. 2012 Apr;25(2):161-5.

16-Mullighan CG, Read SJ, Bird AG, et al. Human cytomegalovirus infection is not increased in common variable immunodeficiency. J ClinImmunol1996;16:272–277.

17- Studies of Ocular Complications of AIDS Research Group, in collaboration with the AIDS Clinical Trials Group. Mortality in patients with the acquired immunodeficiency syndrome treated with either foscarnet or ganciclovir forcytomegalovirus retinitis. N Engl J Med 1992;326:213–220.