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Case Report

Microbiology Section

Chronic Giardiasis in a Case of Common Variable Immunodeficiency (CVID): A Case Report

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ABSTRACT

Common Variable Immunodeficiency (CVID) is a primary immunodeficiency characterized by low antibody levels and recurrent infections. This makes an individual more prone to recurrent respiratory and gastrointestinal tract infections. In cases where there is persistent positive finding of intestinal parasites in stool, a high index of suspicion should be raised to rule out immunodeficiency state. Early diagnosis of such cases will help in reducing the morbidity and better management of the patient. A case of CVID in 18-year-old male with recurrent lower respiratory tract infection and chronic diarrhoea due to *Giardia lamblia* is reported herewith.

Keywords: Chronic diarrhoea, *Giardia lamblia,* Hypogammaglobulinaemia

CASE REPORT

An 18-year-old male, was referred to Chest Medicine Department in February, 2015 with high grade fever, haemoptysis, and 50-70 cc mucoid expectoration since five days. He had pleuritic chest pain, shortness of breath since fifteen days. He had progressive weight loss of about 10 kilos in the past one year. Chest X-ray revealed left sided patchy consolidation. His stool examination revealed cysts of *Giardia lamblia.* Sputum culture did not grow bacterial or fungal pathogens. He was treated with antibiotics and metronidazole in the Chest Medicine Department and had symptomatic relief.

He gave history of recurrent episodes of rhinitis, sinusitis, lower respiratory tract infection and diarrhoea since childhood of which, there were three major episodes. In July 2012, during the episode of respiratory tract infection and diarrhoea, investigations were carried out which revealed that he had moderate leucocytosis, raised ESR. His sputum smear and culture was negative for tubercle bacilli and other respiratory pathogens. His stool examination revealed trophozoites of *Giardia lamblia*. He was treated for the same and he recovered symptomatically. In October 2013, he again had respiratory tract infection and had high fever, mucoid expectoration with streaky haemoptysis. Chest X-ray showed consolidation of left lung and pleural effusion. CT scan was performed which revealed patchy consolidation of left lung with pleural reaction and mediastinal adenopathy suggestive of pulmonary TB. However, considering negative sputum for tubercle bacilli, based on CT findings, diagnosis of basal pneumonia was made and the patient was treated with antibiotics. As he had abdominal pain and discomfort, stool examination was carried out which revealed cysts of *Giardia lamblia*. He was treated for the same with symptomatic relief. In January 2014, he was admitted in the hospital with the same complaints of respiratory tract infection. In addition, he had breathlessness of grade 4 and left sided pleuritic chest pain. Sputum smear and culture was again negative for tubercle bacilli. No bacterial and fungal pathogens were grown. Chest X-ray showed left lung opacities. HRCT was suggestive of air bronchogram, left upper, middle and both lower lobes opacities, interlobular septal thickening throughout the fields. His pO_2 levels were 60mmHg. In view of these findings, he was nebulised, given non invasive ventilation and treated with Tab Faropenem 200mg tds, vasopressors, bronchodilators, and prednisolone. His renal functions were within normal limits, however liver enzymes, alkaline phosphatase levels were raised and serum albumin was low. As the patient had loose motions since admission, stool examination was performed which demonstrated trophozoites of *Giardia lamblia*. He was put on oral metronidazole therapy.

In view of these repeated episodes of respiratory tract infection and diarrhoea, the patient was evaluated to rule out immunodeficiency state. Autoimmune profile did not reveal any autoimmune deficiency disease. He was negative for HIV antibodies. CD4 counts were 545 cells/cu mm. Hepatitis B and C was also ruled out.

Immunoglobulin levels were markedly low, i.e.; IgG 0.42mg/L, Ig A less than 0.255mg/L, Ig M less than 0.161mg/L, Ig E less than 1.5 IU/mL. Considering the above findings, he was diagnosed as a case of common variable immunodeficiency (CVID) as per the European society for immunodeficiencies diagnostic criteria [1] having pneumonia with Acute Respiratory Distress Syndrome (ARDS) and chronic giardiasis. Intravenous Immunoglobulin (IVIG) in the dose of 400 mg/kg body weight was given once in four weeks.

However, due to the present episode of February 2015, making hospitalization again mandatory, and also taking into account the severity and intensity of infection, it was decided to give IVIG in the dose of 400 mg/kg body weight once in three weeks. Repeat investigations could not be carried out as the patient took discharge and was lost to follow up.

DISCUSSION

Common Variable Immunodeficiency (CVID) is characterised by low levels of most or all immunoglobulins classes, a lack of B lymphocytes or plasma cells that are capable of producing antibodies. Some patients lack T-helper lymphocytes which are necessary for a normal antibody response. This has been attributed to intrinsic B cell defects, deficient T cell help and excessive suppressor cell activity [2].

Several mechanisms have been proposed to explain the immune abnormalities in patients with CVID, including an intrinsic B-cell defect, excessive T-suppresser cell activity [3], deficient T-cell helper function [4], cytokine deficiencies [5,6], and suboptimal T cell-B cell interactions through deficient expression of the CD40 ligand [7].

These abnormalities reflect the variability of CVID and support the concept that more than one gene is probably responsible for the immune abnormalities in CVID.

On review of literature no case of chronic giardiasis in CVID has been reported from India. There are few cases of chronic giardiasis in CVID reported from other countries [Table/Fig-1].

S.No	Study	Place	Year
1.	Domínguez-López ME, González-molero I, Ramírez-Plaza CP [8]	Spain	2011
2.	Onbaşi K, Günşar F, Sin AZ, et al., [9]	Turkey	2005
3.	Bloch-Michel C, Viallard JF, Blanco P et al., [10]	France	2003

[Table/Fig-1]: Reported cases of chronic giardiasis in CVID.

CVID manifests usually in 2nd or 3rd decade of life and is therefore also called acquired hypogammaglobulinaemia, adult onset hypogammaglobulinaemia or dysgammaglobulinaemia. Clinical manifestations include recurrent respiratory infections like otitis media, chronic sinusitis, recurrent pneumonia. *Haemophilus influenza* and *Streptococcus pneumoniae* are commonly associated with these infections. In approximately half of the patients with CVID, the gastrointestinal tract is affected, presenting with malabsorption or chronic diarrhoea [11,12]. The chronic diarrhoea is especially due to *Giardia lamblia* [9,13]. Autoimmune diseases, granulomatous diseases and malignancy can also occur [14]. Approximately 50% cases of CVID exhibit diarrhoea and malabsorption related to *Giardia lamblia*, sprue like disorder and small bowel lymphoma. *Giardia lamblia* can produce serious diarrhoeal disease with intestinal malabsorption, steatorrhoea, frequent relapse and marked weight loss and can progress to chronicity [15]. Giardiasis in such patients may be refractory to treatment. There can be excessive enterocyte damage, subtotal villous atrophy and development of nodular mucosal pattern [16].

The mainstay of the treatment is to keep patients free of infections and to minimize the effect of chronic conditions such as giardiasis, sprue, malabsorption, weight loss, etc. It is a common strategy to treat the patients having CVID with intravenous immunoglobulin with a dose of 400mg/kg body weight once in three or four weeks and giardiasis with oral metronidazole. This therapy is to maintain a sufficient serum trough of IgG [17]. However, treatment with IVIG may not be useful for gastrointestinal infections such as chronic diarrhoea. This may be related to the fact that intravenous immunoglobulin does not reach the gut lumen and also intravenous preparations do not contain IgA or IgM. Especially, IgA is important in the gut to deal with infections [18,19]. The index patient also had *Giardia* infection on all four occasions. Repeat examination of stool of the patient was not performed after giving a course of Metronidazole each time and could not label the patient having cured. There was only symptomatic relief. The cause of pneumonia on all four occasions could not be established.

Intravenous IL -2 replacement is viewed as an adjunctive therapy to IVIG. Its use has also been considered in patients with CVID and refractory infections. Improvement in T cell function and formation of antibodies has been observed but no patient has been placed into complete remission. There is also a report by Smith et al., who have treated the patient of CVID with a recombinant human IgG, anti – TNF therapy for three months. tumor necrosis factor- alpha receptor but could not achieve the required goal [20].

Because of the recurrence and infections becoming severe each time, it was decided to give IVIG once every three weeks and also to give oral metronidazole for long term. However, IL-2 or anti TNF could not be considered because of their non-availability and cost.

CONCLUSION

The present case highlights the fact that the clinicians should have a high suspicion of CVID in patients presenting with recurrent respiratory tract infections and chronic gastrointestinal infections which is also recommended by other authors. Even though, intravenous immunoglobulin may not provide improvement in all the patients, early diagnosis of CVID is mandatory. This would prevent significant morbidity, mortality and improve prognosis.

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