

CASE REPORT

COMMON VARIABLE IMMUNODEFICIENCY

Hardik Parmar¹, K M Mehariya², Charul Purani³

Authors' Affiliation: ¹Resident, ²Professor & Head of Department, ³Assistant Professor, Department of Paediatrics, BJ Medical College, Ahmedabad

Correspondence: Dr. Hardik Parmar, Email: hardikdoc@gmail.com

ABSTRACT

Common variable immunodeficiency (CVID) is a form of severe antibody deficiency with an estimated prevalence of 1 in 25,000 to 1 in 100,000. The disorder apparently results from currently undefined immune deregulations resulting in failed B-cell differentiation with impaired secretion of immunoglobulins. A 5-year female presented with fever, cough and shortness of breath at rest. Past medical history of incision and drainage for empyema followed by decortications before 2 years were there. Physical examination was significant bilateral crepitation and bronchial breathing. Laboratory data were significant for leukocytosis. The patient was diagnosed with CVID & started on four week regimen of IVIg. This case emphasizes the need for a high index of clinical suspicion for CVID in patients presenting with recurrent sinopulmonary infections.

Keywords:-Immunodeficiency, sinopulmonary, intravenous immunoglobulin, antibody.

INTRODUCTION

Common variable immunodeficiency (CVID) is a form of severe antibody deficiency with an estimated prevalence of 1 in 25,000 to 1 in 100,000. The disorder results from failed B-cell differentiation with impaired secretion of immunoglobulins. It has a broad range of clinical manifestations including recurrent infections of the respiratory tract and chronic lung disease, autoimmune diseases, gastrointestinal disorders, granulomatous infiltrative diseases, lymphoma and solid tumors. We report a case of a 5-year old female who had presented with classical symptoms of CVID over a period of several years and review the various clinical manifestations, diagnosis and treatment options for CVID.

CASE PRESENTATION

A 5 year old female presented with a history of high grade fever, cough and shortness of breath at rest. The parents' of the patient described chronic dyspnea for approximately last 2 months limiting her ability to perform outdoor activity. Patient was referred from other hospital for further work-up of frequent respiratory infection.

Past medical history of incision and drainage done for empyema before 2 years followed by decortications. History of recurrent cough since 1 year of life requiring antibiotic and frequent hospitalization, multiple episode of ear discharge and perforation of tympanic membrane.

On examination, she appeared chronically ill. She had temperature 100.5 °F was tachycardic (120/min), tachypneic (48/min) with blood pressure 100/58 mmHg, was saturating 92% on 5 Ltr/min of oxygen with mask, had grade-3 clubbing and had some pallor.

Physical examination was significant bilateral crepitation and bronchial breathing, had abdominal distension with hepato-splenomegaly. The remainder physical examinations were within normal limit.

Her white blood cell (WBC) count was elevated at 14,800/mm³, this was 7800/mm³ at discharge. Her renal function test and liver function test were within normal limit. Chest X-ray suggestive of right mid zone & lower zone consolidation. 2D-echo which was showing thin rim of pericardial effusion before 2 months was normal during admission. ABG showed pH of 7.5, PCO₂ of 32 mmHg, PO₂ of 48 mmHg and HCO₃ of 25 mEq/l on 5 l/min of oxygen with mask.

ASO, CRP and RA Factor were negative. HRCT Thorax- Bronchiectatic changes in posterior segment of right upper lobe, right middle lobe, anterior basal, lateral basal, medial basal segment of right lower lobe and inferior lingular segment of left lower lobe. And consolidation with air-bronchogram in right mid zone /lower zone, collapse involving left lower lobe. Multiple enlarged pre & para tracheal and subcarinal lymphnode.

Sputum for gram stain and sputum for AFB were normal. USG-Abdomen was showing hepato-splenomegaly. Otoscopy of right ear showed perforated tympanic membrane with discharge. Blood culture did not had any growth at 72 Hrs. she was started on

intravenous vancomycin and cefepazone-sulbactam, and nebulized with gentamycin and salbutamol.

Given the patient's recurrent respiratory infection since 1 year of life wide differential diagnosis considered to include genetic condition such as; cystic fibrosis, immotile cilia syndrome, alfa-1 antitrypsin deficiency and immunodeficiency. Work-up initiated with a human immunodeficiency virus(HIV)screening test non-reactive and a negative sweat chloride test. Immunoglobulin level were significantly reduced Ig A – 0.217(decreased) (N= 0.7 – 4.0 gm/L), Ig M – 0.601(normal) (N= 0.3 – 2.4 gm/L) and Ig G – 1.009(decreased) (N= 0.7 – 16 gm/L).

The patient was given 0.4 gm/kg of IVIg and planed to give IVIg every 4 weekly and follow regularly to improve quality of life.

DISCUSSION

CVID is a rare form of severe antibody deficiency with an incidence of 1 in 25,000 to 1 in 100,000. The mean age of diagnosis is 30 years, although there can be a delay in diagnosis by many years as demonstrated in our patient¹. The disorder results from failed B-cell differentiation. Thus, plasma cells do not develop and immunoglobulin secretion is impaired. A number of defects of T-cell function and deficits in the memory B-cell pool have been identified, but the underlying cause of this defect remains unknown¹. CVID has variable clinical manifestations, the most common being recurrent bacterial infections caused by encapsulated bacteria¹. Bacterial infections commonly involve the sinuses and respiratory tract leading to sinusitis, otitis media, bronchitis and pneumonia. Chronic sinusitis and bronchiectasis are frequent complications in untreated patients leading to significant morbidity and mortality¹.

Giardiasis is a frequent infection in patients leading to chronic diarrhea. They can also have diarrhea secondary to dysgonic fermenter 3, which is unusual in immunocompetent patients². They are prone to severe herpes simplex, cytomegalovirus infections of the gastrointestinal tract^{3,4} and meningoencephalitis from enteroviral infection. Patients who are not receiving IVIG owing to a delay in diagnosis may develop sepsis or meningitis, which can be fatal¹.

These patients are also at higher risk of developing other autoimmune diseases such as thrombocytopenic purpura, hemolytic anemia and/or neutropenia⁵. In the largest published case series of 248 patients, a 7.7% incidence of non-Hodgkin's lymphoma (NHL) was reported¹. Mucosal associated lymphoid tissue lymphomas, an uncommon form of NHL, can occur in these patients in the stomach or bronchial tissue^{6,7}.

Other uncommon manifestations include granulomatous lung disease, follicular bronchiolitis, inflammatory bowel disease, sprue-like illness, nodular lymphoid hyperplasia and lymphoid interstitial pneumonia.⁸

CVID should be suspected in any patient with recurrent infections, especially of the upper or lower respiratory tract. IgG, IgA or IgM levels should be less than two standard deviations below the mean for age-adjusted standardized reference. They should also have inadequate antibody response to pneumococcal vaccine and tetanus toxoid or absent isohemagglutinins to confirm the diagnosis⁹. The mainstay of treatment is IVIG. The target trough level should be 400–500 mg/dl, which is achieved by infusing a dose of 200–400 mg/kg every three or four weeks. The dosage varies from patient to patient, and IgG levels should be checked periodically to attain a target trough level. Autoimmune and granulomatous components of this disease do not respond to treatment with IVIG. There has been recent interest in the use of tumor necrosis factor (TNF) antagonists and anti-CD20 immunomodulators in treating autoimmune and granulomatous diseases based on the dramatic improvement of some clinical manifestations documented in some case reports¹⁰⁻¹². However, long-term immunomodulators should be used with extreme caution as these patients are at high risk of developing malignancies.

CONCLUSION

The case presented here emphasizes the need for a high index of clinical suspicion for CVID in patients presenting with recurrent sinopulmonary infections. Although IVIG provides improvement in these patients, early diagnosis is the key to preventing significant morbidity and mortality and improving prognosis.

Abbreviations

ABG: arterial blood gas;
CT: computerized tomography;
CVID: common variable immunodeficiency;
HIV: human immunodeficiency virus;
Ig: immunoglobulin;
IVIg: intravenous immunoglobulin;
TNF: tumor necrosis factor;
WBC: white blood cell count.

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