Case Report

A Rare Case of Common Variable Immunodeficiency in Children Mimicking Sarcoidosis

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ABSTRACT

Common variable immunodeficiency (CVID) is the most prevalent clinically significant antibody deficiency syndrome in children. It is characterized by a low serum immunoglobulin IgG and a low IgA and/or low IgM resulting in recurrent and severe infections, associated in some cases with autoimmune manifestations and granulomatous lesions in which case it can be mistaken for sarcoidosis. We report a child who was initially diagnosed as sarcoidosis but later turned out to be CVID requiring a significantly different therapeutic approach. Prompt recognition of CVID is important to allow early introduction of immunoglobulin replacement therapy to decrease infection frequency, reduce development of secondary disease complications and retard progression of tissue damage. We report this case to increase awareness amongst general paediatricians regarding CVID which is the one of the commonest primary immunodeficiency seen in children.

Keywords: Sarcoidosis, common variable immune deficiency, hypogammaglobulinemia

INTRODUCTION

Sarcoidosis is a multisystem disorder characterized by mediastinal lymphadenopathy, pulmonary parenchymal infiltration with cutaneous and ophthalmic manifestation. It is a diagnosis of exclusion. The demonstration of granulomatous inflammation, while valuable in the appropriate clinical setting, does not rule out the possibility of alternative diagnoses. Differential diagnosis includes tuberculosis, malignancy, fungal infections, immunodeficiency, foreign body and drug therapies which need consideration. Common variable immunodeficiency (CVID) is characterized by a low serum immunoglobulin IgG and a low IgA and/or low IgM resulting in recurrent and severe infections, associated in some cases with autoimmune manifestations and granulomatous lesions[1]. We describe a fourteen year old male child who was initially diagnosed as sarcoidosis by physicians but later turned out to be CVID based on the clinical course and immunological investigations, requiring a significantly different therapeutic approach.

CASE DESCRIPTION

A fourteen year old male, initially diagnosed with sarcoidosis at the age of ten years on oral corticosteroids presented to us with fever, generalized lymphadenopathy, cough and progressive dyspnoea. The patient was well until 10 years of age when he presented to a physician with fever, weight loss, and cough for the last six months. He was diagnosed as sarcoidosis and managed on variable doses of corticosteroids with transient efficacy on the basis of high ESR, X-ray chest suggestive of hilar lymphadenopathy with bilateral infiltrates, cervical lymph node biopsy suggestive of non-caseation granulomas (Figure 1) and non-response to anti-tuberculosis therapy. However, subsequent clinical course was marked by the development of bilateral knee arthritis, persistence of clinical signs and worsening of radiological signs. On presentation to us, clinical examination revealed wasting, tachycardia, tachypnea, bilateral wheeze, crepitations and hepatosplenomegaly. Family history was not significant and immunization was complete with no adverse events. Laboratory investigations revealed anaemia (Hb=7.4 gm/dl), neutrophilic leucocytosis (WBC=12.2 x 10.8 x 10^9/L Neutrophils=70%, Lymphocytes=30%), increased platelets (6, 70000/cmm), raised ESR (74 mm at end of one hour), normal urine, liver, renal function and bone

marrow examination. Direct Coombs test was negative. Sputum was negative for acid-fast bacilli (GeneXpert) Culture studies were negative. High resolution CT chest showed bilateral lower lobe bronchiectasis (Figure 2). Immunological investigations revealed negative ANA, ANCA, RF, decreased serum immunoglobulin levels (IgG -1.1g/L, IgA- 0.3 g/L, IgM- 0.2g/L), reduced isohaemagglutin titres to antigen with Anti-A titre of IgM 1:1 ; IgG 1:1 and Anti-B titre of IgM:1:2; IgG:1:3, normal lymphocyte subset analysis and dihydrorhodamine flow cytometry. Based on evidence of hypogammaglobulinemia with normal T cell count, impaired antibody response, autoimmune manifestation of arthritis, bronchiectasis, and granuloma on lymph node biopsy the diagnosis was revised to CVID and counselled for immunoglobulin therapy (IVIG) along with oral corticosteroids with respiratory physiotherapy.

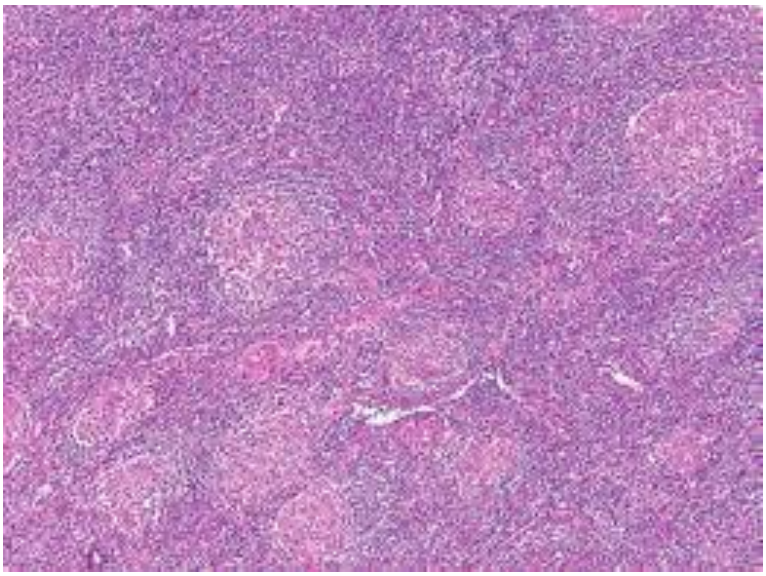

***Figure* 1:** Hematoxylin-eosin stain of a lymph node shows non-caseating granulomas

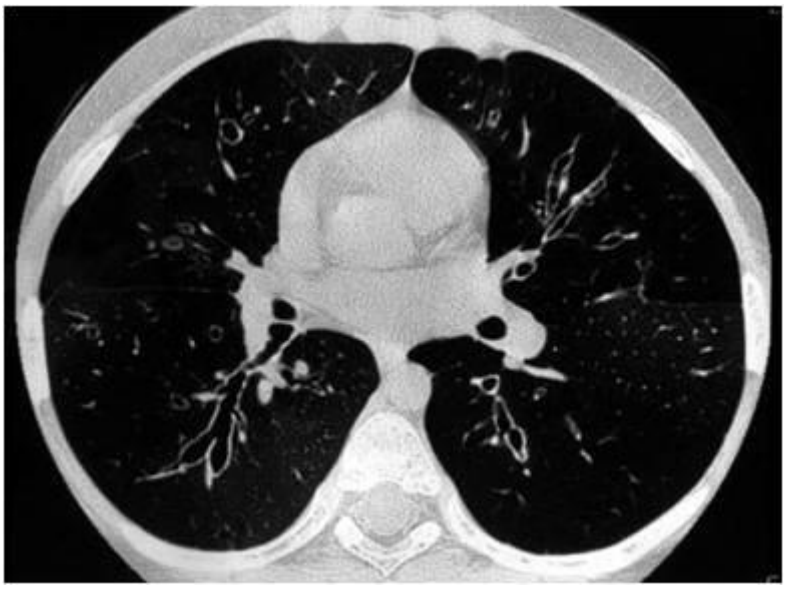

***Figure 2*:** High resolution CT chest showed bilateral lower lobe bronchiectasis

DISCUSSION

Our patient fulfilled the Revised European society of immune deficiencies (ESID- 2014) diagnostic criteria for CVID [1]. The underlying causes of CVID are largely obscure with genetic mutations identified as the cause of CVID in about 10% of patient. Mutations in the genes encoding ICOS, TACI, CD19, CD20, CD21, CD80 and

BAFFR have been identified as causative of CVID [2]. The disease has varied presentations with combination of infections with features of autoimmunity or granulomatous inflammation. Autoimmune manifestations of CVID include immune thrombocytopenic purpura, autoimmune haemolytic anaemia, rheumatoid arthritis, pernicious anaemia, thyroiditis, inflammatory bowel disease, primary biliary cirrhosis, vitiligo, systemic lupus erythematosus [3]. Hypogammaglobulinemia is a characteristic feature of CVID unlike polyclonal gammopathy in sarcoidosis. Multisystem granulomatous inflammation with chronic lung disease manifestations of bronchiectasis and granulomatous lymphocytic interstitial lung disease occurs in 25% of CVID patients [4]. CVID manifestations may develop over many years, and should be considered if a patient with sarcoidosis has a combination of unusual clinical course including autoimmune manifestations (e.g. arthritis as in our case) or any unusual, recurrent, severe infection(s) (bronchiectasis in our patient) or hypogammaglobulinemia (present in our patient). Similar reports of delayed diagnosis of CVID presenting initially with granulomatous disease do exist primarily in adults [5, 6], [7, 8] IVIG remains the mainstay of therapy in CVID. The standard recommendation dose for IVIG is 400-600 mg/kg body weight every 3-4 weeks. Antimicrobial therapy is also indicated as immunoglobulin replacement alone may not adequately prevent or treat persistent infections. It is to be noted that the presence of granulomatous and autoimmune manifestations require a multidisciplinary approach requiring specific treatment because they can evolve independently and may not respond to immunoglobulin replacement alone [8]. Immunosupression in the form of corticosteroids, rituximab, azathioprine, cyclosporine A, infliximab are given but they do have an increased risk of infectious complications. Prospective trials on the effectiveness of immunosuppressive drugs in CVID are still lacking. Bronchiectasis which is a poor prognostic factor is managed with respiratory physiotherapy, bronchodilators and antibiotics. The life expectancy of CVID patients has considerably improved over the past 30 years from initially 12 years to currently over 50 years very likely because of the now-standard doses of replacement IVIG [10]. In essence, we would emphasize that the presence of non-caseating granuloma and bronchiectasis, along with extra pulmonary features required a step by step approach to differentiate between CVID and sarcoidosis which includes serum immunoglobulin estimation

CONCLUSION

Suspect CVID if a patient of apparent 'sarcoidosis' has an unusual clinical course, autoimmune manifestations or hypogammaglobulinaemia. We report this case in order to increase awareness amongst paediatricians which will lead to early introduction of immunoglobulin replacement therapy decreasing the morbidity and mortality of CVID.

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Nil.

CONFLICTS OF INTEREST

There are no conflicts of interest

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