

## AN UNUSUAL CASE OF SINUSITIS

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### Abstract

**Background:** Common Variable Immunodeficiency (CVID) is the commonest form of severe antibody deficiency. It is characterized by reduced levels of IgG (<400mg/dL) and low IgA and/or IgM levels, recurrent bacterial infections, impaired antibody responses despite the presence of B Cells and normal or near normal T immunity in 60% of patients. There is a high mortality from infections without treatment. The main stay treatment is to replace the immunoglobulins.

**Case Presentation:** We describe a British soldier with a 10 year history of recurrent chest infections, sinusitis and otitis media. He repeatedly presented 2 to 3 times a year complaining of either a green nasal discharge or a cough productive of yellow/green sputum. He presented three years ago with severe sinusitis which resulted in investigations highlighting hypogammaglobulinaemia. Subsequently he was started on immunoglobulin therapy with Flebogamma 40g three weekly.

**Recommendations:** Despite being a relatively rare condition, CVID when diagnosed, can be easily treated and improve patients' prognosis. Medical Officers should be aware of the condition as a differential diagnosis for individuals presenting with recurrent infections.

### Introduction

Common Variable Immunodeficiency disorder (CVID) is the commonest form of severe antibody deficiency and clinically it has a variety of presentations, the commonest being some form of infection [1]. The condition can be diagnosed easily with simple laboratory testing of immunoglobulin levels and further, more sophisticated, testing of vaccine responses. We describe a soldier who presented with recurrent infections, who was diagnosed with low immunoglobulin levels and successfully treated with immunoglobulin replacement therapy, which is of interest from both a medical and occupational perspective.

### Case Presentation

A 34 year old British Infantryman was deployed as a storeman and he presented to the Medical Centre with symptoms of recurrent sinusitis. He also complained of daily cough productive of yellow/green sputum, sinus pain over the past two weeks and night sweats intermittently over the last few years. He may have lost some weight over recent years. His past medical history included a hospital admission with pneumonia in 1995 and symptoms of colds and coughs since 1991. There was no history of chronic diarrhoea or joint pain. His current medication included Pencillin V 500mg qds for his sinusitis and a bronchodilator. He had no known allergies. He reported that he took two or three courses of antibiotics each year. His father had chronic bronchitis and died at the age of 59. He had one stepson and one brother with a chest problem. He was a non smoker, married and Caucasian. On examination he was thin, afebrile with stable observations. There was no significant cervical, axillary or inguinal lymphadenopathy. Cardiovascular,

respiratory and abdominal examination were entirely normal.

His initial blood tests showed a raised white cell count (WCC) and inflammatory markers with low serum immunoglobulin levels (IgG, IgA and IgM). A chest x-ray showed patchy consolidation in the right middle lobe adjacent to the right heart border. He was referred to the local immunology clinic for further investigation. Urgent CT chest, sinuses and abdomen showed mucosal thickening in the sinuses, with the abdomen and thorax being entirely normal with no evidence of adenopathy or bronchiectasis. Further detailed blood tests including functional antibody and lymphocyte function studies are shown in Table 1. He was commenced on an aggressive combination regime of therapy for his sinusitis including Flixonase nasal spray x2 puffs per nostril mane, Telfast 180mg mane and Montelukast 10mg at night. He was diagnosed with CVID and commenced on therapy with 40g of Vigam liquid on a x3 weekly basis. Within a year the soldier transferred to home immunoglobulin therapy. At 18 months after diagnosis he underwent an uneventful sinus drainage procedure. His weight has increased by 6kg and he has had no further chest infections.

### Discussion

Common Variable Immunodeficiency disorder occurs in 1-4 per 100 000 people. It has a higher prevalence in those of Northern European descent. Onset is usually between puberty and 30 years with a bimodal distribution at 1-5 and 18-25 years. The pathophysiology of the disease is unknown.

Clinically the disease has many presentations, the majority of which are infections such as pneumonia, bronchitis, sinusitis, conjunctivitis, otitis and meningitis. Pneumonia is particularly common in patients lacking IgM producing B cells as they lack the ability to produce anti pneumococcal polysaccharide IgM. There is also an increased susceptibility to mycoplasma in

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patients with hypogammaglobulinaemia [2]. Pneumonia is a rare presentation in patients who have been treated with intravenous immunoglobulin (IVIg) [3]. Bacterial meningitis and sepsis were also found to be common before IgG treatment.

A study of 248 patients found a high proportion of patients presented with chronic lung disease, the commonest being bronchiectasis. Autoimmune disease was also common (22%) with the most frequently observed manifestations being autoimmune haemolytic anaemia, thrombocytopenia, rheumatoid arthritis and pernicious anaemia. Patients have been shown to present with gastroenterological problems such as inflammatory bowel disease, pernicious anaemia, giardiasis and malabsorption. Also some present with hepatitis B or C, primary biliary cirrhosis and granulomatous disease such as sarcoidosis [4,5]. There is an increased incidence of cancer in patients with CVID, particularly Non-Hodgkins Lymphoma [6].

FBC	Normal
Urea and Electrolytes	Normal
Liver Function Tests	Normal
ESR	9.0mm/hr (1-12)
CRP	15.9mg/L (<10.0)
IgG subclasses	All low
IgA	0.13 (0.8-4.7)
IgM	<0.17 (0.5-3.0)
Lymphocyte function/ CD45 RA expression/ Total Lymphocyte count	All Normal
Test immunity	No response
Hepatitis serology	All negative

Table 1. Blood Results

Table 2 outlines the criteria for the diagnosis of CVID; the differential diagnosis includes the effects of drugs such as sulphasalazine, phenytoin, steroids or cytotoxics, lymphoproliferative diseases (CLL/ Myeloma/Thymoma), other primary immunodeficiencies, protein losing enteropathy and nephrotic syndrome.

The patient (male or female) fulfills all the following criteria:

1. Onset of immunodeficiency at greater than 2 years of age
2. Absent isohemagglutins and/or poor response to vaccines
3. Defined causes of hypogammaglobulinemia have been excluded

in association with a marked decrease (at least 2 SDs below the mean for age) in serum IgG and IgA (probable diagnosis) or in one of the major isotypes (IgM, IgC and IgA) (possible diagnosis).

Table 2: Diagnostic Criteria for Common Variable Immunodeficiency [7]

As early as the 1950s, passive immunization with the immunoglobulin fraction of pooled normal human sera was found to have a dramatic impact on reducing the frequency of sepsis and severe invasive bacterial infection. However, doses were limited to the volume tolerated by the intramuscular route of administration. With the subsequent availability of commercial preparations of IgG for intravenous administration in the United States, several studies demonstrated the efficacy of higher doses that more closely approximate normal physiological levels in slowing the progression of chronic lung disease, as well as decreasing antibiotic use, hospitalizations, and numbers of pneumonias [8]. The use of IVIG has dramatically altered the clinical course of this disorder and

rescued many patients from the burden of frequent infections.

All patients who meet the diagnostic criteria [7] should receive IVIG therapy titrated to provide adequate replacement of IgG levels. The consensus dosing for IVIG is 400 to 500 mg/kg every three to four weeks, which generally results in increases in the trough level of IgG 400 to 500 mg/dL over pretreatment levels. The half-life is approximately three weeks, although variability among individuals exists. Steady-state levels are usually achieved after three to six months of therapy. An alternative to IVIG for maintenance therapy is subcutaneous administration of immunoglobulin (SCIG).

Although replacement immunoglobulin therapy has been clearly shown to reduce the infection-related complications of CVID, its administration will not prevent other complications of this disease [9]. Treatment with IVIG does not entirely eliminate infections in most patients, and antibiotics are essential for managing acute infections of the sinopulmonary, gastrointestinal, and genitourinary systems. In addition, patients with bronchiectasis may have chronic infections that require long-term treatment with broad-spectrum antibiotics, sometimes with rotation of agents to avoid resistance.

Patients with CVID must be monitored carefully for the onset of lymphoproliferative disorders. Although patients typically have marked lymphadenopathy and splenomegaly, the onset of constitutional symptoms or rapidly expanding lymph nodes should prompt evaluation for clonality or malignancy [10]. Bronchoscopy occasionally may be indicated for focal pulmonary findings associated with infection that fail to resolve with treatment.

Patients with CVID have decreased overall survival. In one large series, survival 20 years after diagnosis of CVID was 64 and 67 percent for males and females, respectively, compared to the expected 92 percent population survival for males and 94 percent for females. The parameters found to be associated with a higher mortality were lower levels of serum IgG, poorer T cell responses and a lower percentage of peripheral B cells. In general, the incidence of death associated with acute bacterial infection in primary humoral immunodeficiencies, including CVID, fell off dramatically with the advent of intramuscular (IM) immunoglobulin treatment. However, the immunoglobulin levels obtainable in patients when administered intramuscularly failed to protect against chronic lung disease, which is the major source of morbidity and mortality.

Soldiers are expected to be medically fit for "full combatant duties (in any area) in any part of the world" [11] and their functional capacity is graded according to prescribed criteria [12]. Soldiers in the field are likely to be exposed to endemic diseases, those associated with living in close quarters under sub optimal conditions and the threat of biological and chemical agents. Medical resources including simple medications are likely to be limited and may not be available for prolonged periods. The occupational assessment of this soldier is unusually straightforward since in his current role, with access to full medical support, he has the functional capacity to perform the duties of storeman, can safely carry firearms and drive military vehicles. He therefore he remains an asset to an infantry unit on operational duty in Northern Ireland. He is however unfit to deploy overseas in any capacity.

The Army owes a duty of care to those it has recruited [13] and takes its responsibility for the morale and physical wellbeing of soldiers seriously. [14] To successfully relocate this soldier within the UK would require identification of a suitable post with ready access to appropriate medical support. If this combination were to prove too difficult to achieve, a medical discharge would be indicated. This soldier is currently employed as a storeman and has a PULHHEEMS grading of P7HO.

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