

Case Report:
A Subclinical Presentation of Common Variable Immunodeficiency

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Introduction: Common Variable Immunodeficiency (CVID) is a primary immunodeficiency disorder characterized by hypogammaglobulinemia and recurrent bacterial infections. The phenotypic defect is failure in B cell differentiation with impaired secretion of immunoglobulins, although T cell abnormalities are common.

The patient is a 51-year-old female who was referred to our center by her primary care physician secondary to a history of recurrent episodes of sinusitis, otitis media, and upper respiratory infections. She denied having prior episodes of pneumonia or other serious infections. Her sister had been recently diagnosed with Immunoglobulin A deficiency, and this prompted an investigation into the patient's immune status. She was found to have hypogammaglobulinemia and was referred to our center for further evaluation.

Past medical history was significant for seasonal allergic rhinitis, mild intermittent asthma, and multiple drug allergies to penicillin, polymyxin B, and sulfonamides for which she developed generalized urticaria and angioedema of the pharynx. She had never been hospitalized except for a tonsillectomy at the age of four years. Family history was significant for multiple family members with asthma, allergic rhinitis, and a sister with IgA deficiency and systemic lupus erythematosus. Social history was non-contributory and review of systems was negative. Physical examination findings were entirely within normal limits.

Results: Despite her asymptomatic presentation, a thorough immunologic evaluation was undertaken at our center, which confirmed hypogammaglobulinemia (IgG 387 mg/dL [normal 638-1349], IgA <6.7 mg/dL [normal 70-312], IgM 23.1 mg/dL [normal 56-352]). In addition IgG subclass levels were very low (IgG₁ 268 mg/dL [normal 455-875], IgG₂ 71 mg/dL [normal 188.9-458.6], IgG₃ 14.6 mg/dL [20-90.8], IgG₄ <0.2 [normal 7.2-64.2]). Tetanus titer was within normal limits, however pneumococcal titers were that of an unimmunized individual, despite the patient's history of having received pneumococcal vaccine in the past year. T cell percentages and absolute lymphocyte counts were normal. ANA to screen for SLE was negative. Complement C3 was within normal limits. Specific IgE levels to *D. pteronissinus*, *D. farinae*, dog epithelium, timothy grass, *A. fumigatus*, *A. tenuis*, maple, birch, ragweed, and latex were all negative. A complete blood count was also normal. The patient was instructed to return for follow up in one month.

At the second visit the patient had no complaints of interval infections. Her physical exam was completely benign, however the clinical picture appeared to be consistent with the diagnosis of common variable immunodeficiency. Three months later, the patient continued to be asymptomatic and a decision was made to refrain from treatment with intravenous gammaglobulin due to her borderline total IgG level and lack of symptomatology. The patient was instructed to return every 6 months to monitor immunoglobulin levels and to aggressively treat any intercurrent infections.

Conclusions: The clinical spectrum of CVID is quite broad, with many patients, such as this patient, not presenting with symptoms until late adult life. Bronchiectasis is a common problem leading to frequent hospitalizations, and rarely, severe respiratory impairment. Patients may also present with atypical inflammatory gastrointestinal disease resulting in diarrhea, malabsorption, and weight loss. Autoimmune hemolytic anemia, autoimmune thrombocytopenia, rheumatoid arthritis, and pernicious anemia are relatively common amongst CVID patients. Of particular concern is the increased incidence of cancer, namely lymphoma. Standard treatment is periodic IgA-deficient intravenous immunoglobulin (IVIG). However due to our patient's lack of current clinical symptoms and IgG level > 200 mg/dL, IVIG is not indicated at this time. The patient continues to be symptom-free and we will continue to monitor her every six months.