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## CLINICAL VIGNETTE

# Transient Hypogammaglobulinemia Associated with a Parapneumonic Effusion

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### Introduction

Immune responses to infection are swift and dynamic. Proliferation of immune cells and production of humoral antibodies are key adaptive immune functions, essential for protection against sinopulmonary infections. A physiologic response to infection can result in the consumption of antibodies that may mimic hypogammaglobulinemia. We present a patient with large physiologic fluctuations in IgG levels in response to pneumonia, with spontaneous recovery of IgG levels after resolution of infection.

### Case Presentation

A 31-year-old male presented to the Emergency Department for evaluation of fever, dyspnea and chest pain for two days. Cross sectional imaging of the chest revealed consolidations in the left lower lobe, with a loculated pleural effusion. Infectious evaluation included negative PCR testing for COVID and influenza, and negative urine legionella and sputum cultures. He was treated with empiric intravenous antibiotics for pneumonia. Thoracentesis of parapneumonic effusion not feasible based on size and fluid windows. Immune evaluation revealed isolated IgG hypogammaglobulinemia with an IgG level of 511 mg/dL, normal IgA and IgM. Other evaluation was normal including lymphocyte counts of T, B, and NK cells, and negative HIV testing.

Further immunologic history was pertinent for childhood history of recurrent otitis media requiring ear tubes, tonsillectomy and adenoidectomy. He also had perirectal abscess at age 19, which was treated with oral antibiotics. He did not report other recurrent infections and did not have a personal or family history of immunodeficiency or autoimmunity. Replacement immune globulin for hypogammaglobulinemia was considered but deferred due to clinical improvement on antibiotics. Two months post hospitalization, the pneumonia and parapneumonic effusion had resolved on serial imaging with robust recovery with an IgG level of 1,256 mg/dL. He was advised to continue annual follow up of his immunoglobulin levels and to monitor for recurrent infections.

### Discussion

The transient nature of hypogammaglobulinemia in this case sheds light on the large physiologic fluctuations that can occur in the setting of effective immune responses to pneumonia. Hypogammaglobulinemia can result from insufficient production or increased losses into abdominal or pleural spaces, or urine. The immunoglobulin isotypes IgG, IgA, IgM provide

vital humoral immune defenses against bacterial pneumonia. The subclasses of IgG include IgG1(60-70%), IgG2(20-30%), IgG3(5-8%) and IgG4(1-3%).<sup>1</sup> IgG1 and IgG3 are the most prevalent isotypes and are responsible for protection against protein and polypeptide antigens, viral infections and bacterial toxins such as tetanus and diphtheria. IgG3 is also widely known to be preferentially consumed in the setting of pneumonia, sinusitis and infections. IgG2 (and IgG4 to a lesser extent) are responsible for protection against carbohydrate/polysaccharide capsular antigens such as *Streptococcus pneumoniae*, *Haemophilus influenzae type b*, and *Neisseria meningitidis*.

This patient's pneumonia and hypogammaglobulinemia resolved, without unnecessary immune globulin. When hypogammaglobulinemia was first discovered, the differential diagnosis included primary immunodeficiencies such as Common Variable Immunodeficiency (CVID), and secondary immunodeficiencies (such as medication induced). The most common medication induced secondary immunodeficiencies are caused by oral corticosteroids, rituximab infusions, or other immunosuppressants. In this patient, secondary hypogammaglobulinemia due to medications was ruled out as the patient was not using immune suppressing medications. Hypogammaglobulinemia due to CVID was considered due to the severity of his pneumonia. However, diagnostic criteria for CVID requires confirmation of low IgG on repeat evaluation. Additional criteria include: 1) a marked decreased (at least 2 standard deviations below the mean for age) in serum IgG and IgM or IgA, 2) impaired responses to vaccines, 3) recurrent serious sinopulmonary infections, a combination of recurrent, severe, or unusual infections and 4) lack of other defined immunodeficiency state. The typical vaccine challenge is performed with pneumococcal vaccination and assessment of vaccine titers four to six weeks after vaccination.<sup>2</sup> In addition, immune globulin infusions are most beneficial in cases with severely low IgG below 400 mg/dL.

As in this case, atypical presentations of pneumonia can be associated with lab findings of hypogammaglobulinemia similar to those found in immunodeficiency disorders. The transient hypogammaglobulinemia observed in this case could represent an early risk factor for later development of CVID, and close monitoring for immunodeficiency is warranted. Awareness of fluctuations in immune lab profiles can help guide clinical decision making and identification of patients who may require immunodeficiency treatment.

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