



Hypogammaglobulinemia without Infection

Dennis K. Ledford, MD



Each month we present highlights from the Ask the Expert section of the American Academy of Allergy, Asthma & Immunology (AAAAI) Web site written by Dennis K. Ledford, MD. For more questions and answers, visit www.aaaai.org/ask-the-expert.aspx.

Question:

My patient is a 71-year-old Asian woman without a history of recurrent infection who was referred for hypogammaglobulinemia by her primary care physician 6 years previously. At that time routine blood work showed mild thrombocytopenia without associated bleeding episodes. A hematologist/oncologist consultant requested quantitative immunoglobulins, which demonstrated hypogammaglobulinemia, an IgG level of 272 mg/dL, an IgA level of less than 15 mg/dL, and an IgM level of 2 mg/dL. Initial specific antibody was positive/protective to protein antigens, tetanus and diphtheria, but low for pneumococcal polysaccharide antigens. Lymphocyte subsets were normal. Observation over several years has shown no recurrent infection or additional cytopenias. Repeat quantitative immunoglobulins are unchanged. Any thoughts on IgG replacement or any other thoughts?

Answer:

I could not tell for certain from your question if the quantitative immunoglobulins had changed significantly during the 6 years after which the low levels were first recognized. I think a level that is progressively declining would lead me to treat with subcutaneous or intravenous gamma globulin, even with limited clinical infections. You could discuss this with your patient and document the patient's preference, but she is at risk of serious infection and the infections could be unpredictable with rapid onset. There is no absolute value at which everyone agrees gamma globulin replacement is indicated and gamma globulin therapy should be tailored to the individual, with respect to both decision to initiate therapy and dose.

There is an interesting article by Agarwal and Cunningham-Rundles¹ that provides a scoring system to evaluate laboratory and clinical criteria for the decision to initiate gamma globulin therapy. This decision is a clinical judgment and there is no criterion standard by which to judge the decision, but this article

is by a group, with a senior investigator having extensive clinical experience in making this decision. The article describes a scoring system that assigns a number to the laboratory and clinical findings of a patient to be assessed for gamma globulin therapy. The median IgG concentration in the 46 patients treated with gamma globulin was 263 mg/dL and they had a median laboratory score of 17 and a clinical score of 11 (total 28). The 19 patients for whom gamma globulin was not recommended had a median IgG concentration of 575 mg/dL and a median laboratory score of 7 and clinical score of 10 (total 17). I think you will find this article and the scoring system helpful. The article points out that the clinical score, reflecting the number of infections and other clinical complications, was not greatly different between the 2 groups, but the laboratory score, reflecting the immunoglobulin concentration and immune response to vaccination, showed a greater difference. Applying this scoring system to your patient and the information provided provides a laboratory score of 13 to 16 and a clinical score of 3 to 5 (total 16-21), closer to the group not treated with gamma globulin. I would encourage you to obtain the scoring system and more accurately assess the value.

Another issue to be considered is the possibility of a monoclonal gammopathy or thymoma, although I would have expected the lymphocyte count to be low with the latter. Nevertheless, I would verify the lack of a mass in the mediastinum on chest radiograph and a negative immunofixation for monoclonal protein. The presence of monoclonal gammopathy would lead me to initiate gamma globulin replacement in the setting of a greater IgG concentration. Other causes of hypogammaglobulinemia, such as intestinal lymphangectasia, seem unlikely without symptoms.

In summary, the decision to initiate gamma globulin therapy is a complex clinical choice that should include the patient's input, estimate of future infections, overall risk, and current clinical burden. Despite the absence of infection and the normal protein antibody response, I would favor initiating gamma globulin replacement at 200 to 300 mg/dL even without a history of infections due to increased risk of future infections. The Agarwal/Cunningham-Rundles scoring system may be of value in helping to quantify this risk but cannot be the final arbiter. I would also be sure that there is no evidence of a thymoma or monoclonal gammopathy and initiate gamma globulin therapy at the current level if either was found.

I hope this information is of help to you and your patient.

REFERENCE

1. Agarwal S, Cunningham-Rundles C. Treatment of hypogammaglobulinemia in adults: a scoring system to guide decisions on immunoglobulin replacement. *J Allergy Clin Immunol* 2013;131:1699.

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