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A case of relapsing polychondritis and hypogammaglobulinemia

Relapsing polychondritis (RP) is a rare immune-mediated disease of unknown origin that causes recurrent cartilage inflammation. Its peak incidence is in the 4th or 5th decade of life with a female to male ratio of 3:1. Whereas auricular cartilaginous inflammation is the most common presentation, relapsing polychondritis can also involve cartilaginous components of the respiratory tract, joints, heart, and blood vessels. Corticosteroids are the first line of treatment. Immunosuppressants such as cyclosporine, azathioprine, methotrexate, and cyclophosphamide are possible alternatives. Additionally, the biologic agent antiCD20 monoclonal antibody (rituximab) has been found to be helpful in treating RP.¹

Relapsing polychondritis is suspected to be autoimmune in origin, and other systemic autoimmune phenomena have been linked with this condition. Immunodeficiency, however, is rarely associated with RP. Furthermore, RP has not yet been reported in an adult patient with hypogammaglobulinemia. We report a case of a 37-year-old Hispanic man referred to the allergy and immunology clinic with a 3-year history of recurrent ear inflammation and superimposed secondary infections. There was no shortness of breath, stridor, wheezing, or hoarseness to suggest tracheal involvement. His medical history was significant for controlled asthma, seasonal allergies, recurrent sinusitis, and nasal polypectomy. There was no family history of immunodeficiency. Over the course of the duration of his condition he received multiple, intermittent courses of oral amoxicillin and prednisone for infections and chronic swelling of his ears. This treatment was temporarily beneficial. Prior investigations failed to identify a definitive cause. At the time of presentation, the patient's medications were prednisone 20 mg by mouth daily, fluticasone/salmeterol 500/50 dry powder inhaler twice daily, and albuterol metered dose inhaler as needed. Physical examination findings included erythema and swelling of bilateral pinna, with sparing of the earlobes. There was no evidence of otitis media or nose involvement on examination. Based on the patient's clinical presentation, the diagnosis of RP was made.

At the time of evaluation, the patient's workup showed negative antibody for double-stranded DNA, rheumatoid factor, Sjogren's syndrome antibodies, Smith antigen antibody, and ribonucleoprotein antibody. Complete blood count and basic metabolic studies results were normal. The erythrocyte sedimentation rate was 4 mm/hr. A chest X-ray obtained at the time of initiating follow-up with the clinic was without any evidence of tracheobronchial involvement or fibrosis. A subsequent unenhanced computed tomography image of the chest identified biapical pleural thickening and did not identify any pulmonary nodules, mediastinal adenopathy, interstitial fibrosis, or evidence of a thymoma. Pulmonary function test inspiratory and expiratory loops were unremarkable and showed forced vital capacity 118%, forced expiratory volume in 1 second

115%, forced expiratory volume in 1 second/forced vital capacity 81%, forced expiratory flow 25–75% 90%. Complement levels were within normal limits, specifically C3 119 mg/dL (normal: 90–180 mg/dL) and C4 24 mg/dL (normal: 10–40 mg/dL). Immunoglobulin levels on 2 occasions, which were predated by treatment with corticosteroids but obtained before starting immunosuppressants such as methotrexate, showed consistent hypogammaglobulinemia (Table 1). The patient was therefore evaluated for possible causes of hypogammaglobulinemia, including primary immunodeficiency, protein-losing diseases, and hematologic malignancies. Lymphocyte subsets were within normal limits (Table 1). Serum protein electrophoresis was consistent with hypogammaglobulinemia but did not identify a monoclonal spike. Urinalysis did not identify any proteinuria. Infectious causes were ruled out, including tuberculosis. The patient's condition failed a course of azathioprine but demonstrated significant clinical improvement on treatment with prednisone 15 mg by mouth daily and methotrexate 20 mg by mouth weekly.

Relapsing polychondritis is primarily a clinical diagnosis usually made in the presence of 3 out of 6 of the following criteria: chondritis of pinna, nasal chondritis, nonerosive inflammatory polyarthritis, ocular inflammation, respiratory tract chondritis, and cochlear or vestibular dysfunction.^{2,3} Laboratory findings are not diagnostic, and histologic confirmation may not be necessary. Relapsing polychondritis is most prevalent among whites, with the typical age of onset being between the ages of 40 and 60 years. Its hallmark feature is intermittent inflammation and destruction of cartilaginous structures such as the ear, nose, trachea, bronchi, and joints. Involvement of the respiratory tract, specifically the tracheobronchial tree, can present as wheezing that can be misinterpreted as asthma. Keratouveitis, albeit rare, can also be an initial presentation of RP.⁴ Although auricular chondritis is the most common presentation, involvement of the respiratory tract carries the greatest risk for mortality.⁵ Approximately 30% of patients have additional autoimmune or hematologic disease.³

Corticosteroids are the mainstay of treatment of RP, with immunosuppressive agents serving as possible corticosteroid-sparing alternatives. Biologic agents such as tumor necrosis factor alpha inhibitors and interleukin-1 receptor antagonists can be effective for refractory RP.⁶ Tocilizumab, an anti–interleukin-6 agent, has also been used in cases of refractory RP.⁷

Hypogammaglobulinemia is a form of immunodeficiency marked by antibody deficiency. This condition can be primary or acquired, with causes ranging from primary immunodeficiencies such as common variable immunodeficiency to acquired conditions such as drug-induced hypogammaglobulinemia or nephrotic syndrome–associated hypogammaglobulinemia. The clinical complications of hypogammaglobulinemia are increased risk of infections with encapsulated bacteria, and it is therefore important that clinicians recognize this clinical entity.⁸ Treatment ranges from

Table 1

Laboratory data

Immunoglobulin Levels before Immunosuppressants			
Immunoglobulin	7/15/11	12/5/11	Reference range
IgM (mg/dL)	26	<25	40–230
IgE (IU/mL)	4,133	2,373	0–100
IgG (mg/dL)	563	493	700–1,600
IgA (mg/dL)	340	289	70–400
Lymphocyte subset panel			
Lymphocyte	Result	Reference range	
Total lymphocytes	1,083/ μ L	1,000–2,800/ μ L	
CD3+%	71.80%	55.0–83.0%	
CD3+	781/ μ L	700–2,100/ μ L	
CD4+/CD3+%	48.90%	28.0–57.0%	
CD4+/CD3+	520/ μ L	300–1,400/ μ L	
CD8+/CD3+%	23.20%	10.0–39.0%	
CD8+/CD3+	247/ μ L	200–900/ μ L	
CD56+CD3–%	14.80%	7.0–31.0%	
CD56+/CD3–	164/ μ L	90–600/ μ L	
CD19+%	11.70%	6.0–18.0%	
CD19+	130/ μ L	100–500/ μ L	
CD4+/CD8+	2.11	1.00–3.60	

monitoring of asymptomatic patients and discontinuing possible aggravating agents to replacing immunoglobulin in cases of refractory hypogammaglobulinemia with frequent, severe infections. At his initial presentation our patient did not have evidence of such severe infections and therefore did not require immunoglobulin replacement. Although there have been case reports documenting recurrent infections suggesting immunodeficiency in patients with polycondritis,^{1,9} hypogammaglobulinemia, in the absence of other identifiable primary or acquired immunodeficiency has not been reported in adult patients with RP. This is the

first case report of RP being linked with hypogammaglobulinemia in an adult patient, and it may be important for clinicians to be aware of this association.

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