

Optimal use of ivig in a patient with Behçet syndrome and common variable immunodeficiency

Behçet syndrome is a multisystemic autoimmune disease with vascular manifestations, oral and genital aphthous ulcers, skin lesions, ocular involvement, and pathergy phenomenon as defined by the 2006 International Criteria for Behçet's Disease, which has been deemed the most sensitive diagnostic criterion.¹ Therapy typically involves immunosuppression aimed at dampening the autoimmune response to the disease with agents such as colchicine, which inhibits neutrophil chemotaxis; disease-modifying compounds, such as azathioprine; the alkylating agent cyclophosphamide; anti-tumor necrosis factor α agents, and surgical intervention for issues such as arterial aneurysms.² Reports exist of patients successfully treated with intravenous immunoglobulin (IVIG) for ocular manifestations of the disease.³

Behçet syndrome may be complicated by the presence of an immunodeficiency disorder. This syndrome has been associated with thymoma with hypogammaglobulinemia, transient hypogammaglobulinemia, severe combined immunodeficiency, Bruton agammaglobulinemia, Nezelof syndrome, and common variable immunodeficiency (CVID).^{4–6}

CVID is diagnosed on the criteria of a considerable reduction in levels of IgG and IgA and possibly IgM when compared with an age-matched population and impaired or absent specific antibody production.⁷ A key symptom in most cases is recurrent sinopulmonary infections, but additional features, such as gastrointestinal infectious or inflammatory disease, lymphadenopathy, splenomegaly, and autoimmune diseases, are not uncommon.⁸ The coexistence of Behçet syndrome and CVID in a single patient has been only reported twice in the literature. One instance describes treatment using IVIG at suboptimal low-dose replacement therapy (200 mg/kg).⁵ The other is that of the case presented here, originally reported by Tuttle et al with regard to the patient's 24 nonmelanoma skin cancers that developed after immunosuppressive therapy for Behçet syndrome.⁶

A 48-year-old woman with a medical history of Behçet syndrome unresponsive to multiple immunosuppressive medications presented for further evaluation of episodic pneumonia infections occurring 3 to 4 times per year, frequent sinusitis, and recurrent skin infections. Pathergy test results were negative. The patient was diagnosed as having Behçet syndrome when she was 38 years old. Her symptoms included arthralgias, diarrhea, headache, aphthous and genital ulcers, uveitis, focal neurologic deficits, frequent cutaneous squamous cell carcinomas, and episodes of sepsis. Various immunomodulatory therapies were attempted with only minimal symptom improvement, including colchicine, hydroxychloroquine, dapsone, prednisone, rituximab, methotrexate, cyclosporine, leflunomide, cyclophosphamide, infliximab, interferon alfa, penicillin, and acyclovir.

Immune evaluation was initiated, and the patient was found to have low levels of IgG (315 mg/dL) and IgM (30 mg/dL) and no response to pneumococcal immunization. CVID was diagnosed at this time. The patient was subsequently prescribed IVIG infusions at optimal doses (1 g/kg) every 3 weeks. Since beginning IVIG, the

patient reported a decreased number of sinopulmonary and skin infections and a marked decrease in the amount of oral aphthous and genital ulcers, symptoms of uveitis, and arthralgias. At 6-month follow-up, IgG trough levels were well within range (1,502 mg/dL).

In this patient, the proper dose of immunoglobulin controlled the previously unresponsive inflammatory processes of Behçet syndrome and preserved remission for a period of at least 2 years. The case at hand describes the first patient diagnosed as having Behçet syndrome complicated by CVID in which immunosuppressive therapies for Behçet syndrome failed but was successfully treated with ideal doses of IVIG. Although this is the second case of CVID combined with Behçet syndrome, it is the only documented case with the successful use of a therapeutic dosage of IVIG.

Patients who possess the dual diagnosis of Behçet syndrome and CVID might pose a treatment dilemma in that they are immunocompromised, requiring thoughtful therapeutic strategies. An optimal dose of γ -globulin might provide the necessary effect to decrease symptoms in these patients.

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