



Letter

Common variable immunodeficiency associated with birdshot-like chorioretinopathy

Common variable immunodeficiency (CVID) is a primary hypogammaglobulinemia. It is associated with autoimmune phenomena, such as cytopenia, Sjögren syndrome, inflammatory bowel disease, and arthritis. There have been a number of reported cases of autoimmune disorders that involve the retina in association with CVID.

Birdshot retinochoroidopathy is a rare, chronic disorder that typically occurs in otherwise healthy patients with a mean age of 50 years that is classified as an inflammatory multifocal chorioretinopathy. The pathogenesis of this disorder is unknown, although its treatment (ie, steroids and other immunosuppressive drugs) and the presence of retinal S-antigens in afflicted patients suggest an organ-specific autoimmune origin. The retinal characteristics are described as small, multiple, white-spotted lesions in the fundus, and patients most often present with decreased vision, floaters, and glare. We present what we believe to be the second report of a patient with CVID and birdshot-like retinochoroidopathy.¹

The 25-year-old patient had a history of CVID that was diagnosed when she was a child. She initially presented to our clinic as a teenager with multiple episodes of hemolytic anemia and immune thrombocytopenia with recurrent infections for which she was treated with intravenous γ -globulin (IVIG) (400 mg/kg every 3 weeks) on an episodic basis for 15 years. Later, she developed persistent diarrhea that prompted a colonoscopy biopsy revealed T-cell infiltrates of her entire gut that resembled graft-vs-host disease. Serum immunoglobulin levels gradually decreased below 2 SDs of normal, and we began monthly γ -globulin therapy. Unfortunately, we transitioned to subcutaneous immunoglobulin therapy after port complications made peripheral access unavailable. Weekly subcutaneous γ -globulin treatment was administered for approximately 12 months (100 mg/kg per week), but the patient became nonadherent with her treatment.

During this time of nonadherence, the patient experienced dimness of sight. HLA-A29 and B5 test results were negative. Serum immunoglobulin measurement revealed an IgG level of 320 mg/dL (reference range, 800–1500 mg/dL), IgA level of 25 mg/dL (reference range, 90–325 mg/dL), and IgM level of 20 mg/dL (reference range, 45–150 mg/dL) after 12 months of intermittent subcutaneous γ -globulin. She had been followed up by a retina specialist who diagnosed birdshot-like retinopathy and used intraocular steroid injections for serous retinal detachment. Examination did not reveal anterior chamber or vitreous inflammation. Her visual acuity fluctuated, but after 2 months of IVIG nonadherence, visual acuity measured 20/15 in the right eye and 20/300 in the left eye. Although the patient began IVIG therapy again and received photodynamic therapy, the retinal insult did not resolve. As time evolved, her liver enzyme levels acutely increased; the patient developed liver failure and subsequently died.

CVID-associated retinal and posterior uveal changes have been reported. Three of these were related to a granulomatous response seen in the posterior pole.^{2–4} There is a reported case of CVID linked to an asymptomatic birdshot-like retinopathy in a 17-year-old girl who was treated with hydroxychloroquine for 4 years. She had annual screening eye examinations that revealed no abnormalities until asymptomatic bilateral disc edema with chorioretinal granulomas were discovered in her fourth year. Her HLA-A29 test result was likewise negative.¹ Two additional articles report CVID with posterior uveitides: diffuse placoid choroidopathy and multifocal choroiditis with panuveitis.^{5,6} A final 2 reports document retinal vasculitis and loss of retinal function or pigment epithelium changes associated with CVID.^{7,8}

This is the second report, to our knowledge, of CVID associated with birdshot-like chorioretinopathy. Birdshot retinopathy is an ocular inflammatory disease of unknown origin, although some posit an autoimmune cause supported by an *in vitro* proliferation of peripheral blood lymphocytes in response to bovine retinal S-antigens and bovine interphotoreceptor retinoid-binding protein in patients with birdshot retinopathy. The HLA-A29 phenotype likely plays a strong role in ocular inflammatory changes in birdshot retinopathy; 12 of 15 HLA-A29 transgenic mice developed ocular inflammation with histologic findings of retinal vasculitis, vitritis, subretinal fluid, disruption of photoreceptor cells, and choroid and optic nerve inflammation.¹⁰ Birdshot chorioretinopathy shares one of the strongest HLA associations for any human disease with a sensitivity and specificity of 96% and 93%, respectively, although not required for the diagnosis.^{9,10} The clinical diagnostic characteristic is hypopigmented choroidal lesions that may be white or cream-colored and oval or round (Fig 1). The lesions are most often bilateral, although they may be unilateral. The chorioretinal changes can appear after the onset of clinical symptoms, and patients will experience disabling visual disturbances, such as floaters, decreased vision, glare, photopsia, dyschromatopsia, and nyctalopia.¹¹ Their clinical symptoms are often out of proportion to their visual acuity, and there is no definitive diagnostic test for the disorder. Its patchy-white appearance in the posterior pole of the retina is easily visible on retinal examination and color fundus photographs. Fluorescein angiography will reveal vascular leakage (Fig 1F), and lesions may show early hypofluorescence with late hyperfluorescence. In some cases, lesions may not be visible on fluorescein angiography.¹⁰ Treatment is initiated with periorbital or systemic corticosteroids, and, if vision does not improve, immunomodulatory medications can be used.

Although her fundus and fluorescein angiography photographs resemble birdshot chorioretinopathy, the patient's young age, lack of HLA-A29 allele, and history of CVID direct us to a final diagnosis of birdshot-like chorioretinopathy because birdshot

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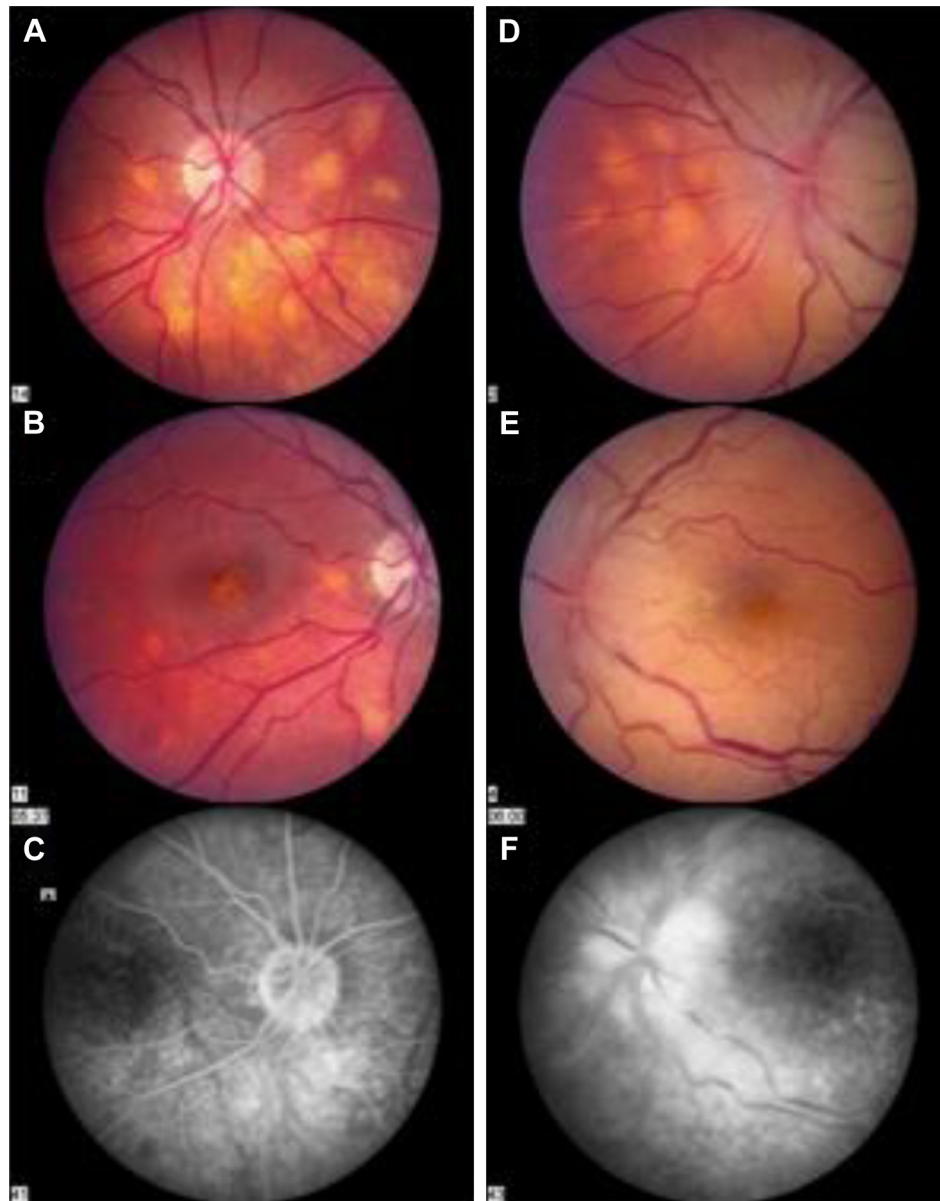


Figure 1. A-C. Right eye. A, B: Areas of patchy, cream-colored hypopigmentation predominantly inferior to the disc with pigment disturbance at the macula. C: Fluorescein angiogram (FA) at 5.5 minutes without evidence of vascular leakage, disc swelling, nor hyper or hypo fluorescence corresponding to creamy patches from A, B. D-F. Left eye. D, E: Patches of hypopigmentation similar to those seen in right eye, nasal to an edematous disc. F: FA at 6 minutes captures the impressive vascular leakage at the disc and along the inferior arcade. Photographer: John DuBois, CRA.

chorioretinopathy is seen in otherwise healthy HLA A29 positive patients with a mean age of 50 years.

Our patient did not outlive her final diagnosis. Her experience allows for us to report a unique association between CVID and birdshot-like chorioretinopathy adding to the small but growing body of literature on ophthalmologic findings associated with the primary immunodeficiency. Currently, however, we believe there is no indication for screening ophthalmic examinations in visually asymptomatic patients with CVID because of the low prevalence of retinal findings. If, however, vision changes are reported by the patient or found on examination in patients with CVID, retinal evaluation should be completed.

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