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Recalcitrant Granulomatous Sclerouveitis in a Patient with Granulomatous ANCA-associated Vasculitis

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Abstract

Purpose—To report an unusual case of granulomatous sclerochoroiditis.

Design—Interventional case report.

Methods—A patient with ANCA-associated granulomatous vasculitis presented with nodular necrotizing scleritis, which was recalcitrant to multiple systemic immunosuppressive therapies and progressed to a blind painful eye, which was enucleated.

Results—Histopathology revealed extensive occlusive vasculitis, diffuse T- and B- cellular infiltration, and lymphoid granulomatous formation. Enhanced MHC class II antigens, adhesion molecules, and Fas (CD95) and FasL (CD95L) were detected in the lesion.

Conclusion—Granulomatous sclerochoroiditis with aggressive immune reaction can be a complication of ANCA-associated granulomatous vasculitis.

Keywords

ANCA-associated granulomatous vasculitis; necrotizing scleritis; sclero-choroiditis; Wegener granulomatosis

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CASE REPORT

A 32-year old Caucasian male was initially seen in August 2002 with bilateral episcleritis, symmetric migratory polyarthritis, and lower extremity rash. Evaluation revealed cANCA titer of 1:640 and PR3-ANCA level of 50.5 EU (normal <5.0 EU). Biopsy of rash showed necrosis of blood vessels and dense inflammatory infiltrates (Figure 1). Urine analysis showed dysmorphic RBCs, WBCs, and granular casts. This confirmed the diagnosis of ANCA-associated granulomatous vasculitis. In February 2006 (visual acuity 20/20), he developed progressive, unilateral nodular scleritis OD (Figure 2) that was unresponsive to methotrexate (20 mg/week) and prednisone (20 mg/day) and infliximab 5 mg/kg. Four months later, he developed a choroidal granuloma (Figure 3), methotrexate was substituted with cyclosporine (2.5 mg/kg), pulse methylprednisolone, and tapering oral prednisone. After 3 months there was stability of the ocular disease (visual acuity 20/63), with secondary maculopathy. In January 2007 he had an exacerbation (visual acuity 20/100) and in March 2007, cyclophosphamide was initiated at 2.5 mg/kg with adjuvant pulse methylprednisolone. He became recalcitrant to therapy, with progressive disease (counting fingers) (Figure 4A). Scleral biopsy showed an ill-defined granuloma without acid-fast bacilli and fungi.

Subsequently, the patient developed extensive exudative retinal detachment (Figure 4B), multiple areas of scleral and perilimbal necrosis, rubeosis iridis (Figure 5), and hypotony. The eye became painful and blind. A diagnostic and therapeutic enucleation was performed. Histopathology revealed diffuse lymphoid granulomatous infiltrations replacing normal architecture of the temporal posterior ciliary body, choroids, and sclera (Figure 6). The infiltrations were composed of numerous T- (CD4 and CD8) and B-lymphocytes, macrophages, giant cells, and few eosinophils. The inflammatory areas were strongly positive for adhesion molecules (CD54, CD11a/CD18), class II antigens (HLA-DR, HLA-DQ), and Fas (CD95, CD95L). No microorganisms or neoplastic cells were identified.

Postenucleation, the patient is stable on 200 mg daily of azathioprine and 15 mg of prednisone, being tapered. He is being closely followed by a team of oculoplastics, uveitis, and rheumatology physicians. The left eye remains uninvolved.

DISCUSSION

ANCA-associated granulomatous vasculitis (such as Wegener granulomatosis) typically affects the respiratory tract, but systemic small vessel vasculitis can involve multiple organs. Ocular complications have been reported in as much as 28-87% of patients.¹ The etiology for these complications is necrotizing vasculitis, either focal or contiguous. Ocular findings include eyelid and conjunctival inflammation, episcleritis and scleritis, orbital pseudotumor, proptosis, optic nerve compression, and nasolacrimal duct obstruction.² Posterior segment involvement, especially choroidal granuloma, is uncommon. Our case shows similar histopathology reported previously.³ It also highlights the immunopathological findings, with enhanced expressions of adhesion molecules (CD54) and its ligand (CD11a/CD18). This supports the role of ICAM in the pathogenesis of inflammatory response seen in vasculitis associated with scleritis.⁴

Several studies have evaluated therapeutic modalities for ANCA-associated vasculitis. A randomized, placebo-controlled multicentric trial showed etanercept was ineffective at inducing remission⁵ though increasing the risk of solid malignancy in combination with cyclophosphamide.

Our case highlights several important points: a rare, potentially blinding case of severe sclerochoroiditis and the immunopathology findings of diffuse granulomatous inflammation with expression of ICAM.

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Figure 1.
Histopathology of skin rash on lower extremity showing vessel necrosis and dense inflammatory infiltrates.

Figure 2.
Slit-lamp examination of the right eye in February 2006. Engorged episcleral and scleral vessels in the superior and inferior temporal regions (clinical grading 1+ scleritis).

Figure 3.
Fundoscopic photograph of the right eye in June 2006 (left panel), September 2006 (right panel). A large choroidal granuloma.

Figure 4. Fundoscopic photographs of the right eye in May and July 2007. Progressive choroidal granuloma with exudative retinal detachment is observed; (A) May 2007; (B) July 2007.

Figure 5. Slit-lamp examination of the right eye in May 2007. Large necrotic scleral nodules, multiple perilimbal infiltrates, engorged deep scleral vessels, and rubeosis iridis.

Figure 6.

Photomicrographs of the enucleated right eye. (A) A large sclero-choroidal mass (arrow) extending into choroid. Detached retina (*) and cataractous lens seen. (B) Multiple granulomas (*) totally replace normal architecture of sclera and choroid. (C) Multiple giant cells (arrow) admixed with numerous inflammatory lymphocytes, macrophages, and granulocytes. (D) An occluded blood vessel with organized thrombus (arrow) and broken, necrotic collagen fibers observed. (E) Fresh thrombus in a small blood vessel (arrow) without identifiable endothelial cells. (F) Positive T-cell infiltration (arrow) forms a pseudo-follicle (CD45RO). (G) Positive B-cell infiltration (arrow) forms a pseudo-follicle (CD20). (H) Diffuse macrophage infiltration (CD68).