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Retinal Pigment Epithelium Tear After Immunosuppressive Treatment for Sarcoidosis-related Choroidal Granuloma

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Abstract

Purpose—To describe the formation of a retinal pigment epithelial (RPE) tear following immunosuppressive treatment of a large choroidal granuloma in a patient with sarcoidosis-related panuveitis.

Case Description—A 25 year-old woman presented with bilateral sarcoidosis-related panuveitis and optic disc edema in both eyes with a large choroidal granuloma temporal to the fovea in the left eye. She was started on high-dose oral prednisone therapy with improvement in her panuveitis with reduction in size of the left choroidal granuloma. An RPE tear overlying the flattening choroidal granuloma developed by three weeks of treatment.

Conclusions—Treatment of choroidal granuloma with rapid reduction in size may result in an RPE tear.

Keywords

Pigment epithelial tear; sarcoidosis; panuveitis; immunosuppression

Introduction

Sarcoidosis is a granulomatous inflammatory disease that may affect multiple organs, including the eye and ocular adnexa.¹ Sarcoidosis may cause inflammatory lesions in nearly all ocular structures. Additionally, ocular manifestations are often the presenting signs of systemic sarcoidosis.² Sarcoidosis-related posterior uveitis has been associated with poor visual outcomes and requires prompt diagnosis and treatment.³ Posterior segment manifestations of sarcoidosis include vitreous cellular reaction or haze, retinal vasculitis, chorioretinal lesions of various size, and granulomas of the choroid or optic nerve.¹

Tears of the retinal pigment epithelium (RPE) are most commonly reported in patients with pigment epithelial detachments (PEDs) associated with neovascular age-related macular degeneration (nAMD).⁴ RPE tears can result from the natural history of PED but have been reported more often following treatment with anti-VEGF agents.⁵ RPE tears have also been

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

described in patients with central serous chorioretinopathy^{6, 7} and Vogt-Koyanagi-Harada disease.^{8, 9} Here, we describe a case of an RPE tear overlying a large choroidal granuloma in a patient with sarcoidosis-related panuveitis after immunosuppressive treatment.

Case Description

A 25 year-old African American woman presented with a three-month history of red sore eyes and two months of decreased vision in the left eye. Best-corrected visual acuity (BCVA) was 20/40 and 20/200 in the right and left eyes, respectively, without a relative afferent pupillary defect in either eye. Intraocular pressure was normal in both eyes. Examination of the right eye revealed inferior granulomatous keratic precipitates, 1+ cells without flare in the anterior chamber, 1+ cell without haze in the anterior vitreous, vitreous snowballs, hemorrhagic disc edema with exudates tracking from the nerve to the fovea, and macular folds. Examination of the left eye revealed inferior granulomatous keratic precipitates, 2+ cells without flare in the anterior chamber, 2+ cells without haze in the anterior vitreous, vitreous snowballs, severe disc edema, macular folds, and a large (>3 disc diameters) elevated yellow choroidal mass temporal to the macula (Fig. 1). OCT of the right macula showed subretinal fluid nasally adjacent the nerve and inner retinal folds. OCT of the left macula showed large intraretinal cystic fluid pockets nasally and temporally, subretinal fluid nasally adjacent to the nerve, foveal detachment with nasal and temporal choroidal elevation (Fig. 2). Fundus autofluorescence (FAF) of the right eye showed hypo-autofluorescence in the areas of hemorrhage, and FAF of the left eye showed small speckled hypo-autofluorescence overlying the choroidal mass (Fig. 3). Fluorescein angiography (FA) of the right eye showed disc hyperfluorescence, blockage in the areas of hemorrhage, and diffuse small vessel leakage. FA of the left eye showed early hyperfluorescence of the optic nerve that was maintained into late frames, diffuse small vessel leakage, and early hypofluorescence with late speckled hyperfluorescence of the large temporal choroidal mass (Fig. 3).

Given the granulomatous nature of her inflammation, sarcoidosis was suspected. Her serum angiotensin converting enzyme (ACE) level was normal, but her lysozyme level was mildly elevated. Computed tomography of the chest showed pericardial adenopathy and bibasilar and right middle lobe ground-glass opacities compatible with interstitial lung disease. Bronchial biopsy of her left upper lobe revealed non-caseating granulomas confirming the diagnosis of sarcoidosis. Importantly, testing for syphilis (syphilis IgG and rapid plasma reagin) and tuberculosis (Quantiferon-TB Gold) were negative. MRI of the brain was normal, and lumbar puncture demonstrated a normal opening pressure. Therefore, the patient was diagnosed with bilateral granulomatous panuveitis secondary to sarcoidosis with a large choroidal granuloma in the left eye.

The patient was started on high-dose oral prednisone 100mg daily with taper to 60mg daily over one week. Nine days after starting therapy, her VA was 20/32 OD and 20/200 OS with improved anterior chamber cellular reaction and less subfoveal fluid in both eyes, as well as flattening of the choroidal granuloma in the left eye. Three weeks after starting prednisone, she was taking 15mg daily, and VA was 20/32 OD and 20/100 OS. Her anterior chamber cellular reaction and subfoveal fluid had resolved in both eyes. At this time, an RPE tear was

noted over the area of choroidal granuloma, which had flattened significantly (Fig. 1). OCT of this area showed elevation of the RPE with discontinuity at the temporal edge, adjacent to the highest area PED, as well as overlying subretinal fluid (Fig. 2). At seven weeks, visual acuity improved to 20/25 and 20/40 in the right and left eyes, respectively. On OCT, the subretinal fluid had resolved, and the PED was shallower with a highly hyper-reflective area on the nasal edge, likely reflecting scrolled RPE. At three months, FAF showed an area of hyper-autofluorescence in the nasal portion of the previous choroidal granuloma, likely representing scrolled RPE, surrounded areas of relative hypo-autofluorescence, likely representing areas of denuded RPE (Fig 3). FA at this time showed blockage in the area of scrolled RPE surrounded by areas of relative hyperfluorescence.

Steroid-sparing immunosuppressive therapy was also initiated because of the severity of her intraocular inflammation. After developing hypertension on cyclosporine A, she was started on mycophenolate mofetil. Due to recurrent posterior segment inflammation with further steroid taper, she was also started on infliximab, after which she was able to successfully taper off of oral prednisone. She is currently maintained on mycophenolate mofetil 1 gram twice daily by mouth and infliximab 5mg/kg intravenously every four weeks. At last follow up approximately two and a half years after presentation, her VA was 20/80 OD (decreased from presentation due to organization of lipid exudate in the fovea) and 20/25 OS, and her inflammatory eye disease remains quiet.

Discussion

RPE tears are most often reported in patients with nAMD. While RPE tears may occur as part of the natural history of nAMD, treatment with anti-VEGF agents appears to increase their frequency.⁵ Rapid contraction of choroidal neovascularization (CNV) with anti-VEGF treatment may cause tractional forces opposing the adherent forces at the junction of attached and detached RPE leading to anatomic failure and subsequent scrolling of the loose end of the RPE.^{10, 11} RPE tears have also been described in conditions without CNV, including central serous chorioretinopathy and Vogt-Koyanagi-Harada disease.⁶⁻⁹ The mechanism of RPE tear in these cases likely differs from that described in CNV. In the current case of RPE tear overlying a large choroidal granuloma, the granuloma lies below Bruch's membrane in the choroid and elevates the RPE/Bruch's membrane complex in the absence of a PED. Rapid contraction of the granuloma with corticosteroid therapy may have predisposed the overlying RPE to tear. Furthermore, it is possible that inflammatory damage to the RPE in the setting of sarcoidosis-related posterior uveitis compromised the anatomic integrity of the RPE predisposing to tear formation.

Several risk factors have been identified to help predict RPE tear formation in the setting of nAMD. PED height, especially lesions greater than 400 μ m, have a higher risk for RPE tear formation than smaller lesions.¹² Increased PED surface area and large PED diameter have also been reported as risk factors for RPE tear development.¹³ As mentioned above, the current case of RPE tear overlying a choroidal granuloma lacks a PED; however, the RPE/Bruch's membrane complex was significantly elevated from its normal position, and the granuloma measured ~3 disc diameters. Therefore, the height and surface area of the RPE elevation was quite large and may have predisposed this area to RPE tear formation.

To our knowledge, this is the first case of an RPE tear following immunosuppressive treatment of a sarcoidosis-related choroidal granuloma. The specific risk factors associated with RPE tears overlying choroidal granulomas remain unknown, but large granuloma height as well as large surface area and diameter of RPE elevation, as has been previously described in eyes PED from nAMD,^{12, 13} may be predisposing factors. Patients with large choroidal granulomas undergoing treatment should be monitored closely for the development of overlying RPE tears.

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Figure 1.

Color fundus photographs of the left eye of a 25 year-old African American woman with sarcoidosis-related posterior uveitis. Note the large choroidal granuloma temporal to the macula in the left eye prior to treatment. After 3 weeks of oral prednisone therapy, the choroidal granuloma had significantly decreased in height, and an RPE tear was noted over the area. At 7 weeks, the RPE tear had progressed nasally over the area of previous choroidal granuloma.

Figure 2.

OCT images of the same patient before and after an RPE tear overlying the choroidal granuloma in the left eye. Note the large area of RPE/Bruch's membrane elevation temporally corresponding to the area of choroidal granuloma prior to treatment (the area of temporal retina folded back toward the RPE is image artifact due to the extreme height of the lesion). After 3 weeks of oral prednisone therapy, an area of RPE elevation is apparent with discontinuity at the temporal edge, adjacent to the highest area of pigment epithelial detachment (PED), as well as overlying subretinal fluid. At 7 weeks, note the intensely hyper-reflective band representing scrolled RPE on the nasal half of the area where the granuloma had been.

Figure 3.

Fundus autofluorescence (FAF) and fluorescein angiography (FA) of the left eye of the same patient. FAF prior to treatment (top left) showed scattered small speckled areas of hypo-autofluorescence over the area of the choroidal granuloma. FA prior to treatment (top right; 3 minutes) showed early hypofluorescence with late hyperfluorescence in the area of granuloma. Three months after treatment, FAF (bottom left) showed an area of hyper-autofluorescence in the nasal portion of the previous choroidal granuloma, likely representing scrolled RPE, surrounded areas of relative hypo-autofluorescence, likely representing areas of denuded RPE. FA at three months (bottom right; 3 minutes) showed blockage in the area of scrolled RPE nasally surrounded by areas of relative hyperfluorescence.