

Histological findings of birdshot chorioretinopathy in an eye with ciliochoroidal melanoma

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Abstract

Purpose To describe the histological findings of birdshot chorioretinopathy.

Design/participant This is a case study of a single patient who has both birdshot chorioretinopathy and ciliochoroidal melanoma.

Methods A 55-year-old woman who was HLA-A29 positive and had birdshot chorioretinopathy had a large ciliochoroidal melanoma (T4b N0 M0) and underwent enucleation.

Outcome measures Using histopathology, we hope to further define the pathological findings in an eye with both birdshot chorioretinopathy and coexistent ciliochoroidal melanomas.

Results The eye showed a ciliochoroidal melanoma. In addition, elsewhere, there were multiple choroidal nodules of lymphocytes that showed the presence of CD3-positive cells, which also stained for CD4 or CD8. There were only a few CD20-positive B cells and rare CD68-positive histiocytes. No granulomas were present.

Discussion To our knowledge, there are only two previous reports describing the histological findings in birdshot chorioretinopathy: one that was HLA-A29 negative showing choroidal granulomas and another that was HLA-A29 positive exhibiting histological findings similar to our case. Incidentally, the latter case had a history of cutaneous melanoma.

Conclusion Birdshot chorioretinopathy is a nongranulomatous nodular infiltration of the choroid.

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Introduction

Birdshot chorioretinopathy is a chronic inflammatory disease that is seen mainly in persons who have the HLA-A29 haplotype. There are very few reports of the histological findings in this disease.^{1,2} We present the histological findings in a patient who had a ciliochoroidal melanoma in one eye.

Case report

A 55-year-old woman noted decreased vision in her left eye for 3 weeks. She was asymptomatic in her right eye. Aside from having had Lasik in both eyes 5 years earlier, she also used topical cyclosporine ophthalmic emulsion for dry eyes (Restasis-Allergan, Irvine, CA, USA) and had cataract surgery in her right eye in 2008. Her medical history was unremarkable. Family history revealed that her mother had a previous skin melanoma and a sister had throat cancer with pulmonary metastasis. The patient had worked as a welder in the past.

When we examined her, visual acuity was 20/20 in the right eye and 20/70 in the left. Anterior segment examination of the right eye showed a faint corneal scar from the prior Lasik and a posterior chamber implant. There were trace-1+ cells in the anterior vitreous of the right eye. The anterior segment examination of the left eye also showed the faint corneal scar. There were also sentinel vessels nasally. There was a sectoral nasal anterior cortical cataract and a diffuse posterior subcapsular cataract with trace cells in the vitreous.

Fundus examination of the right eye showed multiple small yellowish deep choroidal lesions (Figure 1a). Fundus examination of the left eye showed that from 730 to 1030 there was an 18 × 13 × 9 mm³ partially melanotic

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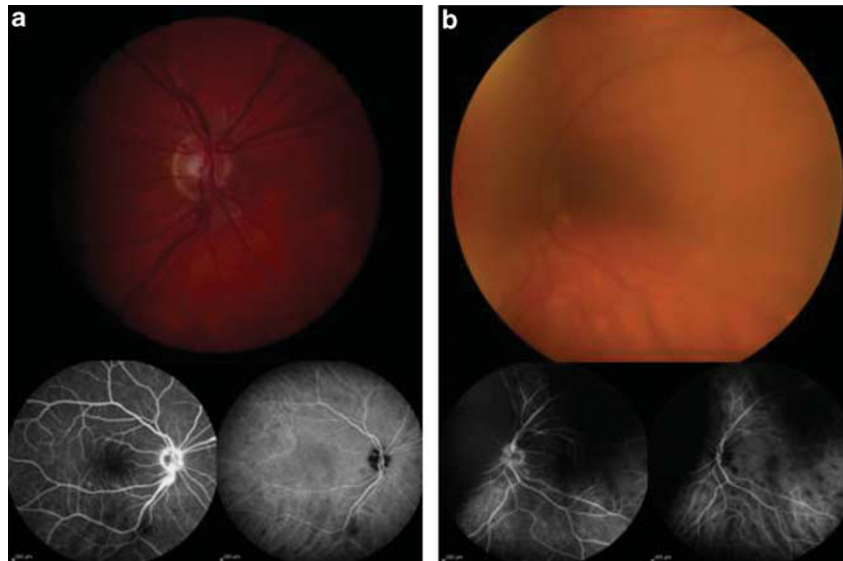


Figure 1 (a) Color fundus photograph centered over the right optic nerve showing multiple small yellowish deep choroidal lesions radiating from the optic nerve. Note the correlation between the lesions and the hypopigmented spots in green indocyanine angiography. There also is a localized phlebitis in the right eye. (b) Color fundus photograph of the left eye. There are multiple creamy white choroidal lesions and a nasal choroidal melanoma. The view is obscured by posterior subcapsular cataract. The correlation between the lesions and the hypopigmented spots in green indocyanine angiography is more prominent in this photograph.

dome-shaped mass with two mushroom-shaped excrescences anteriorly involving the ciliary body. An inferior serous retinal detachment was present. A few deep yellowish spots were noted in the choroid of the left eye as well (Figure 1b).

Fluorescein angiogram of the right eye showed leakage of the retinal veins and some blocked fluorescence from the deep lesions (Figures 1a and b). The left fundus fluorescein angiogram showed some leakage from retinal veins and intrinsic vascularity of the ciliochoroidal melanoma. The indocyanine green angiogram confirmed the internal vascularity of the melanoma and showed blocked fluorescence in the areas of the choroidal lesions. Ultrasound confirmed the presence of a 9-mm-thick ciliochoroidal melanoma with low internal reflectivity and no extrascleral extension. Visual fields showed a mild altitudinal defect in the right eye and a dense superior defect in the left eye, which correlated with the inferior detachment. Multifocal electroretinography of both eyes was similar to the visual fields.

Laboratory studies showed normal angiotensin-converting enzyme levels, normal complete blood count, normal serum protein electrophoresis, and absent Lyme and syphilis antibodies; quantiferon testing for prior tuberculosis exposure was negative. A positron emission tomogram showed high fluorodeoxyglucose uptake in the left eye in the area of the melanoma but no other uptake anywhere else in the body. HLA class 1 typing was remarkable for HLA-A29.

A diagnosis of large (T4d N0 M0) ciliochoroidal melanoma and birdshot chorioretinopathy was made. After discussion with the family, the left eye was enucleated.

Materials and methods

The eye was fixed in buffered formalin. Histological sections were stained with hematoxylin and eosin. Unstained sections were sent for fluorescent *in situ* hybridization for chromosome 3 and for mRNA gene expression (Castle Biosciences, Houston, TX, USA). Immunostaining was performed with CD20, CD3, CD4, CD8, and CD68 (Dako, Glostrup, Denmark).

Results

The ciliochoroidal melanoma was of mixed cell type and involved the ciliary body and peripheral choroid. The neoplasm invaded the overlying retina. No extraocular extension was seen (Figure 2).

Separate from the melanoma, there were nodular lymphocytic infiltrates in the choroid and the ciliary body. In immunoperoxidase studies, the lymphocytic infiltrate had a mixture of T cells (CD3), which were both CD4 (helper) and CD8 (cytotoxic), as well as B cells (CD20 positive; Figures 3a–e). No granulomas were seen, and only scattered histiocytes were present (CD68 positive).

Discussion

This patient had a ciliochoroidal melanoma and HLA-A29-positive birdshot chorioretinopathy including

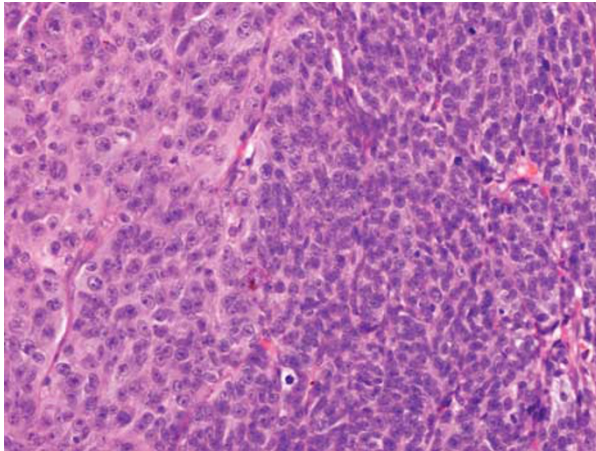


Figure 2 Pathological specimen of the ciliochoroidal melanoma demonstrating numerous mitoses (16 per powered field). There is a moderate amount of tumor-infiltrating lymphocytes but no tumor necrosis demonstrated.

retinal vasculitis and choroidal infiltrates. No evidence of other granulomatous diseases including sarcoidosis, syphilis, Lyme, tuberculosis, or variable combined immunodeficiency was present.

The focal uveal nodules present were nongranulomatous and similar to one of only two other cases of birdshot chorioretinopathy with histological findings described in the literature that we were able to find.¹ This other case reported by Gaudio *et al*¹ was also in a patient who was HLA-A29 positive. To our knowledge, the only other case in the literature had a history of prior penetrating trauma, and the patient was HLA-A29 negative and the enucleated eye showed the presence of granulomas.² Considering that our case was similar to the HLA-A29-positive case, we suspect that cases that are HLA-A29 positive have nongranulomatous focal nodular infiltrates and that this is the histological finding that correlates with the deep whitish lesions seen ophthalmoscopically. Interestingly, the patient in the other case of HLA-A29-positive BSCR histology reported by Gaudio *et al*¹ had a skin melanoma removed 5 months before the diagnosis of BSCR.

In conclusion, we present the histology of BSCR similar to the only other case of HLA-A29 disease

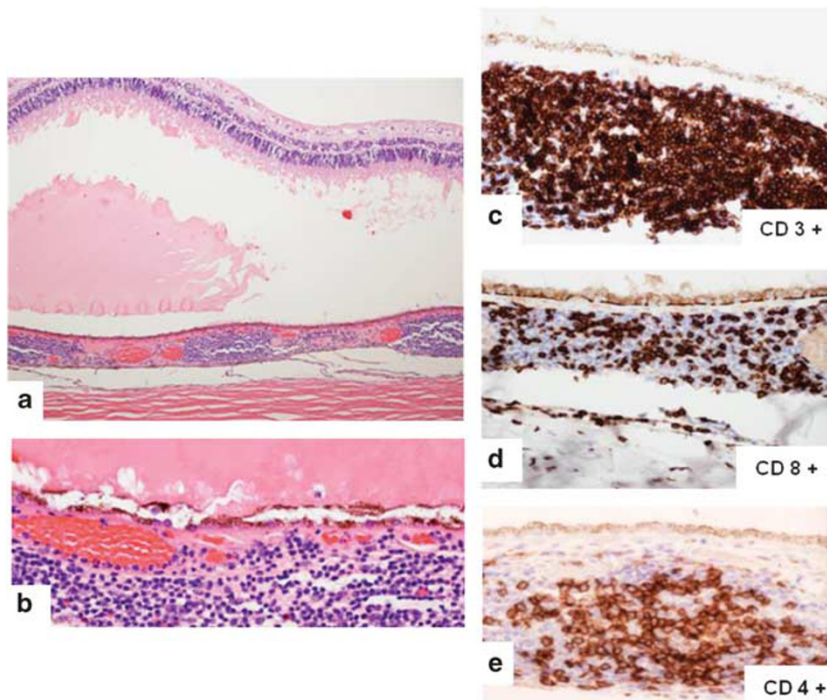


Figure 3 Immunoperoxidase studies demonstrating the lymphocytic infiltrate had a mixture of T cells (CD3), which were CD4 (helper) and CD8 (cytotoxic), as well as B cells. (a) A serous retinal detachment is seen and nodular infiltrates are seen in the choroid. (b) Higher power of the nodular infiltrates show that they are composed of lymphocytes. (c) Immunohistochemical staining shows that the lymphocytes in the nodular infiltrate are mainly T cells. (d) Immunohistochemical staining shows that there are CD8 lymphocytes in the nodular infiltrates. (e) Immunohistochemical staining shows that there are CD4 lymphocytes in the nodular infiltrates.

described in the literature and confirm that this is a nongranulomatous disease.

Summary

What was known before

- There was conflicting information as to the histological findings in birdshot chorioretinopathy.

What this study adds

- Our findings confirm that birdshot is caused by nongranulomatous lymphocytic infiltrates.
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Conflict of interest

The authors declare no conflict of interest.

Acknowledgements

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