JAMA Ophthalmology Clinical Challenge

# Anterior Chamber Snowflake After Keratoplasty

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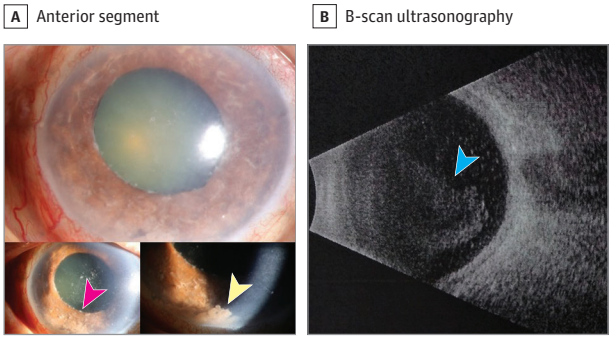


**Figure 1.** A, The iris showed atrophy, along with severe cataract, a diffuse white tiny nodular on the iris (pink arrowhead), and a small pile of snowflakelike deposit (yellow arrowhead). B, A massive opacity at anterior vitreous body (blue arrowhead).

**A 62-year-old woman** presented with painless vision reduction and eye redness in the right eye for a week. The initial best-corrected visual acuity (BCVA) was 4/20 (approximately 20/100), and an irregular superficial corneal ulcer with an epithelial defect size of 3 mm × 5 mm was found in the center of edematous cornea. She received penetrating keratoplasty 4 months later, as the ulcer did not heal with intensive medication. Then, topical tobramycin dexamethasone, topical tacrolimus, and daily oral prednisone, 40 mg, were prescribed, with a gradual taper of prednisone to a maintenance dose of 10 mg.

At 5-month postoperative follow-up, some thin snowflakelike matter was found deposited on the iris and in the angle, with rare cell and mild flare in the anterior chamber. She was then diagnosed with uveitis and subsequently prescribed topical prednisone, subconjunctival triamcinolone acetonide, oral prednisone, 40 mg, and daily intravenous ganciclovir, 5 mg/kg. An aqueous sample was obtained for diagnostic polymerase chain reaction, and Epstein-Barr virus (EBV) was detected with a DNA load of $3.12 \times 10^7$ cells.

Nine months after the keratoplasty, when she presented to the Zhongshan Ophthalmic Center, her BCVA was 2/100 OD (approximately 20/1000 OD), and her intraocular pressure was 19 mm Hg. Diffuse tiny nodules were observed all over the iris, along with more snowflake and severe cataract (**Figure 1**A). The fundus could not be seen. B-ultrasonography showed a dense opacity in the anterior vitreous body (Figure 1B).

**WHAT WOULD YOU DO NEXT?**

- **A.** Perform intravitreal injection of ganciclovir
- **B.** Repeat aqueous sampling without an iris biopsy
- **C.** Repeat aqueous sampling with an iris biopsy
- **D.** Perform intravitreal injection of corticosteroid

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## Diagnosis

**Ocular polymorphic posttransplant lymphoproliferative disorders in the left eye**

## What to Do Next

**C.** Repeat aqueous sampling with an iris biopsy

## Discussion

Although EBV had been detected with high DNA load, intravitreal ganciclovir was not recommended (choice A), as there was no evidence-based antiviral drug for EBV.[1] Nonetheless, EBV-associated diseases, such as uveitis, viral endophthalmitis, or cellular proliferative disease, should be considered. Her iris nodules and atypical anterior chamber deposits were uncommon in uveitis or viral endophthalmitis, which supported our consideration of a cellular proliferative condition. Therefore, we thought repeated aqueous sampling without an iris biopsy could not assess the pathological nature of the nodules directly (choice B); we also chose to withhold intravitreal corticosteroids (choice D) until results of the iris biopsy were known.

The iris specimen was composed of a polymorphic mixture of lymphoid cells that include medium-sized to enlarged irregular lymphocytes. The tumor cells showed nuclear atypia and expressed B-cell antigens (diffuse positivity for CD20 and CD79a) and were EBV positive by Epstein-Barr encoding region in situ hybridization (**Figure 2**). Genetic studies showed gene rearrangement of immunoglobulin heavy chain, immunoglobulin κ light chain, and immunoglobulin light chain loci. A diagnosis of polymorphic posttransplant lymphoproliferative disorders (PTLD) associated with EBV infection was made by a lymphoma subspecialty pathologist.

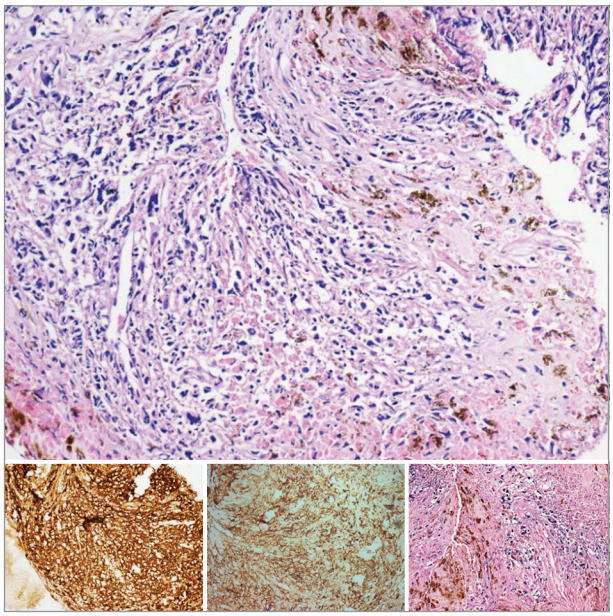

**Figure 2.** Photomicrographs of the iris specimen (top; hematoxylin-eosin, original magnification ×200), with CD20 staining (lower left; original magnification ×200), CD79a staining (lower middle; original magnification ×200), and positive for Epstein-Barr encoding region (lower right; in situ hybridization, original magnification ×200).

PTLD is defined as a series of complications that occur after organ transplant or hematopoietic cell transplant, characterized by varying degrees of lymphocyte hyperplasia, ranging from benign hyperplasia to malignant lymphomas.[2] PTLD usually arise under immunosuppressive condition and are mainly (around 85%) driven by EBV.[2,3] PTLD can be divided into 4 histological categories.[4] Early lesions and polymorphic PTLD account for about 5% and 15% to 20% of PTLD, respectively. The most common type is monomorphic PTLD, including B-cell subtypes (more than 70%) and T-cell subtypes (less than 5%).[5] Less than 5% of PTLD is classical Hodgkin lymphoma. Even though PTLD usually involves lymphoid-rich organ or tissue, various cases of extranodal organ involvement have been reported.[6] Ocular involvement is uncommon and can be easily misdiagnosed for masquerade feature, such as iris nodule, subretinal mass, anterior chamber flare, or vitreous opacity.[7,8]

Algros et al[9] reported a case of gastric PTLD in a patient after keratoplasty who was diagnosed with EBV-induced gastric PTLD (B-cell lymphoma) after receiving oral cyclosporine for a year. Similarly, this patient had received systemic prednisone for 5 months, which might cause her immunosuppressive condition.

## Patient Outcome

Central nervous system lymphoma involvement was ruled out by enhanced 3.0-Tesla magnetic resonance imaging. Systemic and topical prednisone along with topical tacrolimus were discontinued on diagnosis. Intravitreal methotrexate (methotrexate, 0.4 mg) was given every 2 weeks for a total of 5 doses.[10] As cataract progressed, extracapsular cataract extraction was performed without intraocular lens implantation, while its impact on PTLD was unclear. The anterior chamber deposit, iris nodules, and vitreous opacity had resolved. There were no obvious retinal lesions. EBV DNA load from aqueous humor was 0 at the fifth methotrexate injection, without antiviral medication. Unfortunately, she developed corneal edema, presumably associated with chronic endothelial dysfunction, which might be due to PTLD as well as repeated intraocular procedures. At 1-year follow-up, her BCVA was 1/100 OD (approximately counting fingers OD) and intraocular pressure was 12 mm Hg, without recurrent sign of iris nodules.


### ARTICLE INFORMATION

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