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CIBMTR/EBMT expert review of ocular graft-versus-host disease

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Ocular involvement occurs in more than half of patients with chronic graft-versus-host disease (GvHD) after allogeneic hematopoietic cell transplantation (HCT), associating with poor prognosis.[1] Yoshihiro Inamoto from the Department of Hematopoietic Stem Cell Transplantation, National Cancer Center Hospital, Tokyo, Japan, and colleagues analyzed ocular GvHD, in collaboration with transplant hematologists and ophthalmologists, on behalf of the Late Effects and Quality of Life Working Committee of the Center for International Blood and Marrow Transplant Research and the Transplant Complications Working Party of the European Society of Blood and Marrow Transplantation. The expert review was published ahead of print in *Biology of Blood and Marrow Transplantation*.[2]

Recent updates in ocular GvHD, regarding pathophysiology, preclinical models, risk factors, prevention, screening, diagnosis, response criteria, evaluation measures, and treatment were included and assessed in this analysis.

Methods

- Database: Medline (PubMed)
- Search terms: “hematopoietic transplantation AND (eye OR ocular)”
- N = 552 articles were identified as of 31 March 2018

Pathophysiology

- T cell mediated inflammation leads to fibrotic changes and ocular surface damage that cause lacrimal gland dysfunction, meibomian gland dysfunction, and corneoconjunctival inflammation
- Other affected areas may include the cornea, limbus, and conjunctiva

Incidence

- Ocular GvHD incidence may differ due to different diagnostic criteria
- The incidence of ocular GvHD widely varied between 16% and 65%

Common symptoms

- Keratoconjunctivitis sicca (KCS; typically occurs 6–9 months after allogeneic HCT)
- Irritation
- Burning

- Pain
- Redness
- Photophobia
- Blurry vision
- Excessive tearing
- The sensation of having sand or grit in the eyes
- Conjunctival injection

Risk factors

- Prior acute GvHD
- Use of peripheral blood stem cells
- Transplantation from a female donor to a male recipient
- Absence of anti-thymocyte globulin prophylaxis
- Larger number of organs involved with GvHD
- Non-Caucasian
- EBV-seropositive donor

Evaluation measures (diagnosis and response measure) – hematologist assessment

- NIH eye score: A-II and A-II
- Schirmer test without anesthesia: A-II and D-II
- Ocular surface disease index (OSDI): B-II and B-II
- Lee eye subscale: B-II and B-II
- Patient-reported global rating of eye symptoms (0-10): B-II and B-II

Diagnosis, staging and response criteria

- 2014 NIH criteria: new onset of dry, gritty or painful eyes with decreased values in the Schirmer test without anesthesia in a patient after allogeneic HCT
- Severity: 0–3
- International Chronic Ocular GvHD Consensus Group (ICOGCG) criteria: corneal staining and conjunctival injection, patient-reported dry eye symptoms (i.e., OSDI), presence of systemic chronic GvHD

Treatment

- Systemic immunosuppressive therapy should be considered in patients with a moderate or severe NIH global score
- Lubricant therapy: viscous eye drops and viscous ointments are recommended
- Patients with severe KCS: hyaluronic acid and dexpanthenol-containing eye drops are recommended

- Patients with dry eye disease and ocular GvHD: mucin secretagogue eye drops (diquafosol and rebamipide) are recommended
- Patients with more than mild symptoms: punctal occlusion with collagen or silicone plugs is recommended
- Patients with blepharitis: warm compresses and lid care with ointment are recommended; in case of bacterial superinfection, topical antibiotic ointment and eye drops (low-dose oral tetracycline/doxycycline for at least 3–6 weeks) are recommended
- Patients with inflammatory signs of ocular GvHD: cyclosporine eye drops
- Acute exacerbation of ocular GvHD: topical corticosteroids are recommended to administer for a short period of time with close monitoring by an ophthalmologist
- Surgical intervention is recommended for filamentary keratopathy

The authors concluded that "future research should be directed towards establishing reliable and widely-available tools for diagnosis and response measurement of ocular GvHD."

References

1. Lee S. *et al*. Chronic graft-versus-host disease. Biol Blood Marrow Transplant. 2003 Apr;9(4):215-33.

2. Inamoto Y. *et al*. Ocular graft-versus-host disease after hematopoietic cell transplantation: expert review from the late effects and quality of life working committee of the IBMTR and Transplant Complications Working Party of the EBMT. Bone Marrow Transplant. 2018 Dec 7. DOI: 1038/s41409-018-0340-0. [Epub ahead of print].