Commentary: Ocular surface involvement heralds graft-versus-host disease: Time to act

With the advancements in the techniques of allogeneic hematopoietic stem cell transplantation (HSCT), as in other streams of medicine, there has been an increase in the utilization of this therapeutic modality for a variety of indications. For its long-term survival, it becomes imperative to carefully monitor the course of the treatment and recognize any signs of complications such as graft vs host disease (GvHD) at the earliest.

Classically, systemic GvHD has been categorized as acute and chronic.[1] Chronic GvHD develops within 3–6 months after allo-HSCT. Chronic GvHD may develop after acute GvHD, but it can also develop de novo.[2] Besides these, late-onset acute GvHD (>3 months after allo-HSCT) and overlap syndrome, in which features of chronic and acute GvHD appear together (no time limit), have also been added to this clinical spectrum.[3] GvHD is frequently seen during the tapering off of systemic immunosuppression or after its discontinuation. It can also manifest itself up to 3 years after allo-HSCT.[4]

Classical acute GvHD usually involves three organ systems: skin, gastrointestinal tract, and liver.[5] Ocular involvement is quite rare during acute systemic GvHD and develops in about 10% of patients with acute disease. It is usually considered a poor prognostic factor for mortality caused by systemic acute GvHD.[6]

The most common sites involved at the initial diagnosis of chronic GvHD are skin (75%), mouth (51%–63%), liver (29%–51%), and eyes (40%–60%) of the patients.[4] The ocular manifestations may be in the form of surface inflammation, e.g. keratoconjunctivitis sicca, cicatrizining conjunctivitis [Fig. 1], eyelids, lacrimal and/or meibomian glands, and later corneal involvement.[7]

In the light of this evidence of ocular involvement at any stage of the disease, the transplant specialists should ensure documentation of an initial ophthalmic evaluation and regular follow-up visits to the ophthalmologist as part of the routine monitoring of patients who have received allo-HSCT. These visits have to be continued even when the systemic immunosuppression is being tapered or has been stopped. Schirmer’s test without anesthesia (which is inexpensive and does not require an ophthalmic setup) can indicate the presence of dryness, and can be done by the transplant specialists themselves.
The actual data on the prevalence of GvHD across different regions also needs to be collected by various centers treating and monitoring allo-HSCT, with special emphasis on ocular manifestations, to have an improved understanding of the disease. The current study in this issue has successfully attempted to characterize the ocular surface in patients who had undergone allo-HSCT in their center, using simple and easily available clinical tests like Schirmer’s test, ocular surface disease index (OSDI) scoring, oxford scale for corneal staining with fluorescein eye drops, and tear film break up time (TBUT). The combination of these tests could be a useful screening tool for ocular GvHD. Further, the use of conjunctival impression cytology technique to chart CD8 + lymphocytes in these patients was also done and compared to control eyes. These could potentially be used as biomarkers of inflammatory activity to modify topical and systemic therapy.

As ophthalmologists, we should be aware of the ocular manifestations of GvHD and start treatment at the earliest sign of the disease. We should promptly warn the treating transplant specialist regarding the onset or worsening of subtle signs such as dry eye disease as it could be the first manifestation of GvHD. This will ensure that the crucial window of opportunity in such cases is not missed and prompt systemic treatment is initiated. Networking of local ophthalmologists and transplant physicians should be encouraged.

It is important that patients are referred early, because the lacrimal gland damage and dry eye disease can be irreversible. We strongly recommend that the ophthalmologist and immunologist should work together in deciding the dose and duration of systemic immunosuppression. If lacrimal secretion is salvageable, then systemic immunosuppression should not be stopped.

Further, the patients undergoing the HSCT must be counseled accordingly and should be made aware of the symptoms they should watch out for and seek immediate medical advice. All these steps will definitely help in improving the long-term graft survival and have a positive impact on the quality of life of these patients.

References

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