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Case report

GVHD dry eyes treated with autologous serum tears

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Summary:

Two cases of GVHD with severe dry eyes are reported where conventional therapy failed to control ocular signs and symptoms. Autologous serum tears, however, resulted in a beneficial clinical effect with marked attenuation of the symptoms. This therapy proved to be safe during 10 months of treatment. *Bone Marrow Transplantation* (2000) **25,** 1101–1103.
Keywords: GVHD; dry eye; autologous serum tears; allogeneic PBPC transplantation

The treatment of ocular disorders with biological fluids has long been advocated.[1] More recently, autologous serum (AS) tears have been indicated for the treatment of dry eye in Sjögren's syndrome. The rationale for this is based upon the fact that vitamins and growth factors present in tears are also present in serum.[2,3] In this report, we describe the treatment of dry eyes with AS tears in two adult women with extensive chronic graft-versus-host disease (GVHD) following allogeneic peripheral blood progenitor cell transplantation (PBPCT).

Case 1

A 44-year-old woman underwent PBPCT for chronic myeloid leukemia (CML) in the first chronic phase and developed sicca syndrome along with extensive chronic GVHD. Her previous ophthalmic history included only spectacles for myopia. The GVHD was treated with cyclosporin A and prednisone systemically and with commercial artificial tears, including preservative-free tears for 6 months, with minimal improvement in the ocular symptoms which included the sensation of presence of a foreign body, and redness.

Examination revealed a corrected visual acuity of 20/25 for both eyes, conjunctival hyperemia and severe punctate staining of the cornea and conjunctiva (Figure 1, top and bottom). A rapid tear film break-up time (BUT) and a Schirmer test I of 4 mm for each eye confirmed the previous diagnosis.

At this point, we introduced AS tears, prepared as previously described,[2] with instructions to keep the bottles in a refrigerator and apply the drops several times a day. Four weeks later, the patient returned and reported an improvement in her symptoms from the day she started using the preparation. Compared to her previous tear substitute, the effect of AS tears lasted longer, allowing her to apply fewer drops throughout the day and also provided considerably more comfort in the morning, which was the most critical part of the day. Examination of her eyes showed a dramatic improvement in punctate staining, a reduction in hyperemia

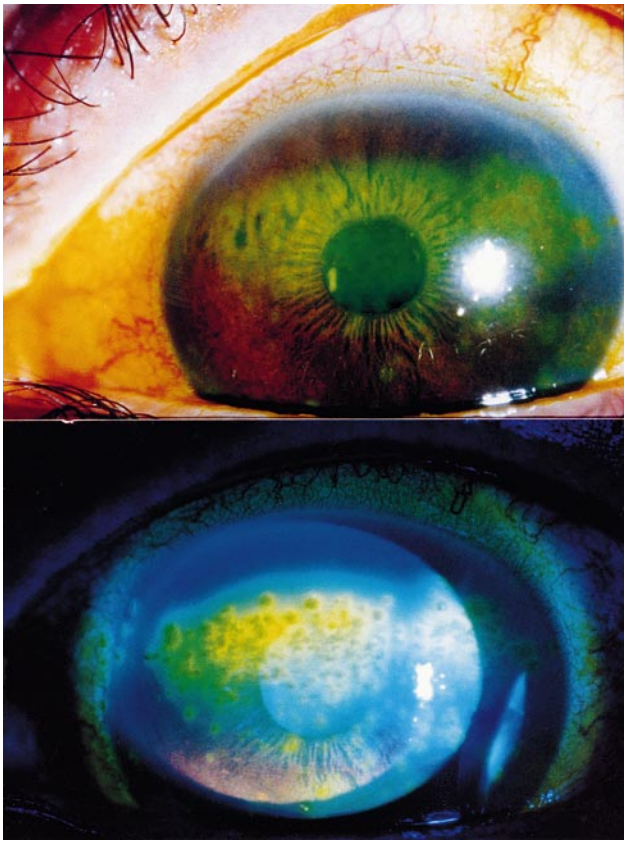

Figure 1 Slit lamp photograph (top) and fluorescein staining (bottom) of the OD in patient 1, showing diffuse punctate keratitis in the latter panel.

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and a longer BUT, with no change in the Schirmer test I (Figure 2, top and bottom). After 10 months of uninterrupted use of AS tears, her condition stabilized; an episode of bacterial conjunctivitis resolved without complications using regular therapy. During this period, the patient interrupted her use of cyclosporin A for GVHD, the only effect of which was that she increased the use of serum tears from five drops to eight drops a day for each eye.

Case 2

A 42-year-old female underwent an allogeneic PBPCT for CML in first chronic phase which was complicated by extensive chronic GVHD, leading to severe sicca syndrome. The patient had no relevant ocular history and had tried commercial artificial tears which she substituted with a preservative-free artificial tear solution, used hourly. Despite systemic treatment with cyclosporin A and prednisone for 9 months, and topical treatment with various formulations of artificial tears for $2\frac{1}{2}$ years including preservative-free eye drops in the last 4 months, the patient complained of the sensation of a foreign body and fluctuations in visual acuity which had worsened, mainly in her right eye, 3 days before presenting to the hospital.

Her visual acuity for OD and OS was 20/30 and 20/25, respectively. Examination revealed conjunctival hyperemia and extensive fluorescein staining of the cornea and conjunctiva, which was more intense in the lower third of her right eye (Figure 3, top and bottom). A Schirmer test showed 7 mm of wetting in both eyes at 5 min.

Topical therapy with AS tears was initiated for both eyes every hour, with the same recommendations as in case 1 above, together with a lubricant ointment at bedtime. One month later, the patient reported an improvement in her symptoms which began 3–4 days after changing to AS tears. She also observed that the effect of AS tears lasted longer than that of previous lubricants. After 8 months, there was a considerable reduction in corneal punctate staining and greater comfort than at the beginning of the treatment (Figure 4, top and bottom). However, the BUT was reduced and the Schirmer test yielded 3 and 4 mm in OD and OS, respectively. During this period, the only complication was bilateral conjunctivitis which was treated with topical antibiotics and resolved in 1 week.

Discussion

GVHD can lead to blindness and also cause persistent ocular discomfort in a variable number of patients who undergo allogeneic BMT.[4] The exact etiopathogenesis of GVHD is unknown and may involve numerous factors, including previous disease, the type of treatment before and after BMT

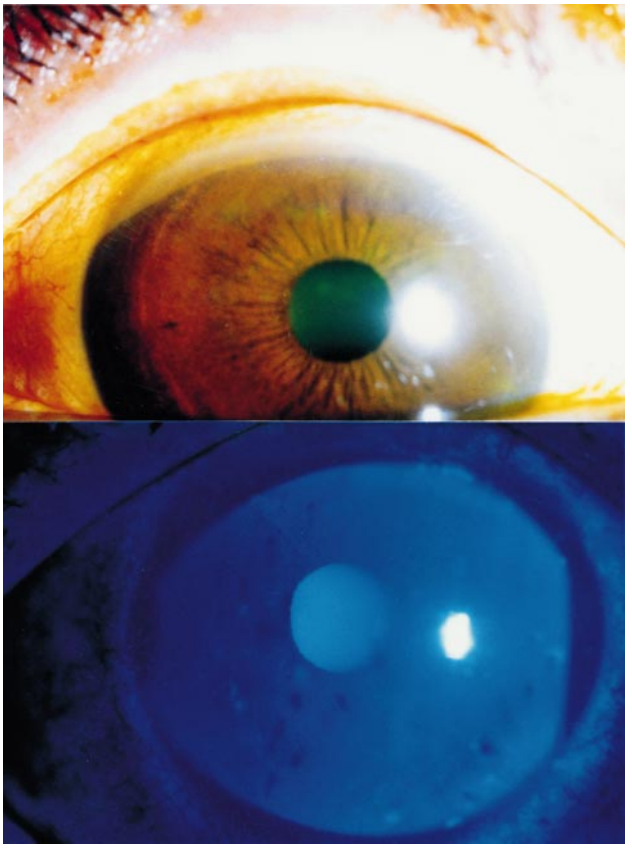

Figure 2 Slit lamp photograph of patient 1 after using AS tears for 1 month (top) and fluorescein staining of the OD in this patient after using AS tears for 1 month (bottom).

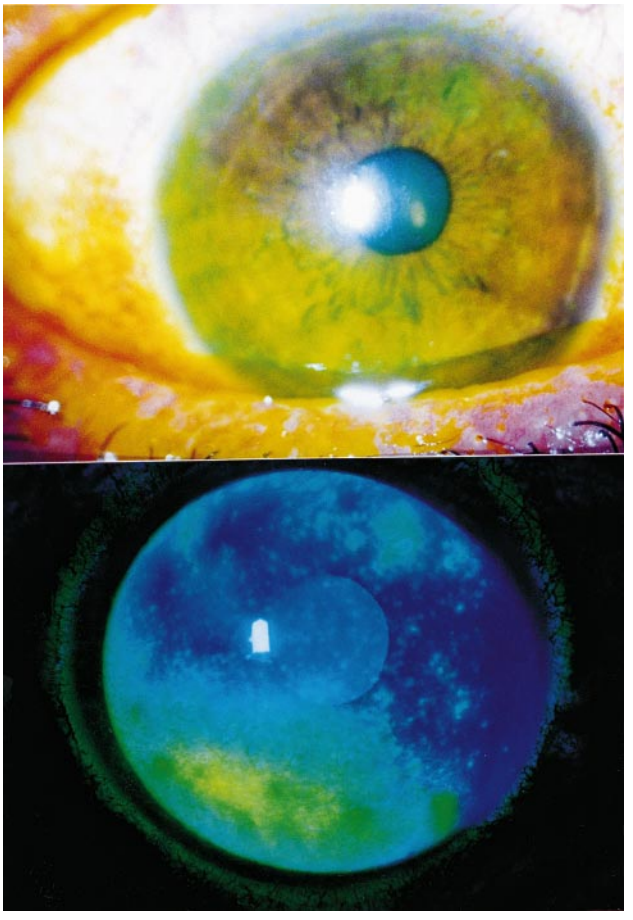

Figure 3 Slit lamp photograph (top) and fluorescein staining (bottom) of the OD in patient 2, showing diffuse punctate keratitis in the latter panel.

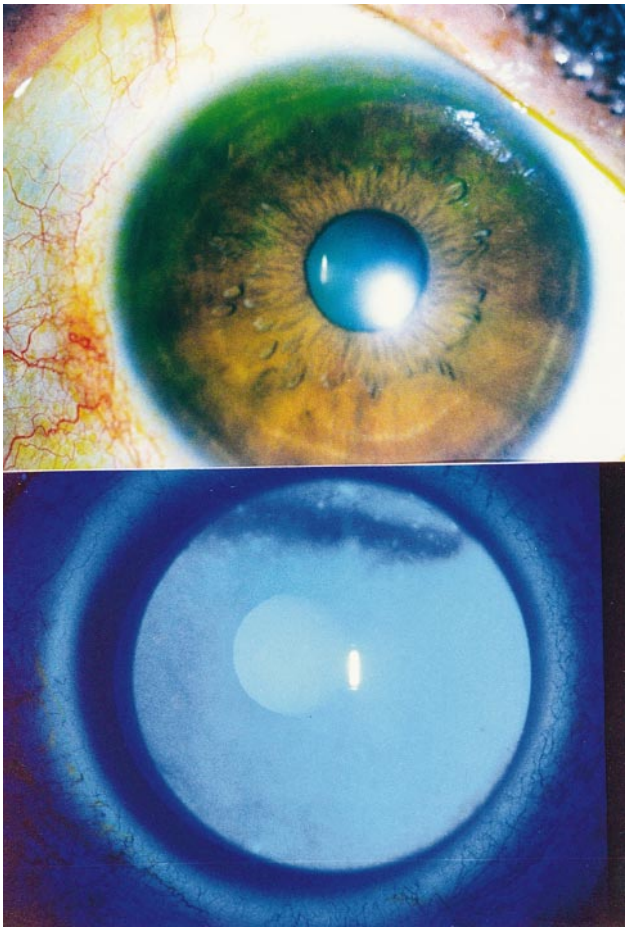

Figure 4 Slit lamp photograph of patient 2 after using AS tears for 8 months (top) and fluorescein staining of the OD in this patient after using AS tears for 8 months (bottom).

and genetic and environmental influences.[5] There is currently no cure or specific treatment for sicca syndrome related to GVHD or other etiologies. However, anedoctal descriptions have reported beneficial results with routine topical retinoic acid[6] and collagen shields for secondary corneal ulceration.[7] In addition, topical cyclosporine A has been investigated for dry eye treatment based on immunoregulatory and lacrimomimetic effects, but its utility in GVHD remains to be established.[8]

Topical AS considerably improved the ocular surface and patient symptoms in both cases described above. These observations suggest that AS tears offer the elements necessary to equilibrate the ocular surface environment, without changing the physiology of tear secretion, and also provide greater comfort to the eye. In support of this, recent research has shown that AS tears contain epidermal growth factor, vitamin A, transforming growth factor-β and induce increased expression of mucine in cultured conjunctival cells.[3] A major concern of this therapy is the possibility of contamination, which could result in serious infection of the fragile ocular surface of GVHD patients. Technical procedures such as sterile manipulation of the bottles and the blood, as well as clear instructions to the patient about the need to keep the bottles in a refrigerator and about possible symptoms of discomfort or blurred vision, are helpful and are recommended to enhance the safety of this therapy. While AS tears may provide an alternative treatment in moderate and severe cases of dry eye which have not responded to conventional tear replacement therapy, a randomized, double-blinded, clinical study would be useful to determine whether the benefits and safety of AS tears are generally applicable to dry eye in different situations involving GVHD.

References

1 Hirschberg J. *The History of Ophthalmology. Volume 1: Antiquity*. JP Wayenborgh Verlag: Bonn, 1985.
2 Fox RI, Chan R, Michelson JB *et al*. Beneficial effect of artificial tears made with autologous serum in patients with keratoconjunctivitis sicca. *Arthr Rheum* 1984; **27**: 459–461.
3 Tsubota K, Goto E, Fujita H *et al*. Treatment of dry eye by autologous serum application in Sjögren's syndrome. *Br J Ophthalmol* 1999; **83**: 390–395.
4 Franklin RM, Kenyon KR, Tutschka PJ *et al*. Ocular manifestations of graft-vs-host disease. *Ophthalmol* 1983; **90**: 4–13.
5 Sullivan KM. Graft-versus-host disease. In: Forman SJ, Blume KG, Thomas ED (eds). *Bone Marrow Transplantation*. Blackwell Scientific Publications: Boston, 1994, pp 339–362.
6 Murphy PT, Sivakumaran M, Fahy G, Hutchinson RM. Successful use of topical retinoic acid in severe dry eye due to chronic graft-versus-host disease. *Bone Marrow Transplant* 1996; **18**: 641–642.
7 Spraul CW, Lang GE, Lang GK. Hornhautulzeration bei chronischer Graft-versus-Host disease (GVHD): Behandlung durch Collagen-Shields. *Klin Monatsbl Augenheilkd* 1994; **205**: 161–166.
8 Tauber J for the Cyclosporine Study Group. A dose-ranging clinical trial to assess the safety and efficacy of cyclosporine ophthalmic emulsion in patients with keratoconjunctivitis sicca. *Adv Exp Med Biol* 1998; **438**: 969–972.