

## Resolution of Autoimmune Polyglandular Syndrome–Associated Keratopathy With Keratolimbic Stem Cell Transplantation

### To the Editor:

I read with great interest the report and literature review of Shah et al<sup>1</sup> on keratolimbic stem cell transplantation in keratitis associated with autoimmune polyglandular syndrome. However, there are some important issues that should be addressed.

First, I have examined and followed up 4 of these patients for a considerable time (6 years), and none of them needed stem cell transplantation. The keratitis was often self-limited and responded well to hormone replacement therapy and management of the dry eye with lubricants and punctal occlusion. The authors simply overlooked my previous reports<sup>2,3</sup> in their review of literature.

Second, they did not pay enough attention to the dry eyes and its management. The normal Schirmer test in their patient may be caused by reflex hypersecretion that is usually seen in these patients and includes dry eye, because the patient also reported dry, itchy, red, and irritable eyes with photophobia.

In my experience, aggressive treatment of dry eye always yielded significant improvement of keratopathy because the stem cell deficiency in these patients is partial<sup>2,3</sup> and not total (as the authors mentioned). One can easily notice (in Figure 2 in their report) that the limbal deficiency is not total simply by comparing the corneal clarity and vascularization of this patient with patients with history of severe alkaline burn and total corneal haziness, vascularization, and even conjunctivalization.

Interestingly, the authors hypothesized that the patient had total stem cell deficiency with inadequate documentation!

Even more severe forms of partial stem cell deficiency usually respond well to superficial keratectomy with or without amniotic membrane transplantation and do not need keratolimbic allograft.

Third, this patient has an underlying immune disorder with multiple endocrine deficiency. Keratolimbic allografts that need lifelong immunosuppressive therapy that may affect the health status of the patient should not be considered as the first step for treatment of these patients. There is no report of side effects of long-term immunosuppressive therapy in similar cases with considerable follow-up. These patients have preexisting immunosuppression, and candidiasis is a common comorbidity in them. Aggressive immunosuppression such as a combination of tacrolimus, mycophenolate, cyclosporine, and prednisolone, as was prescribed for this patient, may exacerbate the innate immunodeficiency and lead to recalcitrant fungal infections.

In conclusion, the first step of treatment in these patients should be limited to sufficient management of dry eye, adequate hormone replacement therapy, and if needed, superficial keratectomy with or without amniotic membrane transplantation and keratolimbic allograft, which needs lifelong immunosuppression, should be reserved only for cases for which initial treatments have failed.

**Mehrdad Mohammadpour, MD**

Farabi Eye Hospital  
Tehran University of Medical Sciences  
Tehran, Iran

### REFERENCES

1. Shah M, Holland E, Chain CC. Resolution of autoimmune polyglandular syndrome-associated keratopathy with keratolimbic stem cell transplantation. *Cornea*. 2007;26:632–635.
2. Mohammadpour M, Javadi MA. Keratitis associated with multiple endocrine deficiency. *Cornea*. 2006;25:112–114.
3. Mohammadpour M, Javadi MA, Karimin F. Limbal stem cell deficiency in the context of autoimmune polyendocrinopathy. *Eur J Ophthalmol*. 2006;16:870–872.

### Reply:

We read with interest the comments raised by Mehrdad Mohammadpour, MD, to our recently published article

and would like to reply to his observations as follows.

He correctly points out that patients with ocular surface disease should have a complete evaluation for dry eye as part of their workup. However, his statement that “they did not pay enough attention to the dry eyes and its management” is inaccurate. This patient had been treated for dry eye and blepharitis for years with frequent nonpreserved artificial tears, lid scrubs, and topical steroids, only to have progression of the epitheliopathy, which resulted in a profound loss of visual acuity. The clinical findings and histopathology of the corneal epithelium confirmed the diagnosis of limbal stem cell deficiency.

Another inaccuracy is his statement, “One can easily notice (in Figure 2 in their report) that the limbal deficiency is not total simply by comparing the corneal clarity and vascularization of this patient with patients with history of severe alkaline burn and total corneal haziness, vascularization, and even conjunctivalization.” Patients with total limbal deficiency do not necessarily end up with loss of corneal clarity until the epitheliopathy has been present for a long time. The early stages of limbal stem cell deficiency result in peripheral epithelial disease followed by migration to central epithelial disease. Only after the central epithelium has been affected for a significant period do we see secondary stromal haze and finally central neovascularization. This patient was fortunately referred with progressive epitheliopathy without significant stromal disease, and that is why he did well with stem cell transplantation without requiring a subsequent keratoplasty.

Dr. Mohammadpour’s next inaccurate statement is, “Keratolimbic allografts that need lifelong immunosuppressive therapy that may affect the health status of the patient should not be considered as the first step for treatment of these patients.” First, we do not consider keratolimbic allograft as a first-step therapy. It is only when the patient failed all of the supportive ocular surface therapies that he was referred for a keratolimbic allograft. Second, patients do not necessarily need lifelong immunosuppression for successful ocular surface transplantation. In fact, patients with normal conjunctiva

without inflammation such as seen with this disorder or that with congenital aniridia or old chemical injuries often do well with a course of immunosuppression for 2–3 years. If the patients do not develop rejection in the first couple of years, we taper the oral immunosuppression completely and maintain the patients on topical immunosuppression only. Indeed, that is what happened in this patient's case, because he is off oral

immunosuppression and doing well on topical medications only.

In conclusion, we agree with Dr. Mohammadpour that evaluation of dry eye is important to patients with limbal stem cell deficiency; however, we recommend that clinicians understand the findings of total limbal deficiency. We recommend consideration of keratolimbal allograft as a treatment of total limbal deficiency with significant

visual loss, as was performed in this patient with autoimmune polyglandular syndrome.

**Edward J. Holland, MD**

Cornea Services  
Cincinnati Eye Institute  
Cincinnati, OH  
Department of Clinical Ophthalmology  
University of Cincinnati  
Cincinnati, OH