Research sheds new light on corneal graft rejection in atopic patients

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A SERIES of elegant mouse experiments conducted in the US opens promising avenues for research on corneal graft survival in atopic patients. The research also sheds new light on the mechanisms underlying corneal graft rejection.

"This model clinically and histologically resembles corneal allografts in humans. And typically 50% of the grafts survive and remain clear well beyond 100 days."

The research also produced very early-stage evidence that anti-interferon gamma treatment combined with dampening the expression of the vascular cell adhesion molecule (VCAM) may possibly enhance corneal graft survival in atopic patients, delegates to the Moorfields Bicentenary Scientific Meeting heard.

Jerry Niederkorn PhD, director of ophthalmic research at the University of Texas Southwestern Medical Centre, Dallas, Texas, told EuroTimes that he launched the research when ophthalmologist colleagues lamented the low level of corneal graft survival in atopic patients.

"Current immunological thinking believes that when challenged, the immune system chooses to go down either a Th-1 pathway, which produces interferon gamma, or a Th-2 pathway, which produces such cytokines as interleukin (IL)-4, IL-5, IL-10 and IL-13," he said.

"Given that the Th-1 pathway may be responsible for organ graft rejection, a Th-2 response may in turn impede a Th-1 response and enhance the chances of graft survival," he explained.

But numerous reports show that allergy is a risk factor in corneal grafts in keratoconus patients, even though 90% of grafts in non-atopic keratoconus patients are successful, said Dr Niederkorn.

"There is a growing body of evidence that allergy is a risk factor in corneal graft rejection in fellow eye."

Dr Niederkorn said future directions of research needed to examine the mechanism of rejection.

"What role, if any, do eosinophils play in rejection? We've had 50 years of immunological research on organ graft rejection, with implications for rejection post-transplantation in some of the keratoconus patients with allergic conjunctival and cutaneous disease. This is a newly recognised pathway to corneal allograft rejection, with implications for rejection treatment and prophylaxis in this patient group."

"The work is of interest to corneal transplant surgeons, as we encounter early and vigorous rejection post-transplantation in some of the keratoconus patients with allergic conjunctival and cutaneous disease."

In a subsequent series of experiments, Dr Niederkorn's team used a combination of anti-IFN-g and anti-VCAM treatment before and after applying B6 corneal allograft onto BALB/c mice. Here graft rejection was at a lower tempo and incidence than in untreated atopic mice, or in atopic mice treated with anti-IFN-g only. Dr Niederkorn stressed, however, that these were early results in series of just 20 mice.

Findings raise new questions

Dr Niederkorn told delegates that this series of experiments showed that mice with allergic conjunctivitis reject corneal grafts faster and at a higher incidence than non-allergic mice. Furthermore, histocompatible, grafts are not rejected in mice with allergic conjunctivitis. Atopic mice produce Th-2 cytokines and interferon gamma. Atopic mice also mount a delayed hypersensitivity response to donor alloantigens, but inflammatory lesions are predominantly eosinophilic and