

Atopic dermatitis as a risk factor for graft rejection following normal-risk keratoplasty

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Received: 28 August 2008 / Revised: 22 September 2008 / Accepted: 24 September 2008
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Keywords Keratoplasty · Immune rejection · Atopy · Risk factor · Transplantation

Dear Editor,

In patients undergoing normal-risk penetrating keratoplasty (PK), corneal transplantation is very successful with regard to graft survival. Still, endothelial corneal allograft rejection (TR) remains the most frequent cause of irreversible graft failure. Controlled prospective studies have so far only been

conducted for high-risk PK or a mixture of normal- and high-risk PK. Therefore, the Erlangen prospective non-high-risk keratoplasty study was initiated to analyze the outcome of normal-risk PK and potential risk factors for endothelial TR (study design, inclusion/exclusion criteria, and first results have previously been published [1, 2]). Patients with atopic keratoconjunctivitis and severe dry eyes/Sjögren's syndrome were excluded. Overall, out of 397 patients recruited so far (median follow-up: 18 months [6/2001]), 5.5% (22) developed an episode of graft rejection and 3% (12) presented newly developed retrocorneal precipitates without other signs or symptoms of TR ("suspects"). Here we report the results of a sub-study evaluating atopic diseases as potential risk factors for TR since retrospective analyses have suggested that atopic dermatitis with ocular involvement may increase the risk of TR [3].

Patients from the Erlangen study were prospectively evaluated for history of atopic diseases using a questionnaire modified from the "Erlangen atopy score" [4]. The questionnaire was filled in preoperatively or at the first routine postoperative control and asked for acute or past history of hay fever, atopic asthma, contact allergic reactions, allergic reaction to insect bites, contrast allergy, cradle cap, atopic dermatitis, food allergy, and family history of atopic diseases ($n=165$). Possible answers were "yes", "no", and "don't know." All patients were evaluated preoperatively and at every routine control (at least 3 monthly) in a specialized outpatient service at our department for symptoms and signs of endothelial graft rejection (including laser flare tyndallometry/cell count [1, 2]). Regarding the atopy questionnaire, atopic dermatitis demonstrated to be a significant risk factor for subsequent TR using Cox time-to-event regression analysis evaluating

There is no financial relationship with the organization that sponsored the research. The authors have full control of all primary data and they agree to allow Graefe's Archive for Clinical and Experimental Ophthalmology to review their data if requested.

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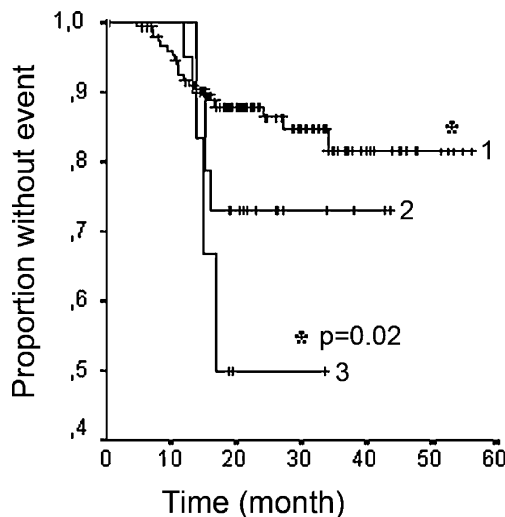


Fig. 1 Graft-rejection-free survival for patients with (3) and without history of atopic dermatitis (1; 2: patients with “don’t know-answer”) after normal-risk keratoplasty (Kaplan-Meier survival curve). Note significantly increased risk of graft rejection for patients with history of atopic dermatitis without clinically detectable ocular involvement (* $p=0.02$; odds-ratio: 4.2)

manifest TRs and suspects together ($p=0.02$; odds-ratio: 4.2; for Kaplan-Meier survival curve see Fig. 1; for the 22 episodes of manifest endothelial graft rejection alone: $p=0.05$; odds-ratio: 4.3). All other questions didn’t prove to be significant risk factors (isolated or in combination), but there was a positive correlation between cradle cap, atopic dermatitis, and family history of atopy and TR following PK. The increased risk of TR in patients with atopic dermatitis may be related to an upregulation of inflammatory/costimulatory molecules on Langerhans’ cells (observed in atopic skin lesions [5]), potentially also affecting the conjunctiva/cornea without obvious clinical changes. Although the Th1-immune response being responsible for TR is downregulated in acute atopic dermatitis, in chronic

disease, both mechanisms seem to be active, thus allowing Th1-delayed type hypersensitivity mediated TR. Nevertheless, we cannot rule out confounding variables such as the association between atopy, keratoconus, and larger graft diameters leading to a higher risk of graft rejections.

Whereas PK in atopic dermatitis with ocular involvement can be regarded as high-risk-PK [3], to our knowledge, this is the first prospective study identifying atopic dermatitis (without clinically detectable ocular involvement) as a risk factor for immunological graft rejection following normal-risk keratoplasty. In conclusion, patients with a history of atopic dermatitis, even without obvious ocular involvement, should receive special attention after PK.

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