

## Role of Photopheresis in the Treatment of Refractory Cellular Rejection in Kidney Transplantation

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### Case Report

Extracorporeal photopheresis is an immunomodulatory technique based on the apoptotic effects of 8-methoxypsoralen (8-MOP) and ultraviolet A (UVA) radiation on leukocytes. This technique is widely used in T-cell mediated disorders such as cutaneous T-cell lymphoma, graft-versus-host disease, rheumatoid arthritis and systemic lupus erythematosus. The use of this technique in the prophylaxis of acute rejection of lung or heart transplant is promising; however, scarce articles have been published on its application in case of acute cellular rejection refractory to conventional treatment in patients with kidney allograft.

We present the case of a 56-year-old patient who underwent kidney transplantation from deceased donor, on May 2013; immunosuppression was induced with basiliximab, tacrolimus, mycophenolate mofetil and corticoids. He presented immediate kidney function and showed improvement up to 16 days post-transplant, however with subsequent deterioration. Percutaneous kidney biopsy showed acute cellular rejection of type IB Banff. Laboratory results for anti-HLA, anti-MICA and anti-endothelial antibodies were negative. He was treated with bolus of methylprednisolone (3 × 500 mg) and thymoglobulin (1.25 mg/kg; total accumulated dose 410 mg) without favorable outcome; 17 days afterwards a second kidney biopsy was conducted, which evidenced acute cellular rejection of type IIA Banff with mild intimal arteritis. Due to the progression and refractory nature of the condition, photopheresis (14 sessions, weekly periodicity, equipment Therakos UVAR XTS System) and infusion of unspecific human gamma globulin (200 mg/kg, total dose 80 grams) were prescribed. After this treatment, progressive improvement of the kidney function was observed with 2.3 mg/dl serum creatinine (Cr<sub>s</sub>) upon discharge. Renal function remained stable for the following 9 months, after which mild deterioration was observed with Cr<sub>s</sub> 2.62 mg/dl. A new photopheresis series (6 weekly sessions) was prescribed with favorable outcome (7 months afterwards Cr<sub>s</sub> was 1.9 mg/dl). No relevant treatment-related infection occurred.

Prophylactic photopheresis treatment in kidney transplantation together with standard immunosuppression therapy has been reported to improve renal function after 6 months and to increase the levels of regulatory T-cells (Tregs) as compared to control [1]. However, very few and occasionally contradictory articles have been published on the use of photopheresis in patients with RA refractory to conventional treatment. Horina et al. described three cases of patients treated with monthly photopheresis sessions, which failed to improve the kidney function so that they had to go back to dialysis in a few months [2].

However, other authors reported improvement of the kidney function in association with more frequent photopheresis sessions [3]. Dall'Amico et al. described 4 patients with different types of cell rejection, previously treated with OKT3, whose renal function improved after the first treatment cycle and kept stable up to one year afterwards, thus allowing for reduction of the immunosuppressive load [4]. These authors used weekly, biweekly or monthly schedules up to a maximum of 19 sessions.

The mechanisms behind the beneficial effects of photopheresis are not fully understood. Apparently, it triggers immunomodulatory response of the alloreactive T lymphocytes exposed to 8MOP and UVA radiation, where the synthesis of interleukins (especially TNF, IL-10 and IL-6) and the progressive increase, session by session, of the number of regulatory T cells (CD4+, CD25+ and FoxP3+) probably play a relevant role. Such mechanisms could account for the fact that the beneficial effects of this therapy on cutaneous T-cell lymphoma are observed after two or three months of treatment, while the effects on RA appear in a few days [5].

Up to the moment, photopheresis as a rescue treatment in cases of acute cellular rejection of renal allograft refractory to conventional treatment seems to be useful and safe. However, studies with larger patient populations are needed to confirm this result.

**Conflicts of Interest:** None

### References

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