Anaphylaxis following Intravenous Methylprednisolone Sodium Succinate in a Renal Transplant Recipient

R. Peces \textsuperscript{a}
M. Gorostidi \textsuperscript{a}
J. Azofra \textsuperscript{b}
L. Sánchez \textsuperscript{a}
J. Alvarez \textsuperscript{a}

Departments of \textsuperscript{a}Nephrology and \textsuperscript{b}Allergy, Hospital Covadonga, Oviedo, Spain

Dr. R. Peces, Servicio de Nefrologia, Hospital Covadonga, Celestino Villamil s/n, E-33006 Oviedo (Spain)

Dear Sir,

Intravenous methylprednisolone is currently used before transplantation as well as for the treatment of acute rejection episodes. Hypersensitivity to methylprednisolone is extremely rare and the reported cases were mostly in atopic or asthmatic patients \cite{1-7}. Among them, only 2 cases were renal transplant recipients \cite{6, 7}.

We report a 49-year-old male with a history of seasonal asthma who underwent cadaveric renal transplant in December 27, 1989. Before transplantation he received intravenous azathioprine (100 mg), ceftriaxone (1 g) and methylprednisolone sodium succinate (500 mg). Within 2 min the patient complained of generalized itching and dyspnea, and became pale, cold and diaphoretic. Blood pressure was 80/50 mm Hg. He was cyanotic, and a skin rash and bronchospasm were evident. His condition improved with the administration of intravenous amino-phylline, fluids and oxygen. It was believed that the patient had suffered an anaphylactic reaction to one of the administered drugs. The patient was intubated and transplantation surgery was performed successfully. The following morning he received the routine medication including methylprednisolone sodium succinate (30 mg) intravenously and developed both inspiratory and expiratory wheezes. A diagnosis of bronchospasm disease was made and a regime of inhalating albuterol and a sustained-release theophylline were administered. On the 2nd day after transplant, methylprednisolone sodium succinate was replaced by oral prednisone (30 mg/day) without any adverse effect. He was also receiving cyclo-sporine (300 mg/day). The patient was discharged from hospital on the 9th day after transplantation with good graft function. He was then receiving prednisone (30 mg/day), azathioprine (50 mg/day) and cyclosporine (300 mg/day). His blood cyclosporine levels ranged from 562 to 834 ng/ml using a polyclonal radioimmunoassay kit (Sandoz, Basel, Switzerland).

One month after transplant he had an acute rejection episode and intravenous methylprednisolone sodium succinate, 500 mg in 200 ml of 5% glucose, was administered. When he had received 2 ml of the solution, he developed facial itching, shivering and bronchospasm with acute breathlessness. An anaphylactic reaction to methylprednisolone sodium succinate was suspected and the infusion stopped. He responded within 15 min to discontinuation of the solution, intravenous injection of 5 mg dexchlorpheniramine maleate and oxygen. The acute rejection episode was managed successfully with high dose oral prednisone...
and two intravenous pulses of 2,500 mg hydrocortisone phosphate. The allograft continues with good function 11 months later.

Intradermal tests [8] were performed by injection of 0.03 ml of methylprednisolone sodium succinate and methylprednisolone acetate to concentrations of 0.1, 1 and 10 mg/ml into the forearm. A strongly positive reaction was observed with all concentrations of methylprednisolone sodium succinate, as shown by a 16-mm wheal with many pseudopods at the site of injection. The tests with methylprednisolone acetate were negative. On the other hand, the patient was able to tolerate oral prednisone and intravenous hydrocortisone phosphate without problems. Then, it is possible that the succinate compound may act as a hapten by combining with proteins, forming complexes with specific antigenic activity [2].

This patient suffered an anaphylactic reaction to methylprednisolone sodium succinate on three consecutive occasions. The last reaction occurred despite concurrent prednisone and cyclosporine treatment. Whereas oral corticosteroids do not alter IgE-mediated skin test reactivity [9,10], little is known about cyclosporine effects on histamine and allergen-induced reactions.

Much attention has recently been focused on the ability of lymphokines secreted by helper T cells to induce or suppress IgE synthesis. IL-3 and IL-5 exert their function on mast cells and eosinophils while IL-4 and interferon-γ have been shown to be the natural regulators of IgE production [11,12]. The actions of cyclosporine seem to be inhibition of macrophage and monocyte-mediated antigen presentation, inhibition of IL-2 production as well as other lymphokines such as interferon-γ [13].

From this perspective, cyclosporine could imply a defective immune responsiveness in patients with immunologic abnormalities due to allergy. However, it has been demonstrated that cyclosporine does not prevent the transfer of specific IgE in recipients of bone marrow from atopic donors [14]. Moreover, cyclosporine is an adjuvant in murine IgE antibody responses [15] and may enhance IgE antibody production to a solvent detergent component, such as cremophor, especially in those patients who were previously exposed and sensitized to this component [16]. Furthermore, the anaphylactic reaction and positive skin test showed by our patient suggest that cyclosporine has no inhibitory influence in the IgE-mediated reactions, on the contrary they could be enhanced.

In summary, clinicians should be aware of the potential risks of methylprednisolone sodium succinate administration particularly in atopic individuals. If there is a reaction in the initial transplant period, these patients, who undoubtedly will require future corticosteroids therapy, may benefit from alternative medication with other corticosteroids. Skin testing can be the most useful way to identify the sensitizing compound and establish the safety of a particular corticosteroid compound.

References
