LETTER

The role of tacrolimus in the step-up induction therapy of refractory childhood-onset lupus nephritis

Dear Editor,

There is growing evidence that tacrolimus (Tc) -a calcineurin inhibitor- is a promising agent for the induction therapy of Lupus Nephritis (LN). Most publications involve Asians with aggressive and resistant disease while relevant data from Caucasians are limited[1,2]. We report the first Greek case of a refractory childhood-onset LN (cLN) that responded to Tc as a step-up induction therapy.

In 2011, a 9-year-old Caucasian girl was referred to us for persistent feverish arthritis, malar rash, and nasopharyngeal ulcers. Her medical and family history was unremarkable. She additionally had a urine sediment characterized by pyuria (18-20/cfu), microscopic hematuria (8-10/cfu) and hemegranular casts, a moderate proteinuria (525 mg/24h), anemia (Hemoglobin 9.9 g/dL), positive antinuclear antibodies (ANA 1:640) and antibodies to double-stranded DNA 1:160. Her estimated glomerular filtration rate was 98 mL/min/1.73m^2. Thus, her established diagnosis was Childhood-Onset Systemic Lupus Erythematosus (cSLE). The renal biopsy showed a stage III focal proliferative cLN. Despite the 6-month initial regimen of hydroxychloroquine (200 mg once daily), prednisolone (1 mg/kg/d) and mycophenolate mofetil (MMF) (600 mg/m^2/12h), proteinuria persisted (585 mg/24h), and urine sediments persisted. Tacrolimus (Tc) was added at that time in a dose of 0.2 mg/kg/d per os, divided into two doses, after being approved. Serum tacrolimus levels were not measured according to the Center's administration policy for calcineurin inhibitors in rheumatic patients. This 3-month regimen led to the complete remission of proteinuria (147 mg/24h), normalization of the urine sediment and hemoglobin levels and allowed steroid discontinuation. Six months later, Tc was withdrawn, and MMF remained for six more months. No adverse events were noted. Since then she remains in complete remission for four years, receiving only hydroxychloroquine.

Proliferative LN is a predominant cause of morbidity. The reported Cyclophosphamide's toxicity and the unfavorable impact of steroids on the growth velocity led to the introduction of newer immunosuppressants, such as of MMF and lately of Tc. Tc has been shown to be a more potent efficacious and safe agent, compared to cyclosporine as reported in Asian SLE patients[1-4].

Tc prevents the activation and proliferation of T helper cells, exhibits less hypertensive and adverse cosmetic effects than older immunosuppressants, rapidly tames proteinuria, and leads to lower risk of lupus flares and less severe infection rates. Tc has also been published to be well tolerated as a component of multi-agent treatment[1,2,4].

This case, of a Caucasian preadolescent with a refractory and proliferative cLN, highlights that Tc can be effectively used as a step-up induction therapy in young patients.

We thus propose that Tc deserves to be applied in resistant cLN, complementary to the conventional therapy. Future and larger studies are needed to determine the optimal dosage, the duration of the regimen, and its long-term efficacy.

References

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Conflict of interest

None declared.

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