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Treatment of Cogan's Syndrome With FK 506: A Case Report

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Cogan's syndrome is characterized by ocular inflammation, most commonly interstitial keratitis, vestibuloauditory symptoms, and (in about 50% of cases) systemic vasculitis. A recent review¹ cites the evidence for an autoimmune pathogenesis of this rare disease. This includes the presence of lymphocytes in ocular and vestibuloauditory tissue,² and the detection of serum antibodies against antigens present in the cornea and inner ear.³ Successful treatment can be achieved with corticosteroids,⁴ while other immunosuppressive agents, including cyclophosphamide and cyclosporine (CyA),⁵ have proved useful in severe cases. FK 506 is a powerful new immunosuppressive agent which shares many of the properties of CyA,⁶ including a very similar inhibitory effect on CD4⁺ T-lymphocyte activation and proliferation. In clinical trials, it has proved highly effective in the prevention⁷ and reversal⁸ of organ allograft rejection, with a reduced incidence of rejection and fewer side effects compared with CyA. FK 506 also shows considerable promise for the treatment of certain autoimmune diseases,^{9–11} including disorders unresponsive to high-dose steroids. We report here on the successful use of FK 506 in the treatment of a patient with Cogan's syndrome.

A 48-year-old Caucasian woman presented to the Ocular Immunology service at the Eye and Ear Institute with a 9-year history of ocular inflammation. She also had a 20-year history of hearing loss. She had lost all vision in the left eye from intractable glaucoma, which was secondary to uncontrolled uveitis and scleritis.

At the time of presentation, she had active, diffuse anterior scleritis, anterior uveitis, and interstitial keratitis of the right eye and mild arthralgias of the knees. She was on low-dose oral steroids (0.25 mg/kg per day). Fluorescence *Treponema* antibody absorption test, rheumatoid factor, antinuclear antibodies, and Lyme titer were negative, and the complete blood count was normal. Audiogram was consistent with severe, bilateral sensorineural hearing loss.

She was diagnosed as having Cogan's syndrome and her oral steroids were increased to 1 mg/kg per day. Cardiology assessment revealed aortic insufficiency. She became dependent on prednisone (0.5 mg/kg per day) to control her ocular inflammation. As the steroid side effects accumulated, she entered our prospective, clinical trial comparing the efficacy and safety of oral FK 506 (0.15 mg/kg b.i.d.) with conventional immunosuppressive drugs for the treatment of ocular autoimmune disease. She was randomized to FK 506. Early during treatment, she experienced a pruritic papular rash on her chest. Her ocular inflammation began to improve in 3 weeks and was mostly resolved in 3 months. Over a 10-month period, oral steroids were tapered and discontinued. She has had no progression of her hearing loss or recurrent arthralgias and has been free of ocular inflammation for 6 months. Only minimal systemic side effects of FK 506 (> 10 mg BID) have been observed. Specifically,

there was a transient rise in creatinine to 158 mmol/L compared with a pretreatment level of 79 mmol/L. Renal function responded to a decrease in FK 506 dose; her current creatinine level is 106 mmol/L. No change in blood pressure, hepatic function, electrolytes, amylase, or blood glucose was observed.

This case report demonstrates the powerful immunosuppressive activity and safety of FK 506. It suggests that FK 506 may prove valuable in the management of this and other ocular inflammatory disorders, as well as showing promise for the treatment of other autoimmune diseases.

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