Retinal Vasculitis and Uveitis – An Adverse Reaction to Intravenous Immunoglobulins?

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Dear Sir,

Intravenous immunoglobulins (ivIg) have been found to reduce disease activity in diverse autoimmune diseases, e.g. immuno-thrombocytopenia, immunoneutropenia, myasthenia gravis, SLE, vasculitis and acquired inhibitors of factor VIII [1,2]. Although involvement of idiotype-antiidiotype interactions has been suggested, the exact mechanism of action remains to be defined. Currently the use of ivIg is entirely empirical. It is therefore of note that uveitis was reported after Ig substitution in a patient with X-linked agammaglobulinemia [3]. We observed a similar case after intravenous administration of Ig in a patient with Wegener's granulomatosis.

A 70-year-old female presented in 1991 to another hospital with a history of chronic conjunctivitis, amaurosis fugax in the left eye, sinusitis maxillaris, serous otitis media and bilateral mastoiditis. The diagnosis of Wegener's granulomatosis was based on a positive c-ANCA titer (1:160), but histological confirmation was not available. The patient was treated with cyclophosphamide and methylprednisolone for 2 months. Then a relapse occurred with oral ulcerations, pulmonary infiltrates, retinitis and iridocyclitis of the right eye.

Immunosuppression was intensified resulting in clinical improvement. The course was complicated by the repeated demonstration of Salmonella enteritidis in stool and urine cultures. Treatment with cyclophosphamide was interrupted and ciprofloxacin instituted. The patient presented to our institution with erosive rhinitis and hypacusis of the left ear. She had an elevated sedimentation rate (67/110 mm), anemia (Hb 9.6 g/dl), elevated alkaline phosphatase (191 U/l, normal < 170) and γ -GT (100 U/L, normal < 18). Serological analysis disclosed a positive c-ANCA (1:20), a marginally elevated CRP (1.7 mg/dl, normal < 0.8) and decreased concentrations of IgM (29.7 mg/dl, normal > 63) and IgG (277 mg/dl, normal > 723). Results of the following serological tests were negative: ANA, ds-DNA-ab, complement, cryoglobulins, paraproteins. In order to eradicate S. enteritidis which was still demonstrated in

stool and urine cultures despite 4 months of ciprofloxacin treatment, steroids were withdrawn and treatment with cephalosporine and TMP/SMX was instituted. We also considered the possibility that low IgG might contribute to the failure of eradicating *S. enteritidis*. An IgG preparation with high titer against *S. enteritidis* was given, i.e. the patient received 0.2 g/kg = 10 g/day of Endobulin® for 3 days. At a concentration of 1 g/l no ANCA activity was demonstrable in the preparation (ANCA by IF; proteinase-3 by ELISA). One week later the patient noticed decreased visual acuity of the right eye. Retinal vasculitis with retinal branch vein occlusion, cotton wool exudates and parapapillary bleeding were noted. Steroids were reinstituted and retinal vasculitis improved. Subsequently, steroids were tapered to 15 mg prednisolone/day. Two months later, when the patient was readmitted, IgG concentrations had again decreased to 421 mg/dl. Prior to ivIg substitution ophthalmological examination did not show active ocular disease. The ANCA test was negative. One day after 0.2 g/kg of Endobulin the patient developed severe anterior and posterior uveitis with cellular infiltration of the vitreous and retinal

vasculitis of the right eye. High doses of steroids were required to control the inflammation. Although a temporal coincidence cannot be entirely excluded, the occurrence of ocular complications on two separate occasions with shortening intervals after ivIg suggests an adverse effect of ivIg substitution. The observation further extends reports of a flare-up of immune-mediated diseases, e.g. SLE [4], after ivIg. It cannot be excluded that ivIg causes paradoxical and unpredictable exacerbations of immune-mediated diseases. The present case documenting adverse ocular effects of ivIg substitution in autoimmune disease calls for caution also when ivIg treatment is considered in cases with vasculitis.

References

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