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Deposition of Eosinophil Granule Proteins in Conjunctiva and Sclera in Patients with Wegener's Granulomatosis: A Harbinger of Disease Progression?

C. Stephen Foster, M.D.

Drs. Virender Sangwan, Charalampos Livir-Rallatos, Panayotis Zifirakis, and Blanca Rojas from my laboratory made the striking observation that the presence or absence of certain proteins in eosinophils may be "markers" for the likelihood that patients with the so called limited form of Wegener's Granulomatosis will progress eventually to the more generalized, lethal form.

We analyzed the state of eosinophil "activation" in conjunctival and scleral biopsy specimens cared for on the Immunology Service of the Massachusetts Eye and Ear Infirmary for their Wegener's Granulomatosis. Immunohistochemical analysis of the biopsied tissue was performed on snap-frozen tissue which had been embedded in Tissue Tec OCT compound. Six-micron cryostat sections were then mounted on poly-L Lysin-coated slides, and the sections were in acetone at 4 • C, followed by an incubation with normal rabbit serum for 20 minutes. The slides were then probed with antibodies designated BMK-13, EG1 and EG2. BMK-13 antibody recognizes major basic protein (MBP) of the eosinophils. EG1 and EG2 antibodies recognize the stored and secreted forms of eosinophil cationic protein (ECP). Antibody binding to the eosinophils present in the biopsied, inflamed conjunctiva or sclera of the patients with Wegener's granulomatosis was then visualized by using an alkaline phosphatase/anti alkaline phosphatase/fast red method, with negative controls consisting of specimens processed in an identical way, with the exception that the primary antibody was omitted.

Conjunctiva and sclera from two patients with well-controlled Wegener's inflammatory eye disease showed no indication of the major basic protein or eosinophil cationic protein in these probing studies. Specimens from one patient with active scleritis, but the limited form of Wegener's granulomatosis revealed intense presence of major basic protein and ECP, and this patient's Wegener's disease progressed to the complete form, with renal involvement, within six weeks. A specimen from yet another patient with active scleritis in the limited form of Wegener's granulomatosis, showing no presence of MBP or ECP in the biopsied specimens remained in its limited form during the succeeding two years of observation.

We hypothesize that the presence of "activated" eosinophils in sclera or conjunctiva of patients with the limited or even the "very limited" form of Wegener's granulomatosis is a sign that might be predictive of which patients will have their limited disease progress to the more generalized form. These patients then probably deserve much closer scrutiny (and possibly even more aggressive therapy) than do those patients without signs of activated eosinophils in their biopsied tissue.