Biologics and treatment of uveitis

By Gary Culliton 22nd April 2008

Mr Micheal J Gallagher, Consultant Ophthalmic Surgeon at the Hermitage Medical Clinic, on the treatment of uveitis and how the use of biologic agents has benefited many patients in recent years

Intraocular inflammatory disease, or uveitis, is a serious problem and has great potential for visual morbidity and visual loss. In one large series of patients with uveitis, 35 per cent had visual loss to a level of worse than 6/18 in at least one eye and 22 per cent became unilaterally or bilaterally blind (worse than 6/60).

{openx:269}
Cicatricial pemphigoid, if untreated, often results in blindness. Scleritis, particularly necrotising scleritis, and necrotising keratitis may threaten the structural integrity of the eye and may herald the onset of a potentially life-threatening systemic vasculitis. As such, the correct treatment of ocular inflammatory disorders is important for preserving vision and for preventing both ocular and nonocular morbidity.
Recent studies quote the prevalence of ocular inflammatory disorders at 115.3 per 100,000 people, a number considerably higher than was previously reported. For many years, uveitis was considered a single disease entity, and the approach to treatment varied very little. As knowledge of the disease process grew and the sophistication of immunologic and microbiologic testing improved, the fact that uveitis entails a multitude of diseases became clear.
Although some diseases represent local ocular immune phenomena, many of them are systemic diseases with ocular manifestations. The spectrum of disease pathogenesis ranges from autoimmunity to neoplasia to infective etiologies and requires an understanding of internal medicine, infectious diseases, rheumatology and immunology.
h4. Paradigm shift
The treatment for uveitis underwent a tremendous paradigm shift more than 50 years ago with the introduction of corticosteroids into the ophthalmic therapeutic armamentarium. Although corticosteroids represent one of the mainstays in the management of patients with ocular inflammation, in many patients, the severity of the disease, the presence of corticosteroid side effects, or the requirement for doses of systemic corticosteroids highly likely to result in corticosteroid complications supports the rationale for immunosuppressive drugs (for example, antimetabolites, T-cell inhibitors, and alkylating agents) being used in the management of these patients.
With the recent turn of the millennium, we entered the era of ‘biologics’. Biologic agents can be broadly defined, but generally include monoclonal antibodies directed against selected cell surface markers or recombinant forms of natural inhibitory molecules.
The clinical impact of neutralising tumor necrosis factor alpha activity in inflammatory diseases has been compared efficaciously to that of corticosteroids and highlights the revolutionary impact these agents have in the treatment of chronic ocular inflammatory disorders such as juvenile idiopathic arthritis, Behcet’s disease and sarcoidosis.
Other biologic agents include daclizumab, adalimumab, rituximab, alemtuzumab, abatacept, interferons and intravenous immunoglobulin. Understandably, there has been a great deal of excitement as the medical literature has reported successful treatment of treatment-resistant inflammatory disorders with various biologic agents.

This enthusiasm has extended to ophthalmology as dramatic remissions have been observed in patients with ocular inflammation that has failed all other treatments. Inflammatory eye disease and its subtypes are heterogeneous disorders and as new biologics are launched, clinical trials must aim to establish which subsets may be responsive.

Because of the potential for side effects, treatment of patients with ocular inflammatory disease must be individualised and regular monitoring performed. Serious side-effects are however rare and must be compared with the considerable risks of conventional therapy. With careful, judicious use of immunomodulatory therapies for the treatment of ocular inflammatory disorders, many patients will benefit both from improved control of their ocular inflammation and a decrease in corticosteroid related morbidity.

* **Mr Micheal J. Gallagher,**
M.M.L. FRCOphth,
Consultant Ophthalmic Surgeon.Fellow of Massachusetts Eye Research and Surgery Institute,
Harvard Medical School. International Uveitis Specialist.
Medico-legal Consultant.
Aut Even Hospital, Kilkenny.
Hermitage Medical Clinic,
Old Lucan Road,
Dublin 20.