Uveitis and neurological diseases

L K Gordon

Therapeutic and diagnostic challenges

Systemic disease associations in uveitis are widespread, ranging from inflammatory bowel disease (IBD), such as ulcerative colitis or Crohn’s disease, to demyelinating diseases such as multiple sclerosis. In some cases, the systemic disease is diagnosed before onset of uveitis, whereas in others uveitis is the initial presentation of the underlying or associated condition. Two significant questions arise regarding neurological concomitants of uveitis. What is the incidence and identity of neurological diseases seen in individuals with uveitis? Are there particular clues in the clinical examination of an individual patient with uveitis that would help lead to diagnosing an associated neurological condition? In the current issue of BJO (p 1498), Smith and Rosenbaum attempt to address these important questions through a retrospective analysis of 1450 patients examined in a tertiary care uveitis clinic.

Increased use of biological agents such as the tumour necrosis factor (TNF-α) inhibitors intensifies the relevance of this study. Targeted immunotherapy for specific immune mediated diseases is rapidly advancing. The immune tolerance network (ITN) is an international consortium with investigators from more than nine countries with the goal of developing clinical therapies for tolerance induction in transplantation, allergy and asthma, and autoimmune diseases. In contrast with the goals of tolerance, clinical trials in cancer therapy now include methods for boosting antitumour immunity through autologous dendritic cell transplantation, allergy and asthma, and autoimmune diseases. This is an exciting time in therapeutic development targeted towards immune regulation. However, unanticipated responses to these therapeutic agents provide us with clues about the unknown aspects of disease pathogenesis. For example, use of the TNF-α inhibitors, whose positive therapeutic utility was predicted for multiple sclerosis, may actually increase demyelinating events.

Use of biological agents in uveitis therapy has received increasing attention and there is now evidence for the utility of specific agents in the therapy of refractory uveitis or for specific uveitis syndromes—for example, Behcet’s disease. However, therapy using an anti-TNF-α medication should probably not be initiated in a patient with underlying multiple sclerosis. Additionally, immunosuppressive medications, commonly used in treatment of refractory uveitis, may mask or worsen certain infectious or neoplastic disease concomitants of uveitis. Understanding the magnitude of the neurological associates of uveitis and developing preferred patterns for the comprehensive evaluation of patients with specific uveitis syndromes is critical in this emerging therapeutic era.

In the series presented here by Smith and Rosenbaum, almost 8% of all patients in their clinic had neurological disease underlying and associated with the ocular inflammatory disease. The authors note, but do not describe, cases with neurological diseases that were presumably unrelated to uveitis. These cases were excluded from the present report; however, additional descriptions of these patients may have been helpful to understanding the magnitude of neurological diseases in this patient group. For example, associations of HIV infection with both infectious diseases and uveitis are well characterised. The absence of AIDS or HIV as a diagnosis in the present series probably reflects the exclusion of these patients from this report.

Future prospective studies will provide the basis for developing evidence based indications for both evaluation and therapy of these important diseases.

It is notable, but not unexpected, that specific clinical features of uveitis were helpful in diagnosing Vogt-Koyanagi-Harada (VKH), multiple sclerosis, and herpes virus infections. However, the sensitivity of the clinical examination in making the correct systemic diagnosis was insufficient in 25% of patients with MS and 20% of patients with herpes infections. These numbers are of significant concern as the therapeutic decision making would have great potential negative impact on the underlying disease. Furthermore, 24% of patients in this series with both uveitis and a neurological disease did not have a specific neurological diagnosis, further complicating the therapeutic decision tree.

The authors freely note some of the additional limitations of their study. These limitations include the retrospective nature of the study, the possibility of underestimating the prevalence of diagnosing concomitant neurological diseases, and the changing neurological disease definitions during the time in which patients were examined (1985–2000). One important potential limitation of any retrospective analysis includes the lack of long term follow up data—for example, a patient who is successfully treated for uveitis may subsequently develop an associated demyelinating disease but may not be re-evaluated by the uveitis specialist unless the ocular inflammation recurs. Additional potential limitations include the applicability of data from a tertiary care facility to the larger experience in community treated uveitis patients. These limitations do not detract from the study by Smith and Rosenbaum, but rather suggest additional prospective studies are required to address the magnitude and scope of neurological diseases in patients with uveitis.

How should the present study be used in clinical practice? Awareness of the underlying, uveitis associated neurological diseases should be increased among both comprehensive ophthalmologists and rheumatologists who deliver care to many of these patients. In evaluating patients with uveitis, a comprehensive history must be performed to elicit symptoms that may suggest systemic conditions such as multiple sclerosis, which may initially have intermittent, self limited systemic complaints not typically reported to the ophthalmologist. Certainly, before initiation of anti-TNF-α therapy, demyelinating diseases such as multiple sclerosis, with a prevalence of at least 1% in this series, must be considered. The role for additional diagnostic testing, such as neuroradiological imaging, analysis of spinal fluid, or sampling and pathological evaluation of intraocular fluids must be individually considered for each patient. Importantly, future prospective studies, which define the prevalence and characteristics of specific neurological syndromes in association with uveitis, will provide the basis for developing evidence based indications for both evaluation and therapy of these important diseases.
ROP has shown better functional outcomes at 9 months of age than conventional treatment at threshold. Schelenburg and Tsanaktidis’s paper is timely because early recognition of the serious nature of the high risk signs of this atypical ROP predominantly seen in extremely premature babies of 23–25 weeks gestational age, combined with appropriate early intervention, should improve the visual outlook in these cases.

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Correspondence to: D Clark, University Hospital Aintree, Department of Ophthalmology, Walton Hospital, Rice Lane, Liverpool L9 1AE, UK; david.clark@ahtr.nwest.nhs.uk

REFERENCES
Found in translation

A H K Kwok, D S Pereira, R B Bhisitkul

Introducing BJO in Translation

English, as we at the BJO would be the first to point out, is a perfectly splendid language, but it does have one drawback: roughly six billion people don’t speak it. As a first step in addressing the non-anglophone sector of the ophthalmological world, BJO Online is introducing a new feature: BJO in Translation.

The language barrier has remained surprisingly impervious to advances in the medical journal model. Readers and contributors from around the world still accommodate themselves to the hegemonic languages of the major journals. This was understandable in the pre-digital age, when the printing and distribution costs of the traditional print medical journal precluded the publication of multiple versions in multiple languages. But with the wide adoption of electronic publication over the past decade, such considerations have been obviated. Page limitations are meaningless in cyberspace, added costs of paper and printing are now just a matter of added megabytes, and fast distribution is available to any place on the planet with internet access. The opportunity is at hand for our new translation project.

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The BJO in Translation Chinese edition is edited by Alvin Kwok in Hong Kong. Chinese is the most widely spoken language in the world, with approximately a billion speakers using the leading dialects. The BJO Chinese page uses the simplified version of traditional Chinese characters developed in China’s 20th century language reform, which is the official text used by speakers of Mandarin, Cantonese, Hakka, and other dialects. There are an estimated 22 000 ophthalmologists in China, with only a minority fluent in English. Most Chinese ophthalmologists are trained in a “Western medicine” educational system, but others are trained in schools of traditional Chinese medicine. Developing countries in Asia, like China, have a large load of preventable blindness. In a country of 9.56 million square kilometres with a population of 1.2 billion, nine million people in China have cataract blindness. To keep abreast of advances necessary to address the eye care needs of this huge population, a small portion of ophthalmologists are able to go abroad to receive training or attend conferences. But for the vast majority without this option, peer reviewed ophthalmological journals represent an important means to keep updated on advances in the field. Journals available in libraries have been integral in enhancing the practice of ophthalmology in China for the benefit of patients.

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The BJO in Translation continues our mission to emphasise the international scope of the British Journal of Ophthalmology, and to reaffirm the initiative of the BMJ family of journals to provide free online materials to readers and institutions in the developing world. It’s our hope that the BJO in Translation will continue growing to incorporate other languages and expanded content. Only 6497 languages left to go.


Authors’ affiliations
A H K Kwok, Department of Ophthalmology, Hong Kong Sanatorium and Hospital, Hong Kong

D S Pereira, Santa Casa de São Paulo, Brazil

R B Bhisitkul, UCSF Department of Ophthalmology 10 Kirkham Street, K301 San Francisco, CA 94143, USA

Correspondence to: Dr Robert B Bhisitkul, UCSF Department of Ophthalmology 10 Kirkham Street, K301 San Francisco, CA 94143, USA; bhisi@itsa.ucsf.edu
Threshold ROP

D Clark

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