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The challenge of ocular inflammation in systemic vasculitis: How to address inequalities of care?

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The systemic vasculitides cause considerable morbidity, not least by their potential to affect so many organs. In major referral centres, they are managed optimally, by multidisciplinary teams comprising specialists in the individual organ systems involved, working together to provide a holistic approach and the optimal environment to assess disease activity and deliver optimal therapy. For example, the National Centre for Behçet's syndrome (BS) in Liverpool UK[1] brings together clinicians from disparate disciplines to provide patient-centred state-of-the-art care for this form of vasculitis. Unfortunately, in many countries, access to diagnostic techniques and appropriately experienced specialists in systemic vasculitis can be difficult. In this article, we will highlight the challenges of detecting and managing systemic vasculitis in the eye and consider how advances in "oculomics" and artificial intelligence (AI) may enhance the management of this major complication and help address the current inequalities of care. We will focus on ocular disease in BS, where early diagnosis and prompt treatment can be sight-preserving.

Behçet's syndrome (BS)[2] is a complex inflammatory disease with the potential to affect any organ. It is unique in vasculitis, with the ability to affect both arteries and veins, of any size. The pathogenesis, still poorly understood, demonstrates both autoinflammatory and autoimmune characteristics. The clinical manifestations are protean, variable and can mimic other diseases, causing diagnostic difficulties. The potential for organ and life-threatening disease highlights the need for timely diagnosis and treatment. However, this remains a challenge: there are no diagnostic tests and many disease mimics, including infections, forme-fruste manifestations of other vasculitides, monogenic autoinflammatory syndrome[3] and inflammatory bowel disease to name but a few. The requirement for not only identifying an appropriate clinical picture, but also excluding other conditions, and a dearth of suitably experienced specialists often delays diagnosis. Ocular BS, present in up to 50% of patients can involve many ocular structures, from scleritis and uveitis to ischaemic retinal vasculitis. The consequences can be devastating[4], with significant eye morbidity and blindness.

Relentless advances in ocular imaging methods have allowed for early diagnosis, monitoring and prognostication in specialist centres. The tools available for the ophthalmic diagnostician now include: Optical coherence tomography (OCT - a ubiquitous imaging modality to highlight structural changes in the eye arising as a consequence of inflammation or ischaemia);[5] OCT angiography (a more recent non-invasive functional overview of retinal and choroidal vasculature);[6] fluorescein and indocyanine green angiography (identifying inflammation and vascular occlusions in the retina and choroid respectively),[7] and widefield imaging (allowing a window into more peripheral pathologies which might otherwise be missed).[8] Furthermore, analysis of ocular tissue can also be required, to rule out other diagnoses, such as infection.

Whilst these specialised ophthalmological investigations have transformed the management of ocular vasculitis in centres like ours, neither these techniques, nor the specialists able to assess and interpret them, are available everywhere, resulting in significant inequality of care between (and often within) countries. This is unfortunately not a new situation. Since the

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distinguished English surgeon John Hunter first described inflammation of blood vessels in the eye in his 1784 paper "Observations on the Inflammation of the Internal Coats of the Veins",[9] eye specialists have been hunting clues to discover associations of systemic vasculitis and eye disease and inventing yet more complex (and expensive) tools and instruments to facilitate this. This has, of course, led to many promising consequences – but also some very concerning ones.

It is certainly worthwhile to better understand ocular involvement in systemic vasculitis. Ophthalmic signs can be the first manifestation of disease, and therefore a thorough assessment of the eye may be critical for systemic diagnosis and management, as well as prevent irreversible loss of vision. A wide spectrum of clinical presentations in the eye has been uncovered: from ocular dysmotility, orbital pain, proptosis and eyelid oedema (suggesting orbital inflammation); photophobia or red eyes (suggesting episcleritis and scleritis, anterior uveitis, ulcerative keratitis and cicatrizing conjunctivitis); floaters and reduction of vision (potentially indicating intermediate, posterior or pan-uveitis and retinal vasculitis; loss of colour vision (found in optic neuritis) and painless loss of vision (a presentation of ischaemic optic neuropathy). Ocular inflammation, comprising any of the above pathologies, may be found in Behçet's and must be identified in order to direct optimal treatment.

However, it is also disturbing to reflect on the inequalities of care that have arisen from these technological advances. Patients fortunate enough to be able to access (and afford) a major centre enjoy state-of-the-art care that is simply not available or affordable elsewhere. How can this be reconciled? We believe that the application of not just biomedical and technological advances, but also the emerging fields of oculomics and AI can, together, result in a more equitable and cost-effective approach to diagnose and manage complex ocular vasculitis.

The burgeoning field of Oculomics refers to the use of ocular investigations, principally imaging, to obtain new insights into systemic health and well-being. Ocular biomarkers can help with prognostication, diagnosis of ocular complications, and might even construct personalised treatment plans. Whilst the cost of some of these tests can be prohibitive, especially if only provided in a few limited centres, others have the potential for low-cost - utilising technology that can be more accessible, such as slit lamps or even simpler methods for imaging the retina.

Complementing oculomics, the use of AI brings tremendous promise for medicine and in particular Ophthalmology. Machine learning algorithms, and deep learning systems in particular, can feed from the data within ophthalmic images, automated perimetry and other ophthalmic investigations[10] in order to generate new insights into systemic disease. The most common application of AI in ophthalmology to date has been in the recognition of disease-related features in OCT and fundus imaging. Applying deep learning to automated segmentation has allowed accurate identification of fluid in the retina, vascular changes, geographic atrophy and other abnormalities. More recent imaging, such as OCT Angiography, can be used by machine learning algorithms to differentiate stages of vascular disease,[11] which is encouraging for prognosticating retinal manifestations of disease.

There have been undoubted advances in the understanding and management of the systemic vasculitides, driving forward treatment and improving outcomes. Ocular involvement is an important component. The detailed ophthalmological evaluation required for vasculitis can be expensive and dependent on access to expertise that is currently not generally available. We look forward to the greater equity of care that can be provided by the application of new technology and AI – and call for this to be developed with a view to widespread accessibility to benefit the maximum number of patients with these serious conditions.

Conflict of Interest

Robert J Moots is a Co-Editor-in-Chief of the journal. The article was subject to the journal's standard procedures, with peer review handled independently of the editor.

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