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Lessons Learnt Along the Way: Illustrative Cases

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Tremendous progress has been achieved in the appraisal of uveitis both in diagnosis and management in the last two decades. The objective and quantitative evaluation of intraocular inflammation by laser flare photometry allows a precise follow-up of uveitis by determining the exact inflammation level at each time point and permits exact monitoring of the impact of therapeutic intervention together with other investigational modalities.

Another crucial development in the appraisal and follow-up of uveitis was indocyanine green angiography (ICGA) that advantageously completed fluorescein angiography in investigating and monitoring inflammation in the choroidal compartment. Many lesions that could not be detected before became accessible to imaging investigation and could be treated accordingly. Choroidal inflammation could be classified according to the disease mechanism and no more only by the aspect of fundus lesions, subdividing choroiditis into inflammation of the choroidal stroma (stromal choroiditis including birdshot retinochoroiditis and VKH disease) or inflammation of the choriocapillaris (choriocapillaritis including MEWDS-multiple evanescent white dot syndrome, multifocal choroiditiss and others)

Diagnosis of intraocular infections has been made easier and more precise by PCR and other techniques applied to intraocular fluids and contribute to reach a diagnosis in many more cases, such as in intraocular tuberculosis and granulomatous anterior uveitis such cytomegalovirus uveitis. In case of suspected intraocular tuberculosis, interferon-gamma release assay (IGRA) tests allow to orient diagnosis into this direction.
In parallel with new performing investigational techniques, a tremendous advancement in therapy occurred, with the availability of less toxic immunosuppressive agents such as mycophenolate mofetyl and the development of more specifically acting biologic agents, the first and most used being the anti-TNF agents.

Unfortunately, too often these new modalities that allow to investigate uveitis cases with great precision, are neglected Therefore, the course has been organized against the background of these novel investigational tests that have improved diagnostic performance, improved accuracy of follow-up and have achieved unprecedented precision in monitoring therapeutic intervention, accounting for lessons that were learnt along this way of improved appraisal and management of uveitis.

1. Management of ocular TB: lessons learnt along the way. (Vishali Gupta, MD Professor, Advanced Eye Centre, PGIMEr Chandigarh, India)
The management of intraocular Tb is a major challenge. After diagnosing intraocular TB, one expects that the further course will be easy where we just have to administer anti-tuberculosis therapy (ATT) to the patients. On the contrary, there are several challenges that come along the way. Here are some of those:

1. Dosage, and schedule of concomitant corticosteroids : this is one of the most challenging issue. Many of these patients represent a hypersensitivity response to Mycobacterium tuberculosis and would need concomitant corticosteroids.
2. Paradoxical worsening on initiation of ATT: Nearly 20% of the patients would show paradoxical worsening when started on ATT. Once needs to identify this phenomenon very carefully and differentiate it from the non-responsiveness to therapy either because of wrong diagnosis or due to drug resistance.
3. Muti-drug Resistance: Multi-drug resistance to Mycobacterium tuberculosis is another challenge. We have started doing PCR /Gene-Xpert to identify Rifampicin resistance.
4. Co-existent complications: Development of retinal angiomatous proliferans is very common in TB granulomas because of high VEG-F levels in these granulomas.

This presentation aims to discuss these issues with illustrative cases.

2. Choroiditis cases (Carl P. Herbort Jr, MD, PD, University of Lausanne and Centre of Ophthalmic Specialised Care (COS), Lausanne, Switzerland)

2a. Choriocapillaritis : how to save the macula. Inflammatory lesions of the choriocapillaris are at the origin of diseases such as MEWDS, APMPPE, Multifocal choroiditis, Serpiginous choroiditis and unclassifiable choriocapilaritis cases. Often the lesion process can only be detected by ICGA while fluorescein angiography is silent. If such occult are not detected (as early as possible) and not treated by corticosteroids and/or immunosuppression this can lead to chorioretinal atrophy.

2b. How can one follow stromal choroiditis closely other than with ICGA? Primary stromal is an inflammatory disease for which inflammation originates primarily in the choroidal stroma. Vogt-Koyanagi-Harada disease is typically a primary stromal choroiditis. When the panuveitis is brought under control by corticosteroid treatment, the challenge is to monitor subclinical occult disease in order to avoid progression of lesions and evolution to sunset glow fundus and to detect response to immunosuppressive treatment.

3. Managing Behçet's disease in the biologic era. (Ilknur Tugal-Tutkun, MD, Istanbul University, Istanbul, Turkey)
Behçet's uveitis is a potentially blinding disease characterized by chronic recurrent nongranulomatous panuveitis and occlusive retinal vasculitis. Our main goals in the management of Behçet's uveitis include rapid control of intraocular inflammation, prevention of recurrences, and achievement of durable remission. Corticosteroids are widely used for the treatment of acute inflammatory episodes; however, severe adverse effects of high-dose corticosteroids and occurrence of rebound attacks during tapering are the limitations. Furthermore, recurrences cannot be prevented by corticosteroid therapy. Conventional immunosuppressive agents have to be added to first-line therapy, as steroid-sparing drugs and for the prevention of recurrences. Both the large dose of steroids and long-term use of immunosuppressive agents may lead to severe adverse events and may not prevent visual loss in a substantial proportion of patients who have severe disease. The development of biologic agents has heralded a new era in the management of Behçet's uveitis. Both interferon-alpha and anti-TNF agents are superior to immunosuppressive drugs regarding their anti-inflammatory potential and long-term disease control. Recent studies have shown that the visual outcomes have improved with the use of these biologic agents. Based on available evidence, anti-TNF agents have been recommended as first-line steroid-sparing therapy in Behçet's uveitis. On the other hand, interferon-alpha therapy can induce durable remissions of uveitis and may be recommended as first-line of biologic therapy especially in countries where tuberculosis is endemic.

4. How to best manage birdshot retinochoroiditis (Carlos Pavesio MD FRCOphth, Moorfields Eye Hospital, London, UK)
Probably the most important development related to the management of Birdshot Retinochoroiditis (BRC) was the recognition that visual acuity was not the best measure to indicate need to initiate therapy. Significant loss of visual function could have developed by the time central vision dropped to levels for which treatment would be considered necessary. The use of visual fields and electrophysiology tests for monitoring disease activity has added a new dimension to the management of these patients. Another important point was the recognition that use of systemic steroids monotherapy was not the best approach to treat this condition and early introduction of immunosuppressive therapy allowed better control and reduced side effects of exposure to higher levels of steroids. More recently attempt to achieve control of the disease by local therapy has gained strength with the use of slow-release steroid devices, which allow for high intraocular levels of therapy with no systemic side effects. A general discussion of the current status and future directions in the management of BRC will be presented.

5. Infectious anterior uveitis (Nikos N. Markomichelakis, Athens, Greece)
Infectious anterior uveitides represent approximately 20 percent of the total anterior uveitis cases. Although many different pathogens may induce anterior uveitis, viruses are by far the most common cause. Herpes Simplex, Varicella Zoster, and Rubella virus are considered the most common cause of infectious anterior uveitis in the Western countries. Cytomegalovirus has recently been implicated as a frequent cause in Asia, but not only. Infectious diseases, known previously only in some regions of the world and especially in the Southeast Mediterranean, Sub-Saharan Africa or Far East, today tend to become a global threat. Also anterior uveitis may develop as part of systemic bacterial infections such as tuberculosis, syphilis leprosy, Lyme disease, relapsing fever, leptospirosis, brucellosis and cat scratch disease.In this presentation will deal with the etiology, clinical presentation, diagnostic approach and treatment of infectious anterior uveitis.

6. Choriocapillaritis same mechanism, different consequences. (Marina Papadia, Genova, Italy)

Choriocapillaritis are usually classified among the “white dot syndromes”, which is not telling us anything about the mechanism. When there is inflammation within the choriocapillaris the outer retina is suffering. Different degrees of choriocapillaris involvement determine different entities from the benign side (MEWDS) to the more severe involvement (APMPPE, Multifocal Choroiditis & Serpiginous choroiditis). In order to monitor disease evolution, evaluate the need for treatment and judge the response to treatment, among several imaging procedures, indocyanine green angiography (ICGA) is the most appropriate investigational modality. Illustrative clinical examples will be presented, showing how ICGA gives us precise information, crucial in the management of such cases.

7. A masquerade not to miss. (Moncef Khairallah, MD, Rim Kahloun, MD, Imen Ksiaa, MD Dpt of Ophthalmology, Fattouma Bourguiba University Hospital, Faculty of Medicine, University of Monastir, Monastir, Tunisia)
Failure to differentiate central serous chorioretinopathy (CSC) from inflammatory chorioretinal disease usually leads to inappropriate use of corticosteroids. Corticosteroid therapy is not only ineffective, but it usually exacerbates the condition, leading to bilateral, severe, and chronic CSC with multifocal retinal pigment epithelial detachments or diffuse retinal pigment epitheliopathy. Unusual findings can occur including acute bullous retinal detachment, subretinal fibrin, subretinal fibrosis, hard exudates, and even neovascularization. A careful analysis of clinical findings and appropriate use of multimodal imaging are mandatory to differentiate CSC from any chorioretinal inflammatory condition to prevent severe and irreversible visual damage resulting from misdiagnosis and management mistakes.

8. How semantics can sometimes be confounding in uveitis: a practical approach
(Piergiorgio Neri, MD, PhD, FEBOphth, Director of Ocular Immunology Service,The Eye Clinic, Università Politecnica delle Marche, Ancona, Italy)
Posterior uveitis is one of the leading causes of visual impairment in ophthalmology. Although classification of uveitis plays a pivotal role in the diagnostic process, in the past years there have been an excessive compartmentalization, particularly among multifocal choroiditis. The hypertrophic number of denominations of such diseases can lead to confusion, which is not useful both for the diagnostic and the therapeutic process. The recent approach to such diseases is based on a more rational classification, based on the topographic involvement of the choroidal tissue.
Furthermore, despite differences in clinical course and outcome, different clinical patterns of multifocal choroiditis may represent manifestations of the same disease, given their similar genetic associations with IL-10 and TNF-α loci, which are known to be associated with non-infectious uveitis and several autoimmune diseases. However, the data also support the notion that epigenetic factors have a strong effect on clinical phenotype. Although we are still far from a precise knowledge of multifocal choroiditis pathophysiology, these evidences can demonstrate that the classification system of multifocal choroiditis should be profoundly revised: the simplification of multifocal choroiditis classification can allow a more practical and targeted approach of disease management. Two cases will be presented, illustrating the condition of idiopathic multifocal choroiditis, a vision threatening disease.

9. Challenging cases. The two great imitators: Lyme and Syphilis. (Pia Allegri, MD, Rapallo Hospital Uveitis Referral Center, Genova, Italy)
Two main Spirochaetal (bacterial infectious) disorders, Lyme disease and Syphilis, can affect many organs of the human body, including the eye. At ocular level they present with proteiform aspects which can mimic many other diseases; that’s the reason why they are called “imitators”. Our presentation will show two cases, recently visited at our tertiary referral center, who were both incorrectly treated with steroids because of an acute unilateral papillitis but were discovered to be affected, the first by the tick-bite disease (Lyme disease) which is endemic in our region (Liguria) in the North-Western part of Italy and the other patient, by a secondary stage form of luetic ocular involvement misdiagnosed by the dermatologist who saw the palmo-plantar eruption without making the correct diagnosis.
We show our diagnostic and therapeutic procedure which permitted to our patients to successfully recover from the general and ocular disease.