June 29 (Saturday) 8:30-12:00 Room 1 (Auditorium)

5th International Workshop on Ocular Behçet's Disease

Chairs / Moderators: Shigeaki Ohno *(Japan)*
Moncef Khairallah *(Tunisia)*
Massimo Accorinti *(Italy)*

8:30-8:45 **Global perspective /EULAR recommended treatment of Behçet's Disease and ocular Behçet's Disease**
Toshikatsu Kaburaki *(Japan)*

8:45-9:00 **Treatment of ocular Behçet's disease and its duration in Japan**
Nobuyoshi Kitaichi *(Japan)*

9:00-9:15 **Treatment of ocular BD and its duration in Korea**
Hyeong Gon Yu *(South Korea)*

9:15-9:30 **Treatment of Ocular Behçet's Disease and its Duration in Iran**
Masoud Soheilian *(Iran)*

9:30-9:45 **Treatment of ocular BD and its duration in Turkey**
Ilknur Tugal-Tutkun *(Turkey)*

9:45-10:00 **Treatment of ocular Behçet disease and its duration in North Africa and Middle East**
Moncef Khairallah *(Tunisia)*

10:00-10:15 **Treatment of ocular BD and its duration in Germany**
Manfred Zierhut *(Germany)*

10:15-10:30 **Treatment of ocular BD and its duration in Italy**
Massimo Accorinti *(Italy)*

10:30-12:00 **Panel Discussion**

Panelists: Nobuhisa Mizuki *(Japan)*
Hyeong-Gon Yu *(South Korea)*
Yih Shiou Hwang *(Taiwan)*
Thanapong Somkijrungroj *(Thailand)*
Masoud Soheilian *(Iran)*
Ilknur Tugal-Tutkun *(Turkey)*
Hassan Al-Dhibi *(Saudi Arabia)*
Manfred Zierhurt *(Germany)*

It is our great pleasure to meet all of you to discuss ocular lesions in Behçet's disease. This meeting is the 5th International Workshop on Ocular Behçet's Disease.

In the GOIWs 2019, treatment of intraocular inflammation is the main topic. In our Ocular Behçet's Disease workshop, we would also like to discuss the recent treatment of Behçet's disease. Nowadays in the developed countries, biologic therapy with infliximab, interferon, or adalimumab has widely been used. They seem to be more effective than the conventional immunomodulating drugs. However, biologic therapy is not perfect and there are several adverse events. The other problem is that anti-TNF drugs are quite expensive, and it is sometimes difficult to use them in the developing countries.

In this workshop, we have excellent 8 speakers and 9 panelists from various parts of the world such as Asia, Middle East, Europe, and North America, who have much experience with the management of Behçet's patients with ocular lesions.

We sincerely hope that all of you will actively join this workshop on Behçet's disease, and have meaningful discussion.

Global perspective /EULAR recommended treatment of Behçet's Disease and ocular Behçet's Disease

Toshikatsu Kaburaki

Faculty of Medicine and Graduate School of Medicine, University of Tokyo, Tokyo, Japan

Behçet's syndrome (BS) is a chronic systemic inflammatory disorder characterized by recurrent oral aphthae, genital ulcers, ocular disorders, and skin lesions. The aim of treatment in BS is to prevent irreversible damage that mostly occurs early in the course of disease, especially in the high-risk group, young men. In 2008, the recommendations for management of BS was published by European League Against Rheumatism (EULAR), that consisted of 9 recommendation statements. Recently, in 2018, the recommendation was revised that would be reflected the new data of recent treatment modalities. As for ocular disease, the recent recommendation noted that (1) Patients with BS and inflammatory eye disease affecting the posterior segment should be on a treatment regime such as azathioprine, cyclosporine-A (CYA), interferon-alpha or monoclonal anti-TNF antibodies. Systemic glucocorticoids should be used only in combination with azathioprine or other systemic immunosuppressives (2) randomized clinical trials have shown the efficacy of azathioprine and CYA in preserving visual acuity and preventing relapses in patients with uveitis. (3) Interferon-alpha and monoclonal anti-TNF antibodies were treatment choice for the patients with refractory uveitis against azathioprine and CYA. (4) Patients presenting with an initial or recurrent episode of acute sight-threatening uveitis should be treated with high-dose glucocorticoids, infliximab or interferon-alpha. Intravitreal glucocorticoid injection is an option in patients with unilateral exacerbation as an adjunct to systemic treatment.

Treatment of ocular Behçet's disease and its duration in Japan

Nobuyoshi Kitaichi[1,2]

[1]Institute of Preventive Medical Science, Health Sciences University of Hokkaido, Sapporo, Japan, [2]Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Japan

Behçet's disease is a chronic systemic disease with poor visual prognosis. The disease is distributed between Japan and Mediterranean countries along the historic Silk Road.
First line systemic drugs vary according to gender, age, clinical features, and countries. Conventional treatments of Behçet's disease with systemic corticosteroids or immunosuppressive drugs such as colchicine, azathioprine, methotrexate, are not effective enough to suppress the recurrent ocular attacks. Cyclosporine shows a passable efficacy, however, neurological symptoms were reported.
Japanese national insurance system delivered the approval to use Infliximab, a biological monoclonal antibody against tumor necrosis factor alpha on Behçet's disease in 2007. It was the world's first approval. Also, national "Practice guideline for uveitis" is now in press.
Treatment of ocular Behçet's disease will be presented according to the recent accumulation of the clinical experience.

Treatment of ocular BD and its duration in Korea

Hyeong Gon Yu[1,2]

[1]Department of Ophthalmology, Seoul National University Hospital, Seoul, South Korea, [2]Seoul National University College of Medicine, Seoul, South Korea

Biologics are increasingly used to treat uveitis that is unresponsive to steroid or more conventional forms of immunosuppression. Humira, as the first and the only approved biologics in Korea as a second line treatment for endogenous uveitis, is being used more and more in Korea Behçet patients. Behçet disease is a good indication of the effective but costly biologics because the cost is supported by Korean government as one of the designated orphan diseases.
In this talk, the early experience of biologics in Korean Behçet patients will be discussed.

Treatment of Ocular Behçet's Disease and its Duration in Iran

Masoud Soheilian[1,2,3]

[1]Department of Ophthalmology, Shahid Beheshti University of Medical Sciences, Tehran, Iran, [2]Labbafinejad Medical Center, Tehran, Iran, [3]Negah Eye Hospital, Tehran, Iran

Adamantiades-Behçet's disease (ABD) is more common and often more severe along the countries bordering the Silk Road, and Iran is known to have the second highest prevalence of ABD in the world (68/100,000). Ocular manifestations occur in 25-75 percent of ABD patients, and often progresses to blindness if left untreated. Adalimumab (ADA) is the only biologic agent to receive EMA and FDA approval for the treatment of noninfectious uveitis and a number of observational studies have shown its efficacy in the treatment of ABD-associated ocular symptoms. CinnoRA is the biosimilar product of ADA, manufactured by CinnaGen pharmaceuticals. CinnaGen is one of the top biotech companies in the MENA region and is certified with the EU-GMP certification by the EMA. We here report the successful experience with CinnoRA in patients with active uveitis. 181 ABD patients received CinnoRA between Oct. 2016 and Feb. 2019, of which 93 were presenting ocular disease. There were 31 female and 62 male patients [mean (SD) age, 38.3 (13.7) years]. The mean duration of treatment with CinnoRA was 43 weeks (median 248 days; range 6-870), and the mean duration of disease prior to CinnoRA was 4.3 years (median 900 days; range 30-9060). Intraocular inflammation reduced and visual acuity improved in a significant number of patients. Furthermore, CinnoRA allowed a remarkable reduction in daily corticosteroid use among patients. Within the reporting period, most adverse reactions were mild, no new safety signals were found, and the safety profile was consistent with the known information about ADA.

Treatment of ocular BD and its duration in Turkey

Ilknur Tugal-Tutkun
Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey

Purpose: To analyze therapeutic regimens and treatment duration in Turkish patients with ocular Behçet disease who achieved angiographic remission.
Methods: We reviewed the medical records of 118 patients who underwent wide-field fluorescein angiography between March 2016 and January 2019 and were found to be in angiographic remission.
Results: There were 95 males and 23 females with a mean age of 29±8 years at presentation. 34 patients presented in less than a month after the onset of ocular symptoms; and in 84 patients, the median disease duration was 12 months (1 month-10 years). Remission was achieved after conventional therapy in 38 patients (32.2%), interferon alpha in 56 patients (47.5%), infliximab in 16 patients (13.6%), adalimumab in 6 patients (5.1%), and tocilizumab or canakinumab in 1 patient, each. 69 patients (58.5%) received 2-5 lines of therapy. The median duration of therapy was 50 months (range, 5-243 months). 31 patients were off treatment at the time of last visit, and 18 of them had sustained remission for 1-10 years, after IFN-induced remission in 12 and conventional therapy in 6. During follow-up, 7 patients (10 eyes) lost visual acuity by 2 lines or more; 4 of them were noncompliant patients.
Conclusion: Conventional treatment had been employed as first line due to the local regulations in Turkey. Administration of interferon alpha or biologic agents has been required to achieve angiographic remission in 68% of the cases.

Treatment of ocular Behçet disease and its duration in North Africa and Middle East

Moncef Khairallah
Fattouma Bourguiba University Hospital, Faculty of Medicine, University of Monastir, Monastir, Tunisia

Behçet disease (BD) in prevalent in North Africa and the Middle East (NAME). Behçet uveitis (BU) is a chronic recurrent disease with explosive attacks of severe inflammation that may cause significant damage to the eye. Diagnosis of BD in our region is usually made based on the association of ocular features and extraocular manifestations according to the ISG for BD criteria or the new International criteria. However, diagnosis of BD may be challenging in incomplete forms and isolated ocular disease, which may occur in up to one fifth of our Behçet cases. Imaging modalities that are most contributive to diagnosis are fluorescein angiography and OCT. Treatment of BU in the NAME region primarily relies on systemic corticosteroids and conventional immunosuppressive agents. Azathioprine and cyclosporine A are the most commonly used immunosuppressants. There is a wide variation between NAME countries regarding the use of biologics as first line or as second line therapy, due to disparities between these countries in drug availability and insurance regulation. Immunosuppressive therapy with or without associated biologics are maintained for at least two years. Steroids and conventional immunosuppressives are usually prescribed by ophthalmologists, whereas biologics are often administered by internists. Monitoring of treatment side effects usually requires a close collaboration between ophthalmologist and internist. Response to treatment is often assessed by clinical examination, OCT, and sometimes fluorescein angiography.

Treatment of ocular BD and its duration in Germany

Manfred Zierhut
University Eye Clinic, Tuebingen, Germany

While the incidence of Behçet's Disease (BD) seems to drop in Germany, the treatment becomes less complicated and more effective.
Following the updated EULAR criteria we use alpha-interferon in nearly all situations of posterior or panuveitis. As published before the response rate is more than 90%. The dosage we use starts with 3-6 Mio IU per day (depending on the body weight), reducing it every 4 weeks for 1 more day. Typically patients need treatment for app. 9-12 months. With this treatment we achieve a very high permanent response, with 25% staying without further recurrence during the next 109 months, (75% without recurrence after 19 months) after 1 course of alpha interferon. Typical drug induced effects (fever, arthralgia) are wellcome, because they demonstrate the effectiveness of the drug, and the non-existence of anti-interferon antibodies. Such effects are limited to a few days and can mostly covered by additional drugs, very rarely leading to discontinuation. Due to the extremely rapid effect of this drug we do not need any prophylactic treatment anymore.

Treatment of ocular BD and its duration in Italy

Massimo Accorinti[1] for the Italian Study Group for Behçet's Disease[2]
[1]*Sapienza University of Rome, Department of Ophthalmology, Rome, Italy*
[2]*Italian Study Group for Behçet's Disease (participants in alphabetic order): P. Allegri (Rapallo), L. Berchicci (Milan), A. Cerquaglia (Perugia), L. Cimino (Reggio Emilia), P. Fontana (Bergamo), M. Gilardi (Roma), B. Iaccheri (Perugia), L. Iannetti (Roma), L. Latanza (Napoli), F. Machetta (Torino), E. Miserocchi (Milano), G.M. Modorati (Milano), P. Mora (Parma), M. Nebbioso (Roma), G. Spinucci (Fermo), I. Testi (Padova), M.S. Tognon (Padova), P. Torino-Rodriguez (Pescara), L. Vannozzi (Firenze)*

Purpose: to study the diagnostic and treatment strategies for Ocular Behçet's Disease (OBD) in Italy and to assess differences due to regional/hospital rules.
Methods: a questionnaire was sent to Italian Society for Uveitis and Ocular Inflammatory Diseases members.
Results: 17 complete questionnaires returned and were considered. The 2010 revised criteria for BD is used in 76.5% of the sites. Fluorescein angiography and OCT are always used at onset in 82.3% and 88% of the centres, respectively, and during follow-up in 41.2% and 58.8%. A team of specialists are responsible for OBD therapy in 70.6% of the cases while ophthalmologist alone are in charge of corticosteroid (47% of the cases), conventional immunosuppressive (47%), and biologic (17.6%) therapies. In OBD patients without systemic manifestations, there is no consensus on the use of an immunosuppressive drug in relation to: - anatomic location of uveitis and - presence of retinal vasculitis. Isolated anterior uveitis is treated with topical, periocular and systemic corticosteroids by 88.2% of the responders. Different approaches are used to treat the first episode of bilateral intermediate, posterior or panuveitis, the most frequent being systemic corticosteroids + conventional immunosuppressive drugs (23.5%) or biologics (23.5%), and systemic corticosteroids alone (17.6%). Among biologics, adalimumab is the first choice drug and 64.7% of the centres are allowed to give it since the onset of OBD.
Conclusion: in Italy the subdivision of the Health National System on a regional basis might influence the way of treating OBD.