RECENT TRENDS IN TREATMENT OF EYE MANIFESTATIONS OF BEHÇET'S DISEASE

Essay
Submitted by

Radwa Taher Hassan El-Zanaty, (M.B.B.Ch.)

In Partial Fulfillment Of The Master Degree(MSc) in Ophthalmology

Under Supervision
Of

Prof. Dr. FADIA MAHMOUD SAMY ELGUINDY

Professor of Ophthalmology
Faculty of Medicine
Cairo University

Prof. Dr. EMAD ABD-EL-AAL SAWABY

Professor of Ophthalmology
Faculty of Medicine
Cairo University

Lect. Dr. AHMED ABD-ELAZIM ABD-ELKADER

Lecturer of Ophthalmology
Faculty of Medicine
Cairo University

Cairo University
Faculty of Medicine
2009

Abstract:

Behçet's disease is probably one of the most challenging conditions to treat. Reasons are the still unclear aetiology of this syndrome as well as multiple manifestations possibly affecting all organ systems, moreover complicated by varying appearances of the disease in different ethnic groups. A good therapy for Behçet's disease should be highly effective for preferably manifestations, should work rapidly, should be low in side effects and at the same time be as cheap as possible. At present these contradictory requirements are not compatible. This may be a reason for the fact that standardized treatment regimens for Behçet's disease are still missing. Due to its poor prognosis, eye involvement is one of the most worrying manifestations for patients with Behçet's disease.Without treatment, vision is usually lost on average 3.4 years after the onset of eye symptoms ***(Mamo JG, 1970).*** Thus it is often necessary to treat the condition earlier and more aggressively than other forms of uveitis.

Keywords:

Behçet- Uveitis- IFN-α2a- Ulcer- Steroids- Infliximab- HLA-B51- Syndrome

Acknowledgments

All praise goes to **ALLAH**, the most merciful and mightiest, for all his great blessings.

First I would like to dedicate this work to my **parents** and **husband**, without them none of this would have been possible.

I am deeply grateful to **Professor Dr Fadia Mahmoud Samy El-Guindy** for her constant support and sincere advice. Her wisdom and her keenness for high standards of performance have always guided me.

I would like to express my deep appreciation to **Professor Dr Emad Abd-El Aal Sawaby** for his overwhelming kindness, fatherly support, his guidance and endless cooperation throughout this work.

A very sincere thank you to **Dr Ahmed Abd El-Azim Abd El-Kader**, learning from him and working with him have always been a great pleasure.

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Aim of the Work

This review of literature aims to give an overview of the treatment of Behçet's Disease, with emphasis on the recent emerging treatment modalities, their advantages and common side effects.

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List of Abbreviations

AECA: Anti-Endothelial Cell Antibodies

ANA: Anti-Nuclear Antibodies

ASO: Anti-Streptolysin O

AZA: Azathioprine

BD: Behçet Disease

BS: Behçet Syndrome

CAIs: Carbonic Anhydrase Inhibitors

CCP: Cyclophosphamide

CME: Cystoid Macular Edema

CML: Chronic Myeloid leukemia

CNS: Central Nervous System

CSA: Cyclosporin A

eNOS: endothelial Nitric Oxide Synthase

FA: Fluorescin Angiography

GDD: Glaucoma Drainage Device

HDIST: High Dose Intravenous Steroid Therapy

HLA: Human Leucocytic Antigen

Hsp: Heat shock proteins

ICAM: Intercellular Adhesion Molecule

IFN: Interferon

IgM: Immunoglobulin M

IgG: Immunoglobulin G

IOP: Intra Ocular pressure

IL: Interleukin

IVTA: IntraVitreal Triamcinolone

LPO: Lipid PerOxidation

mfERG: Multifocal ElectroRetinoGram

MHC: Major Histocomptability Complex

MICA: Major Histocomptability Complex Class I Chain-related gene A

MIF: Migration Inhibitory Factor

MRI: Magnetic Reasonance Imaging

MS: Multiple Sclerosis

MTX: Methotrexate

Nd;YAG: Neodymium-Yettrium Aluminium Garnet

NKcell: Natural Killer Cells

NSAID: Non-Steroidal Anti-Inflammatory Drug

PMNLs: Polymorph Nuclear Leucocytes

PMMA: Polymethyl methacrylate

PPV: Pars Plana Vitrectomy

Retinal S-Ag: Retinal S antigen

TA: Triamcinolone Acetonide

TGF: Tumour Growth factor

Th cytokines: T-helper cytokines

TNF: Tumour Necrosis Factor

VA: Visual Acuity

VCAM: Vascular Cell Adhesion Molecule

VEGF: Vascular Endothelial Growth Factor

INTRODUCTION

Introduction

I.Definition

Behçet's disease (BD) is a recurrent systemic disorder, characterized by an immune-mediated occlusive vasculitis. Four major symptoms characterize BD: oral aphthous ulcers, ocular lesions, skin lesions and genital ulcerations. Inflammation of other locations may also be found in these "complete Behçet's patients".

II.History

The first description of the symptoms of BD was in the fifth century BC by Hippocrates in his third book of epidemiology ***(Zafirakis P and Foster CS, 2002)***. Since that time and especially during the nineteenth century, isolated symptoms of BD have been reported ***(Dilsen N, 1996)***. In 1937, Hulusi Behçet, a Turkish dermatologist, described three patients with findings of oral and genital ulcers and recurrent iritis ***(Zafirakis P and Foster CS, 2002)***. The disease is therefore commonly known by his name, despite the fact that in 1930 the Greek ophthalmologist Benedictos Adamantiades presented at the Medical Society of Athens the case of a 20 year old man who was suffering from recurrent iritis with hypopyon resulting in blindness, associated with phlebitis, mouth ulcers, genital ulcers, and knee arthritis. One year later he published this case in the *Annales d Óculistique* ***(Adamantiades B, 1931)***. The name "Behçet's disease" therefore led to a long discussion between Turkish and Greek scientists. One explanation for the use of "Behçet's disease" might be the wider distribution of the paper by H.Behçet in the medical literature ***(Zafirakis P and Foster CS, 2002)***. However, the combination of "Adamantiades- Behçet's disease" is also acceptable.

Almost any organ system in BD can be affected. The diagnosis of BD is based on the criteria of the International Study Group from 1990 (Table 1.1) ***(International Study Group for Behcet's Disease, 1990)***. As these were developed as a classification and not as diagnostic criteria and especially early stages of the disease often do not allow diagnosis ***(Lee S, 1997)***, older sets of criteria, most commonly those by O'Duffy and Dilsen ***(Dilsen N et al., 1985)***, and in Asia those of the Japanese ***(Mizuki N et al., 1997)*** are still in use.

Although there are some recent improvements regarding the management especially of ocular BD, by new biological agents ***(Saenz A et al., 2004).*** However, a debate exists regarding the terminology of this unique disorder. Is BD or Behçet syndrome (BS) preferable? Although these two terms are the subject of disagreement, they are used synonymously and are generally thought to be readily exchangeable.

Table 1.1: Criteria of the International Study Group 1990

(International Study Group for Behcet's Disease, 1990)

Recurrent oral aphthous ulcers	Small or large aphthous or herpetiform ulcerations recurring at least 3 times in a 12month period.
❖ ***Plus 2 of the following:*** 1.Recurrent genital ulcerations	Aphthous ulcerations or scarring
2.Eye lesions	Anterior uveitis, posterior uveitis or cells in vitreous on slit lamp examination or retinal vasculitis observed by an ophthalmologist
3.Skin lesions	Erythema nodosum, pseudofolliculitis or papulopustulous lesions or acneiform papules in post-adolescent patients without steroid treatment.
4.Positive pathergy testing	Intracutaneous needle stick with 21G on forearm(inside), read by a physician after 24-48 h

III. Epidemiology

This ubiquitous disorder exhibits a distinct geographic variation and is endemically higher particularly in Turkey, Iraq, Iran, Korea and Japan, the population derived historically from the ancient Silk Road that was used for centuries as a trade-making passage from the East to the West ***(Önder M and Gūrer MA, 2000).*** Behçet disease accounts for up to 20% of cases of endogenous uveitis in some of these countries, particularly in Japan and Turkey (when compared with only 0.2% in the USA) and the highest prevalence is reported in Turkey where family occurrence has been note ***(Nishiyama M et al., 2001)***.This is most probably due to the association of environmental factors together with the histocompatibility antigen.

Also Behçet disease occurs more frequently in Europeans who live between the latitudes of 30º and 45º compared to those in Northern Europe, and Behçet uveitis represents about one-third of all uveitides in Saudi Arabia ***(Kurumety U et al., 1999)***. By contrast, the disease is far less common in the USA, the United Kingdom, and among Black Africans, and it is almost absent in American Indians ***(Direskeneli H, 2001)***.