THE RECENT TRENDS IN MANAGEMENT OF REFRACTORY UVEITIS

Essay submitted for partial fulfillment of the Master Degree in Ophthalmology

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List of Abbreviation

ACE	Angiotensin-Converting Enzyme
AIDS	Acquired Immune Deficiency Syndrome.
AMPPPE	Acute Multifocal Posterior Placoid Pigment Epitheliopathy.
ANA	Antinuclear Antibody
ANCA	Antineutrophil Cytoplasmic Antibody.
APC	antigen-presenting cells
ASOT	Antistreptolysin-O Titre.
BD	Behçet Disease.
CD	Cluster of Differentiation
CMV	Cytomegalovirus.
CNV	Choroidal Neovascularization.
DC	dendritic cells
DME	Diabetic Mcular Edema.
DSF	Diffuse Subretinal Fibrosis
FFA	Fundus Fluorescein Angiography.
Fig	Figure.
ECCE	Extracapsular Cataract Extraction .
ESR	Erythrocyte Sedimentation Rate.
HTLV-1	The Human T-lymphotropic virus Type I
IBD	Inflammatory Bowel Disease.
ICG-A	Indocyanine Green Angiography.
IE	Infective Endocarditis.
IFN-a	Interferon Alpha.
Ig	Immunoglobulin.
IL	Interleukein
IMT	Immunomodulatory Therapy.
IOL	Intraocular Lens.
IOP	Intraocular Pressure
IVTA	Intravitreal Triamcinolone Acetonide.
IU	Intermediate Uveitis.
JRA	Juvenile Rheumatoid Arthritis.

JIA	Juvenile Idiopathic Arthritis.
KPs	Keratic Precipitates.
MCP	Multifocal Choroiditis with Panuveitis
MHC	Major histocompatability complex
NSAID	Nonsteroidal Anti-Inflammatory Drugs.
OCT	Optical Coherence Tomography.
PCR	Polymerase Chain Reaction.
PIC	Punctate Inner Choroidopathy
PLP	Peripheral Lser Photocoagulation.
POHS	Presumed Ocular Histoplasmosis Syndrome.
PPV	Pars Plana Vitrectomy.
PSCC	Posterior Subcapsular Cataract.
PSII	Posterior segment intraocular inflammation.
PVR	Proliferative Vitreoretinopathy.
RD	Retinal Detachment.
RF	Rheumatoid Factor.
RPE	Retinal Pigmented Epithelium.
SLE	Systemic Lupus Erythematosis.
SO	Sympathetic Ophthalmia.
SPCA	Short Posterior Ciliary Arteries.
STOI	Sight threatening ocular inflammation.
TB	Tuberculosis.
TCR	T-cell receptor
TLR	Toll-like receptor
TINU	Tubulointerstitial nephritis and uveitis
TNF	tumor necrosis factor
VKH	Vogt-Koyanagi-Harada Syndrome
5-FU	5-Fluorouracil

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INTRODUCTION

Uveitis is defined as inflammation of the uveal tract, the vascular coat of the eye which is composed of the iris, ciliary body and choroid. Inflammation of these structures is frequently accompanied by involvement of the surrounding ocular tissues, including the cornea, sclera, vitreous,retina and optic nerve **(foster & vitale 2002).**

So the term uveitis is used clinically to describe a heterogeneous group of diseases characterised by inflammation of intraocular structures**(suhler et al,2005)**

Refractory uveitis refers to uveitis which may be progressive and diblitating despite aggressive treatment with conventional therapy **(Bodaghi et al,2003)**

Uveitis as an inflammatory eye disease is a leading cause of blindness especially in the working age population **(Choudary et al, 2006) & (Fraser R et al, 2007)**

The incidence of blindness in uveitis can be as high as 35% with bilateral loss in 10% **(Choudary et al.,2006)**

Management of refractory uveitis remains a significant clinical challenge.The course is persistant,with periods of improvement and flare,leaving a significant ocular morbidity **(C-Elga Rabinovich et al.,2007)**

Systemic corticosteroids are typically used in acute stage of when local steroid theraby doesn't control the inflammation.

The long term use of systemic steroids is problematic because of its adverese side effects **(VA Shanmuganathan et al.,2005)**

This has led to the formulation of a therapeutic philosophy that calls for complete elimination of active inflammation ,limited tolerance for the use of corticosteroids and the early implantation of immunomodulatory therapy (IMT),as either a steroid replacing therapy or first line treatment,when indicated,in an effort to minimize secondary side effects and to preserve visual function **(vitale et al.,2006)**

A step ladder algorithm that is steroid sparing and is titrated to the clinical picture in its aggressiveness may be used by an ophthalmologist who is experienced in the use of immunomodulatory therapy and the management of the potentially serious toxicities that may arise from using this step ladder algorithm.It is used in the following order:

1-Initial treatment with corticosteroids.

2-Systemic non-steroidal anti-inflammatory medications for selected indications.

3-Systemic immunomodulatory therapy(IMT)as:

a-Anti-metabolities e.g.:methotrexate and azathioprine.

b-T-cell signal transduction inhibitors as cyclosporine.

c-Alkylating agents e.g.:chlorambucil

d-Intravenous immunoglobulins.

e-Biologic agents:Interferonalpha, Infliximab, Etanercept, Daclizumab and Anakinra.

4-Peripheral retinopexy or lazer photocoagulation in certain patients with intermediate Uveitis and parsplanitis.

5-Surgical treatment of uveitis and therapeutic parsplana vitrectomy.

6-Surgical treatment of complications of uveitis **(vitale et al.,2006)**

Contents:

-Uveal tract anatomy and physiology.

-Eoidimiology and pathology of refractory uveitis

-Classification and diagnosis of uveitis

-Treatment of refractory uveitis

-Work up for specific disease enteties

AIM OF THE WORK:

This essay aims to review the litratures concerned with the recent trends in management of refractory uveitis.

ANATOMY OF THE UVEAL TRACT

INTRODUCTION

The uvea (from the Latin *uva,* meaning grape) is a pigmented structure that primarily lies between the retina and the sclera and constitutes the vascular portion of the eye. Its blood supply comes from the ophthalmic artery, which nourishes most of the eye through branches of the anterior and posterior ciliary arteries. A separate branch of the ophthalmic artery, the central retinal artery, supplies the inner retinal layers and part of the optic nerve. The uvea also has secretory and mechanical functions including production of aqueous humor, improvement of aqueous outflow, and control of near accommodation. The uvea may become involved in disease processes through inflammation, known as uveitis, neoplasia (e.g., melanoma), and growth of abnormal vessels, known as choroidal neovascularization. **(Yanoff,2004)**

IRIS

The anterior portion of the uvea is called the iris . It is composed primarily of vascular stroma as well as melanocytes, nerves, clump cells, collagen, and hyaluronidase-sensitive acid mucopolysaccharides.The vascular supply to the iris originates in the anterior and long posterior ciliary branches of the ophthalmic artery. These branches join in the ciliary body to form the major arterial circle before entering radially into the iris. The vessels lack an internal elastic lamina and are lined by nonfenestrated endothelial cells.(FINE BS, YANOFF M,1972)

The anterior surface of the iris is composed of a fibroblast cell layer folded into many ridges and crypts, with a pupillary aperture located slightly inferonasal to the center.**(Hogan MJ, Alvarado JA,1971).** Eye color is determined by the number and degree of melanin granules in the stromal melanocytes **(Apple DJ, Rabb MF,1992)**

Muscular and pigment epithelial structures are located in the posterior portion of the iris. Smooth muscle is tightly arranged in a circle to form the pupillary sphincter and is primarily innervated by parasympathetic nerves coming from the third cranial nerve nucleus. The radially oriented dilator muscles extend from their cell bodies in the anterior pigment