ENDOGENOUS UVEITIS ETIOPATHOGENY

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Abstract: *Uveitis represents the inflammation of the structures that make up the uveal tract: the iris, the ciliary body and the choroid, or of the adjacent ocular structures (the retina, the optic nerve, the vitreous, the sclera). The etiology is attributed, in most cases, to the autoimmune mechanisms. In terms of the location of the pathological processes, uvea can be divided into two portions: the anterior portion, irrigated by the ciliary arteries and the long posterior ciliary arteries; the posterior portion, irrigated by the posterior short ciliary arteries. The vascular arrangement explains the limitation of some inflammatory processes to one of the two territories. The existence of two vascular territories, one anterior (iridociliary) and one posterior (choroidal) explains the possibility of limited inflammation occurrence, either in the first territory or in the posterior one. Still, there are cases when both territories can be covered by an inflammation, either simultaneously or successively.*

Cuvinte cheie: *uveită, inflamaţie*

Rezumat: *Uveita reprezintă inflamaţia structurilor care alcătuiesc tractul uveal: irisul, corpul ciliar şi coroida, sau a structurilor oculare adiacente (retina, nervul optic, corpul vitros, sclera). Etiologia este atribuită în cele mai multe cazuri mecanismelor autoimune. Din punct de vedere al localizării proceselor patologice, putem împărţi uveea în două porţiuni: porţiunea anterioară, irigată de arterele ciliare anterioare şi arterele ciliare lungi posterioare; porţiunea posterioară, irigată de arterele ciliare scurte posterioare. Dispoziţia vasculară explică limitarea unor procese inflamatorii la unul din cele două teritorii. Existenţa a două teritorii vasculare, unul anterior (iridociliar) şi altul posterior (coroidian) explică posibilitatea apariţiei de inflamaţii limitate, fie la primul teritoriu, fie la cel posterior. Se întâlnesc totuşi cazuri când ambele teritorii pot fi cuprinse de o inflamaţie, fie simultan, fie succesiv.*

INTRODUCTION

The classification of uveitis is the result of various research centres, aiming at standardizing some aspects of uveitis, establishing certain criteria for diagnosis and treatment, evolution and prognosis.

1. The classification according to the International Uveitis Study Group (IUSG-1987) is based on the anatomical location of the inflammation and it is the most used one (table no. 1):

Table no. 1. Classification of uveitis according to IUSG

Anterior uveitis	Intermediate uveitis	Posterior uveitis
Inflammation of the iris and / or pars plicata anterior ciliary bodies	Pars plana (posterior ciliary body and / or pars plana)	Choroid and retina
Iritis	Pars planitis	Diffuse multifocal choroiditis
Anterior cyclitis	Posterior cyclitis	Chorioretinitis
Iridocyclitis	Basal retinochoroiditis	Neuroretinitis
Panuveitis is the inflammation of the anterior chamber, of the vitreous, retina and choroid.		

2. Anatomical, etiological classification (O'Shea amended):

Granulomatous, idiopathic; associated with HLA-B27; juvenile idiopathic arthritis; glomerulonephritis; ankylosing spondylitis; psoriatic arthritis; herpes simplex; LES; leukemia; Reiter's syndrome; anterior uveitis induced by drugs; Posner-Schlossman syndrome; Lyne's disease; inflammatory bowel disease.

Nongranulomatous (UANG): sarcoidosis; syphilis; TB; Behcet's disease; ankylosing spondylitis; multiple sclerosis; Herpes simplex; systemic viral infections; fungal infections; Fuchs heterochromic iridocyclitis; persistent postoperative uveitis; traumatic uveitis; inflammatory bowel disease; Reiter's syndrome; psoriatic arthritis.

3. Classification according to the International Uveitis Study Group (IUSG-2008) is based on the etiological criterion:

a. infectious (bacteria, fungi, viral, parasitory)
b. non-infectious: with known systemic association / without known systemic association
c. neoplasia masquerading, non-neoplastic

4. Classification according to IUSG-2008 takes into account the evolution criterion:

a. acute;
b. chronic;
c. recurrent.

5. Classification according to IUSG -2008 in terms of nature:

a. pathologic - granulomatous; nongranulomatous
b. lesional - focal; multifocal; disseminated; diffuse

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c. associated indices – synechiae; fibrin; nodules
d. configuration precipitates - focal; central; disciform; stellate or diffuse; peripheral

6. Other classification:

A. Anatomical classification (IUSG)

1. Anterior: iritis, anterior cyclitis, cyclitis.
2. Intermmediate: posterior cyclitis, hialitis, basal retinochoroiditis.
3. Posterior: chorioretinitis, retinochoroiditis, choroiditis.
4. Panuveitis represents the inflammation of the entire uveal tract

B. Etiological classification:

1. Idiopathic: 1. ocular manifestations; 1b. with ocular and systemic manifestations
2. Infections: 2a. with ocular manifestations; 2b. with ocular and systemic manifestations
3. Non-infectious: 3a. with ocular manifestations; 3b. with ocular and systemic manifestations

C. Clinical classification, according to onset and evolution length:

1. According to the evolution criterion:

a. Acute, with a maximum period of 6 weeks, often bringing about recurrences;
b. Subacute, with insidious onset, lasting for months or years with acute exacerbations;
c. Chronic, they evolve with attenuated inflammatory phenomena, sometimes absent when examined with the naked eye, the evolution lasting months and years, being hard to distinguish between the non-progressive periods of time. There may occur lens and corneal opacities, occlusion or secondary glaucoma or pupillary seclusion. The patient comes to the doctor in a late phase, generally when decreased vision occurs.

2. According to the clinical manifestations: granulomatous, nongranulomatous
3. According to severity: medium, severe
4. According to complications: simple, complicated.

D. Anatomical, pathological classification:

1. Anterior uveitis

Ø granulomatous uveitis with insidious onset, long development, clinical picture with discrete manifestations, characterized by the presence of iris nodules, large corneal precipitates and nodulated lesions at the level of the fundus. No systemic associations: idiopathic; glaucomatous crisis; keratouveitis; u.a.induced by drugs; post-traumatic; post-laser; post-surgical.

Ø nongranulomatous uveitis presenting an acute onset, short evolution but with strong symptoms, small corneal precipitates, diffuse lesions on fundus examination. With systemic associations: ankylosing spondylitis; juvenile rheumatoid arthritis; Reiter's syndrome; TB; leprosy; Behcet's syndrome; sarcoidosis; diabetes; hypothyroidism etc.

2. Intermediate uveitis

Idiopathic; toxoplasmosis; tuberculosis, sarcoidosis; syphilis; Borrelia; multiple sclerosis.

3. Posterior uveitis

Ø No systemic associations: idiopathic; serpiginous choroidopathy; posterior scleritis; post-surgically; myopia with fibrous postretinal syndrome

Ø With systemic associations: sympathetic ophthalmia; toxoplasmosis; sarcoidosis; TB; Behcet's syndrome; syphilis; intraocular lymphoma; retinopathy associated to AIDS.

Posterior uveitis may be suppurative or exudative (non-suppurative).

According to the lesions appearance, the exudative choroiditis may be:

- Diffuse, in case of acute forms, exudative spots appear, of dirty-gray or yellow colour, poorly defined, which may outline the edematous appearance of the fundus, whereas the chronic forms may also present areas of choroidal atrophy.
- In focal, with lesional appearance: acute lesions, with an appearance of prominent yellowish-white nodules of about 1 mm, which can merge, and scar lesions with the appearance of atrophic areas over which the retinal vessels pass.

Ø Disseminated circumscribed, with focal disease in different developmental stages (different ages), or of the same age, with dissemination throughout the retinal surface.

Of uttermost importance is the general clinical examination, as well as the specialty exams: dentistry, ORL, urogenital, dermatological and internal examinations, designed to detect the focal diseases. Note that an infection is not truly represented by an acute infectious process, such as a dental abscess or acute pultaceous tonsillitis. Focal diseases are represented by secluded processes, seemingly off in which the microbes are closed off and from where they are put into circulation, either germs of attenuated virulence or microbial toxins or microbial degradation products, which play the role of antigen triggers of the uveal process with immunologic mechanism. This is the manner in which dental granulomas, cryptic tonsils, chronic hypertrophic sinusitis etc. develop.

Focal reactions can be triggered by a number of microbial agents, among which, we first mention the BK and streptococcus, then gonococcus, pseudomonas pneomococus, bacillus coli, staphylococcus and pleuropneumonia group. A systematization of the germs incriminated in producing the granulomatous uveitis was made by Aronson (table no. 2).

Table no. 2. Germs incriminated to produce uveitis

No.	Pathogenic germs	Eye clinical appearance
1.	Treponema	Diffuse choroidal ("salt and pepper" appearance)
2.	Koch's bacillus	Granulomatous iridocyclitis
3.	β-hemolytic streptococcus	Exudative iridocyclitis
4.	Brucella	Exudative iridocyclitis
5.	Toxoplasmosis	Focal retinochoroiditis
6.	Histoplasmosis	Diffuse choroiditis with secondary macular damage
7.	Anaerobic	Macular lesion
8.	Leptospira	Exudative iridocyclitis
9.	Nematode	Fibroblast focal chorioretinitis

Clinical picture of endogenous uveitis

- Acute endogenous iridocyclitis presents a sudden and noisy symptomatology with paroxysmal onset and rapid evolution. In etiology, there are encountered infectocontagious diseases (measles, scarlet fever, chicken pox, typhoid fever, influenza), as well as tuberculosis, syphilis, chronic rheumatism, in whose evolution, recurrent acute iridocyclitis may occur. Their prognosis is favourable if the treatment is applied early, correctly and systemically, the aim being to obtain during the treatment a mydriasis as pronounced as possible.
- Chronic endogenous iridocyclitis have milder symptoms, the onset is insidious, with discrete reactive signs, a long term evolution (months, years), the periods of activity alternating with the quiet ones; they are accompanied by

ocular complications (secondary glaucoma, complicated cataracts), as well as the extension of the process in the entire uveal membrane.

- Their etiology is a subject of discussion, generally being brought about the chronic inflammatory diseases (focal infection, rheumatism, viral infections, syphilis, tuberculosis), but in most cases, their etiology remains unknown. The prognosis is reserved, even in the mild forms due to the torpid evolution, complications frequently encountered. In the cases diagnosed late or due to the late presentation to the doctor, or in the case of an incorrect or inadequate treatment, the prognosis is unfavourable.

Anterior uveitis

The subjective symptoms of the acute anterior uveitis are: ocular or periocular pain, intermittent, with onset in a few hours or days, with the exception of the traumatic cases that are aggravating due to strong light, redness, photophobia, excessive tearing, decreased visual acuity.

The subjective symptoms of the chronic anterior uveitis are: decreased visual acuity. There may be periods of remission and exacerbation with mild acute symptoms (e.g. juvenile idiopathic arthritis / juvenile rheumatoid arthritis).

Critical signs: cells and hyperemia in the anterior chamber, ciliary congestion, the presence of keratic precipitates that can be:

- fine, stellate, usually covering the entire corneal endothelium: herpetic, Fuchs heterochromic iridocyclitis (FHI), cytomegalovirus retinitis etc.
- small, nongranulomatous: HLA-B27 associated system, trauma, juvenile idiopathic arthritis, glaucomatocyclitic crisis and all of granulomatous entities.
- granulomatous: large, dirty which occur most often on the bottom of the cornea: sarcoidosis, syphilis, tuberculosis, Vogt-Koyanagi-Harada syndrome etc.

Other signs: pupillary miosis occurs, caused by a spasm reflex of the pupillary sphincter as a result of the irritation of the iris tissue; changes in intraocular pressure, in the sense of its decrease, the most common situation, secondary to the decrease of the ciliary body secretions or to its increase; the presence of fibrin (HLA-B27 or endophthalmitis); hypopyon (HLA-B27, Behcet's disease, infectious endophthalmitis, tumours); iris nodules (sarcoidosis, syphilis, tuberculosis); iris atrophy (herpetic); iris heterochromia; synechiae (HLA-B27 in particular, sarcoidosis) etc.

Intermediate uveitis

Symptoms are represented by: decreased visual acuity, presence of painless cotton wool spots, mild photophobia or external inflammation. It is usually seen in people aged 15-40 years old and bilaterally.

Critical signs: vitreous cells; presence of exudative white deposits above the lower portion of the serrata and pars plana; groups of cells floating in the inferior vitreous; the younger patients may experience bleeding in the vitreous.

Other signs: peripheral neovascularisation; mild inflammation of the anterior chamber; posterior subcapsular cataract; secondary glaucoma; retinal detachment.

Posterior uveitis

Subjective symptoms: blurred vision; myodesopsia; pain, hyperemia and photophobia are usually absent except for the case when the inflammation exists in the anterior chamber.

Clinical signs: cells in the anterior and/or posterior chamber; blurred iris; retinal or choroidal inflammatory lesions; vasculitis.

Other signs: inflammatory signs of the anterior segment.

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