ENDOGENOUS ENDOPHTHALMITIS

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CLINICAL CASE

83 year-old female, caucasian.

Chief complaint:

- History of 3 weeks pain,redness and decreased vision in OS

- Patient was been treated by her ophthalmologist with topical steroids,cycloplegics and 40 mg of oral Prednisone.

- No improvement of the ocular condition despite local and systemic treatment.

Past ocular history:

- Glaucoma OU under control with medical treatment.

- BRAO OD

- Idiopathic band keratopathy OU that required EDTA scrub.

Review of system:

- Hypertension

- Pacemaker

- Previous colonoscopy for recurrent episodes of melena: negative

Examination:

- VA: OD=20/100 OS = CF

- Anterior segment:

OD: BK, cataract 2+

OS: diffuse conjunctival and limbal injection, BK, diffuse corneal edema, hypopyon 3 mm, 3+ cells and fibrin clots in anterior chamber, posterior synechia, non reactice pupil, cataract 2+.

- Intraocular pressure: OD=17mmHg OS = 26mmHg

- Posterior segment : no view in OU because media opacity.

Assessment:

- Acute anterior uveitis OS with hypopyon formation, that did not improve on steroid

Treatment

- Elevated IOP OS

- Glaucoma OU

- BRAO OD

- Band keratopathy OU

Plan:

- Serolgical tests

- AC tap: the decision to proceed immediately with the tap, without waiting for the laboratory results, was principally dictaded by the absence of response to topical and oral steoids. This fact associated with elevated ocular pressure made us suspicious for infectious rather than autoimmune etiology of the uveitis.

- B-scan

Follow up:

- First AC tap: growth of Staphilococcus hominis in the meat broth after 5 days

- Second AC tap + intraocular injection of Vancomycin 1mg: growth of Staphilococcus epidermidis in the meat broth after 2 days.

- B-scan: posterior vitreous detachment, absence of choroidal or retinal involvement. Absence of vitreous opacity.

- Laboratory results: elevated levels of parathyroid hormone.

- Infectious disease consult: absence of systemic syntomps or signs of active infections in the body.Blood culture negative. Risk factors: previous colonoscopy.

- Definitive diagnosis: bacterial endogenous endophthalmitis(diffuse anterior endophthalmitis). Band keratopathy most likely caused by elevated levels of PTH.

- Treatment: intraocular Vancomycin injection 1mg, topical steroids 2QD,cycloplegics TID,antiglaucoma medications.Since no source of infection was found and patient was afebrile and asymptomatic, systemic antibiotic treatment was not prescribed.

- Three weeks follow-up:

- Absence of hypopyon and cells in the anterior chamber,improvement of corneal edema. The VA was still CF because of the dense cataract. The patient was adressed back to her ophthalmologist with the idea of planning a further cataract extraction in OS to improve the visual acuity. In addition, a endocrinologic consult was suggested to investigate the possibility of primary or secondary hyperparathyroidism.

ENDOGENOUS ENDOPHTHALMITIS

Endophthalmitis is a severe inflammation of intraocular structures. Although is not a common occurrence, it is considered one of the most severe vision threatening ocular condition. It is most frequently caused by microbial organisms and much less commonly results from direct physical or chemical tissue injury or from immunologic or neoplastic processes. In clinical practice the term endophthalmitis generally refers to microbial causes.

Classification

According to the clinical setting in which the infection occurs, endophthalmitis can be classified as:

Exogenous:

the organisms usually gain access to the eye via the external environment.

-Postoperative: 50-75%. Although the incidence of endophthalmitis following intraocular surgery has decreased due to modern surgical techniques and antibiotic and other prophylaxis, cataract surgery is still the most important cause of post surgical endophthalmitis. Less commonly, endophthalmitis can occur after pars plana vitrectomy, penetrating keratoplasty and pneumatic retinopexy. The majority of cases of endophthalmitis are caused by the patient's own lid and conjunctival flora. Operative risk factors include vitreous loss, wound abnormalities, prolonged surgery and contaminated instruments. The clinical evidence of postoperative infection can be acute, usually within two weeks from surgery or chronic, even after months(more than 3) from ocular surgery. In patients with chronic endophthalmitis the organism has been present in the eye since the surgical procedure itself.

-Post-traumatic:16-23%. As a result of penetrating ocular trauma organism may gain access to the eye.

-Bleb related: 4-18%. Patients who undergo glaucoma filtering surgery can develop early or late signs of endophthalmitis. The factors that can increase the risk to develop an infection are the use of antimetabolites (5-fluorouracile and mitomicin C), inferior filtering bleb, persistent postoperative hypotony, blebitis,and contact lens wear.

Endogenous:0-15%. Differently from the exogenous type, in endogenous endophthalmitis the infection results from hematogenous spread of the organism to the eye from a site elsewhere in the body. Moreover, differently from exogenous endophthalmitis which is most frequently caused by bacteria, fungal endogenous endophthalmitis is more frequently seen than bacterial or metastatic endogenous endophthalmitis.

Etiology

<u>Fungal endogenous endophthalmitis:</u>

-Candida

-Aspergillus

-Cryptococcus

-Histoplasma

-Coccidioides

Bacterial endogenous endophthalmitis

Gram positive organisms: Gram negative organisms:

-Streptococci 32% -E. coli 18%

-Staphylococci 25% -Klebsiella 4%

-B. cereus 4% -Serratia 4%

-P. acnes 4% -Neisseria 4%

The incidence of different bacteria in causing endogenous bacterial endophthalmitis has changed over the years. Until the fortys,before the introduction of antibiotics (particularly penicillin), Neisseria meningitidis accounted for more than 50% of all infections, while during the seventys Bacillus cereus was most frequently reported in endophthalmitis.

Clinical classification

The clinical presentation of endogenous endophthalmitis can be extremely variable and led Greenwald to propose a system of classification for bacterial (reasonably useful also for fungal) endophthalmitis into several clinical presentations.

-Anterior: focal/diffuse

-Posterior: focal/diffuse

-Panophthalmitis

Focal endophthalmitis: localized inflammatory nodules are present in the iris,ciliary body, retina and choroid.The inflammation in the anterior chamber can be associated with hypopyon but never obscure the view of the fundus. Lesions involving the choroid and retina are white or yellowish accompanied by moderate vitreous haze. The intraocular pressure is usually normal. The prognosis in these cases is good.

Diffuse anterior endophthalmitis: it is a severe anterior segment inflammation characterized by conjunctival chemosis, marked anterior chamber reaction with fibrin clots and significant hypopyon that hampers the view of the retina. Intraocular pressure is typically elevated. It is an ocular emergency and if not promptly and adequately treated the infection can spread to the entire eye.The visual prognosis is excellent with aggressive and appropriate treatment. Blindness usually results from delay in treatment.

Diffuse posterior endophthalmitis: the vitreous inflammation is so intense that it obscures retinal details. Nevertheless, during the early stages of the disease whitish emboli and perivascular hemorrhages can be noted. As the infection progresses, the retina becomes totally necrotic and vitreous abscess frequently occur. The anterior segment remains moderately involved. The intraocular pressure is low. The poor visual prognosis is most likely due to retinal ischemia as a result of occlusion of the central retinal artery by a septic embolus.

Panophthalmitis: it is a severe involvement of either anterior and posterior segment presenting with marked lid edema, proptosis and limitation of ocular movements. All details of anterior as well as posterior chamber are lost because of the prominent hypopyon. Typically the intraocular pressure is high. It is a disastrous and rapidly developing infection that destroys the globe and invades the orbit, resulting in blindness, phthisis or enucleation. Depending of the virulence of the pathogen, progression of a panophthalmitis may be life threatening.

Symptoms

The most common ocular symptoms referred from a patient with endogenous endophthalmitis are blurred vision, pain, redness and external discharge. Associated systemic symptoms may be present such fever, malaise, weight loss especially when the disease is advanced, these are more severe in sepsis.

Ocular signs include ciliary and conjunctival injection, hypopyon, corneal edema, posterior synechia with bombe' iris, cells in the anterior chamber and vitreous cavity, retinal and choroidal lesions.

Risk factors

Endogenous endophthalmitis rarely occurs in healthy patients. Since the disease occurs secondary to the hematogenous spread of microrganisms to the eye from a site of infection in the body, any disease process that produces septicemia can lead to development of endophthalmitis.

Well known predisposing factors are active foci of infection in the body (even occult), debilitating conditions like diabetes, malignancies, alcoholism and liver diseases, heart abnormalities (valve abnormalities and endocarditis), recent surgery, long postoperative course, intravenous catheters and hyperalimentation, intravenous drug abuse, prolonged use of corticosteroids and, in case of fungal endophthalmitis, broad spectrum antibiotic therapies.

Diagnosis

The high incidence of misdiagnosis of endogenous endophthalmitis ranging from conjunctivitis, acute glaucoma or other ocular conditions should alert the ophthalmologist to make a correct diagnosis of this insidious entity. The possibility of endogenous endophthalmitis should be considered in any patient who manifests a pronounced anterior reaction that is refractory to steroid treatment. The appropriate diagnosis is necessary to start the appropriate treatment and influence dramatically the visual outcome as well as reduce the incidence of systemic complications, sometime fatal. Therefore the crucial point is diagnostic suspicion.

-Accurate ocular and systemic history.

-Investigation of risk factors.

-Search source of infection: cooperation with internal medicine and infectious disease.

-B and A scan: to exclude posterior involvement, during the follow-up to monitor the adequacy of treatment.

-Intra-ocular fluids: anterior aqueous tap, vitreous tap or vitrectomy.

-Non-ocular fluids: blood, urine, CSF, all suspicious source of infection, others.

-Culture of fluids.

Differential

Diagnosis

In cases when there is no suspicion for endogenous (and this can happen especially if the clinical setting is negative or the patient is healthy), other common causes of uveitis must be excluded with the usual serologic tests.

-Autoimmune causes.

-Other infectious diseases: viral, protozoal, fungal.

-Malignancies, masquerade,metastatic tumors.

Whether, a negative response is obtained after a carefully exclusion of these causes, ocular and non ocular fluids culture must be considered.

Pathogenesis

In endogenous bacterial endophtalmitis the microrganisms enter into the uveal tract or retinal circulation as scattered organisms or in a bolus, and lodge in small capillaries. To invade ocular

tissues and produce infection these bacteria must cross the blood-ocular barrier and establish a septic focus that can develop in the retina prior to breaking into the vitreous. The infectious embolus is usually in proximity to the retinal vessels. If a large septic embolus pass through the central retinal artery and disseminates throughout the retina, retinal necrosis and ischemia may occur,allowing the microrganism to quickly invade the vitreous and further the anterior segment. Similarly, in cases of fungal endophthalmitis a localized inflammatory reaction surrounding a small nidus of fungi forms in the inner choroid, breaks through Bruch's membrane into the retina forming a microabscess and spreads into the vitreous cavity.

Medical treatment

-Bacterial: prompt and intensive intravenous antibiotic treatment continued for 3 weeks or longer is imperative. Initial doses should be those recommended for systemic infections. The selection of antibiotics prior to define identification of the causative agent reflects the characteristics of the patient and the likely source of bacteriemia.In other cases, broad spectrum coverage is indicated. Vancomycin is used for Gram positive bacteria, while gentamycin, amikacin or ceftazidime are indicated in cases of Gram negative infection. Intraocular and intravitreous injections are effective. Generally gentamycin and amikacin are now less commonly used because of associated risk of retinal toxicity and macular infarction; ceftazidime has been preferentially used more recently. Subconjunctival and topical antibiotics are also employed as well as intravitreal and oral steroids. The role of systemic antibiotic analyzed by the endophthalmitis vitrectomy study group (EVS) is not applicable for the endogenous forms.

-Fungal: intravitreal and intravenous amphotericin B is currently the drug of choice. Treatment duration and total dose of intravenous drug are determined by the clinical response and the degree of systemic or non-ocular involvement. Toxic side effects, including renal and hepatic toxicity, must be carefully monitored. Flucytosine can be used in combination with amphotericin B in cases of macular involvement and extensive inflammatory response, but its use alone is not recommended because of the frequent occurrence of drug resistance.

Surgical treatment

Surgical treatment is controversial and moreover criteria formulated from the EVS regarding the benefits of vitrectomy versus vitreous tap are not applicable. In general vitrectomy is indicated in cases of prominent vitreous involvement showing progressive disease despite intensive medical treatment. In these cases vitrectomy is effective in clearing the vitreous of inflammatory debris. Other advantages include the possibility to have larger sample to make the diagnosis and also to deliver a therapeutic level of drug in the vitreous.

Prognosis

The visual outcome is usually good in the anterior form of endophthalmitis, differently from posterior diffuse and panophthalmitis forms. Ultrasonography negative prognostic factors are vitreous and subhyaloid opacities, choroidal and retinal detachment. Other factors that are associated with a poor visual outcome are the patogenicity of organism, delay in time between the diagnosis and treatment, low intraocular pressure, initial visual acuity of light perception, severe hypopyon and absent red reflex.

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Review Questions for ENDOGENOUS ENDOPHTHALMITIS

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1. What is endogenous edophthalmitis?

a) An inflammation affecting anterior and/or the posterior segment.

b) A form of refractive uveitis that must be treated with steroid drops.

c) A severe vision-threating ocular condition.

d) A panuveitis always associated with elevated intraocular pressure.

e) A severe form of anterior uveitis characterized by sterile hypopyon.

2. Choose the right statements.

a) Exogenous endophthalmitis are caused by microrganism that gain access to the eye via the external environment.

b) Endogenous endophthalmitis are caused by organisms that spread hematogenously into the eye.

c) Glaucoma filtering surgery is the most frequent cause of endophthalmitis.

d) Endophthalmitis after cataract surgery can occur acutely and also after months from the surgery.

e) Endogenous endophthalmitis more frequently occurs in healthy patients.

3.The more frequent clinical presentation of endogenous endophthalmitis are

a) Bombe' iris and blood clots in the pupillary area.

b) Giant papillary conjunctivitis and mucous discharge.

c) Acute angle closure glaucoma.

d) Anterior hypopyon that obscure the view of the fundus.

e) Retino-choroidal lesions in cases of fungal infection.

4.Which statements are correct.

a) When the infection involves the anterior segment even if severe, the prognosis is good because the barrier effect of lens and iris hampers the spread of microrganisms in the posterior segment.

b) The panophthalmitis can be a life-threatening condition especially if the pathogen organism is virulent.

c) The most severe complication of endogenous endophthalmitis is orbital cellulitis.

d) Patients with metastatic endogenous endophthalmitis have elevated levels of eosinophils in peripheral blood.

e) Intravenous drug abusers are more exposed to develop bacterial than fungal endogenous endophthalmitis.

5. The diagnosis of endogenous endophthalmitis.

a) It is a clinical diagnosis.

b) Is always made by culturing anterior aqueous and vitreous.

c) Is a diagnosis of exclusion.

d) Is made in cooperation with internal medicine and infectious disease consult.

e) Needs to be prompt to allow a prompt initiation of adequate treatment.

6. Which statement is correct regarding treatment of endogenous endophthalmitis

a) Bacillus cereus endophthalmitis are treated with intraocular gentamycin.

b) Local antibiotic and steroid injections are the treatment of choice for metastatic endophthalmitis caused by Streptococcus pneumonia.

c) Intraocular injection of ceftazidime have shown retinal toxicity, therefore gentamycin is the preferred agent.

d) Fungal infections are better treated with oral flucytosyne.

e) Patients with Candida endophthalmitis are treated with oral or intravenous Amphotericin .

7. Surgical treatment in endogenous endophthalmitis is indicated .

a) In cases of pupillary glaucoma from extensive posterior synechia.

b) In infections with severe vitreous involvement.

c) If the visual acuity at onset is light perception or worse.

d) When the vitreous cultures are negative.

e) Always in cases of fungal endophthalmitis.

8. The prognostic factors that correlate with a poor visual outcome in endogenous endophthalmitis are:

a) Fluorangiographic evidence of macular edema.

b) High hypopyon level.

c) Associated endocarditis and heart valve abnormalities.

d) Initial visual acuity less than 20/200.

e) Evidence of vitreous opacities and retinal detachment on the B-scan exam.

9. Choose the right statements.

a) Patients treated with long term broad spectrum antibiotics have high risk of developing E. coli endophthalmitis.

b) The pathogenesis of endogenous endophthalmitis is related to emboli formation in the choroid and retina.

c) Candida endophthalmitis typically form retinal and vitreous microabscess.

d) Endocarditis is one of the most important risk factors for fungal and bacterial endophthalmitis.

e) Patients with metastatic endophthalmitis must always be hospitalized.

10. A patient presents with severe uveitis and anterior hypopyon that has been treated with topical and oral steroids without any improvement, what would you like to do?

a) Request an ESR, CRP and HLA typing.

b) Perform an AC tap.

c) Give the patient an intraocular injection of steroid .

d) Place the patient on broad-spectrum oral antibiotic treatment.

e) Request a fluorescein angiogram

CORRECT ANSWERS:

1.a,c.

2.a,b,d.

3.d,e.

4.a,b.

5.d.

6.e.

7.a,b.

8.b,e.

9.b,c,d.

10. b.