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INFLAMMATORY CNVM BY TOXOPLASMOSIS: A REVIEW ARTICLE

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ABSTRACT

Choroidal neovascular membrane (CNVM) formation is a well-documented sight-threatening complication of posterior segment intraocular inflammation like Toxoplasmosis. Necrotizing retinochoroiditis caused by an obligate intracellular parasite, *Toxoplasma gondii*, is a common inflammatory lesion of the fundus accounting for up to 70 % of cases with retinochoroiditis . By virtue of high affinity for neural tissue and retinal ganglion cells , the *T. gondii* localizes in retina and causes recurring ocular inflammation. Focal necrotizing retinitis adjacent to old retinochoroidal scar is the characteristic lesion in ocular toxoplasmosis. The diagnosis of ocular toxoplasmosis can be made on the basis of clinical findings alone. Choroidal neovascularization (CNV) developing at the margins of the healed *Toxoplasma* scar lesion is an important cause of vision loss in young patients. The prevalence of choroidal neovascular membrane (CNVM) in toxoplasmosis cases is reported to be 2–19 % during the late stage of the disease . CNV has been well reported to occur during the stage of healed toxoplasmosis.

Figure : 00 References : 23 Table : 00

KEY WORDS :CNVM, Scar, Sight threatening, Toxoplasmosis.

Introduction

Infection with *Toxoplasma gondii* is a frequent cause of retinal disease. *Toxoplasma gondii* is an ubiquitous obligate intracellular parasite, which infects both humans and warm-blooded animals as a zoonotic pathogen widespread in nature.[10,21]

In the United States, it is estimated that approximately 20% to 70% of adults are seropositive for antibodies to Toxoplasma.[1]

Ocular toxoplasmosis is a progressive and recurring necrotizing retinitis, with vision-threatening complications such as retinal detachment, choroidal neovascularization and glaucoma, which may occur at any time during the clinical course. There lies a matter of controversy about diagnosis and treatment for ocular toxoplasmosis and to date, many treatment options are applied clinically.

Other causes of inflammatory CNVM are: Rubella, Sarcoidosis, Birdshot choreoretinopathy, ocular Histoplasmosis, Multiple evanescent white dot syndrome, serpinginous choroiditis, Vogt Koyanagi Harada syndrome.

Discussion:

Organism and life cycle:

The infection is a zoonosis and members of the cat family are definitive hosts.[11,22]

T. gondii exists in 3 forms, all of which are possible to infect hosts as a form of zoonosis. Tachyzoites can infect almost all nucleated cells through a process of active invasion, tissue cysts (containing bradyzoites) are formed primarily in the brain and skeletal muscles during the chronic phase of infection and oocysts are produced during the sexual cycle that takes place in the intestine of acutely infected felines [2,3]

The main routes of infection have been thought to be by ingestion of oocytes from the cat faeces present in soil and sand boxes. Oocysts attached to fruits and vegetables and oocysts in

water which might be resulted from the process of washing may be a route of infection. However, ingestion of tissue cysts in raw or undercooked meat from several intermediate animals may be the main cause of infection in some countries. [6]

Pathogenesis:

Most of acute systemic toxoplasmosis in normal hosts tend to be subclinical, but some may present with mild flu-like symptoms. If parasites reach an eye and they yield a focus of inflammation, the lesion is progressed to retinitis and involves the choroid secondarily. Immune responses of the host appear to induce conversion of the parasitic forms, from tachyzoites to bradyzoites and their encystment.[19] The cyst may remain inactive in the scar or nearby for a long time. However, when the cyst ruptures with release of organisms into the surrounding retina, retinitis may be reactivated[3]. The reactivation of retinitis is known to develop at the border of old scars and is attributed to the rupture of tissue cysts which are located within old lesions. Sometimes, however, new lesions are found at locations distant from old scars.

Clinical features:

Ocular toxoplasmosis most often presents as a focal necrotizing retinitis. It is generally associated with vitritis and often with anterior uveitis. Less commonly, it may present as a papillitis. The age of the first attack of ocular toxoplasmosis is typically in the second decade and during a long-term follow-up, 5-year recurrence rate was 79%, and some patients had multiple recurrences[4,17]

The severity of anterior uveitis can range from a quiet anterior chamber reaction to an intense anterior uveitis, masking the inflammation of the posterior segment. It can be either granulomatous or non-granulomatous inflammations. Also, intense anterior inflammation may occur secondary to retinochoroiditis, near the ora serrata, which may be missed at initial examinations[7,18].

In children with congenital toxoplasmosis, cataracts may occur as a complication of retinochoroiditis and may follow severe iridocyclitis. Cataract may cause severe amblyopia in children and may need to be removed surgically.[14]

The complications of ocular toxoplasmosis include chronic iridocyclitis, cataract formation, secondary glaucoma, band keratopathy, cystoid macular edema, retinal detachment, and optic atrophy secondary to optic nerve involvement. Choroidal neovascularization has been described as a late complication of ocular toxoplasmosis. Other retinal vascular lesions, described as complicating toxoplasmosis, include branch artery occlusion, periphlebitis and toxoplasmic scleritis.

Choroidal neovascularisation is a vision threatening complication of posterior segment inflammation. It's development is promoted by infiltrating myeloid cells and also the choroidal and retinal myeloid cell activation, subsequent vascular endothelial growth factors, cytokine and chemokine production and complement activation acting in consort to mediate angiogenic responses.[13]

Choroidal neovascularization (CNV) developing at the margins of the healed *Toxoplasma* scar lesion is an important cause of vision loss in young patients[5]. The prevalence of choroidal neovascular membrane (CNVM) in toxoplasmosis cases is reported to be 2–19 %[2,20] during the late stage of the disease[9,16] . CNV has been well reported to occur during the stage of healed toxoplasmosis.

Diagnosis:

The diagnosis of *Toxoplasma retinitis* is made on the basis of the characteristic lesion (i.*e.*, an area of active retinitis adjacent to an inactive chorioretinal scar). Differential diagnosis can be sarcoidosis, tuberculosis, syphilis, viral and fungal infections.

Serological tests like Sabin Feldman dye test, indirect fluroscent antibody test, indirect hemagglutination test, complement fixation test, and enzyme linked immunosorbent assay test. However because the prevalence of antibodies can persist for years in otherwise healthy individuals, the interpretation of these tests is often fraught with difficulty.

Polymerase chain reaction (PCR) has been investigated recently as a useful technique to identify Toxoplasma on specimens obtained from ocular fluids and from paraffin embedded retinal tissue.[8,12]

Treatment:

Decision to treat is based on whether the toxoplasmosis is congenital or acquired, the immunocompetency of the host and nature and location of the lesion.

Treatment is generally given to congenital toxoplasmosis, immunocompromised host, lesions in the posterior pole and large destructive

lesions.

Drugs used:

Pyrimethamine, two 50 mg loading doses 12 hours apart, then 25 mg by mouth twice daily

Sulfadiazine, 2g loading dose, then 1 g by mouth four times daily

Prednisolone, 20 to 40 mg by mouth once daily

Surgical treatment:

Photocoagulation may be considered in the treatment of choroidal neovascularisation which can be a late complication of ocular toxoplasmosis.[15]

Treatment of inflammatory CNVM:

The routine options available for managing inflammatory CNVM include observation, laser photocoagulation, local and systemic corticosteroids and surgical removal; all with some limitations. Although, Photodynamic therapy combined with systemic corticosteroids and immunosuppressives has shown the best potential in treating inflammatory CNVM.[23]

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