Parasites and the eye

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INTRODUCTION

Systemic parasitic infections can result in intraocular inflammation. They are a major cause of blindness in many parts of the world. Infection usually results from bloodborne transmission of the organism to the eye or ocular adnexal structures. Diagnosis is often made from clinical patterns of disease in the eye, with laboratory investigations and imaging to support the diagnosis. Various local and systemic therapies are available, but may have limited success in preserving vision.

TOXOPLASMOSIS

Toxoplasma gondii is the most common infectious cause of retinochoroiditis (Rowe and Durand, 1998). It is an obligate intracellular protozoan that can infect humans and other animals, but felines are the definitive host.

Transmission

T. gondii exists in three forms: oocysts or soil forms are produced in the intestinal mucosa of the cat and shed in the faeces; tachyzoites are the active form present in the intermediate host and capable of invading various host tissues; and tissue cysts are the latent form and contain bradyzoites.

Infected cats shed oocysts in the faeces, which sporulate and are ingested by intermediate hosts, giving rise to tachyzoites. These invade the intestinal mucosa, enter the circulatory system and are carried into the host tissues where they replicate and cause tissue destruction. The chronic stage of the disease is characterized by the formation of tissue cysts containing thousands of bradyzoites protected from the host immune system (Edwards and Pordell, 1985). These cysts may lie dormant for years. Recurrences are thought to occur with rupture of the cysts.

Human infection may be through ingestion of undercooked or raw meat containing cysts or exposure to faeces containing oocysts (cat litter, contaminated food or water). Congenital infection occurs via transplacental passage of tachyzoites during primary maternal infection in pregnancy. Maternal infection early in pregnancy may cause stillbirth, abortion or multiple organ involvement. Transmission across the placenta is greater later in pregnancy, but has less severe sequelae (Edwards and Pordell, 1985). It was believed that most ocular toxoplasmosis was caused by reactivation of congenital infection, but studies in Brazil suggest that in this population, ocular toxoplasmosis more commonly results from acquired postnatal infection (Sharma et al, 2003).

Ophthalmic manifestations

There is a wide range of clinical presentations of ocular toxoplasmosis. Patients are often asymptomatic but ocular lesions may be present. These classically appear as a white-centred chorioretinal scar with pigmented border.

Some patients present with a single episode of mild intraocular inflammation while others suffer severe visual loss from recurrent uveitis. Worldwide, toxoplasmosis accounts for 28–55% (Edwards and Pordell, 1985) of posterior uveitis. Symptoms include floaters, visual blur and photophobia. Uveitis may involve the anterior chamber and be granulomatous or non-granulomatous with keratic precipitates on the corneal endothelium, cells in the anterior chamber, posterior iris synechiae and raised intraocular pressure. Signs in the posterior segment include a mild vitritis overlying an area of retinitis or a diffuse vitritis obscuring most of the retinal details. Areas of retinitis appear as creamy-white patches of retinal oedema adjacent to an old chorioretinal scar (satellite lesion) (*Figures 1* and *2*), which suggests recurrence of disease from tissue cysts in the old scar (Rowe and Durand, 1998). Other manifestations include perivascular sheathing, papillitis and cystoid macula oedema (Bosch-Driessen et al, 2002a).

Complications of ocular toxoplasmosis may result in legal blindness in at least one eye in up to 24% of patients (Bosch-Driessen et al, 2002a). Decreased vision results from macula scarring, macula dragging from a peripheral lesion, optic atrophy, cataract, retinal detachment (Hougard et al, 2002), cystoid macula oedema, dense vitritis or choroidal neovascularization. Macula lesions and bilateral involvement are more common in patients with congenital infection whereas peripheral lesions are more frequent in patients with postnatally acquired infection (Bosch-Driessen et al, 2002a).

Diagnosis

Diagnosis of ocular toxoplasmosis is based upon the clinical picture, however, serological tests may be performed to confirm exposure to the parasite. Recently acquired systemic infection is indicated by elevated anti-*T. gondii* immunoglobulin (Ig) M and/or IgA while the chronic phase is defined by positive IgG without IgM or IgA (Tran et al, 1999). Polymerase chain reaction in aqueous (Pearson et al, 1999) or vitreous (Abiose et al, 1993) samples can confirm ocular toxoplasmosis when the clinical picture is not diagnostic.

Treatment

Ocular toxoplasmosis is usually self-limiting in immunocompetent patients. Anterior uveitis can be treated with topical cycloplegic and steroid drops.

Treatment of posterior uveitis depends upon the severity of the clinical presentation and may not be necessary for small, peripheral retinal lesions with only mild inflammation. Indications for treatment include significantly reduced visual acuity, a macula or peripapillary lesion, large or multiple lesions, severe vitritis, persistent inflammation for over

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1 month, an immunocompromised patient (Hibberd et al, 1994) or involvement of an only seeing eye.

There are multiple treatment regimens combining antimicrobials with or without steroids. Combinations include pyrimethamine with folinic acid and sulfadiazine or trimethoprim/sulfamethoxazole, pyrimethamine with folinic acid and azithromycin (Mets et al, 1996), clindamycin alone or in combination, or new agents, e.g. atovaquone (Zygulska-Mach et al, 1993). Treatment is continued for at least 6 weeks (longer in immunocompromised individuals) and systemic corticosteroids may be introduced after antimicrobials are started in immunocompetent individuals to hasten resolution of inflammation. Corticosteroids should not be used without antimicrobial cover as this gives a poor visual outcome (Bosch-Driessen et al, 2002a).

ONCHOCERCIASIS

Onchocerciasis, or river blindness, is caused by *Onchocerca volvulus*, a filarial nematode that is transmitted to humans by the bite of the blackfly. The fly requires a high oxygen content and breeds in fast-flowing rivers. It is endemic in Africa, parts of the Middle East, Central America and some areas of South America. It is estimated to have infected at least 18 million people worldwide and caused blindness or vision impairment in almost 1 million (de Souza and Nakashima, 1995). The prevalence of ocular lesions increases with age (Montoya et al, 1999).

Figure 1. Active area of toxoplasma chorioretinitis near old scar.

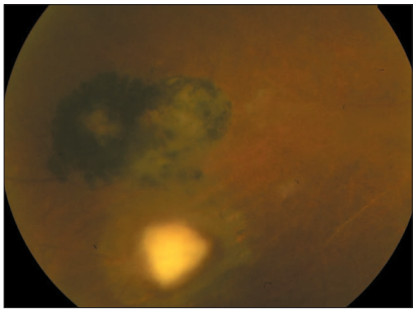
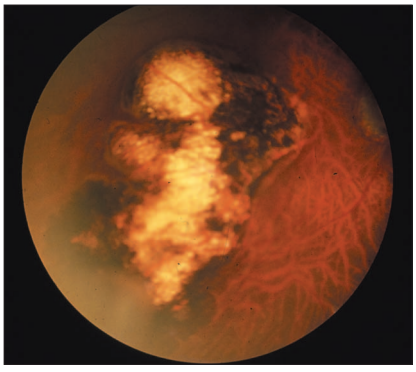


Figure 2. Large inactive scar from old toxoplasmic chorioretinitis.



Transmission

Transmission occurs when the bite of an infected blackfly deposits larvae, which migrate subcutaneously and mature into adult worms. These can survive for up to 10 years. They gather in an encapsulated mass (onchocercoma) where worms undergo sexual reproduction and release microfilariae that migrate throughout the body and infiltrate the skin and eyes (Bajaj and Pushker, 2002). The blackfly may then take up microfilariae after biting an infected human to complete the cycle.

Ophthalmic manifestations

Microfilariae migrate to the eye via the bloodstream, along nerves or from adjacent tissues. They invade the cornea at the limbus then pass into the aqueous and anterior segment, or can reach the posterior segment via the posterior ciliary nerves and vessels supplying the retina and choroid (Pushker et al, 2001). Severe inflammation accompanies dead microfilariae.

The cornea may be affected by punctate keratitis with white corneal opacities in the superficial stroma. A more severe sclerosing keratitis may develop that begins as an inflammatory vascular pannus then encroaches on the visual axis and causes devastating visual loss (Cooper et al, 1995).

In the anterior segment microfilariae may be seen and can cause a granulomatous or non-granulomatous uveitis with posterior synechiae, raised intraocular pressure and cataract.

Posterior segment involvement with chorioretinitis usually begins in the peripheral retina and causes visual field loss. The retinal pigment epithelium shows areas of alternating hyperplasia and atrophy and may be accompanied by chorioretinal atrophy. Optic atrophy may also develop following inflammatory optic neuritis in response to dead microfilariae and cause severe visual loss (Kayembe et al, 2003).

Diagnosis

Diagnosis of onchocerciasis can be made by recognition of the dermatological and ocular manifestations in endemic areas or by identifying the worms or microfilariae on skin biopsy. The Mazotti test provokes an urticarial reaction after administration of diethylcarbamazine. It is rarely used because of the risk of anaphylaxis and death. Serum antibody detection using enzyme linked immunosorbent assays (ELISAs) is useful to screen for infection or exposure while polymerase chain reaction testing for parasite DNA in skin snips or urine helps monitor infection and response to treatment (McDonald, 2003).

Prevention and treatment

The World Health Organization (WHO) has attempted to prevent infection in endemic areas. For over 30 years the Onchocerciasis Control Programme in West Africa has instituted vector control programmes to spray blackfly breeding sites with larvicides, and managed therapeutic treatment programmes so that onchocerciasis is no longer a major public health problem in these areas (Sabrosa and Zajdenweber, 2002). Education campaigns are aimed at individuals in endemic areas, encouraging use of insect sprays, protective clothing and avoidance of breeding grounds (Bajaj and Pushker, 2002).

Treatment of established onchocerciasis with a single annual dose of ivermectin is effective in killing microfilariae and is well tolerated (Holland, 1999). It can induce regression of anterior segment inflammation and reduces the incidence of optic nerve involvement and visual field loss (Pavesio and Lightman, 1996).

TOXOCARIASIS

Toxocariasis is caused by human infestation with the canine nematode *Toxocara canis* or less often the feline nematode *Toxocara cati*. Infection presents as either systemic visceral larva migrans in younger children (2 years old) or ocular

larva migrans in older children (7 years old), but they rarely coexist.

Transmission

Toxocara ova are excreted in canine or feline faeces and ingested by humans through contact with animals, contaminated foods or geophagia. In the human intestine the ova develop into larvae that penetrate the mucosa, enter the portal circulation and are then distributed via the systemic circulation to tissues including the eyes, lungs, muscle and CNS (Cooper et al, 1995).

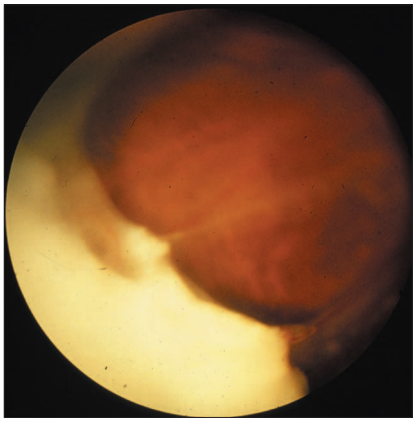
Ophthalmic manifestations

Larvae are thought to enter the eye via the choroidal circulation then migrate through the retina into the vitreous. Children may be asymptomatic or experience central or peripheral visual loss. Parents may notice leukocoria (white pupil reflex) or strabismus. It is an important differential diagnosis of retinoblastoma.

Ocular larva migrans commonly presents unilaterally as a retinal granuloma (*Figure 3*), endophthalmitis or rarely as optic neuritis. A retinal granuloma appears as a white elevated globular mass in the retinal periphery, posterior pole or directly involving the optic nerve. Complications such as retinal folds, 'dragging' of the macula as the inflammatory mass contracts, or a retinal detachment may occur.

Endophthalmitis is characterized by marked posterior segment inflammation with mild or no anterior segment activity and the eye may appear white externally.

Figure 3. Peripheral retinal mass from toxocara infection.



Diagnosis

Most cases of ocular larva migrans are diagnosed clinically. If the ocular media are opaque, imaging studies can be used to assess the posterior segment. Ultrasound may show pseudocyst transformation of the peripheral vitreous (Mets et al, 2003) while computed tomography (CT) (Bosch-Driessen et al, 2002b) and magnetic resonance imaging (MRI) studies may further delineate intraocular lesions. Serological tests, e.g. ELISA, can confirm diagnosis.

Prevention and treatment

Toxocariasis may be prevented by regular antihelminthic treatment of dogs and cats and limiting the contamination of the environment with animal faeces, particularly in children's play areas.

Treatment of ocular toxocariasis depends upon the severity of the clinical picture, taking into account the visual potential of the eye, degree of inflammation and macular involvement (Pushker et al, 2001). Systemic or periocular corticosteroids are useful for active inflammation. Antihelminthics such as thiobendazole may be used if the patient is unresponsive to steroids or has systemic signs of infection. Vitrectomy, laser photocoagulation and cryotherapy are useful in eyes with dense vitreous opacities, vitreomacular traction or retinal detachment (Casella et al, 1998).

CYSTICERCOSIS

Cysticercosis is caused by infestation with the larval form (cysticercus cellulosae) of the tapeworm *Taenia solium*. Infections are common in Asia, Central and South America, Africa and Europe.

Transmission

Humans are the definitive host of the adult tapeworm and shed ova in the faeces. Pigs are the intermediate hosts that become infected after ingestion of ova. The ova hatch, penetrate the intestinal epithelium and then spread throughout the body and encyst in tissues. The cycle is completed after human ingestion of poorly cooked pork containing larval cysts. This results in taeniasis with the development of adult tapeworms in the intestine (Gass and Braunstein, 1983).

Cysticercosis results when humans act as intermediate hosts and ingest the ova from food or water contaminated with human faeces, poor personal hygiene resulting in faecal–oral contamination or autoinfection from reverse peristalsis (vomiting) in a patient with a tapeworm in the bowel. These hatch in the intestine and migrate throughout the body to encyst in tissues including the eye, skin, CNS and muscles.

Ophthalmic manifestations

The cysticercus is a fluid-filled bladder containing a white head or scolex. Cysticerci can develop in the orbit and adnexa, involving the lacrimal gland, extraocular muscles, eyelids, retrobulbar optic nerve and subconjunctival space. The manifestations of cysticerci include proptosis, diplopia, motility disorders, orbital pain and redness, and vision loss (Sutisna et al, 1999). These are caused by their space-occupying effect and local inflammatory response.

The globe may be affected by subconjunctival cysts, free cysts floating in the anterior chamber, intravitreal cysts and vitritis, subretinal cysts with macula scarring, chorioretinitis, and retinal vasculitis (Silveira et al, 2001). The optic nerve can be involved by a compressive optic neuropathy, papilloedema or atypical optic neuritis (Pushker et al, 2002).

Diagnosis

The diagnosis can be made clinically with the organism being directly observed in the eye. Imaging (Pushker et al, 2002) with ultrasound (A or B scan) shows echoes corresponding to the cyst and scolex. CT scan and MRI (Figueroa et al, 2000) may also reveal the cysts in the orbit and ocular adnexae. A head CT scan is recommended to assess for coexistent neurocysticercosis. Systemic investigations such as serology using ELISA and detection of eosinophilia may support the diagnosis.

Treatment

Method of treatment depends on the location of the cyst and the degree of disease activity. Medical treatment consists of a combination of antihelminthics, e.g. albendazole, and oral corticosteroids in a tapering dose to

reduce inflammation. Serial ultrasound can be used to monitor the response to treatment (Pushker et al, 2002).

Where cysts are accessible, surgical removal may be the treatment of choice (Silveira et al, 2001). Subretinal cysts anterior to the equator of the globe can be removed by transscleral excision, whereas more posterior subretinal cysts or intravitreal cysts can be removed by pars plana vitrectomy (Chung et al, 2002).

DIFFUSE UNILATERAL SUBACUTE NEURORETINITIS

Diffuse unilateral subacute neuroretinitis (DUSN) is caused by an as yet unidentified species of motile nematode that wanders through the subretinal space causing progressive ocular damage. It usually affects otherwise healthy children or young adults and has been reported in some areas of North America, South America and Northwestern Europe.

Transmission

There are two sizes of nematode (WHO, 1987); one smaller 400–700 μm long worm that may be *Toxocara canis* or *Ancylostoma caninum*, and a longer 1500–2000 μm worm that is thought to be a racoon nematode *Baylisascaris procyonis* (Abiose, 1998).

Ophthalmic manifestations

Patients may present with a unilateral scotoma, transient visual loss or ocular pain. The early phase of the disease is characterized by multiple clusters of grey-white lesions in the retina that may be confined to one quadrant, mild vitritis and papillitis (Vincent et al, 2000). The nematode may be visualized moving in the retina causing linear tracks.

During the second phase of the disease there is progressive visual loss as a result of extensive degeneration of the retinal pigment epithelium, optic atrophy, arteriolar attenuation and electroretinogram abnormalities.

Diagnosis

Diagnosis is made on the clinical picture presenting in a patient from an area where DUSN is found. Systemic investigations for toxoplasmosis, syphilis and sarcoidosis are useful to rule out other causes of chorioretinitis that may present in a similar way (Vincent et al, 2000). Careful fundus examination to search for subretinal nematodes may confirm the diagnosis.

Treatment

Laser photocoagulation is used to kill the nematode if it is visualized and situated away from the fovea, otherwise it can be chased peripherally with a less intense laser (Vincent et al, 2000). This results in minimal inflammatory or toxic damage to the eye. Vitreoretinal surgery may be considered to extract the parasite for diagnostic and therapeutic purposes (Hovakimyan and Cunningham, 2002). Systemic antihelminthic drugs such as thiobendazole and ivermectin have limited success (Ongkosuwito et al, 1999). HM

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