

Treatment of ocular toxoplasmosis

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SYNOPSIS

Ocular toxoplasmosis is a potentially blinding cause of posterior uveitis. It predominantly affects children and young adults and is often recurrent. Current treatments do not effect a cure nor do they prevent recurrences. Their role lies in minimising the damaging effects of inflammation and limiting lesion size, particularly when sight is threatened.

Index words: blindness, parasite, abnormal laboratory results.

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Introduction

Ocular toxoplasmosis is the commonest identifiable cause of posterior uveitis. It predominantly affects children and young people (25–45 years) and is characterised by recurrences that can ultimately lead to significant visual loss. *Toxoplasma gondii* is an obligate intracellular parasite with the cat as the definitive host. It is transmitted to humans by accidental ingestion of the egg form (oocysts) in cat faecal matter which may contaminate fruit and vegetables, ingestion of the cyst form (bradyzoites) in undercooked or raw meat, and vertical transmission to the fetus during maternal primary infection by the replicating form (tachyzoites). Most clinical episodes of ocular toxoplasmosis represent reactivation of an infection that was acquired *in utero*. It is likely however, that more patients with ocular disease acquire toxoplasmosis after birth than was previously recognised.

Clinical features

Only a small proportion of infected people develop significant ocular disease. The commonest symptoms are floaters and reduced vision. The hallmark clinical signs are a vitreous cellular infiltrate associated with a creamy white retinal lesion that is typically adjacent to a pigmented chorioretinal scar (see Fig. 1). The eye may be painful and red with anterior uveitis and high intraocular pressure.

Assessment and investigations

Ocular toxoplasmosis can be confused with a large number of other causes of posterior and pan uveitis. The differential diagnosis depends largely on the clinical setting and the clinical signs. For example disease processes such as

herpetic retinitis, metastatic endophthalmitis, lymphoma, metastatic carcinomas and sarcoidosis may closely mimic the signs of ocular toxoplasmosis.

The diagnosis is predominantly clinical. Using the polymerase chain reaction to test the vitreous and aqueous humours for toxoplasma DNA can be useful when the diagnosis is uncertain but is limited by low sensitivity.

Serology is of limited value, as the presence of IgG antibodies to toxoplasma is usually not helpful in determining the cause of uveitis in patients with chorioretinitis. Positive IgG antibodies to toxoplasma imply past exposure and are very common in teenagers and adults in our community. The concentrations of IgG do not alter with ocular relapses. In patients with chorioretinal lesions that are consistent with ocular toxoplasmosis, the absence of specific IgM and IgG effectively excludes the diagnosis. This knowledge is particularly important for pregnant women as primary infection during pregnancy may result in infection of the fetus. If there are IgM antibodies and no IgG antibodies, this implies that the ocular lesions are a primary infection with toxoplasma. A fourfold increase in IgG concentrations over a four-week period may also suggest primary infection.

Management

The need for therapy, type of drug treatment and duration of therapy needs to be individualised. It is determined by factors such as the location of the lesion, severity of the inflammatory response, threat to vision, status of the other eye and the immune status of the patient.

An episode of ocular infection is ultimately self-limiting in immunocompetent patients. If the infection involves the peripheral retina, has only mild associated inflammation and there is no involvement of the optic disc or macular region of the retina, then treatment is not necessary.

Therapy is usually needed for 6 to 12 weeks in immunocompetent patients and a response is determined clinically when the retinal lesions lose their fluffy white appearance, the vitreous clears and an atrophic chorioretinal scar with sharp margins develops (see Fig. 2).

Immunocompromised patients such as transplant recipients and patients with HIV infection may require long-term suppressive therapy. Pyrimethamine and/or sulfadiazine can be used to maintain control of infection.

Fig. 1

Active ocular toxoplasmosis

The lesion is indistinct due to cloudy media, there is an area of retinal opacification and associated retinal vascular sheathing, contiguous with a focus of pigmented retinal scarring. The lesion is adjacent to the optic disc and is therefore a serious potential threat to vision. Toxoplasmosis in this location usually requires therapy.

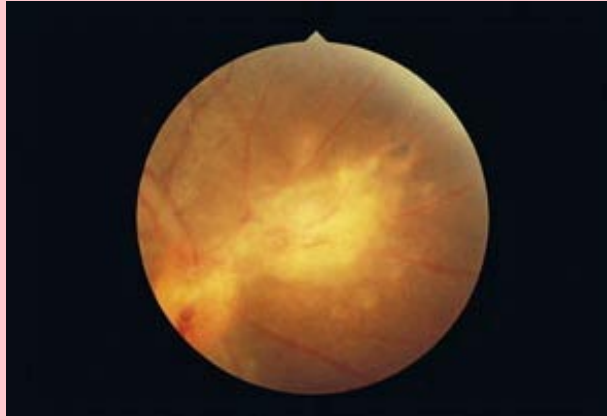
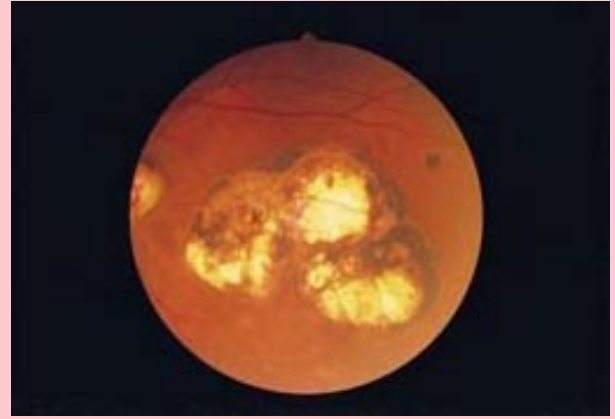


Fig. 2

Inactive ocular toxoplasmosis

There is a large retinal and choroidal scar with typical clinical features of inactive ocular toxoplasmosis. The scar involves the macula, is large in area, has heavily pigmented margins and is white centrally. It is well demarcated from the surrounding retina and the overlying media is clear.

**Drug treatment**

Most treatments are active against the replicating form of the parasite (tachyzoite). Some newer antimicrobials kill encysted organisms (bradyzoites) in animal models, however there are no data available for human disease.

Combination drug therapy is preferred to achieve rapid resolution, minimise inflammatory damage and to minimise resistance. The most commonly used combinations are clindamycin and corticosteroids, and pyrimethamine, sulfadiazine and corticosteroids. Combination treatment results in smaller retinal scars and is frequently used to treat patients with macular involvement. Other combinations of antimicrobials can be used, but data are limited.

Pyrimethamine

Pyrimethamine is probably the most effective single drug. It interferes with replication as it inhibits the enzyme dihydrofolate reductase in the folate production pathway. Treatment consists of a loading dose of 25 mg three times on the first day followed by a daily dose of 25 mg. The main adverse reactions are bone marrow depression (particularly leucopenia and thrombocytopenia), nausea and other gastrointestinal adverse effects.

Human cells are able to utilise exogenous folate, while toxoplasma, which lacks transmembrane transport mechanisms for folate, depends on intracellularly derived folic acid. Folinic acid 15 mg should be taken orally three times weekly to provide adequate dietary folic acid to prevent adverse effects, particularly bone marrow suppression, whenever pyrimethamine is used. A weekly full blood count is essential.

Sulfadiazine

This is a sulfur analogue and acts as a competitive antagonist for para-aminobenzoic acid (PABA), one of the precursors of folate production. Treatment consists of a loading dose of 2 g

followed by 1 g four times daily. Its main adverse reactions are malaise, gastrointestinal adverse effects and hypersensitivity. Other important adverse reactions include bone marrow suppression and crystallisation in the renal tubules.

Clindamycin

Clindamycin interferes with protein synthesis. It is frequently used as a single drug or in combination with corticosteroids with excellent results. Recommended doses are 300 mg four times daily for 3–4 weeks followed by 150 mg four times daily for a further 3–4 weeks. Its serious adverse effects are diarrhoea and pseudomembranous colitis. Clindamycin has also been used as intraocular therapy by direct injection into the vitreous.

Azithromycin

This azalide antimicrobial is well absorbed. It reaches high and sustained tissue concentrations and penetrates the blood-brain and blood-ocular barriers when they are inflamed. The recommended dose is a 500 mg loading dose followed by 250 mg daily. Adverse effects are infrequent.

Atovaquone

Most experience with atovaquone has been in patients with HIV infection and toxoplasma. Poor absorption and gastrointestinal adverse effects limit its use.

Spiramycin

Spiramycin is infrequently used in Australia, but it has the lowest toxicity to the fetus and is recommended when a pregnant woman needs treatment. The recommended dose is 1 g twice daily.

Corticosteroids

Oral corticosteroids are used to limit the damaging effects of inflammation. They should always be used in conjunction with antimicrobial therapy.

Anterior uveitis and raised intraocular pressure can occur from spillover of inflammation to the anterior segment of the eye. Topical corticosteroids and ocular hypotensive medications are the treatment.

Surgery

Surgery may be needed to treat complications such as retinal detachment, cataract and epiretinal or choroidal neovascular membranes involving the macula.

Recurrences

Following primary infection, recurrences of ocular infection are common. They are managed in the same manner as primary infection. During pregnancy, relapses of ocular infection cannot transmit toxoplasmosis to the fetus.

Prevention

Ensure that fruits and vegetables are cleaned and washed. Cook all meats adequately to destroy any harboured cysts. Pregnant women should avoid cat litter pans. Adequate contraceptive precautions are needed for six months in women of childbearing age following primary toxoplasmosis infection.

Conclusion

Toxoplasmosis is the commonest identifiable cause of posterior uveitis in our community accounting for about 20% of cases. Treatment can control episodes of infection but cannot prevent recurrences.

FURTHER READING

Dodds EM. Ocular toxoplasmosis: Clinical presentations, diagnosis, and therapy. American Academy of Ophthalmology Focal Points 1999: Volume XVII Number 10.

Conflict of interest: none declared

Self-test questions

The following statements are either true or false (answers on page 99)

3. Oral corticosteroids should always be used in combination with antibiotics to treat symptomatic ocular toxoplasmosis.
4. All patients who are exposed to *Toxoplasma gondii* should be treated with a combination of antibiotics.

Dental notes

Prepared by Associate Professor R.G. Woods and Associate Professor N. Savage of the Australian Dental Association

Consumer Medicine Information: dental requirements

The recommendation made in the 1991 report on the future of drug evaluation in Australia¹, that patient information be provided with all medication, is being implemented. Consumer Medicine Information (CMI) has been developed for almost all drugs in Australia. It is based on the approved product information for each drug.

CMI involves all health professionals.² Dentists giving or supplying drugs are required to make CMI available to patients who request it irrespective of the route of administration. In practice, most CMI will be provided by pharmacists. CMI should also be provided for medicines available from supermarkets or other non-pharmacy outlets.

A convention has been developed that dentists advise patients that CMI is available for the drugs they administer

and can be provided on request. This includes CMI for local anaesthetics and other drugs given parenterally, for instance intramuscular antibiotics.

In an emergency, for instance treatment of collapse, there is unlikely to be an opportunity to offer or provide CMI before treatment. However, CMI can be made available afterwards.

A CMI supply can be obtained for manufacturers. It is also available in some electronic databases, such as E-MIMS, and to subscribers to the Australian Dental Association web site (www.ada.org.au).

REFERENCES

1. Baume PE. A question of balance: report on the future of drug evaluation in Australia. Canberra: Australian Government Publishing Service; 1991.
2. Dowden JS, Clear PR, Fogg S, Appel S, Joseph P. Consumer product information affects us all. Aust Prescr 1996;19:30-4.