Reminder of important clinical lesson

Atypical toxoplasmic retinochoroiditis

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Summary

We report a case of re-activation of *Toxoplasma gondii* as a cause of atypical retinal necrosis in an immunocompetent individual. The rapid development of necrotising confluent retinochoroiditis and vitreous inflammation necessitated urgent aqueous humor PCR analysis, which was positive for *T gondii*. The patient was treated with two intravitreal injections of clindamycin, along with oral sulphadiazine, pyrimethamine, folinic acid and prednisolone. He developed central retinal arterial occlusion, as a complication of toxoplasmic retinochoroiditis, and immediate anterior chamber paracentesis was performed with visual recovery. The injection of intravitreal clindamycin with concomitant oral therapy was associated with control of toxoplasmic retinochoroiditis and resolution of vitreous inflammation.

BACKGROUND

We present an atypical toxoplasmic retinochoroiditis in an immunocompetent individual, which is unusual, but serves to underpin some important principles in the diagnosis and management of this challenging condition. Atypical cases of ocular toxoplasmosis consist of multifocal disease, large areas of retinal necrosis or retinochoroiditis. Such cases may require a combination of intraocular and oral treatment to control the inflammation. In addition, aqueous humor (AH) analysis to determine local antibody production or PCR tests to detect *Toxoplasma gondii* DNA can help differentiate ocular toxoplasmosis from similar retinal lesions caused by herpes viruses or other infectious agents.

CASE PRESENTATION

A 30-year-old man presented with a history of redness, pain and reducing visual acuity in the left eye. He had a ocular history of a scar and poor vision of the left eye since childhood. He was otherwise well. On examination, best-corrected visual acuity was recorded as 6/5 OD and 6/60 OS. An active nasal retinochoroidal lesion with associated vitritis and retinal arteritis was seen in the left eye. Intraocular pressure was raised in the left eye and was normal in the right eye. A clinical diagnosis of the re-activation of *T gondii* retinochoroiditis was performed. Oral azithromycin for 3 weeks and oral prednisolone for 5 weeks were commenced along with topical dexamethasone, brinzolamide and atropine.

INVESTIGATIONS

Blood investigations of full bloody count (FBC), erythrocyte sedimentation rate (ESR), urea and electrolytes, serum ACE, rheumatoid factor, antinuclear antibody (ANA), anti-neutrophil cytoplasmic antibody (ANCA), Venereal Disease Research Laboratory (VDRL) and serum electrophoresis were normal. The serum *Toxoplasma* IgG was positive. Despite treatment, 1 month later there was significant clinical deterioration, with development of necrotising confluent retinochoroiditis and increased vitreous inflammation. Further tests including HIV serology were negative and lymphocyte levels were normal. Although the clinical

findings suggested atypical toxoplasmic acute retinal necrosis (ARN), an urgent AHPCR analysis for cytomegalovirus (CMV), herpes simplex virus (HSV) and toxoplasmosis was performed. All PCR results were negative except for toxoplasmosis. His medication was changed to sulphadiazine and pyrimethamine with folinic acid (15 mg three times weekly), but given the previous failure of oral treatment, he received intravitreal clindamycin 1 mg. He later developed lymphopaenia as an unusual pyrimethamine-related side effect, which only resolved with more frequent daily dosing of folinate once pyrimethamine was discontinued.

DIFFERENTIAL DIAGNOSIS

Differential diagnoses for uveitis with associated retinitis include toxoplasmosis, ARN caused by CMV, HSV or varicella-zoster virus, endophthalmitis, sarcoidosis, tuberculosis, fungal retinitis and lymphoma.

TREATMENT

The patient received two intravitreal injections of clindamycin 1 mg, along with oral sulphadiazine, pyrimethamine, folinic acid and prednisolone. A 0.1 ml solution containing 1 mg of clindamycin was prepared for each intravitreal injection using aseptic techniques. 0.5 ml of clindamycin (150 mg/ml) was withdrawn and injected into 1 ml L/L syringe using a filter needle. 7 ml of sodium chloride 0.9% was withdrawn and injected into a 10 ml L/L syringe. 0.5 ml of clindamycin 150 mg/ml was transferred and injected into the 10 ml L/L syringe containing 7 ml of sodium chloride 0.9%. A final volume of 7.5 ml had a concentration of 10 mg in 1 ml, which is equal to 1 mg/0.1 ml. Using a fluid dispensing connector, 0.2 ml of the solution was transferred into a 1 ml L/L syringe.

OUTCOME AND FOLLOW-UP

Objective improvement in the vitritis was noted 2 weeks following the first injection (figure 1). Given the fact that the vitreous inflammation was still significant and given the intolerance of the patient to the oral treatment, repeated intravitreal injection of clindamycin was

Figure 1 Fundus photography showing significant retinitis and vitritis.

required. However, following the second injection, the patient experienced sudden loss of vision as a result of retinal artery occlusion. Immediate anterior chamber paracentesis was performed with visual recovery. The vitritis improved 2 weeks later (figure 2). After 2 months, there was significant improvement of the vitritis and the retinochoroidal lesions appeared inactive (figure 3).

DISCUSSION

The diagnosis of ocular toxoplasmosis depends largely on the presence of typical lesions, with retinochoroiditis as a key feature. PCR is a quick reliable tool that is useful for the prompt diagnosis of ocular toxoplasmosis, particularly in patients presenting with atypical features. A high index of suspicion and the choice of appropriate investigations are crucial in the diagnosis of ocular toxoplasmosis. Medications traditionally used include sulphadiazine, pyrimethamine with folinic acid, clindamycin and antimicrobials, such as azithromycin. However, some patients are intolerant of or allergic to or have infections resistant to systemic therapy. Pyrimethamine has been described to produce side effects, including leukopaenia and thrombocytopaenia, in 26% of patients taking the medication

Figure 2 Fundus photography showing resolving vitritis 4 weeks after the first intravitreal injection of clindamycin.

Figure 3 Fundus photography showing inactive retinochoroidal lesions and significant improvement of vitritis 2 months after the intravitreal injections of clindamycin.

for ocular toxoplasmosis. Our patient developed lymphopaenia during the course of the triple anti-Toxoplasma therapy; to our knowledge, this is the first report of lymphopaenia in an immunocompetent patient. In addition, his infection was resistant to azithromycin treatment. There is clearly a role for intravitreal therapy in the treatment of ocular toxoplasmosis, and intravitreal injection of clindamycin appears to be an effective strategy especially in patients who are intolerant or resistant to (conservative) oral treatment. Ocular toxoplasmosis may cause a variety of retinal vascular changes including retinal arterial occlusion, a rarely reported complication of the disease.¹ Braunstein and Gass² first proposed that the acute necrotising reaction in toxoplasmosis causes branch retinal artery occlusion. Recurrent ocular toxoplasmosis with branch retinal arterial occlusion within the necrotic lesion has also been described.^{3 4}

Learning points

Although most atypical cases are seen in immune-compromised patients,⁵ toxoplasma remains the primary differential diagnosis in ARN after HSV, CMV and varicella zoster virus.

- ▶ Aqueous Humor PCR is a sensitive and specific tool for the prompt diagnosis of ocular toxoplasmosis, especially when combined with measures of local antibody production⁶.
- ▶ Pyrimethamine-related side effects, including leukopaenia and thrombocytopaenia, are common, occurring in up to a quarter of patients.⁷ Weekly blood counts are therefore essential. To our knowledge, an isolated lymphopaenia, such as in our case, has not been reported in the literature and is reported here for the first time.
- ▶ Intravitreal injection of clindamycin^{7 8} has been demonstrated to be an effective strategy, especially in patients intolerant of or resistant to oral treatment.
- ▶ Ocular toxoplasmosis causes retinal vascular changes, and the ophthalmologist should be aware of possible complications and be prepared to perform immediate paracentesis after intravitreal injection, if needed.

Competing interests None.

Patient consent Obtained.

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