HEALTHCARE DELIVERY

Anterior chamber paracentesis to improve diagnosis and treatment of infectious uveitis in South Africa

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Infectious uveitis is a significant cause of blindness in South Africa, especially among HIV-infected individuals. The visual outcome of uveitis depends on early clinical and laboratory diagnosis to guide therapeutic intervention. Analyses of aqueous humor obtained by anterior chamber paracentesis direct the differential diagnosis in infectious uveitis. However, although safe and potentially cost-effective, diagnostic anterior chamber paracentesis is not common practice in ophthalmic care across Africa. We draw attention to this important procedure, which could improve the diagnosis and prognosis of infectious uveitis.

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Uveitis is a potentially sight-threatening eye condition with an estimated prevalence of up to 714/100 000 in the developing world.[1] HIV impacts on the burden of uveitis, as HIV-infected individuals have increased susceptibility to ocular infections and may present with more severe disease.[1,2] In Uganda, infectious uveitis is the most common cause (41%) of non-correctable visual impairment among HIV-infected individuals.[3] In sub-Saharan Africa, including countries where onchocerciasis is endemic, up to 25% of all blindness can be attributed to uveitis.[1] Uveitis has a wide range of causes, with an infectious origin in up to 50% of cases in Africa.[1]

Diagnostic challenges in uveitis

Early diagnosis and subsequent initiation of targeted antimicrobial treatment is vitally important for good visual outcome in patients with infectious uveitis.[4-6] However, accurate diagnosis is challenging, especially in resource-poor settings and in HIV-infected individuals.[2,3] Firstly, uveitis is generally clinically underdiagnosed owing to lack of ophthalmological expertise.[2] Unrecognised uveitis was reported to result in significant visual impairment among Ugandan HIV-infected individuals.[3] Visual impairment in these cases could possibly have been prevented if the condition had been recognised early. Secondly, if uveitis is diagnosed clinically, the presumed cause may be incorrect as the diagnosis is based on the patient's history and clinical and ophthalmological characteristics. Clinical features have poor predictive value for diagnosing the cause of uveitis, and do not distinguish well between infectious and non-infectious origin. Moreover, in cases of infectious uveitis, clinical features are poorly predictive of the causative pathogen, because different pathogens may present with similar clinical characteristics.[4,5] Based on diagnostic testing in almost a quarter of patients presenting with uveitis in studies from The Netherlands and South Africa (SA), the initial clinical diagnosis was adjusted and treatment altered.[4,5] An exception may be uveitis caused by *Mycobacterium tuberculosis* where the patient's history (e.g. recent history of pulmonary tuberculosis) or specific retinal findings (e.g. granuloma) are strongly indicative of infection by this organism. However, tuberculosis cannot always be ruled out solely on the basis of clinical symptoms.[7] Thirdly, empirical treatment of infectious uveitis is difficult because of the wide range of potential uveitogenic pathogens that require targeted treatment (Table 1). Finally, HIV-infected individuals are at an increased risk of specific opportunistic ocular infections (e.g. cytomegalovirus retinitis).[2] Manifestations of infectious uveitis are often atypical, with immunosuppression resulting in a lower degree of inflammation, even in advanced uveitis, compared with HIV-uninfected individuals. This makes clinical identification of the triggering pathogen in HIV-infected individuals particularly challenging.[2]

Diagnostic analysis of aqueous humor

The clinical diagnosis of infectious uveitis is increasingly supported in Western countries by analysis of ocular fluid[8] obtained through diagnostic anterior chamber paracentesis and aspiration of aqueous humor (Fig. 1). This is a well-documented procedure that is routinely performed in other aspects of ophthalmological care, e.g. management of acute elevation

Table 1. Clinical management of the most common pathogens in infectious uveitis

Aetiology	Treatment
Viruses	
HSV and VZV	Topical and oral or intravenous antivirals (e.g. acyclovir), topical corticosteroids (e.g. prednisolone acetate eyedrops), and intravitreal antiviral agents (e.g. ganciclovir)
CMV	Intravenous and/or intravitreal antiviral agents (e.g. ganciclovir)
Bacteria	
Mycobacterium tuberculosis	Routine treatment for extrapulmonary tuberculosis and topical steroids (e.g. prednisolone acetate eyedrops)
Treponema pallidum	Intravenous antibiotic treatment (e.g. penicillin G or ceftriaxone)
Protozoa	
Toxoplasma gondii	Oral antimicrobial regimens (e.g. pyrimethamine) and systemic steroids (e.g. prednisolone)
Onchocerca volvulus	Oral ivermectin

Note: This table serves as a general guideline for the clinical management of infectious uveitis. Management of these conditions may differ dependent on local guidelines and availability of drugs.
HSV = human simplex virus; VZV = varicella zoster virus; CMV = cytomegalovirus.

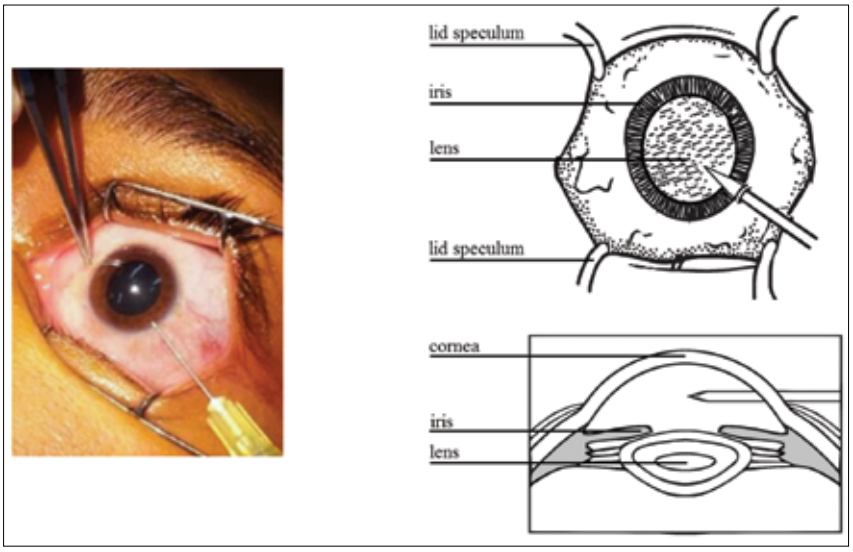

Fig. 1. Photograph and schematic overview of anterior chamber paracentesis for the aspiration of aqueous humor.

of intraocular pressure and diagnosis of suspected intraocular infections, metastasis and lymphoma.[5,6] The two key diagnostic tests of aqueous humor are pathogen-specific serological examination of paired ocular fluid and serum samples, and polymerase chain reaction (PCR) testing of the ocular fluid sample. In serological examination, intraocular pathogen-specific IgG is measured and compared with serum IgG levels (Goldmann-Witmer coefficient) to differentiate between intraocular production of antibody and passive leakage from the blood as proxy for infection, whereas PCR identifies pathogen-specific nucleic acids.[9] In infectious uveitis, pathogen-specific nucleic acids and IgG production are commonly detectable at different times after the onset of disease. During the early phase, nucleic acids are detectable within days after the onset of disease, followed by detection of intraocular IgG levels. Whereas pathogen nucleic acids commonly become undetectable 2 weeks after the onset of disease, specific antibodies remain detectable for many weeks in aqueous humor.[9] The two assays are therefore complementary, and contribute considerably to the differential diagnosis of infectious uveitis.[4-6,9,10] Identification of the triggering pathogen was established by serological examination and PCR in 60% of HIV-infected individuals presenting with undefined posterior uveitis, whereas PCR provided a final diagnosis in 39% of cases in which the initial diagnosis of the causative pathogen was uncertain.[4,10] Furthermore, treatment was altered on the basis of PCR results in 20% of patients with posterior uveitis of suspected infectious origin in a study from the USA.[6]

Anterior chamber paracentesis in uveitis

Anterior chamber paracentesis is a safe procedure that can be performed in a consultation room with a slit-lamp.[11,12] Three studies have reported on the safety of this procedure in diagnosing uveitis.[11-13] Only a few non-serious complications occurred, including traumatic hyphaema (5 cases/1 000 procedures), referring to bleeding in the anterior chamber that may cause blurred vision, but usually resolves spontaneously or is easily treatable with topical eyedrops (e.g. topical steroids); similarly, injection of air into the anterior chamber (4 cases/1 000 procedures) may cause blurred vision, but is usually self-limiting.[11-13]

Uveitis is a serious condition resulting in severe visual impairment and even blindness if not treated promptly and adequately. In SA, referral from lower levels of healthcare to a regional ophthalmology unit for further management and initiation of (empirical) treatment is indicated. However, even in these units treatment outcomes may be poor owing to the low predictive value of the patient's history and clinical characteristics for identifying the cause of the uveitis.

Anterior chamber paracentesis, aspiration and analysis of aqueous humor provide a valuable diagnostic procedure that optimises treatment and subsequent prognosis and poses a very limited risk. We believe that this procedure could be performed in most settings, because a well-trained ophthalmic nurse could perform anterior chamber paracentesis safely in situations where qualified ophthalmologists are not available. Paracentesis is easier to perform than cataract surgery, for which ophthalmic nurses are trained in African countries such as Malawi that lack ophthalmologists.[14] In addition to skills development, strengthening laboratory infrastructure is warranted. Validation of existing diagnostic assays and provision of other resources required to analyse aqueous humor for the most common uveitogenic pathogens should be considered across SA. Furthermore, logistic systems such as a cold-sample transport chain require optimisation to ensure a short turnaround time and maximum clinical impact of this diagnostic test. Providing such a diagnostic service

would be cost-effective, reducing unnecessary use of expensive antimicrobial drugs and avoiding blindness and its associated socioeconomic costs.[15]

Conclusion

We seek to draw attention to the so far unmet need for this valuable diagnostic procedure and to encourage discussion among healthcare providers regarding introduction of anterior chamber paracentesis in the routine work-up of patients with uveitis in SA. Ultimately, these efforts should result in the development of clinical guidelines and a training programme that includes anterior chamber aspiration. This would improve clinical management of uveitis and reduce the burden of avoidable visual impairment and blindness.

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