

Infectious Uveitis, Part 1: Know the Causes and Take a History

Although it can be difficult to distinguish between infectious and noninfectious uveitis, the consequences of that decision are substantial. In the worst-case scenario, failure to recognize an infectious etiology can lead to inappropriate treatment with unopposed steroids, proliferation of the inciting organism, and even loss of vision. Janet L. Davis, MD, at the Bascom Palmer Eye Institute in Miami, said, “Some infections that might have been easily curable at the onset can convert to an infection that cannot be controlled. This can create a situation in which trying to catch up later is difficult.”

A challenge in diagnosing infectious uveitis is that it's uncommon, at least in the United States; a longitudinal study found that infectious uveitis/scleritis constituted about 14% of all uveitis diagnoses, with a mean annual incidence of 19.1 per 100,000 during the study period.¹ However, the figures vary widely across the globe. A 2018 literature review found that between 30% and 60% of uveitis cases in the developing world were infectious.²

The first critical step in making the diagnosis is to have a keen awareness of possible infectious etiologies, and the second is to take a careful history to elicit important clues to guide the subsequent diagnostic investigation. Accordingly, Part 1 of this two-part series covers the four infectious uveitides of

greatest concern for U.S. ophthalmologists and provides pointers for incisive history-taking in patients with intraocular inflammation. Next month, Part 2 will present key diagnostic findings from the eye exam and pertinent results from lab testing and imaging.

Four Concerning Conditions

Scores of organisms can cause infectious uveitis.³ However, because of their frequency and potential for serious visual consequences, the following infections should be on clinicians' radar.

Toxoplasmosis. “Toxoplasma chorioretinitis [Fig. 1] is probably the most common infectious uveitis in the world,” said Ramana S. Moorthy, MD, at Associated Vitreoretinal and Uveitis Consultants, in Indianapolis, Indiana. “It's usually associated with drinking water contaminated with Toxoplasma or eating undercooked meats that may contain Toxoplasma cysts.”

This protozoan organism is found around the world and is estimated to be present in 11% of the U.S. population and in as many as 60% in endemic areas such as Central and South America. However, most infected persons are asymptomatic.⁴

Syphilis. “The second most common infectious uveitis I see is syphilitic uveitis, which has become increasingly common, and it is often accompanied by HIV infection, especially among men who have sex with other men,”



SIGN. Headlight in the fog presentation of *Toxoplasma retinochoroiditis*.

said Dr. Moorthy. (For a more detailed discussion of ocular syphilis, see Ophthalmic Pearls in the *May EyeNet*.)

“Diagnosing syphilitic uveitis is challenging because it can present in almost any form,” said Phoebe Lin, MD, PhD, at the Cleveland Clinic Cole Eye Institute. Manifestations can include granulomatous or nongranulomatous anterior chamber inflammation, vitritis, retinal vasculitis, papillitis, and retinitis.³ Beyond the ocular manifestations, however, this diagnosis can have a public health impact, as patients often don't know that they have syphilis.

Tuberculosis (TB). Similar to syphilis, the ocular signs of TB may be noted by the ophthalmologist before the patient has been diagnosed with the systemic disease. Indeed, only a

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small number of the bacteria can incite exuberant ocular inflammation, even in the absence of any evidence of TB on chest x-ray, said Dr. Moorthy, adding that virtually every form of inflammation that can involve the uveal tract has been reported with TB.

Acute retinal necrosis (ARN). “Viral necrotizing retinitis is a great concern because these infections can change from a simple iritis to extensive retinitis in just a few days,” said Dr. Davis. “Use of oral corticosteroids without antiviral coverage may speed up the process and make it harder to treat. We see cases like this in the referral practices.” The most common culprits in necrotizing retinitis are varicella-zoster virus (VZV) and herpes simplex virus (HSV) types 1 and 2.

Start With a Thorough History

Faced with these and a host of other possible causes of ocular inflammation, what is the ophthalmologist to do? “One of the things that can’t be overlooked is the critical importance of taking a good history—ocular, medical, and social—and teasing out specific details that can point you in the right direction as you put together your initial findings,” said Dr. Moorthy.

It’s important to note that the following questions are examples and are not exhaustive. Every ophthalmologist who sees patients with intraocular inflammation will develop his or her own approach to eliciting key points.

Ocular history. Dr. Davis asks if the patient wears contact lenses, has had any previous ocular trauma, or gotten anything into their eye. “We saw a case recently where someone had spent the whole day working in a garden; that evening his eye was red and kept getting worse and worse. It turned out to be an infectious scleritis related to fungal infection. In other cases, I’ve seen unusual infections in the sclera from people who had a bug fly into their eye. The patient might not think anything of it at the time, but if a red eye develops, that’s a history that needs to be elicited.”

In addition to asking about prior ocular surgery or trauma, Dr. Lin queries the patient on what symptoms they

are experiencing and the time course. Are the symptoms worsening, are there flare-ups, or do they remain steady? Are both eyes affected or just one?

Medical history and review of systems. “Then I try to determine if there are any possible recent systemic illnesses, including a viral prodrome,” said Dr. Lin. “Other pertinent queries in the review of systems might include, Do you have painful cold sores? Do you have genital sores? Both of these suggest herpes infections. Have you experienced fevers, chills, nausea, vomiting, diarrhea, or weight loss recently?”

Dr. Davis noted, “Some people who have herpetic iridocyclitis will have had previous episodes. They may have a history of fever blisters or other herpetic infections, and then you would correlate that with the exam, where there’s often a lot of iris inflammation and loss of iris pigment.”

Dr. Moorthy added other pertinent questions for the medical history: “Have you been in the hospital and had an indwelling IV catheter? Were you receiving hyperalimentation or IV nutrition? Those things automatically tell us we should consider an infectious etiology. Are you immunocompromised because of HIV infection or cancer therapy? Cytomegalovirus retinitis can occur opportunistically in people who are severely immunocompromised [iatrogenically or from HIV].”

Next, he asks about rashes: “For example, did you have a tick bite after which you developed a target-shaped rash or a migrating rash? That might indicate Lyme disease or other arthropod-borne disease.” In connection with such a rash, “we ask whether the patient has achy joints or migratory arthritis. Conditions such as Lyme disease can cause significant arthritis.”

In addition, a bout of shingles on the side of the face or chest wall before the development of floaters and vision loss could indicate VZV-associated retinitis, a very serious infectious process, he said.

“Then we perform a pulmonary review of symptoms, usually asking if the patient has chronic cough or shortness of breath (e.g., TB or sarcoidosis), whether they have significant weight loss, night sweats, fevers, or chills,

which could suggest TB,” he said.

Social history. Information about a person’s national origin and travels can further focus the investigation. Dr. Davis asks patients where they grew up, which can be revealing for diseases that are endemic in areas outside the U.S. For example, she said, “Many people with Toxoplasma were infected in early childhood, so even if they’ve been in the United States for a long time, they could have been infected long ago and are only now having a recurrence of Toxoplasma chorioretinitis.”

Similarly, residence or travel in Southeast Asia and sub-Saharan Africa could raise the possibility of TB and diseases that are uncommon in the developed world.

Leisure or work activities may also be relevant. For example, people who drink from streams or other untreated water while camping or traveling in remote areas may develop waterborne infections including leptospirosis, giardiasis, and toxocariasis, as well as the more common toxoplasmosis.⁵

Dr. Moorthy also inquires about diet. “For example, a patient may recount, ‘I’m a deer hunter, and I like eating rare venison. And a few weeks after I ate it, I got floaters in my left eye.’ That could indicate acquired toxoplasmosis.”

1 Zhang Y et al. *PLoS ONE*. 2020;15(8):e0237995.

2 Tsiroki T et al. *Ocul Immunol Inflamm*. 2018; 26(1):2-16.

3 Lin P. *Curr Ophthalmol Rep*. 2015;3(3):170-183.

4 CDC. Accessed Feb. 18, 2023. www.cdc.gov/parasites/toxoplasmosis/.

5 Ahmad SS. *Saudi J Ophthalmol*. 2018;32(3):227-233.

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