Considerations in Chronic Uveitis Treatment

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Thomas Albini, MD, moderator of the Uveitis Resource Center, spoke with Steven Yeh, MD, of the Emory Eye Clinic, about local treatment options for patients with chronic uveitis. Their conversation follows:

Thomas Albini, MD: Complications of long-term systemic steroid use are a serious concern. What are appropriate long-term systemic steroid doses?

Steven Yeh, MD: Cortical steroids remain a mainstay of therapy for active non-infectious uveitis. For active disease, we will consider .5mg to 1mg per kg as a starting dose, and then we taper according to the level of disease activity aiming for complete lack of inflammation or complete disease inactivity. We try to reduce the steroids to less than 7.5 mg to 10 mg by three months of therapy, and if we're not able to do that then we'll consider alternative agents, including systemic steroid sparing medications, local sustained release cortical steroids or short term cortical steroids.

TA: What complications have you seen in patients who have been on long-term, high dose steroids?

SY: Long-term, high dose steroids can be associated with hypertension, osteoporosis, diabetes, weight gain, insomnia, anxiety and mood swings, among other things. I've actually seen patients become suicidal with long-term use of cortical steroids. Gastro-intestinal side effects, including peptic ulcers, are also something to consider. The most extreme GI-associated side effect I've seen is a perforated peptic ulcer.

TA: The Multicenter Uveitis Steroid Treatment (MUST) study, which looked at visual acuity as a primary outcome in patients who were randomized to either Retisert (fluocinolone acetonide intravitreal) implant or standard systemic therapy and found non-inferiority in terms of VA outcomes, fund that systemic treatment is well tolerated. Would you agree with that?

SY: I would definitely agree. We often think we should steer away from systemic medications because of the side effect profile, when the reality is, as was shown in the MUST study, that they are very well tolerated, at least in terms of severe infectious processes requiring hospitalization.

OTHER TREATMENT OPTIONS

TA: TNF alpha inhibitors and biologics are viable options for uveitis patients. What are your thoughts regarding outcomes and side effects with respect to these agents?

SY: Outcomes and side effects beyond 10 years are still unknown with these agents, however, based on findings from the Systemic Immunosuppressive Therapy for Eye Diseases (SITE) study, which retrospectively looked at whether there was increased mortality or morbidity with these drugs, I think this class of medications is very effective -- particularly infliximab and adalimumab.

There is a rare association with lymphoma, primarily in patients with inflammatory valve disease who were placed on anti-TNF agents. While this was relatively rare, it could certainly be a scary complication. It's also been shown in populations of patients with rheumatoid arthritis on these agents that there may be increased risk of lymphoma, but it's not clear if it's due to the anti-inflammatory agents or whether this is due to the rheumatoid arthritis, which may put them at risk.

SUSTAINED RELEASE AGENTS

TA: One of the most recently approved sustained release options is the biodegradable free-floating dexa-

methasone implant, Ozurdex, which was shown in the HURON Study Group to be effective in the treatment of uveitis. Has this had an impact on your practice patterns?

SY: From practice patterns standpoint, I think Ozurdex is an excellent treatment option. In the HURON study, treatment of CME with vitreous inflammation was effective and sustained for six months. In clinical practice Ozurdex has proven to be effective and sustained for treatment of CME with vitreous inflammation for a four to six month period. In my experience, some patients end up not needing another Ozurdex implant injection, whereas other patients will have some recurrent CME symptomatic and detectable on Optical Coherence Tomography (OCT) that will require retreatment.

TA: What are the benefits of Ozurdex relative to Triesence or Kenalog. What is your thought process on choosing one vs the other?

SY: We know more about the kinetics of Ozurdex over that of retroseptal corticosteroids, which are a little less predictable. The short term side effect profile of Ozurdex is quite favorable as far as progression to cataract or development of glaucoma. It also seems very well tolerated in the short term for patients who have a history of cortical steroid elevation with ocular pressure, and also a history of glaucoma.

TA: Some of the things that prompt me to use Ozurdex over other options are that with Ozurdex we can avoid anterior migration of the drug, pressure elevation is more manageable than with Triesence and studies show that dexamethazone may have decreased toxicity to retinal pigment epithelium photoreceptors relative to Triamcinolone.

TREATMENT STRATEGY

TA: What is your process with regard to choosing a local treatment strategy such as Retisert or Ozurdex vs a systemic approach?

SY: Once we ascertain that it is a condition where we have low grade chronic inflammation that can lead to vision loss over time we know it requires long term systemic immuno-suppressive therapy, or local corticosteroid therapy.

First, I knock down the active inflammation with 1 mg per kg of prednisone. Once the active disease is controlled, the next step in my algorithm is to determine whether the patient will need systemic medication or local sustained cortical steroid. More often than not I'll have a detailed discussion with the patient explaining that we have two very good options for treatment of this disease, and I have a discussion about side effects -- whether it's related to cataract and glaucoma with the Retisert implant or whether it's systemic therapies and the systemic side effects associated with them.

Other considerations include the patient's phakic status. If they still have their native lens and are young, I want to keep their accommodation and avoid cataract so that's one scenario where we have to think about systemic medication first.

TA: What clinical scenario do you most commonly find yourself opting for Ozurdex?

SY: Patients who have CME with vitreous haze respond well to the Ozurdex implant. Also, patients who have not responded to a retroseptal steroid injection, tend to respond well to Ozurdex because it has more predictable kinetics. This is true especially for patients with CME and intermediate uveitis, or for those who have a chronic disease, such as birdshot. ■