Rheum With a View: Management of JIA-Associated Uveitis in Adults

Transcript

Mara Becker, MD: I do think the steps that you take to establish those relationships with the ophthalmologists are really key.

Meghna Rao (Host): Welcome back to season 2 of the *Rheumatology Advisor* podcast, Rheum Advisor on Air. I'm Meghna Rao, the senior editor of *Rheumatology Advisor* and the host of this podcast.

In this series, we will be joined by expert clinicians and researchers to discuss emerging and compelling topics in rheumatology. These perspectives may be related to the management of rheumatic disease, guideline updates, patient care, data from conferences and scientific meetings, and much more.

In the next set of episodes, we're talking with some of the presenters of the all-virtual American College of Rheumatology (ACR) Convergence 2021.

So, let's dive in!

Meghna: Uveitis has been described as the most common extra-articular manifestation of juvenile idiopathic arthritis or JIA.

In today's episode, we're discussing the management of JIA in adults vs pediatric patients, with a focus on uveitis screening and treatment.

Let's welcome Dr Mara Becker, professor of pediatrics in the Division of Rheumatology and vice chair for faculty at Duke University Health System.

Thank you for joining us, Dr Becker, and it's a pleasure to talk with you today.

Dr Becker: Oh, thank you so much for having me. It's a pleasure to speak with you as well.

Meghna: I know we had some back and forth on the dates, but I'm glad we could make this happen finally.

Dr Becker: Absolutely, absolutely.

Meghna: So, we've reached the end of yet another ACR annual meeting that was incredibly insightful on different levels. Your presentation itself on Sunday, November 7, was one of those and it covered a lot of ground about JIA and its subtypes and management.

I think it would be really wise to focus on 1 aspect of JIA today to be able to provide a more comprehensive roundup. What do you think?

Dr Becker: Yeah, sounds perfect. Yeah, it was a big talk and so I appreciate breaking it down in whatever way you see fit. That sounds great.

Meghna: Excellent! So, let's talk specifically about JIA-associated uveitis in adults.

Now my first question, Dr Becker, is about screening, as someone had inquired after your presentation. To your colleagues in adult rheumatology, what would you recommend is the optimal way to go about screening for uveitis in adults with JIA? How can at-risk patients be identified and so on?

Dr Becker: Yeah, that's a great question. What we know so far is that the risk for chronic uveitis in JIA is definitely greatest in young girls, usually less than 7 [years], who [test antinuclear antibody] (ANA)-positive and who present with the subtypes of oligoarticular or rheumatoid factor-negative polyarticular subtypes of JIA. The risk is really the greatest earliest in the course of their disease, so within the first 4 years. So this means, by the time our high-risk pediatric patients are adults, by the time they transition to adults, if they have never had uveitis in all those years that we've been managing them in their pediatric sphere, their risk is starting to get lower by then. And so, really the thought is that they can obtain ophthalmology screening, at least through the recommendations that I was a part of creating, every 6 to 12 months.

Usually what I do is I'll send a referral to the ophthalmologist and explain specifically [that] the patient has JIA and needs screening for anterior uveitis at a frequency of X. You know, usually if they've never had uveitis for the whole time that we've managed them and, say, adult providers are taking on that transition care, then usually I'd say annually.

However, on the flip side, we know that for patients [with JIA] who do get uveitis, we know that that disease extends into adulthood and that those kids that do have uveitis are at definite risk for significant ocular sequelae, right? And those are kids that have chronic inflammation and can have vision-threatening complications. So we need to ensure that those kids continue to get regular assessments.

For the patients [with] well-controlled [disease], the recommendations are to really continue to screen them at least every 3 months. The reason for that, truly, is that we know that this inflammation can be silent, we know it doesn't necessarily have associated external signs that patients can pick up on. And so, if we don't screen it, we can miss it.

When [there are] significant complications and now adult has had increased risk for glaucoma or cataracts or has had surgery [t]o treat some of the consequences from their uveitis, frequency of monitoring might be much less – it might be every month or every 2 months, and that's something that usually gets negotiated between the [patient and the] ophthalmologist who is doing the primary management of some of those sequelae.

Some of the best, the most successful, relationships with ophthalmologists in this sphere have been ophthalmologists that actually have additional expertise in uveitis.

And so, for a patient in adulthood [who] does have uveitis that's being actively treated, [i]f you have the opportunity to partner with an ophthalmologist [who] has expertise in uveitis, I would say grab it because I have absolutely seen that degree of expertise be very useful in monitoring these kids and in monitoring the subtle changes that can occur to suggest that the disease reactivates and needs an adjustment in therapy.

Meghna: I think that's some great advice. On that note, several studies have pointed out barriers in uveitis screening among patients with JIA. Some of them have included the presence of asymptomatic uveitis, like you spoke about, and knowledge gaps.

Now in the wake of how important screening for uveitis is in adults with JIA, and as you also mentioned in your presentation, due to the significant increase in ocular complications over time, could you perhaps suggest a more streamlined approach for how clinicians can address these challenges and provide care at the same time?

Dr Becker: Sure. One obvious solution that may not necessarily realistic for everyone, depending on where you practice, is instituting a joint uveitis clinic. In at least the couple of centers that I worked at, that's been incredibly useful and by far offering the most optimal care. So it really does (a) establish really great relationships between both subspecialties and (b) helps to optimize and make the most efficient care possible to the patient. And there's no like back and forth delay between notes getting faxed to one person versus the other and then setting up a call to talk about next steps, et cetera.

However, I'm not naive to think that, certainly, in the adult world there [are] many more folks in private practice, and being in large groups associated with academic centers that make that kind of multidisciplinary clinic possible, isn't necessarily realistic.

And 1 thing that I did that we did in a previous place that I worked that did have a very large catchment area and required us to really partner with ophthalmologists [who] were in private practice is we started a systematic way of providing all of our patients a letter at their discharge from their clinic to address to their ophthalmologist or to their eye doctor to say, "Hey, this is a patient with JIA and this subtype. They're at risk for anterior uveitis and need to be screened at a frequency of X."

And what that started to do is really started to establish that relationship with the community ophthalmologists and what it really did is it helped them get to know us and helped us get to know them, and helped to streamline some of the

communication between maybe 2 very different types of practices and 2 very different, of course, subspecialties.

So I don't think you have to have a fancy ability to have a multidisciplinary clinic, but I do think the steps that you take to establish those relationships with the ophthalmologists are really key.

Meghna: That's incredible. And I think you're right to highlight that co-management of this population from both rheumatology and ophthalmology can be critical owing to the fact that JIA-U could lead to visually disabling complications and even carry a significant risk for morbidity.

Dr Becker: Absolutely. I think because it is not something that shows up so obviously to the patient, it's not going to be a big swollen joint that's going to impact their ability to walk, for example, or write, for example. It can sometimes be even dismissed by the family, right? They may not necessarily understand the urgency by which they need to be seen by the ophthalmologist to make a change.

Meghna: Kind of shifting our focus to treatment, I want to reiterate what you said at the ACR meeting that "treating children is not the same as treating adults."

Now, a 2-part question here, Dr Becker – how does treatment between these populations differ, and second, why the emphasis on this statement during your talk? Is it not as commonly known in the community?

Dr Becker: That makes me laugh! That statement I think, as a pediatrician, I we have always been trained that, clearly, children are not just little adults.

However, what's been happening in our field recently. I think I made that comment particularly in context of our discussions about JIA and really some of the reclassification discussions that are underway, recognizing that there are some similarities in genetic susceptibility that starts to make us think that, oh, some of these JIA subtypes that we have inadvertently classified based on their clinical phenotype have actually a lot more similarities to adult subtypes of arthritis than we probably originally recognized, with the exception of this early-onset arthritis subtype that is inherently at increased risk for uveitis. There is no real correlate to that subtype of arthritis in adulthood. But even when there are genetic susceptibilities to make us think, "Okay, well, maybe our [patients who test] rheumatoid factor-negative factor polyarticular JIA are really similar to the seronegative patients [with rheumatoid arthritis] as well."

The truth of the matter is, kids are different, right? There are changes in metabolism and drug distribution that happen over time, not just because of their size but also because of the time that certain enzymes turn on just physiologically for kids throughout development. There are definitely differences in the effects of drugs on a growing skeleton compared to one that is

not. Using corticosteroids in children is without question – we try to avoid that because we want their growth trajectories to be undisturbed, if you will.

Clearly the psychosocial development of children in their maturity over time into adolescence plays a role, adherence, and the way that they're coping with their chronic diseases, in addition to things like exposures and comorbidities, and negotiating, honestly, with not just the patient but also their families as well. I imagine that many of the adult rheumatologists that take on [patients with] chronic JIA have an adjustment period because they recognize that those parents might be a little bit more involved in some of the care and decision-making than many of their independent adult patients might be.

That being said, I think that some of the interesting things I've learned about managing pediatric patients different than adults is that parents and families are faced with a lot of really important decisions, right? Treatment decisions for kids that have chronic diseases.

We are providing them with this amazing new armamentarium of treatment choices that we have. I'm excited because I have so many more than I did 20 years ago. But the truth of the matter is, I can't always 100% reassure them of what the long-term consequences are going to be because we don't know that yet. That is anxiety-provoking for families.

On the flipside, what I use in that moment is I try to explain to families what we do know. What we do know though is that letting, say, anterior inflammation, the anterior chamber of the eye, go unchecked will result in visual consequences, will result in your increased risk for surgery, will result in the potential for blindness. Or, on the flipside, from an arthritis perspective, ongoing, untreated arthritis will result in joint damage, which can result in disability or joint replacement. Undertreating those conditions absolutely results in disability.

Meghna: What I'm thinking about what you just said is that critical transition from pediatric to adult rheumatology as well.

So, Dr Becker, what are the treatment goals for children vs adults with JIA and uveitis, knowing that early treatment is key and quality of life is, of course, important for all patients?

Dr Becker: Yeah, I think you just said it. I mean this is an easy one; for me, it's the same when I control the inflammation of the eye as soon as possible and as effectively as possible. What the main goal is to maintain vision and ocular health, period. I think remembering that it's silent, remembering that you can't look at a patient and know it's there unless, God forbid, you're at the end stages with a lot of damage.

I think the other thing to keep in mind that we, as a community and I think in the adult-provider world, also remember as well is that corticosteroids, even

though, ophthalmologists think that they are fairly innocuous – "little drops, just throw some drops in your eye," and that is okay temporarily – but we do know that there are ocular sequelae that can result in poor outcomes like glaucoma and cataracts.

And the truth of the matter is [o]ur comfort level with systemic immune-modulating therapies are much higher than an ophthalmologist's. So, sometimes, it does require us to say, "Hey, we've got medications at our disposal that can work for this and we don't have to keep patients on topical drops for months and months and months." That's where if you have a good relationship with them, you could say, "Let's try methotrexate or let's try a biologic" because truthfully, at some point, the risks for those topical treatments outweigh the benefits.

Meghna: Absolutely. [A]lluding to what you said and speaking specifically in terms of pharmacologic therapies, and again, speaking to the value of rheum-ophtho consults for these patients, would you say that rheumatologists need to consider treatment choices keeping in mind ophthalmalogic outcomes too, for example, with [disease-modifying antirheumatic drugs] (DMARDs) or tumor necrosis factor (TNF) inhibitors?

Dr Becker: Hmm, yeah, that's a good question.

So, not to beat a dead horse, but I would say, for sure, avoid glucocorticoids. I know adults use them probably more; there is more acceptability to using them as an adjunct for some of the treatment in adulthood. But I would say, don't forget about the eye and the consequences of glucocorticoids [on] the eye.

The second is that we, kind of, kill 2 birds with 1 stone but I did want to say that there are times that you're going to have to escalate treatment based on 1 organ or the other. For example, if you have a patient who has arthritis and uveitis and their arthritis is well-controlled but their uveitis is not, you need to cater your treatment choices to the organ that's not affected. That might mean that you have to increase the frequency or increase the dose or switch classes even if the arthritis is well-controlled if the uveitis is flaring or vice versa.

But the truth of the matter is the drugs we use for arthritis we know work pretty darn well for uveitis. So, the basics, like methotrexate, adalimumab, infliximab, and even some of the drugs that we have less exposure and knowledge with from the eye perspective, we have at least some case series and case reports of effective use with things like abatacept and tocilizumab, and now some emerging data on the [Janus kinase] JAK inhibitors.

So I do think that people continue to push the envelope because there are recalcitrant patients [who] just do not respond to the basics, which in my mind are methotrexate and TNF inhibitors. If they do not respond to those treatments, then we need to keep pushing, right, because of the most significant consequence, which is, clearly, visual impairment, which we're trying to avoid.

Meghna: Finally, just 1 last thing I wanted to touch on is in 2019 the ACR developed guidelines for diagnosis and treatment of JIA-associated uveitis in pediatrics. So, are those recommendations something that could be valuable for the management of adults as well or do you think separate guidance may be warranted?

Dr Becker: No, you know, I'm, kind of, a streamlined type of mindset. I would say absolutely they would be useful. [I] respect the fact that adults who are managing patients with JIA are not at the early-onset of their treatment often, right? I mean, there are definitely children who are managed by adult rheumatologists at least would be useful. But the concepts are still the same – treat effectively; treat early; screen frequently.

Remember that there are some helpful guidelines in the approaches to systemic immune-modulating treatment as far as the timing, not allowing topical steroids to go on unchecked forever; utilizing methotrexate TNF-blockade; thinking about escalating the dose, for example, or the frequency of the TNF blocker rather than just switching classes right away.

Also, the recognition that the monoclonal antibodies for TNF inhibition are recommended over etanercept and that is definitely based on data. So, we know that those agents – adalimumab and infliximab – perform way better than etanercept. And so, we don't use etanercept for uveitis anymore. But that's where the guidance is as applicable to adults as it is to children.

And frankly, once you have a patient, and many adult providers may be faced with transitioning new patients [who] are actively being treated for their uveitis when they get them, thinking about the frequency of monitoring for screening, which should be at least every 3 months.

And then some guidelines around the time you want to start to taper, which is if you get to the glorious time that you want to try to taper, even though the data so far are not that reassuring that it is going to be successful, but more data may emerge or there may be circumstances by which you need to taper off a medication, recommendations around the frequency of screening around that taper are also embedded in those guidelines, which I think is useful.

So, if you're tapering something like a systemic immune-modulating treatment, making sure you're partnering with the ophthalmology to screen in less than 2 months is really important because, again, it's the timing. It's not letting that inflammation go unchecked. The closer kind of handle you have on that, the better off that patient will do.

Meghna: Interesting. Dr Becker, thank you for sharing your insights on the subject. We will look forward to more compelling talks by you, hopefully in-person, in the near future.

Dr Becker: Oh, you're very kind. Thank you so much for having me.

Meghna: Please stay tuned for more episodes in this series. For more information on *Rheumatology Advisor* and this podcast, you can reach out to us at editor@rheumatologyadvisor.com.

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