The Journal of Rheumatology 2022;49:661–2
doi:10.3899/jrheum.220163
First Release April 15 2022

The Journal of Rheumatology

Editorial

Uveitis in Juvenile Psoriatic Arthritis: Still So Much To Learn

Kamiar Mireskandari[1]

Psoriatic arthritis (PsA) is a systemic inflammatory disease that includes uveitis as one of its extraarticular associations. Studies involving predominantly adult patients report a significant association between the incidence of uveitis and psoriasis, the risk of which is greatest in patients with severe PsA.[1,2] The literature on uveitis in children focuses mainly on risk factors for the more common forms of juvenile idiopathic arthritis (JIA) associated with uveitis and antinuclear antibody (ANA) positivity.[3,4] Information on juvenile PsA–associated uveitis (JPsA-U) is scarce, with detailed ophthalmic findings restricted to small case series.[5,6]

In this issue of *The Journal of Rheumatology*, Walscheid et al reported the results of a large population-based cohort study on 1862 patients with JPsA.[7] Cross-sectional data from the German National Pediatric Rheumatological Database (NPRD) were used to describe prevalence and risk factors for JPsA-U. The authors report that their cohort from 2002 to 2014 had documented uveitis in 6.6% (122/1862). Patients with JPsA-U were more frequently ANA positive (60.3% vs 37.0%, $P < 0.001$) and younger at JPsA onset (5.3 vs 9.3 yrs, $P < 0.001$) compared to patients without uveitis. Indeed, uveitis developed more frequently in those aged < 5 years at JPsA onset (17.3% [73/423] vs 3.8% [49/1306], $P < 0.001$). Further, patients with JPsA-U received disease-modifying antirheumatic drugs (DMARDs; both conventional synthetic and biologic) significantly more frequently than patients with JPsA (77.0% vs 44.3%; $P < 0.001$). Overall, the data demonstrated a similarly high risk for ocular involvement between JPsA and the JIA subgroup with oligoarthritis, which is the most frequently assessed JIA subtype in the literature.

The strength of the study by Walscheid et al[7] lies in the large sample size and data from a population-based cohort. As with any epidemiological study based on registry data, there is potential for information bias, selection bias, or confounding.[8] The NPRD had uniformity of data input from pediatric rheumatologists in accordance with International League of Associations for Rheumatology criteria.[9] However, data could be entered at any stage in the patient's journey and the majority of patients were included more than a year after their disease onset. Therefore, many confounders could have influenced the data summarized above. For example, the timing of medication used in relation to uveitis onset, the indication for which the medications were given, and their influence on uveitis occurrence are unknown for the whole cohort. In an attempt to address this, a subset of 655 (35%) patients who had their clinical characteristics captured within 1 year of PsA diagnosis was analyzed for information regarding prognostic factors for uveitis development. Multivariable analysis found only higher mean baseline disease activity, calculated using the Juvenile Arthritis Disease Activity Score 10 (cJADAS10; until first uveitis documentation), was significantly associated with the development of uveitis (hazard ratio 1.16, CI 1.02–1.31; $P = 0.03$).

From an ophthalmologist's perspective, the NPRD has the potential to collect valuable data on "anatomical types of uveitis, laterality, best-corrected visual acuity, uveitis complications, and characteristics of flare (sudden or insidious onset) according to the Standardization in Uveitis Nomenclature guidelines."[10,11] Currently, the largest detailed study on JPsA-U is a case series of 6 patients.[5] Therefore, the 122 patients with JPsA-U on the NPRD registry could provide crucial insights on this condition if the information could be obtained. However, the authors acknowledge that the ophthalmic data are available on only 22 patients, 17 of whom have data only at a single timepoint. This is an unfortunate limitation on the utility of large registries when it comes to addressing questions beyond the defined aim of the registry and the data it is designed to collect. Greater collabora-

[1]*K. Mireskandari, FRCOphth, PhD, John and Melinda Thompson Chair in Vision Research, Professor and Staff Ophthalmologist, Department of Ophthalmology and Vision Sciences, Hospital for Sick Children and University of Toronto, Toronto, Ontario, Canada.*

KM is on the advisory boards for Santen Canada Inc. and Novartis; and received research support from Bayer.

Address correspondence to Dr. K. Mireskandari, Department of Ophthalmology and Vision Sciences, Hospital for Sick Children and University of Toronto, 555 University Avenue, Toronto, ON M5G 1X8, Canada. Email: kamiar.mireskandari@sickkids.ca.

See Uveitis in juvenile PsA, *page 719*

tion and direct involvement of ophthalmologists with an interest in pediatrics or uveitis would be a great addition to this type of registry.

Excellent collaboration already exists between rheumatologists and ophthalmologists to prevent vision loss from complications of JIA-associated uveitis, the most devastating outcome for children and families. Development and refinement of screening criteria, monitoring, and treatment for childhood uveitis are well established in many jurisdictions.[12] These efforts have substantially improved long-term outcomes for our patients over the past few decades. A patient diagnosed with JIA-uveitis between 1973 and 1982 had a 7-year uveitis complication rate of 58%, with visual acuity of 20/40 or worse in their better eye of 21.7%.[13] This meant that over one-fifth of children could not reach the driving standard in most countries and their overall quality-adjusted life-years (QALY) was significantly affected. Two decades later, a similar Nordic patient cohort with JIA-uveitis from 1997 to 2000 had significant improvement in uveitis complication rate of 38.8% and visual acuity of 20/40 or worse in the better eye of 5%, even after 18 years of follow-up.[14] These cohorts were prior to our current understanding of the optimal use of conventional and biologic DMARDs.[12] It is likely that a patient diagnosed with JIA-uveitis today should have better long-term outcomes and QALY. In particular, earlier use of DMARDs reduces ocular complications that require surgical intervention, mainly cataract and glaucoma.[15]

To continue down our path toward better patient outcomes, we need to diagnose uveitis in a timely manner. We are reminded that unlike adults with PsA-U who have symptomatic ocular inflammation, children with JPsA-U behave similarly to those in other JIA categories and exhibit asymptomatic uveitis, underscoring the vital importance of ophthalmological screening.[5] JPsA is categorized as high risk for uveitis in screening guidelines and therefore requires monitoring every 3 months when a patient is diagnosed at age < 7 years and has JIA duration < 4 years.[12] This recommendation is further supported by data presented by Walscheid et al,[7] who showed that 45% of children who eventually developed uveitis had presented with JPsA by their 4th birthday.[7] More intriguing, the Kaplan-Meier analysis they present in Figure 1B[7] shows continued and steady incidence of new uveitis beyond 4 years after JPsA diagnosis. Typically, screening can become less frequent if there has been no uveitis 4 years after JPsA diagnosis; therefore, their data may require us to think differently and continue regular screening every 3 months. In this regard, large population-based cohorts such as NPRD can further inform our understanding of the risk factors for JIA-associated uveitis and improve our screening protocols.

REFERENCES

1. Lam M, Steen J, Lu JD, Vender R. The incidence and prevalence of uveitis in psoriasis: a systematic review and meta-analysis. J Cutan Med Surg 2020;24:601-7.
2. Chi CC, Tung TH, Wang J, et al. Risk of uveitis among people with psoriasis: a nationwide cohort study. JAMA Ophthalmol 2017;135:415-22.
3. Angeles-Han ST, Pelajo CF, Vogler LB, et al; CARRA Registry Investigators. Risk markers of juvenile idiopathic arthritis-associated uveitis in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry. J Rheumatol 2013;40:2088-96.
4. Tappeiner C, Klotsche J, Sengler C, et al. Risk factors and biomarkers for the occurrence of uveitis in juvenile idiopathic arthritis: data from the inception cohort of newly diagnosed patients with juvenile idiopathic arthritis study. Arthritis Rheumatol 2018;70:1685-94.
5. Salek SS, Pradeep A, Guly C, Ramanan AV, Rosenbaum JT. Uveitis and juvenile psoriatic arthritis or psoriasis. Am J Ophthalmol 2018;185:68-74.
6. Twilt M, Swart van den Berg M, van Meurs JC, ten Cate R, van Suijlekom-Smit LW. Persisting uveitis antedating psoriasis in two boys. Eur J Pediatr 2003;162:607-9.
7. Walscheid K, Rothaus K, Niewerth M, Klotsche J, Minden K, Heiligenhaus A. Occurrence and risk factors of uveitis in juvenile psoriatic arthritis: data from a population-based nationwide study in Germany. J Rheumatol 2022;49:719-24.
8. Kleinbaum DG, Kupper LL, Morgenstern H. Epidemiologic research: principles and quantitative methods. John Wiley & Sons; 1982.
9. Stoll ML, Lio P, Sundel RP, Nigrovic PA. Comparison of Vancouver and International League of Associations for rheumatology classification criteria for juvenile psoriatic arthritis. Arthritis Rheum 2008;59:51-8.
10. Jabs DA, Nussenblatt RB, Rosenbaum JT; Standardization of Uveitis Nomenclature (SUN) Working Group. Standardization of uveitis nomenclature for reporting clinical data. Results of the first international workshop. Am J Ophthalmol 2005;140:509-16.
11. Standardization of Uveitis Nomenclature (SUN) Working Group. Classification criteria for juvenile idiopathic arthritis-associated chronic anterior uveitis. Am J Ophthalmol 2021;228:192-7.
12. Angeles-Han ST, Ringold S, Beukelman T, et al. 2019 American College of Rheumatology/Arthritis foundation guideline for the screening, monitoring, and treatment of juvenile idiopathic arthritis-associated uveitis. Arthritis Care Res 2019;71:703-16.
13. Skarin A, Elborgh R, Edlund E, Bengtsson-Stigmar E. Long-term follow-up of patients with uveitis associated with juvenile idiopathic arthritis: a cohort study. Ocul Immunol Inflamm 2009;17:104-8.
14. Rypdal V, Glerup M, Songstad NT, et al; Nordic Study Group of Pediatric Rheumatology. Uveitis in juvenile idiopathic arthritis: 18-year outcome in the population-based nordic cohort study. Ophthalmology 2021;128:598-608.
15. Cheung CSY, Mireskandari K, Ali A, Silverman E, Tehrani N. Earlier use of systemic immunosuppression is associated with fewer ophthalmic surgeries in paediatric non-infectious uveitis. Br J Ophthalmol 2020;104:938-42.