Association of Systemic Lupus Erythematosus With Uveitis

Kevin Gallagher, BMBCh, FRCOphth; Ananth Viswanathan, FRCOphth; Narciss Okhravi, FRCOphth, PhD

SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) can be associated with uveitis. The reported prevalence of SLE in patients with uveitis varies from 0.1% to 4.8%. Accordingly, the positive predictive value of antinuclear antibody testing in diagnosing SLE in a patient with uveitis varies enormously. An accurate estimate of SLE prevalence in uveitis is needed to establish the value of routine antinuclear antibody testing in patients with uveitis.

OBSERVATIONS A literature review using the Medline database was performed to find studies reporting data on uveitis etiology from January 1, 1984, to March 20, 2015. Studies were included where there were sufficient data to draw conclusions on the prevalence of SLE as an etiological factor in uveitis. Data for 53,315 patients were reviewed and 63 studies from 30 countries were included. The prevalence of SLE as a cause of uveitis was estimated to be 0.47% (95% CI, 0.41%-0.53%). The positive predictive value of routine antinuclear antibody testing was 2.9% (95% CI, 2.65%-3.19%).

CONCLUSIONS AND RELEVANCE Systemic lupus erythematosus is a rare cause of uveitis. Routine antinuclear antibody testing has a low positive predictive value for SLE. These data suggest such testing should be reserved for patients where there is a higher pretest probability of SLE.

The aim of this brief report was to provide an estimate of the prevalence of SLE as a cause of uveitis in patients attending specialist clinics based on worldwide reports of uveitis etiologies.

Methods

An extensive literature search using the Medline database was conducted from January 1, 1984, to March 20, 2015. Search terms included uveitis, etiology, patterns, epidemiology, and classification. Articles in English and pertaining to humans were included. The inclusion of studies was limited to those reporting on uveitis in adults and those that included sufficient data on etiology from which conclusions about SLE prevalence could be drawn.

In studies where all cases were assigned a diagnosis, the number of cases with SLE was recorded. In a number of studies, disease entities with low frequencies were grouped as other or miscellaneous. In these circumstances, certain assumptions were made to estimate SLE frequency. Such assumptions were designed to give the highest possible estimate of SLE frequency. For example, if a miscellaneous group with 16 patients and any 1 of a possible 6 diagnoses...
were found recorded in a table of etiologies and in the same table, a diagnosis that appeared in 4 or more cases was mentioned specifically, then the assumption was made that no more than 3 of the cases in the miscellaneous group could be secondary to SLE. By using this method, a value for the likely maximum of SLE prevalence in uveitis was determined. We also calculated the prevalence by only counting cases where a diagnosis of SLE was specifically mentioned.

Results

In total, 63 studies were included that reported on the etiology of uveitis in 53,315 patients (eReferences in the Supplement). There was a range of 42 to 8759 patients (median, 548 patients; mean, 833 patients). Five studies reported exclusively on anterior uveitis, 2 reported on intermediate uveitis only, and 1 reported only on posterior and panuveitis combined. One study did not report on cases of intermediate uveitis. All other studies included cases with anterior uveitis, intermediate uveitis, posterior uveitis, and panuveitis.

The mean SLE prevalence for all studies combined was 0.47% (95% CI, 0.41%-0.53%). If cases were only counted where SLE was specifically mentioned, the prevalence estimate was 0.31% (eTable in the Supplement).

The anatomical classification of uveitis associated with SLE was presented in only 18 studies. In these 18 studies, there were 72 cases of anterior uveitis, 3 cases of intermediate uveitis, 26 cases of posterior uveitis, and 4 cases of panuveitis.

Discussion

The overall prevalence of SLE in patients with uveitis seen in specialist clinics was 0.47%. If we used this value as the pretest probability in the Rosenbaum and Wernick analysis1 (specificity, 85%; sensitivity, 95%), we could derive values for the positive and negative predictive values of positive and negative ANA test results (Figure 1). The posttest probability of a patient with a positive ANA test result (ie, positive predictive value) was 2.9% (95% CI, 2.65%-3.19%). Therefore, for every true-positive test result, there were 34 false-positive test results (Figure 2).

Figure 1. Bayesian Analysis of Routine Antinuclear Antibody Testing in Patients With Uveitis

Positive predictive value = \( \frac{447}{447 + 14929} = 0.029 = 2.9\% \)

Negative predictive value = \( \frac{84601}{23 + 84601} = 0.9997 = 99.97\% \)
The specificity and sensitivity of ANA testing in diagnosing SLE varies in the literature. One series found the sensitivity to be only 70%. Other studies calculated the specificity and sensitivity of ANA testing in diagnosing SLE as 92% and 98%, respectively. Substituting these values into the calculations in the eTable in the Supplement gave a positive predictive value of 5.47% and negative predictive value of 99.99% (calculations not shown). Even with this improved sensitivity and specificity, for every true-positive ANA test result, there were 19 false-positive test results. False-positive test results may lead to anxiety for patients as well as costs in time and money in the referral for a rheumatology assessment.

Our estimated SLE prevalence in uveitis of 0.47% is a likely overestimate given the assumptions described earlier. If we use the lower estimated prevalence of 0.31%, the positive predictive value of a positive ANA test result is less than 2%.

Figure 2. Icon Array Showing Results of Antinuclear Antibody Testing in 1000 Patients With Uveitis

Prevalence was 0.47%, sensitivity was 95%, and specificity was 85%. There were 34 false-positive test results for every true-positive test result.

Conclusions

Our theoretical calculations for the positive predictive value of a positive ANA test result in uveitis were very close to those found in another study investigating patients who were referred to a tertiary rheumatology clinic for evaluation of a positive ANA test result. The authors confirmed the poor positive predictive value of a positive ANA test result for SLE was 2.1%. This low positive predictive value was largely due to unnecessary testing in patients with low pre-test probabilities of the disease. Our study reinforces this view and suggests that routine testing of ANA in patients with uveitis is not justified (an exception would be in patients with juvenile idiopathic arthritis and uveitis where a positive ANA test result may influence management and follow-up). A positive test result is much more likely to rep-
resent a false-positive test result than a true-positive test result. Patients with systemic features suggestive of SLE or in cases where the ocular phenotype is in keeping with SLE (eg, scleritis or retinal arteritis) will have a higher pretest probability. Our analysis suggests that ANA testing in these cases would be warranted.

ARTICLE INFORMATION
Submitted for Publication: March 30, 2015; final revision received May 28, 2015; accepted May 29, 2015.
Published Online: July 16, 2015.

Author Contributions: Dr Gallagher had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: All authors.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: All authors.
Critical revision of the manuscript for important intellectual content: Viswanathan, Okhravi.
Statistical analysis: All authors.
Administrative, technical, or material support: Okhravi.
Study supervision: Viswanathan, Okhravi.

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

REFERENCES