Detection of Ro/SS-A antibodies in lupus erythematosus: What does it mean for the dermatologist?

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Background: Lupus erythematosus (LE) is a systemic autoimmune disease. However, some patients have only cutaneous LE (CLE), whereas others develop internal organ involvement. Ro/SS-A antibodies are frequently detected in photosensitive variants of LE.

Objective: The prevalence of LE-specific and LE-nonspecific cutaneous manifestations and their relation to internal organ involvement in Ro/SS-A antibody–positive patients were investigated.

Methods: All Ro/SS-A-positive patients between January 2000 and December 2011 were reviewed. Only patients with Ro/SS-A antibodies and LE were enrolled and retrospectively analyzed.

Results: In all, 215 Ro/SS-A antibody–positive patients were given the diagnosis of LE. Older patients (>50 years old) presenting with subacute CLE or chronic CLE and negative antinuclear antibody usually only experienced skin involvement. In contrast, internal organ involvement was observed in younger patients (<50 years old) with subacute CLE or chronic CLE presenting with the clinical and laboratory markers: fatigue, positive antinuclear antibody, and additional extractable nuclear antigen. Young female patients with acute CLE should be recognized as a separate subset of Ro/SS-A antibody–positive patients because almost a third was given the diagnosis of kidney involvement. Logistic regression analysis revealed that internal organ involvement was observed in patients with LE presenting with LE-nonspecific cutaneous manifestations, arthralgia, leukopenia, positive antinuclear antibody, and fatigue.

Limitations: This was a retrospective study from a single referral center specializing in dermatologic diseases.

Conclusion: The particular cutaneous variant of LE and age at Ro/SS-A detection predict different risks for internal organ involvement in Ro/SS-A antibody–positive patients with LE. (J Am Acad Dermatol 2013;68:385-94.)

Key words: internal organ involvement; lupus erythematosus; lupus erythematosus–nonspecific cutaneous manifestations; lupus erythematosus–specific cutaneous manifestations; Ro/SS-A antibody.

Ro/SS-A antibodies are prevalent among patients with connective tissue disorders.[1-4] They are found in patients with systemic lupus erythematosus (SLE), Sjögren syndrome (SS), SLE/SS overlap, neonatal lupus erythematosus (LE), and homozygous C2 or C4 deficiency. Moreover, they were detected in cutaneous LE (CLE), for instance, subacute CLE (SCLE),[5] chronic CLE (CCLE) such as discoid LE (DLE)[6] and chilblain LE (CHLE),[7] drug-induced LE,[8] and LE tumidus (LET).[9]

So far, several studies[4-11] have described the clinical characteristics of patients with LE and Ro/SS-A antibodies. Ro/SS-A antibodies were detected in 30% to 65% of patients with SLE[11-13] and were

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associated with skin, joint, hematologic, and kidney manifestations.[13-15] In addition, elevated liver enzymes and pneumonitis were described.[11]

Several studies deal with the relationship among LE, photosensitivity, and Ro/SS-A antibodies.[16-19] Ro/SS-A antigen expression in skin and the titer of circulating Ro/SS-A antibodies are greater in patients with LE and photosensitivity than in patients with LE without photosensitivity.[20]

The prognosis of patients with CLE who do not fulfill American Rheumatism Association (ARA) criteria is not always obvious.[21] Determining which patients with CLE are at higher risk for internal organ involvement is of central importance. Given the association of Ro/SS-A antibody with specific organ involvement in patients with LE, studying Ro/SS-A antibody–positive patients with LE may give more insight into this question.

Furthermore, besides having LE-specific skin lesions,[22] patients with LE can also develop so-called LE-nonspecific skin lesions.[23] The identification of LE-nonspecific skin lesions has been highly associated with systemic involvement.[24,25] So far, LE-specific and -nonspecific lesions and their impact on internal organ involvement have not been investigated in Ro/SS-A antibody–positive patients with LE.

Our study aimed to investigate skin manifestations (LE-specific and -nonspecific lesions) in Ro/SS-A antibody–positive patients with SLE, SLE/SS, or CLE and their correlation to laboratory and clinical features.

CAPSULE SUMMARY

- Scant information is available regarding clinical or laboratory features that predict internal organ involvement in Ro/SS-A antibody–positive patients with lupus erythematosus (LE).
- This retrospective study establishes associations among specific and nonspecific LE skin lesions, laboratory features, and additional internal organ involvement.
- Internal organ involvement was most commonly observed in Ro/SS-A antibody–positive patients with LE presenting with LE-nonspecific cutaneous manifestations, leukopenia, positive antinuclear antibody, and fatigue. Ro/SS-A antibody–positive patients presenting with acute cutaneous LE and mucosal LE were considered at high risk among patients with Ro/SS-A antibodies and LE, because they had the highest frequency of lupus nephritis and serositis, respectively.

METHODS

Ro/SS-A antibody positivity was defined by at least 1 positive enzyme-linked immunosorbent assay test result. They were determined by an indirect noncompetitive enzyme immunoassay (Varelisa ANA Profile EIA kit, Phadia GmbH, Freiburg, Germany) using Ro/SS-A (52 kd and 60 kd) as recombinant antigens.

Study cohort

A total of 12,374 consecutive sera were tested for Ro/SS-A antibody in our immunology laboratory (January 2000 through December 2011). Ro/SS-A antibodies were tested in all antinuclear antibody (ANA)-positive patients or if specifically requested by the referring physician (Fig 1). Ethics approval was not required because it was a retrospective study.

CLE was diagnosed according to Gilliam and Sontheimer[22,23,26]: in detail acute CLE (ACLE) (malar rash, morbilliform/maculopapular exanthema), SCLE (annular and/or papulosquamous/psoriasiform rash), DLE (erythematous, discoid hyperkeratotic plaques with scarring), CHLE (tender, bright-red edema, puffy nodules—acral skin), LET (succulent, erythematous/violaceous nonscarring, papules, and urticarial plaques), LE profundus (subcutaneous nodules/plaques that heal with scarring, lesional surface: reddened, unchanged or concomitant DLE), mucosal LE (MLE) (erythematous macules, palatal erythema, ulcers, blisters, erosions on mucosa). The clinical picture was correlated in all patients with histopathology results of skin biopsy specimens. However, biopsy specimens were only taken in 2 patients with MLE and therefore it was usually diagnosed based on the clinical picture. SLE was diagnosed according to the revised ARA criteria[27] and the remaining diseases (SS,[28] antiphospholipid syndrome [APS],[29] etc[30-32]) were diagnosed according to general accepted guidelines. SLE, CLE, SS, SS/SLE overlap, scleroderma, dermatomyositis, rheumatoid arthritis, mixed connective tissue disease, and undifferentiated connective tissue disease were summarized as autoimmune connective tissue diseases. The autoimmune disease group further encompasses diseases such as vitiligo, Hashimoto thyroiditis, and APS.

Demographic data, along with clinical and laboratory findings, were routinely documented at the first and/or following visit (regular intervals, 3-6 months) and retrospectively analyzed by chart review. Clinical features, such as skin involvement (specific and nonspecific LE skin lesions)[23]; arthralgia; myalgia; fever; fatigue; sicca symptoms; kidney, neurologic, lung, and heart involvement; serositis; and