ARTICLE 4

PREVALENCE OF INFECTIVE ENDOCARDITIS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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A B S T R A C T

Background. Compared with the general population, patients with systemic lupus erythematosus, or SLE, have an increased prevalence of functionally impaired cardiac valves due to the presence of Libman-Sacks lesions. These lesions may place patients with SLE at risk of developing infective endocarditis, or IE.

Methods. The authors performed a retrospective chart review to determine the association between SLE with valvulopathy and IE. They reviewed the records of 361 patients from two health care facilities who had the diagnostic code of SLE.

Results. Of the 275 records that met the 1982 revised American Rheumatism Association criteria for SLE, 51 (18.5 percent) were for patients who had a clinically detectable heart murmur that resulted in echocardiography being performed. Nine (3.3 percent) of the 275 patients had a clinically significant valvular abnormality, three (1.1 percent) had a potentially significant valvular abnormality, and one (0.4 percent) had a history of IE that was diagnosed two years before her diagnosis of SLE was made.

Conclusions. The findings suggest that 18.5 percent of this cohort of patients with SLE had a clinically detectable heart murmur that would require further investigation to determine its significance. Furthermore, between 3.3 and 4.4 percent of the study population had cardiac valve abnormalities that potentially required antibiotic prophylaxis before certain dental procedures. However, the authors identified no cases that demonstrated an association between IE and diagnosed SLE.

Clinical Implications. Dentists should query their patients with SLE about their cardiac status and consult with the patient's physician if the cardiac status is unknown. Patients with confirmed valvular abnormalities should receive antibiotic prophylaxis for designated bacteremia-producing dental procedures.

Several cross-sectional, prospective and retrospective studies have demonstrated that patients with systemic lupus erythematosus, or SLE, have an increased prevalence of cardiovascular abnormalities, including endocarditis, myocarditis, pericarditis and coronary artery disease secondary to atherosclerosis or arteritis.[1-4] Of the cardiovascular abnormalities associated with SLE, Libman-Sacks endocarditis (that is, verrucous endocarditis) is the most common endocardial lesion.[5-8] These vegetative lesions consist of sterile fibrin and platelet accumulations that do not shed emboli.

Verrucous lesions are reported to occur in 9 to 60 percent of patients with SLE.[9-16] The pathogenesis of verrucous endocarditis in SLE is not known. Several researchers have reported a correlation between valvular disease and immune mechanisms mediated by antiphospholipid (for example, anticardiolipin) antibodies.[17-23] However, the pathogenic role of antiphospholipid antibodies in the mediation of valvular disease has not been shown definitively. Nevertheless, functionally impaired cardiac valves resulting from the presence of Libman-Sacks lesions are prone to hemodynamic changes and may place patients at risk of developing infective endocarditis, or IE. In spite of this risk association, some physicians have in-

TABLE

PATIENTS WITH CLINICAL AND LABORATORY CRITERIA FOR SYSTEMIC LUPUS ERYTHEMATOSUS.*

FINDING	NUMBER (PERCENT) OF POSITIVE FINDINGS (N = 275)†
Malar rash	140 (51)
Discoid rash	22 (8)
Photosensitivity	99 (36)
Oral ulcerations	79 (29)
Arthritis	213 (77)
Serositis	148 (54)
Renal disorder	83 (30)
Neurological disorder	62 (23)
Hematologic disorder	102 (37)
Immunological disorder	
Anti–double-stranded-DNA test	121 (44)
Anti-Smith test	20 (7)
False-positive serologic test for syphilis	13 (5)
Positive antinuclear antibody	242 (88)

* According to the 1982 revised American Rheumatism Association criteria.[35]
† Laboratory parameters were not obtained for every patient, and the results reflect the percentage of the total number of patient records reviewed that had positive findings.

dicated that IE among patients with SLE is not common (Willie O'Connor, M.D., oral communication, June 1997).

The prevalence of IE in patients with SLE is reported to range from 1 to 4 percent.[2,24-26] However, the true prevalence of patients with SLE who are at risk of developing IE has not been determined, in part because most of the findings have been based on autopsy studies.[6,12] This is potentially problematic because auscultation and echocardiographic findings often underestimate the endocardial findings identified at autopsies of patients with SLE.[8,9,11,27,28] Of even greater importance, it is unclear whether the valvulopathy commonly associated with SLE constitutes a significant risk factor for the development of IE.

The risk of IE developing in patients with SLE as determined in presteroid-era studies (roughly before the mid-1970s) may not correlate with the risk determined in poststeroid-era studies. This may be important because long-term use of corticosteroids, a common treatment for patients with SLE, may predispose them to bacterial infections.[29-32] Conversely, steroid use can result in decreased size and number of Libman-Sacks lesions, which may decrease the risk of IE.[12] However, because steroid healing leads to fibrotic and retracted leaflet tissue, the risk of valvular dysfunction may, paradoxically, be increased.[33] De Rossi and Glick[26] recently reported that up to 3.9 percent of patients with SLE and valvular pathology, if treated with glucocorticosteroids, will develop IE.

The question of whether there is an increased risk of developing IE secondary to cardiac involvement and valvular pathology in patients with SLE who are receiving dental treatment prompted us to undertake this investigation. Our main purpose was to determine the prevalence of IE in a group of patients with SLE and to compare this finding with those of previous prevalence studies of IE in cases of SLE.

MATERIALS AND METHODS

We conducted a retrospective chart review of all inpatients and outpatients attending the University of Kentucky Medical Center, or UKMC, and the Lexington Clinic Foundation (a large community group practice) from 1980 to 1995 who had SLE according to the diagnostic code established by the International Classification of Diseases, 9th Revision, Clinical Modification, or ICD-9-CM.[34] Our goal was to determine the prevalence of IE among these patients. We accepted the diagnosis of SLE only when four of the 11 diagnostic criteria from the revised criteria for SLE of the American Rheumatism Association, or ARA, were fulfilled.[35] The diagnosis of IE was accepted when at least two positive blood cultures were detected in association with a new or changing cardiac murmur and echocardiographic evidence of valvular vegetations. The final cohort consisted of 275 patients with SLE, 117 from UKMC and 158 from the Lexington Clinic.

We recorded the specific criteria for each patient that led to the diagnosis of SLE, as well as the results of immunological tests (that is, lupus anticoagulant; anticardiolipin antibody; Venereal Disease Research Laboratory test for syphilis; anti-Smith, or anti-Sm; antiribonuclear protein, or anti-RNP; anti-Sjögren's syndrome A, or anti-SSA [LA]; and anti-Sjögren's syndrome B, or anti-SSB [RO]). We also noted the presence of a cardiac murmur according to auscultation or valvular abnormality, as determined by electrocardiography; transthoracic echocardiography, or TTE; or other cardiac test. To determine the correlation between SLE and IE, we conducted a computer search of all patients admitted to UKMC between 1980 and 1995 with the diagnosis of SLE and matched their identifiers with diagnostic codes of patients with all types of endocarditis. Statistical analysis was performed with SAS/STAT, release 6.12 (SAS Institute Inc.).

RESULTS

A total of 506,453 hospital admissions and 235,269 outpatient visits for all diagnoses were recorded from the two facilities between 1980 and 1995. Among these, 361 records were identified with the ICD-9-CM diagnostic code for SLE, and 275 patients fulfilled the revised ARA criteria for SLE. The study group was 90.2 percent female (248 patients), 9.8 percent male (27 patients), 88 percent white (242 patients) and 12 percent African-American (33 patients). The mean age of subjects was 44.6 years, with a range of 14 to 89 years. The mean number of ARA criteria that subjects met at the time of review was 4.8 (range, four to nine). The mean duration of the disease was 74 months.

The table summarizes the clinical and laboratory features of the series. Common findings were positive antinuclear antibody, or ANA, test results and arthritis. Infrequent findings were false-positive serologic test results for syphilis, or STS, positive anti-Sm test results and discoid rash. We identified one or more immunological abnormalities (including a positive ANA finding) in 91 percent of patients. One hundred twenty-one (44 percent) of 275 patients had one immunological abnormality, 87 (32 percent) had two abnormalities, 22 (8 percent) had three abnormalities and 18 (7 percent) had four abnormalities. We detected lupus anticoagulant in three (12 percent) of 26 patients, anti-RNP in 24 (20 percent) of 123 patients, anticardiolipin antibody in 21 (39 percent) of 54 patients, anti-SSA (LA) in 46 (44 percent) of 104 patients and anti-SSB (RO) in 12 (13 percent) of 90 patients.

Cardiac murmurs were identified by auscultation in 51 (18.5 percent) of 275 patients.

Cardiac murmurs were identified by auscultation in 51 (18.5 percent) of 275 patients. The mean age (± standard deviation) of patients with a cardiac murmur was 42 ± 9.3 years. TTE was performed on 23 patients with murmurs and revealed significant cardiac disease in 18 patients (78 percent) (that is, mitral valve prolapse [three patients], aortic valve disease [four patients], mitral valve disease [two patients], idiopathic hypertrophic subaortic stenosis [one patient], myocarditis [two patients] and pericarditis [six patients]). No cases of Libman-Sacks endocarditis were identified. Two patients with SLE and murmurs had undergone valve replacements, one as a result of rheumatic heart disease and the other as a result of congenital aortic defect. A third patient with SLE had a history of rheumatic fever and a heart murmur.

Our review of both the patient records and the computer search revealed only one case of IE to have occurred among the 275 patients with SLE. However, the IE occurred two years before the patient received the diagnosis of SLE. The index patient was a 62-year-old woman who was diagnosed with IE in December 1988. The endocarditis was of the mitral valve and the microbe isolated was *Streptococcus viridans*. The patient denied having a history of rheumatic fever, recent dental procedures, dental infections or other risk factors for bacteremia. However, one of us (C.S.M.) conducted a telephone interview with a member of her dentist's staff who indicated that a dental appointment had taken place no more than 30 days before the diagnosis of IE was made. Information about the nature of the dental treatment was not available.

The patient was hospitalized and treated for IE, and recovered without incident. In 1988, her ANA test result was negative. Two years later, she devel-

oped pancytopenia, hemolytic anemia, cerebritis and nephritis. Her ANA test result was positive at 1:160, multiple blood cultures were negative, and the patient was diagnosed with SLE. In 1994, she developed cervical lymphadenopathy and was found to have non-Hodgkin's lymphoma. She died shortly thereafter of acute pulmonary edema.

DISCUSSION

We initiated this retrospective chart review to determine the prevalence of IE in a large cohort of patients with SLE and to correlate this finding with those of previous studies of IE in SLE as well as studies of heart disease in SLE. Previous studies have reported a 10 to 74 percent prevalence of valvular abnormalities in patients with SLE, [8,9,15,26,36,37] with a mean prevalence of about 35 percent.[2,4,11,18,23,38,39] Although the prevalence of valvular problems found in this study is much lower (3.3 to 4.4 percent) than those previously reported, the actual number of undiagnosed cardiac problems may have been higher, since TTE was performed on only 8 percent of patients. Of the 23 patients evaluated by TTE, 18 (78 percent) had significant cardiac disease. In a finding similar to those of other studies, the mitral valve was most commonly involved in patients in our study.[4,38,40]

Valvular disease and renal disease are common in SLE and can result in marked hemodynamic dysfunction. When present, these diseases combined with abnormalities in the reticuloendothelial system and complement pathway presumably place patients who have SLE at risk of developing IE.[41] Other studies have reported a prevalence of IE in patients with SLE of 1 to 7 percent.[2,25,27,42] The 7 percent prevalence was determined from postmortem studies of patients with SLE before the era of corticosteroid therapy.[7,11,43-45] More recent compilations of cases involving patients who received corticosteroid therapy demonstrate a prevalence of 4 percent in postmortem studies[6,12] and 1.3 percent in studies of clinical patients.[2,46] These clinical rates of IE are comparable to those in patients who have prosthetic heart valves.[47-49]

The prevalence of IE in our study, however, was 0 percent,

Patients with systemic lupus erythematosus and known valvular abnormalities should receive antibiotic prophylaxis before undergoing designated bacteremia-producing procedures.

a figure much lower than those of previous studies. The low prevalence reported here approaches that of the general population (0.002 to 0.004 percent)[48] and may be the result of several factors:

- a decrease in the prevalence of IE in patients with SLE as a result of their receiving corticosteroid therapy;
- an overestimation of IE in cases of SLE in previous studies;
- limitations inherent in a retrospective chart review with regard to patient mobility, in that treatment for IE could have occurred at another facility;
- unique immunological status of these patients;
- this study cohort's not being representative of the general SLE population.

The last possibility seems unlikely, in that the demographics and clinical and laboratory criteria for SLE among this patient population appear similar to those found in other studies.[4,36] Alternatively, it is possible that the patient diagnosed with IE in this study had SLE at the same time, but remained undiagnosed for two years. This possibility is plausible because SLE can be a disease of evolution that demonstrates a variable course.[50] If this scenario were true, the prevalence of IE in this study would have been 0.36 percent, a rate similar to that in patients with rheumatic heart disease (0.3 to 0.4 percent).[51,52]

Although the current AHA recommendations for preventing bacterial endocarditis do not mention the need for antibiotic prophylaxis in patients with SLE, acquired valvular dysfunction (for example, owing to collagen vascular disease) is included as an indication.[53] Therefore, patients with SLE and known valvular abnormalities, as defined in the high- or moderate-risk categories according to the AHA recommendations, should receive antibiotic prophylaxis before undergoing designated bacteremia-producing procedures. In this study, at least 3.3 percent of patients would have met the criteria for receiving antibiotic prophylaxis and another 1.1 percent would have required further evaluation to make a determination of the need for prophylaxis. Consequently, den-

tal practitioners should query patients with SLE about their cardiac status before performing invasive dental procedures.

Cardiac pathoses may remain clinically silent and undiagnosed in patients with SLE, potentially placing them at risk of developing IE. This is evident by the fact that only 8 percent of all patients in this cohort underwent echocardiography for evaluation of valvulopathy. The limited number of patients who underwent TTE may have been related to the fact that most patients in this cohort were women, and fewer cardiac diagnostic tests are usually performed on women than men.[54,55]

These data suggest that cardiac pathoses may be undiagnosed in patients with SLE despite the fact that their condition is being followed by a physician. For patients with SLE in whom the presence of a valve defect is uncertain and for whom a bacteremia-producing procedure is planned, we recommend that the dentist refer them for cardiac evaluation. Normal echocardiographic findings dictate that no prophylaxis is required. If the patient's physician detects a murmur, valvular disorder or flow abnormality that would increase the likelihood of bacterial adherence on the valve, then antibiotic prophylaxis is recommended for potentially bacteremia-producing dental procedures. The findings of this study do not support a recommendation to provide prophylaxis for designated bacteremia-producing procedures in patients with SLE and unknown cardiovalvular problems.

CONCLUSION

This retrospective chart review suggests that at least 3.3 to 4.4 percent of patients with SLE were potentially at risk of developing IE; however, IE was not identified in any patients in this cohort who had a confirmed diagnosis of SLE. The data suggest that many patients with SLE did not undergo TTE and their cardiac status is uncertain. Dentists should query patients with SLE about their cardiac status, and consider consulting with the patient's physician if dental procedures are planned that could affect the cardiovascular status of a patient with uncertain cardiac function. Further studies are required to determine the biomedical and biochemical factors that place patients with SLE at risk of developing valvular disease and IE in the corticosteroid era. ■

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