

Frequency of Lymphadenopathy in Rheumatoid Arthritis and Systemic Lupus Erythematosus

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This study aimed to assess the frequency of all palpable lymph nodes during active disease and remission in patients with rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). Hospital records of 100 SLE patients, 100 RA patients, 100 spondyloarthropathy patients, and 150 osteoarthritis patients, treated in our rheumatology department, were evaluated retrospectively. Overall frequencies of enlarged lymph nodes in patients with active RA and SLE were 82% and 69%, respectively. Enlarged lymph nodes associated with RA were mostly

located in the axillary region, and in SLE the nodes were smaller and lymphadenopathy was more generalized compared with RA. Palpable lymph nodes disappeared in the majority of patients during remission. Lymphadenopathy was significantly less frequent in patients treated with steroids before admission. Lymph node enlargement is an important physical finding associated with RA and SLE disease activity. Atypical locations and unusually large lymph nodes should raise clinical suspicion of another underlying disease.

KEY WORDS: LYMPHADENOPATHY; LYMPH NODES; RHEUMATOID ARTHRITIS;
SYSTEMIC LUPUS ERYTHEMATOSUS

Introduction

Lymphadenopathy is seen during the clinical course of both rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). The frequency of detectable lymph nodes reported in different series has ranged from 41% to 82% for RA^{1 - 4} and 12% to 78% for SLE.^{5 - 8} These differences may be due to variations in clinical stage and treatment received. Moreover, in general clinical practice, lymph nodes smaller than 1 cm in diameter are generally considered benign and are not usually taken into

consideration.⁹ This study aimed to assess the frequency of lymphadenopathy in RA and SLE cases. The presence of palpable lymph nodes of any size was determined in RA and SLE patients during active disease and remission. The degree of enlargement and the number of palpable lymph nodes were also noted. The findings were compared with those from patients with spondyloarthropathy (SpA) and osteoarthritis (OA). The effects of steroid therapy on the number and size of the palpable lymph nodes were also evaluated.

Patients and methods

The hospital records of 100 SLE patients, 100 RA patients, 100 SpA patients and 150 OA patients, treated in our rheumatology department, were evaluated retrospectively. More patients with OA were included as more presented to the department. The presence of lymph nodes of all sizes was recorded during both the active phase and complete remission periods of disease, as indicated by clinical and laboratory parameters, for patients with SLE, RA and SpA, and at first admission for patients with OA. Lymph nodes ≥ 0.5 cm in diameter in the axillary and inguinal regions and nodes of 0.2 – 0.4 cm in size in the cervical and supraclavicular regions were included in the analysis. Palpation of smaller nodes is possible in cervical and supraclavicular regions, but not in the axillary and inguinal regions, due to fatty tissue. Patients who had co-existing diseases that can cause lymph node enlargement and those with overlap syndromes (such as SLE and RA, or SLE and scleroderma) were excluded from the study. Patients who failed to reach complete remission were also excluded. All physical examinations were

performed by the same physician, as part of routine patient assessment, and were not performed for a specific study. Intra-observer variability and test-retest data are not available. We believe however, that the reliability of the examinations is high.

STATISTICAL ANALYSIS

The McNemar test and χ^2 test were used to analyse the data. $P < 0.05$ was considered significant.

Results

A total of 100 SLE patients (mean age 42 years, range 23 – 70 years; eight males, 92 females), 100 RA patients (mean age 51.6 years, range 26 – 78 years; 21 males, 79 females), 100 SpA patients (mean age 28.1 years, range 18 – 42; 58 males, 42 females) and 150 OA patients (mean age 51.7 years, range 38 – 71 years; 44 males, 106 females) were evaluated.

The overall frequency of lymphadenopathy in patients with active RA was 82%. Lymph nodes were significantly more common in the axillary region than the cervical, supraclavicular and inguinal regions ($P < 0.001$; Table 1). Lymphadenopathy was present in more than one

TABLE 1:
 Frequency of lymphadenopathy detected at various locations in patients with rheumatoid arthritis and systemic lupus erythematosus during the active phase of disease

	Axillary		Cervical		Supraclavicular		Inguinal	
	No.	%	No.	%	No.	%	No.	%
Rheumatoid arthritis								
Total ($n = 100$)	82	82	7	7	5	5	3	3
Without previous steroid treatment ($n = 80$)	76	95	6	7.5	5	6.25	3	3.75
Systemic lupus erythematosus								
Total ($n = 100$)	43	43	46	46	12	12	6	6
Without previous steroid treatment ($n = 69$)	38	55.1	39	56.5	11	15.9	4	5.8

anatomical location in 12% of RA patients. Eighty of the patients with RA had not used steroids before admission to our clinic (Table 1). Of the patients using steroids ($n = 20$), axillary lymph nodes and cervical lymph nodes were palpated in six (30%) and one (5%) patient, respectively. The difference in the frequency of lymphadenopathy between these two groups of RA patients was statistically significant ($P < 0.001$). The size and number of nodes were variable; a detailed analysis of the size and number of axillary nodes is given in Table 2. All the palpable lymph nodes disappeared during remission, except in three patients ($P < 0.001$). Among these three patients, the lymph nodes decreased in number in one patient and decreased in size in the other two patients during remission.

In patients with active SLE, the overall frequency of lymphadenopathy was 69%. In 29 SLE patients, lymphadenopathy was present in multiple regions. The frequencies of lymphadenopathy in the 69 SLE patients who were not on steroid therapy are given in Table 1. In SLE patients who were using

steroids before admission to our clinic ($n = 31$), the frequencies of lymphadenopathy in the axillary, cervical, supraclavicular and inguinal regions were 16.1%, 22.6%, 3.2% and 6.5%, respectively. The difference in the frequency of lymphadenopathy between these two groups of SLE patients was again statistically significant ($P < 0.001$). In the majority of patients (42 out of 46, 91.3%), the lymph nodes in the cervical region were multiple small nodes. Two patients had one to two small nodes, and the other two patients had more than three nodes > 1 cm in diameter. Similarly, axillary nodes tended to be small; however, 11 of the 43 patients had larger nodes (i.e. > 1 cm in diameter) (Table 2). During remission, multiple small lymph nodes remained present in two of the SLE patients in the cervical region ($P < 0.001$).

In patients with active SpA, axillary lymph nodes 0.5 – 0.9 cm in diameter were palpated in 10% of patients, and nodes 0.2 – 0.4 cm in the cervical and supraclavicular regions were palpated in 4% of patients. All of these nodes disappeared after effective therapy ($P < 0.001$). Axillary lymph

TABLE 2:
 Detailed analysis of the number and diameter of axillary lymph nodes detected in patients with rheumatoid arthritis and systemic lupus erythematosus during the active phase of the disease

	RA ($n = 82$)		SLE ($n = 43$)	
	No.	%	No.	%
1 lymph node				
0.5 – 0.9 cm	13	15.8	9	20.9
≥ 1 cm	14	17.1	1	2.3
2 lymph nodes				
0.5 – 0.9 cm	9	11.0	7	16.3
≥ 1 cm	14	17.1	8	18.6
3 or more lymph nodes				
0.5 – 0.9 cm	19	23.2	16	37.2
≥ 1 cm	13	15.9	2	4.7

nodes 0.5 – 0.9 cm in diameter were palpated in 18% of the patients with active OA. Lymphadenopathy was significantly less frequent in patients with SpA and OA compared with RA and SLE ($P < 0001$).

Discussion

We have demonstrated that the majority of RA patients with active disease who were not on steroids had axillary lymphadenopathy, while the overall frequency of axillary lymph nodes was comparable to that in previous observations of RA patients. Lymphadenopathy is a common finding in RA. It has been reported to occur in 41 – 82% of patients,^{1–4} and is often associated with active disease.¹⁰ Generalized lymphadenopathy has been described,^{10,11} but the enlarged nodes are often located near the inflamed joints. The axillary area is particularly affected,⁴ since the lymphatics draining the hand joints lead to these nodes. In contrast, while lymphadenopathy was also present in most of the SLE patients with active disease, it was more generalized. SLE is primarily an inflammation of the connective tissue, which is widely distributed throughout the body,⁷ causing more widely distributed lymph node enlargement. The most commonly involved glands are the cervical, submaxillary, axillary and supraclavicular lymph nodes,^{5–7} but the lymph nodes in SLE are never very large.⁷

We also demonstrated that, while most RA and SLE patients had lymphadenopathy during the active phase of the disease, these lymph nodes disappeared (or at least were reduced in size or number) after effective therapy. It would seem, therefore, that palpable lymph nodes reflect disease activity in these connective tissue disorders. The frequency of lymphadenopathy found seems

to be higher than previously reported in RA and SLE patients. Even very small nodes were recorded in our study, and their disappearance after effective therapy is evidence that they are associated with active disease. The modulatory effect of steroid administration on the physical findings is also an important observation. Systemic glucocorticoid therapy can change the clinical picture of patients with connective tissue disease without suppressing disease activity, and the rapid immunosuppression induced by steroids may complicate the clinical management.

The vast majority of patients with RA or SLE have reactive lymph node enlargement,^{3,5,10,12} but other causes, especially lymphoproliferative disorders, should be considered in the differential diagnosis. Atypical locations, larger nodes and/or the persistence of lymph nodes despite effective immunosuppressive therapy raise clinical suspicions about the presence of another underlying disease. Based on our observations, clinical concern should focus on the aetiology of cervical and supraclavicular lymph node enlargement in patients with RA, and of larger lymph nodes in patients with SLE.

Lymphadenopathy may be related to disease activity because of its association with the clinical symptoms of RA and SLE.^{8,10} It may also however be an active component of the immunological abnormality in RA.³ The present study indicates that lymphadenopathy is a frequent physical finding in RA and SLE cases. Further work is necessary to outline the importance of lymphoid abnormalities in the pathological basis of connective tissue diseases such as RA and SLE.

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