LETTER TO THE EDITOR / EDİTÖRE MEKTUP

DOI: 10.4274/mjima.galenos.2019.2019.29
Mediterr J Infect Microb Antimicrob 2019;8:29
Erişim: http://dx.doi.org/10.4274/mjima.galenos.2019.2019.29

# A Rare Case of Lupus Lymphadenopathy in the Differential Diagnosis of Lymphadenopathy

## Lenfadenopati Ayırıcı Tanısında Nadir Görülen Lupus Lenfadenopati Olgusu

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**Keywords:** Necrotizing lymphadenitis, pulse steroid, systemic lupus erythematosus, fever, granulomatous infection
**Anahtar Kelimeler:** Nekrotizan lenfadenit, pulse steroid, sistemik lupus eritematozus, ateş, granülomatöz enfeksiyon

**Dear Editor,**

Systemic lupus erythematosus (SLE) is a multisystemic autoimmune disease that can manifest with skin, kidney, hematological, and musculoskeletal involvement. It predominantly affects young females, with 90% of cases seen in women of childbearing age[1]. Lymphadenopathy (LAP) may be localized or generalized, and occurs as a result of neoplastic or inflammatory cell proliferation in or invasion of the lymph node. LAP is common in the course of many infectious diseases and is also included in the differential diagnosis of SLE and other connective tissue diseases, malignancies, and lysosomal storage disorders[2]. The most frequent initial symptoms of SLE are generally polyserositis, pyrexia, arthritis, and skin eruptions[3]. The prevalence of LAP in SLE patients varies between 12-78% and it is rarely an initial symptom[4,5]. LAP is usually generalized in SLE[6]. Herein, we discuss a case that presented with complaints of fever and LAP limited to the cervical and axillary regions as initial symptoms and was diagnosed as lupus lymphadenitis upon pathologic lymph node examination.

A 29-year-old woman with no known comorbidities, first presented to another center with complaints of swellings in the left anterior cervical region for about one month and left axillary region for 15 days, as well as fever that had recurred every day for one week. Complete blood count (CBC) results indicated pancytopenia. Breast ultrasound revealed conglomerated LAPs up to 30x23 mm in size in the left axillary region. Magnetic resonance imaging of the neck also demonstrated conglomerated LAPs approximately 57x51x25 mm in size in the left retromandibular area of the neck, anteromedial to the sternocleidomastoid area and posterior to the left submandibular gland. The patient was referred to our center for further testing. On physical examination, Traube's space was closed, palpable, painful swelling was detected in the left cervical triangle and left axillary region, and malar rash was noted on her face (Figure 1, image used with the patient's permission). In routine laboratory tests, CBC was consistent with pancytopenia (hemoglobin: 9 g/dl, leukocyte count: 1570 $10^3$/µl, platelet count: 78 $10^3$/µl), erythrocyte sedimentation rate was 86 mm/hr, and liver and kidney function tests were within normal range. Peripheral blood smear was also consistent with pancytopenia; no additional pathologies were detected. Blood and urine cultures were negative. *Brucella*, hepatitis B, C, HIV, *Toxoplasma*, and *Leishmania* serologic tests were negative. Epstein-Barr virus and cytomegalovirus serologic tests were consistent with her history of past infection and her tuberculosis interferon gamma release assay was positive. Whole-body and neck computed tomography (CT) demonstrated splenomegaly and LAPs in the left cervical and left axillary region, the largest being approximately 4.7x2.1 cm and having a necrotic center, suggesting granulomatous infectious processes. Excisional lymph node biopsy was planned.

**Cite this article as:** Pullukçu H, Akyol D, Soyer N, Yargucu Zihni F, Özsan N, Işıkgöz Taşbakan M. A Rare Case of Lupus Lymphadenopathy in the Differential Diagnosis of Lymphadenopathy. Mediterr J Infect Microb Antimicrob. 2019;8:29.

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**Received/Geliş Tarihi:** 21.04.2019 **Accepted/Kabul Tarihi:** 16.09.2019


**Published:** 27 September 2019

However, the patient's general condition deteriorated during follow-up before the biopsy appointment and an empirical four-drug antituberculosis treatment regimen was initiated based on her CT findings. Biopsy obtained from LAPs in the left axillary region tested negative in bacteriological and parasitological tests *(Leishmania)*. Antituberculosis therapy was discontinued after 10 days due to negative acid-fast bacilli test and polymerase chain reaction analysis for tuberculosis, and lack of resolution in fever. Mycobacteriological tests yielded no *Mycobacterium tuberculosis*. The results of bone marrow biopsy indicated hemophagocytosis, so the patient was treated with intravenous immunoglobulin 20 g/day for three days. However, she still did not have fever response. Antinuclear antibody (ANA) was positive with a titer of 1/640 and granular pattern, ANA profile was anti-SSA 2 positive, anti-SM 1 positive, and anti-RNP 1 positive; C3 level was 51 mg/dl (90-180), C4 level was 9 mg/dl (10-40), ferritin level was 4668 ng/ml, and protein/creatinine ratio was 0.65 (<0.15) in spot urine sample. Lymph node pathology results indicated widespread necrotic foci in a sporadic patchy pattern that eradicated the normal structure; occasional eosinophils in necrotic areas; histiocytes with crescentic nuclei, immunoblasts, and plasmacytoid dendritic cells in the necrotic area; and hematoxylin bodies in several foci. These findings suggested necrotizing lymphadenitis. The patient's pathological findings were compatible with lupus lymphadenitis, and the patient was diagnosed with SLE and given 1 g/day pulse methylprednisolone for three days. Her fever decreased rapidly and the LAPs decreased in size with methylprednisolone treatment. However, after one year of remission, the patient had a severe exacerbation. The acute exacerbation was accompanied by persistent fever and cervical/axillary LAPs, similar to her initial presentation. Treatment with pulse methylprednisolone 1 g/day for three days and oral mycophenolate mofetil 1500 mg/day resulted in clinical response and the patient continued follow-up. No relapse was observed during the six months follow-up.

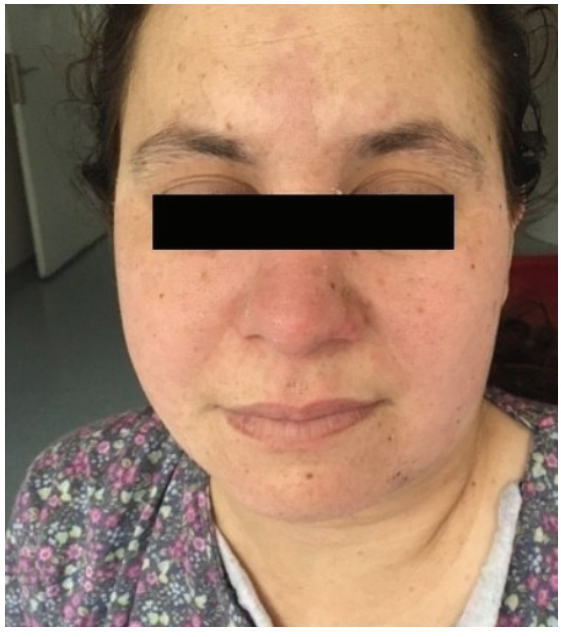

**Figure 1.** Malar rash on the patient's face

Despite multiple genetic, epigenetic, hormonal, and environmental risk factors have been suggested, systemic lupus erythematosus is an autoimmune disease of unknown etiology. Its prevalence is 59 per 100,000 in Turkey. It occurs most commonly in patients aged 15-45 years, but can be seen at any age[7].

The SLE classification criteria defined by the American College of Rheumatology in 1982 and reviewed in 1997 are used to identify SLE patients. Patients with at least 4 of the 11 criteria are accepted as having SLE[8]. Our patient met the clinical criteria for SLE with malar rash, pancytopenia, ANA positivity, and anti-SM positivity, while she did not have discoid rash, photosensitivity, oral ulcers, arthritis, serositis, or any renal and neurological diseases.

While LAP is not among the lupus classification criteria, the most characteristic lymph node lesion seen in SLE is coagulative necrosis containing hematoxylin bodies, or reactive follicular hyperplasia[9]. However, findings of coagulation necrosis should not lead to misdiagnosis with tuberculosis lymphadenitis, which has epithelioid granulomas with characteristic caseous necrosis. Lymph node pathology results from our patient were consistent with the typical SLE lymphadenitis with widespread necrotic foci and hematoxylin bodies.

There may be extreme fluctuations in disease course of SLE patients. Furthermore, they possess high risk of developing malignancy, particularly hematological malignancies like leukemia, Hodgkin's, and non-Hodgkin lymphoma. Hence, classifying the disease and implementing a treatment plan based on clinical findings alone may be insufficient. Definitive diagnosis is based on pathologic lymph node examination[9]. Although our patient met the clinical classification criteria, lymph node and bone marrow biopsies were performed for differential diagnosis. Malignancy and potential infectious pathologies, primarily tuberculosis, were ruled out.

The first adult who presented with LAP and was diagnosed with SLE in Turkey was reported by Türkbeyler et al.[10] in 2011. The second patient diagnosed with LAP in adulthood was reported in 2014, and ours is the third case report from Turkey according to our search of the literature through these keywords as "SLE, lymphadenopathy and Turkey" in PubMed, Turkish Citation Index, and Google Scholar databases on 19 April 2019[9]. Although LAP is rarely an initial symptom, it is important both in diagnosis and early initiation of effective treatment due to the potential of high disease activity.

In conclusion, LAP can be seen in many infectious and noninfectious diseases. It is imperative to rule out firstly the infectious factors, especially tuberculosis. This should be followed by detailed history and physical examination for differential diagnosis that includes connective tissue diseases, primarily SLE.

### Ethics

**Informed Consent:** Consent form was filled out by the patient.

**Peer-review:** Externally and internally peer-reviewed.

### Authorship Contributions

Surgical and Medical Practices: H.P., M.I.T., F.Y.Z., D.A., Concept: M.I.T., Design: H.P., M.I.T., D.A., Data Collection or Processing: D.A., N.S., F.Y.Z., N.Ö., Analysis or Interpretation: H.P., F.Y.Z., N.S., N.Ö., M.I.T., Literature Search: D.A., Writing: D.A., F.Y.Z., M.I.T.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study received no financial support.

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