Tuberculous Meningitis in a Patient with Systemic Lupus Erythematosus

Sistemik Lupus Eritematozuslu Hastada Tüberküloz Menenjit

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Abstract

Systemic lupus erythematosus (SLE) is a chronic inflammatory autoimmune disease of unknown etiology that affects various organs. In patients with SLE, infections are the most important causes of morbidity and mortality. Their risk factors for infection include immune system irregularities due to SLE and immunosuppressive/cytotoxic therapy. Infection is frequent and the unusual spectrum of organisms is thought to be related to the combined effect of immune system anomalies and immunosuppressive therapy. This case is presented to remind us that tuberculous meningitis should be included in the differential diagnosis of central nervous system pathologies in patients diagnosed with SLE.
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Key words: Systemic lupus erythematosus, immunosuppression, vasculitis, tuberculous meningitis

Özet

Sistemik lupus eritematozus (SLE), çeşitli organları etkileyen, etyolojisi bilinmeyen, kronik inflamatuvar otoimmün bir hastalıktır. Sistemik lupus eritematozuslu hastalarda morbidite ve mortalitenin önemli bir sebebi enfeksiyonlardır. Enfeksiyon için risk faktörleri arasında, sistemik lupus eritematozusa ya da immünosüpresif ve sitotoksik tedaviye bağlı immün sistemdeki bozukluk yer alır. İmmün sistemde meydana gelen anormallikler ve kullanılan immünosüpresif tedaviye bağlı olarak enfeksiyonlar sık ve farklı spektrumda görülmektedir. Bu olgu, sistemik lupus eritematozus tanısıyla izlenen hastalarda merkezi sinir sistemi ile ilgili patolojilerde tüberküloz menenjitin ayırıcı tanıda akla gelmesi için sunulmuştur. *(J Pediatr Inf 2013; 7: 106-9)*

Anahtar kelimeler: Sistemik lupus eritematozus, immünosüpresyon, vaskülit, tüberküloz menenjit

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Introduction

Systemic lupus erythematosus (SLE) is a chronic inflammatory autoimmune disease that affects various organs, and its etiology is not known (1). In SLE patients, infections are the most important causes of morbidity and mortality (2, 3). Their risk factors for infection include immune system irregularities due to SLE and immunosuppressive/cytotoxic therapy (4, 5). The infections are usually due to Gram-positive and -negative bacteria. Opportunistic infections are also seen, such as Candidiasis, cryptococcal meningitis, *Pneumocystis jiroveci* pneumonia, invasive aspergillosis, and tuberculosis (TB) (5-8). Infection is frequent and the unusual spectrum of organisms is thought to be related to the combined effect of immune system anomalies and immunosuppressive therapy. This case is presented to remind us that TB meningitis should be included in the differential diagnosis of central nervous system pathologies in patients diagnosed with SLE.

Case Report

A 15-year-old girl complained of a headache and fever for 1~2 days and weakness in her right

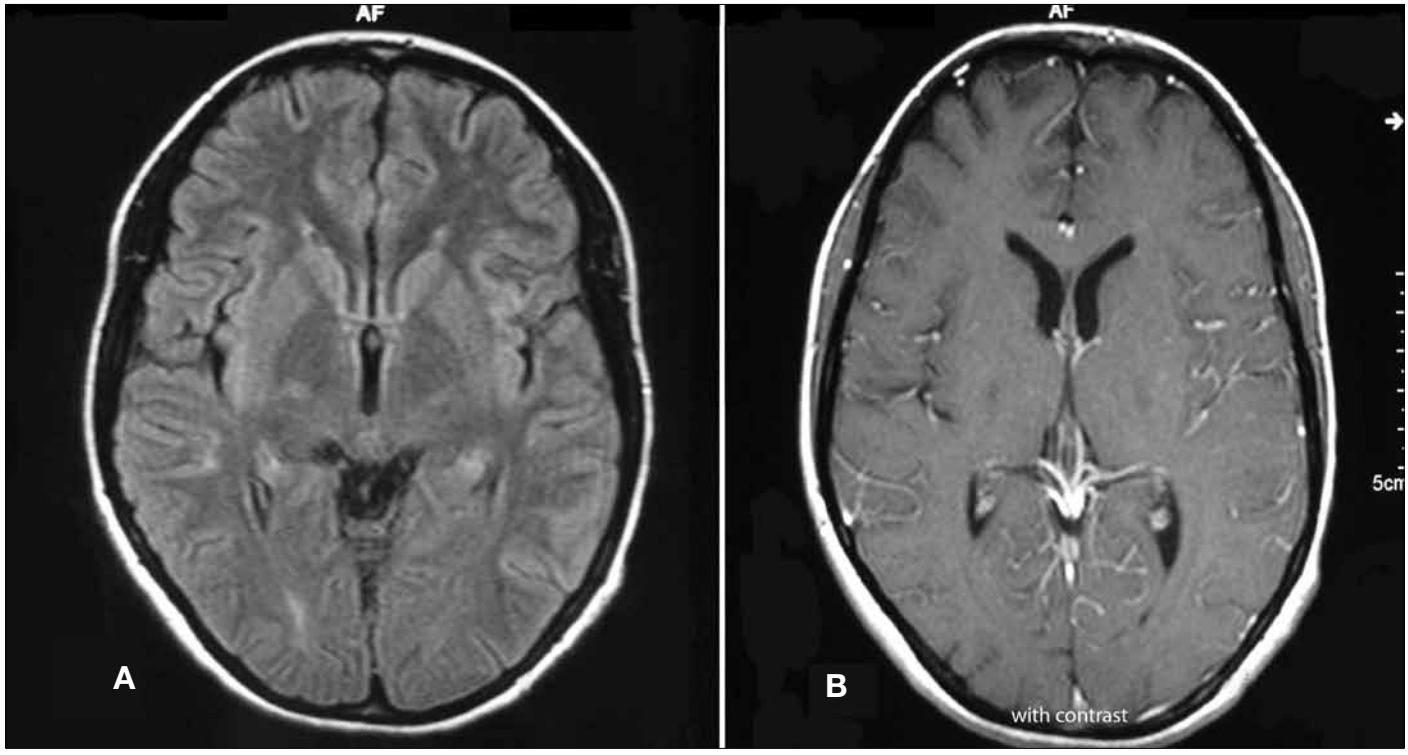

Figure 1. The FLAIR image (A) shows mild hyperintensity in the left Sylvian fissure. Contrast enhanced T1-weighted MRI (B) shows suspect leptomeningeal enhancement in the left Sylvian fissure

arm. She had been diagnosed with SLE 4 years earlier and was taking prednisolone and azathioprine. On examination, she had a fever of 39°C, and had several beats of clonus in the lower extremities. The white blood cell count was 5730 (95% neutrophil, 5% lymphocytes), hemoglobin 10.5 g/dL, platelets 184.000/mm^3, C-reactive protein 39 mg/L, erythrocyte sedimentation rate (ESR) 51 mm/h, C3 154 mg/dL (90–180), C4 35 mg/dl (10–40), and anti-dsDNA 1.08 U/mL (<0.9). On cranial magnetic resonance imaging (MRI), the FLAIR image showed mild hyperintensity in the left Sylvian fissure, and contrast-enhanced T1-weighted MRI showed suspect leptomeningeal enhancement in the left Sylvian fissure (Figure 1). Considering the possibility of vasculitic involvement due to SLE, methylprednisolone (30 mg/kg/dose) was given for 3 days.

The patient developed reduced consciousness and convulsions during follow-up, and a lumbar puncture was performed. The cerebrospinal fluid (CSF) pressure was normal, the CSF was slightly blurry and contained 400 cells/mm^3 (lymphocytes in character), protein 65 mg/dL, and sugar 47 mg/dL (blood glucose 125 mg/dL). Cefotaxime was started based on a diagnosis of bacterial meningitis. Anti-TB treatment (isoniazid (INH), rifampicin, pyrazinamide, and streptomycin) was initiated because it was thought that the patient might have TB meningitis, given that she had SLE, her aunt had a history of lung TB, and the patient was taking immunosuppressants and living in a region endemic for TB. The QuantiFERON test and CSF were positive for TB DNA determined by the polymerase chain reaction (PCR). Cranial MRI conducted approximately 2 weeks later showed prominent leptomeningeal enhancement in the Sylvian fissure (A) and basilar cistern (B) bilaterally (Figure 2). Thoracic computed tomography (CT) showed a nodular infiltrate in the right upper lobes and calcified hilar lymph nodes, consistent with TB.

During the second week of treatment, pyrazinamide was stopped and ethambutol added as the aspartate aminotransferase (AST) was 685 IU/L and alanine aminotransferase (ALT) 405 IU/L; the INH and rifampicin doses were reduced. The liver enzymes decreased subsequently. On day 40, a CSF culture grew *M. tuberculosis*. Since it is INH resistant, the treatment continued with rifampicin, ethambutol, streptomycin, pyrazinamide, and ofloxacin without INH. No complications were observed during the 4-year follow-up.

Discussion

Infections are relatively common in SLE patients and are responsible for 30~50% of their morbidity and mortality (9, 10). In addition, they mimic SLE activation, which delays diagnosis and treatment. Following cardiovascular diseases (41%), infections are the second most important (18%) cause of death (11, 12). The TB risk for patients with SLE is increased seven-fold, as compared to the normal population (13). TB located in the pleura, meninges, skin,

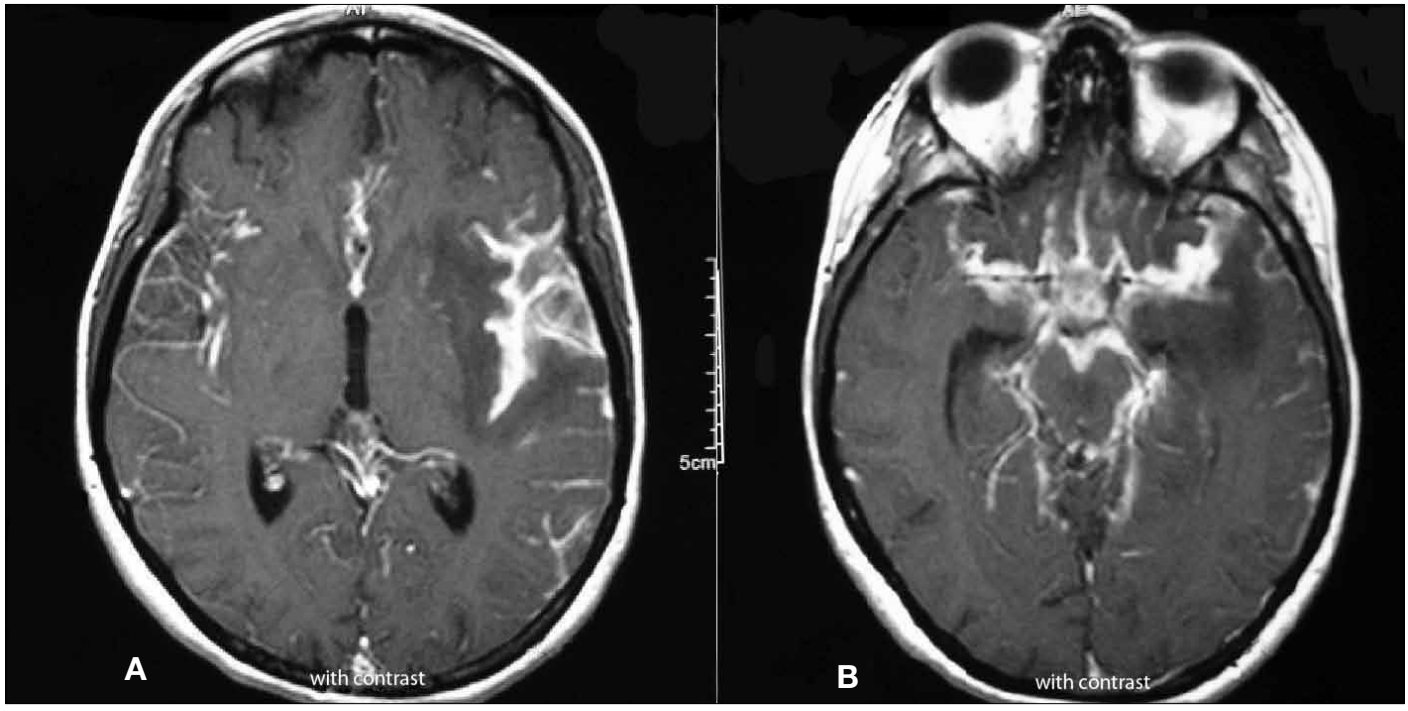

Figure 2. Contrast enhanced T1-weighted MRI obtained at the level of the Sylvian fissure (A) and basilar cistern (B) shows apparent leptomeningeal enhancement

joints, and kidneys is seen more frequently in patients with SLE (7). Baizabal-Carvallo *et al*. (14) observed 25 meningitis episodes in 23 of 1411 patients diagnosed with SLE, and 15 of these grew various microorganisms (*Mycoplasma tuberculosis* 5-33.3%, *Listeria monocytogenes* 5-33%, *Cryptococcus neoformans* 3-20%, *Streptococcus pneumoniae* 1-6.6%, and *Kingella kingae* 1-6.6%). Some of the risk factors for tuberculosis are; high SLE activity, active lupus nephritis, and the use of corticosteroids or immunosuppressive drugs (15, 16). In addition, SLE patients have fewer lymphocytes, T cell dysfunction, and cytokine communication disorders, which are thought to be the probable cause of extrapulmonary tuberculosis (17). Our patient had been given methylprednisolone and azathioprine for 4 years for the SLE.

Sütlaş et al. (18) evaluated 16 patients diagnosed with TB meningitis. The most frequent clinical findings were blurred consciousness, focal neurological disorders, behavioral disorders, signs of increased intracranial pressure, and convulsions. The average time which elapsed from the onset of neurological symptoms was 29 days (2 days to 5 months). Our patient complained of headache for 1 week and then developed a fever, weakness in the right arm, blurred consciousness, and convulsions. *M. tuberculosis* was considered given that the patient was receiving immunosuppressive therapy, her aunt had past lung TB, and she lived in an endemic country (Turkey). Since the morbidity and mortality of TB meningitis is high, quadruple anti-TB treatment was initiated without waiting for the CSF culture results. The CSF was positive for TB DNA determined by PCR and *M. tuberculosis* grew in the CSF culture.

An increased number of lymphocytic cells in the CSF is a characteristic of tuberculous meningitis. On analyzing the CSF in our case, 400 lymphocytes were observed, characteristic of TB meningitis, and the sugar level was 47 mg/dL (blood sugar 125 mg/dL). Sütlaş et al. (18) stated that tuberculoma, basal exudation, hydrocephalus, brain infarct, and edema are the most frequent cranial findings in patients diagnosed with TB meningitis. Cranial MRI at the time of admission showed an increased signal in the frontal lobe white matter, which was consistent with vasculitis. The follow-up cranial MRI showed an increased signal consistent with TB meningitis in the basal regions of the brain.

Conclusion

In patients diagnosed with SLE, corticosteroid and immunosuppressive therapy should be kept at the lowest dose, taking into consideration the severity of the disease and the patient's individual characteristics. Before starting immunosuppressive or high-dose steroid therapy, one should not forget TB screening and consider TB prophylaxis or treatment.

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

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Informed Consent: Written informed consent was obtained from the patient's parents for publication of this case report and any accompanying images.

Author Contributions

Concept - Ö.K., A.T., Ö.K.; Design - Ö.K., Y.C., Ö.K.; Literature Review - Ö.K., A.T., Z.I.H.; Writing - Ö.K., Ö.K., Z.I.H.; Critical Review - Y.C., N.A., H.Ç., Ö.K.

Çıkar Çatışması

Yazarlar herhangi bir çıkar çatışması bildirmemişlerdir.

Hakem değerlendirmesi: Dış bağımsız.

Hasta Onamı: Bu çalışmaya katılan hastalardan yazılı hasta onamı alınmıştır.

Yazar Katkıları

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References

1. Maddison PJ. Is it SLE? Best Pract Res Clin Rheumatol 2002; 16: 167-80.
2. Cervera R, Khamashta MA, Font J, et al. European working party on systemic lupus erythematosus. Morbidity and mortality in systemic lupus erythematosus during a 10-year period: a comparison of early and late manifestations in a cohort of 1000 patients. Medicine 2003; 82: 299–308.
3. Teh C, Ling G. Causes and predictors of mortality in hospitalized lupus patient in Sarawak General Hospital, Malaysia. Lupus 2013; 22: 106-11.
4. Kang I, Park SH. Infectious complications in SLE after immunosuppressive therapies. Curr Opin Rheumatol 2003; 15: 528-34.
5. Vargas PJ, King G, Navarra SV. Central nervous system infections in Filipino patients with systemic lupus erythematosus. Int J Rheum Dis 2009; 12: 234-8.
6. Zhang L, Wang DX, Ma L. A clinical study of tuberculosis infection in systemic lupus erythematosus. Zhonghua Nei Ke Za Zhi 2008; 47: 808-10.
7. Sayarlioglu M, Inanc M, Kamali S, et al. Tuberculosis in Turkish patients with systemic lupus erythematosus: increased frequency of extrapulmonary localization. Lupus 2004; 13: 274-8.
8. Arenas Miras MD, Hidalgo Tenorio C, Jimenez Alonso J. Tuberculosis in patients with systemic lupus erythematosus: Spain's situation. Reumatol Clin 2012; pii: S1699-258X(12)00211-2.
9. Zandman-Goddard G, Shoenfeld Y. Infections and SLE. Autoimmunity 2005; 38: 473-85. [CrossRef]
10. Alarcon GS. Infections in systemic connective tissue diseases: systemic lupus erythematosus, scleroderma, and polymyositis/dermatomyositis. Infect Dis Clin N Am 2006; 20: 849-75. [CrossRef]
11. Bernatsky S, Boivin JF, Joseph L, et al. Mortality in systemic lupus erythematosus. Arthritis Rheum 2006; 54: 2550-7. [CrossRef]
12. Sharma A, Shamanna S, Kumar S, et al. Causes of mortality among inpatients with systemic lupus erythematosus in a tertiary care hospital in North India over a 10-year period. Lupus 2013; 22: 216-22. [CrossRef]
13. Tikly M, Navarra S. Lupus in the developing world–Is it any different? Best Pract Res Clin Rheumatol 2008; 22: 643-55. [CrossRef]
14. Baizabal-Carvallo JF, Delgadillo-Marquez G, Estanol B, Garcia-Ramos G. Clinical characteristics and outcomes of the meningitides in systemic lupus erythematosus. Eur Neurol 2009; 61: 143-8. [CrossRef]
15. Jick SS, Lieberman ES, Rahman MU, Choi HK. Glucocorticoid use, other associated factors, and the risk of tuberculosis. Arthritis Rheum 2006; 55: 19-26. [CrossRef]
16. Tam LS, Li EK, Wong SM, Szeto CC. Risk factors and clinical features for tuberculosis among patients with systemic lupus erythematosus in Hong Kong. Scand J Rheumatol 2002; 31: 296-300. [CrossRef]
17. Kammer GM. Altered regulation of IL-2 production in systemic lupus erythematosus: an evolving paradigm. J Clin Invest 2005; 115: 836-40. [CrossRef]
18. Sütlaş PN, Ünal A, Forta H, Şenol Ş, Kırbaş D. Tuberculous meningitis in adults: review of 61 cases. Infection 2003; 31: 387-91.