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A 46-Year-Old Woman with Systemic Lupus Erythematosus and Brain Mass Lesion

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WHAT IS YOUR DIAGNOSIS?

A 46-year-old woman was referred because of nausea, vomiting and pancytopenia since two months ago. She had experienced frequent nausea, vomiting and generalized weakness following a flu-like syndrome.

She also had painful swelling of hand joints for three months associated with 10 kg weight loss during this time period. The patient had received ranitidine and metoclopramide injection without response. She did not have a history of systemic diseases or smoking and she was a housewife living with her husband and four children who were all healthy. In clinical examination, all findings were normal including neurological exam except for mild hepatomegaly, swelling and tenderness of both MCP, PIP and wrist joints. She was normotensive, the temperature was 37.9°C, pulse rate: 90 beats/min and the respiratory rate: 16/min. Laboratory exams showed pancytopenia (WBC: 2000/ μ l, Hb: 7.9g/dl, RBC: 2.5mil/ μ l, platelet: 50.000/ μ l), ESR 1st hour: 54 mm/h, proteinuria (1204mg for 24h urine collections), BUN: 20mg/dl and Creat: 0.4mg/dl. Liver function tests were abnormal (AST: 245U/l, ALT: 75 U/l, LDH: 1050 U/l). Chest x-ray was normal and blood cultures were negative. Upper GI endoscopy was performed which demonstrated severe pangastritis. Hepatomegaly was detected in abdominal sonography without any abnormal lesion. Bone marrow aspiration and biopsy were normal. Serology of HBV, HCV, EBV, CMV, HIV, syphilis, Brucella and S.typhi was negative. ANA=1/160 and Anti-dsDNA=128 IU/ml were strongly positive. C3, C4 and CH50 had decreased (C3: 19mg/dl, normal range: 89-187, C4: 3 mg/dl, normal range: 16-38, CH50: 60u, normal range: 70-50). RF and Anti CCP were negative. Based on clinical findings and pancytopenia with positive serologic tests for SLE the diagnosis was confirmed and pulse therapy with methylprednisolone (1g daily for 3 consecutive days) was initiated followed by oral prednisolone (50 mg/d). The patient dramatically responded to treatment in terms of clinical symptoms and signs and pancytopenia resolved rapidly. On the 12th hospitalization day, she developed slurred speech and mild dysarthria. Magnetic resonance imaging (MRI) of the brain with contrast was performed that revealed a ring enhancing mass in the left temporoparietal area (Figure 1). (Tanaffos 2008; 7(2): 79-83)

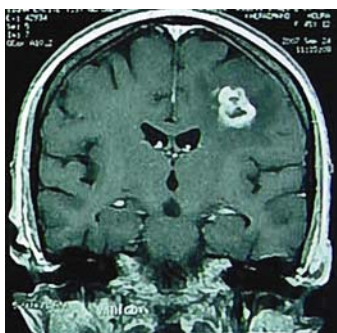


Figure 1. MRI of the brain: a flair image of the brain on the 12th hospitalization day shows a ring enhancing mass in the left side

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Diagnosis: Brain tuberculosis following treatment for SLE

A stereotactic biopsy of the brain was done and microscopical examination of the biopsy specimen is shown in figure 2 which demonstrated brain tissue with necrotizing granulomatous lesions, multinucleated giant cells, and multiple acid-fast bacilli in Ziehl Neelsen staining.

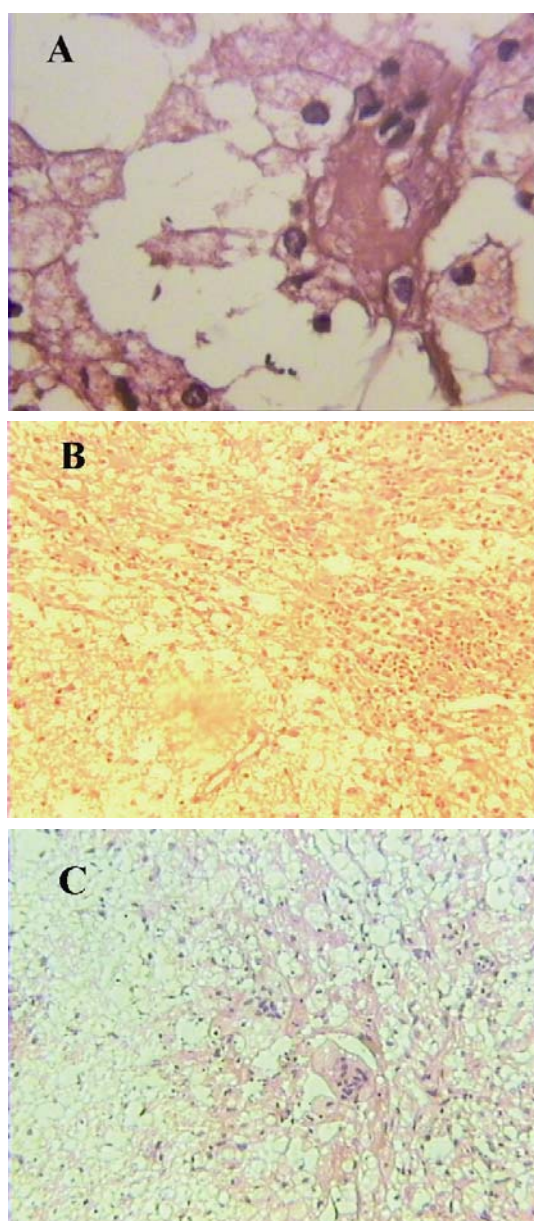


Figure 2. Microscopic examinations of the brain lesion (A,B,C).

The diagnosis of cerebral tuberculosis without pulmonary TB was confirmed and treatment with four anti-tuberculous drugs (isoniazid, rifampin, ethambutol, and pyrazinamide) was initiated. All neurologic symptoms resolved after one week of treatment and the patient was scheduled to continue the standard six-month anti-TB treatment.

DISCUSSION

In our patient with SLE and recent onset of dysarthria, the major question was whether her symptoms were the result of neuropsychiatric SLE alone or a complication such as infection or a malignancy such as lymphoma.

The frequency of which the central nervous system is affected by SLE varies, according to different reports between 13 and 59%.

The most common manifestations are cognitive dysfunction, anxiety and depression (1), headache, seizures and psychiatric conditions, aseptic meningitis, stroke, encephalopathy, syndrome of inappropriate secretion of antidiuretic hormone (SIADH), movement disorders, and myelopathy (2-7).

However, the neuroradiographic appearance of the lesions did not suggest ischemia or a demyelinating disease.

Causes of stroke in SLE include large artery occlusion, intracerebral and subarachnoid hemorrhage. Ischemic stroke in SLE is attributed at least in part to circulating antiphospholipid antibodies (APL), atherosclerosis and other causes (8, 9). Subarachnoid haemorrhage in SLE is well documented in the literature (10-15). Figures of

transient ischemic attacks (TIAs) in SLE indicate their raised incidence (8, 13, 16). Pseudotumor cerebri (benign intracranial hypertension) and brain stem disorder are uncommon presentations of neuropsychiatric SLE (17,18). Tests of cognitive function and psychological status, magnetic resonance imaging (MRI), and electroencephalography (EEG) with evoked potentials are most useful in discriminating functional neuropsychiatric symptoms from organic diseases. Cerebrospinal fluid analysis is useful to exclude infection. A new imaging technique for the diagnosis of neuropsychiatric SLE is "Magnetization Transfer Imaging" (MTI). MTI analysis detects cerebral change in neuropsychiatric SLE (19).

F-18-fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) may help to verify cerebral involvement of SLE earlier than MRI (20).

Infections are common in patients with SLE (21) accounting for about 20% of episodes of fever (22) and are the leading causes of death in hospitalized patients (22, 23). CNS infection occurs infrequently (24, 25) and most often in patients who have received corticosteroid treatment within the previous 6 months as well as concurrent immunosuppressive therapy with cyclophosphamide, azathioprine, or other agents. Our patient had important risk factors for infection including active SLE with leukopenia (26), renal involvement, and the receipt of high doses of corticosteroids.

Tuberculosis is more frequent in SLE patients than in the general population. Predisposing factors for the development of active TB in general include malnutrition, alcoholism, substance abuse, diabetes mellitus, corticosteroid and immunosuppressive drugs, malignancy, HIV infection and homelessness.

The incidence and severity of TB in SLE patients vary greatly among different series. The annual incidence of TB among SLE patients (most of them

from developing countries) varies between 150/100,000 patients in Turkey to 2,450/100,000 in India (27). Higher doses of corticosteroid and low levels of serum albumin are important risk factors for the development of CNS infections in SLE patients (4).

Possible infectious causes in SLE patients include bacterial, viral, fungal, and parasitic pathogens.

Differential diagnosis of an enhancing hemispheric lesion in this patient consisted of:

Bacteria (*Nocardia* and *Mycobacteria*), viruses (CMV, Herpes simplex, and Varicella zooster), protozoa (*Toxoplasmosis* and *Amibiasis*), fungi (*Candidiasis*, *Aspergillosis*, *Cryptococcosis*, *Coccidioidomycosis*, *Mucormycosis*, *Blastomycosis*, and *Histoplasmosis*), helminthes (*Schistosomiasis* and *Neurocysticercosis*), and neoplasms.

Immunosuppressive therapy may predispose SLE patients to lymphoproliferative malignancy such as non-Hodgkin's lymphoma, usually of B-cell origin that may manifest primarily in the CNS; a condition which is observed in HIV or transplant patients (28).

This case illustrates the importance of considering CNS infection (such as TB) in SLE patients particularly during or after immunosuppressive therapy and the importance of brain MRI as a useful tool to differentiate infectious etiologies from ischemic complications of SLE.

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