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Peter Sillevis Smitt and Ton Swaak

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## LESSON OF THE MONTH

## Neuropsychiatric lupus?

Peter Sillevis Smitt, Ton Swaak

## Case history

A 49 year old man with systemic lupus erythematosus (SLE) was admitted in April 1996 with fever, headache, and mental change. In 1984, he noticed discoid changes on sun exposed skin areas. At the same time, he developed pleuritis, myocarditis, pericarditis, haemolytic anaemia, and myositis. Anti-dsDNA antibodies were found in his serum and SLE was diagnosed.<sup>1</sup> Treatment was started with prednisone 80 mg and cyclophosphamide 150 mg. On high doses of corticosteroids he became delusional and therefore, the prednisone was tapered. Over the following years he was admitted several times with relapses of his SLE manifesting as glomerulonephritis (biopsy class IV), thrombocytopenia, and leucocytopenia. In 1994 he had his latest glomerulonephritis relapse and treatment was again started with prednisone and cyclophosphamide. On admission, he presented with a three week history of headache, memory loss, and clouded thinking. For the past two years he had been taking a stable daily dose of 7.5 mg prednisone and 100 mg cyclophosphamide.

Rectal temperature was 38.5°C without signs of meningeal irritation. Orientation and attention were diminished. He could only follow one step commands and was apraxic. Visual field examination revealed right sided homonymous hemianopia. Fundoscopy, motor and sensory exam and coordination were normal. His white cell count was 3300 (per mm<sup>3</sup>) with a differential count of 68% neutrophils, 8% lymphocytes, and 20% monocytes. The serum creatinine was 144 µmol/l (compared with 148 µmol/l in January 1996); erythrocyte sedimentation rate (ESR) was 56 mm in the first hour (compared with 46 mm in January 1996); C reactive protein was negative. Glucose, electrolytes, and gammaglobulins were normal, and his HIV status was negative. Magnetic resonance imaging of the brain showed a ring enhancing, space occupying lesion in the left occipital lobe (fig 1). Examination of cerebrospinal fluid showed pleocytosis with 61/µl white blood cells and increased protein (3.5 g/l). Anti-toxoplasma titre in cerebrospinal fluid was 57 IU and in serum 1140 IU, both IgG. A tentative diagnosis of toxoplasma encephalitis was made and a trial of anti-toxoplasmosis treatment was started.

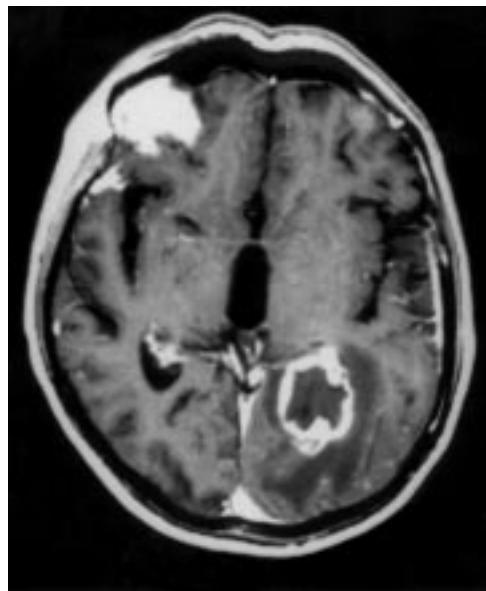


Figure 1 Magnetic resonance imaging after gadolinium administration. Ring enhancing, space occupying lesion in the left occipital lobe surrounded by oedema and compressing the occipital horn of the lateral ventricle.

He was treated with a pyrimethamine loading dose of 200 mg followed by 100 mg pyrimethamine and 4 g sulphadiazine daily for six weeks.<sup>2</sup> After two days he improved dramatically. Two weeks later, the neurological examination was normal and the brain magnetic imaging had greatly improved. Also his serum anti-toxoplasma IgG decreased significantly (fig 2).

## Discussion

The differential diagnosis of a ring enhancing space occupying lesion in the brain comprises primary brain tumour, metastasis, abscess, granuloma, and demyelinating lesions.<sup>3</sup> In our patient, the main differential is between primary or metastatic brain tumour and abscess. The presence of fever and diffuse encephalopathic change strongly suggests infection as the cause of the enhancing magnetic resonance imaging lesion in our patient. Patients with SLE are prone to opportunistic infections because of prolonged immunosuppressive treatment. The array of pathogens involved in brain abscess in such patients differs from the causative agents of brain abscess in the non-immunocompromised population. In patients with disorders mainly affecting the

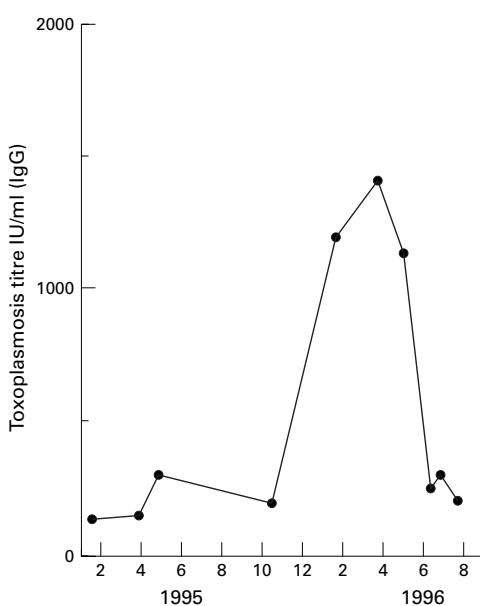
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**Figure 2** Retrospectively, serum toxoplasma titres (ELISA) were determined in the year before admission and after treatment. IgM titres remained negative, suggesting reactivation of a previous toxoplasma infection. Serum samples had been collected prospectively as part of a clinical study evaluating the prognostic significance of autoantibodies in SLE.

cellular immunity, the prevailing causes of brain abscess are *Toxoplasma gondii*, *Nocardia asteroides*, *Cryptococcus neoformans*, *Listeria monocytogenes*, and *Mycobacterium* sp.<sup>4</sup> In SLE, brain abscess may also be caused by *Aspergillus*.<sup>5,6</sup> Most of these pathogens give rise to concomitant systemic infections such as pneumonia, which may help diagnose the brain lesion. Because our patient had very high cerebrospinal fluid titres of anti-toxoplasma antibodies we decided not to perform a brain biopsy but rather give him a trial of anti-toxoplasmosis treatment. The clinical, radiological, and serological response to this treatment proves the diagnosis toxoplasma encephalitis.

“Neuropsychiatric lupus” has become a popular term to refer to all neurological and psychiatric complications in patients with SLE.

Consequently, neuropsychiatric lupus covers a vast array of disorders ranging from peripheral neuropathy to stroke, psychosis, and dementia. Mechanisms that have been associated with the pathogenesis of neuropsychiatric lupus include antineuronal antibodies, antiphospholipid antibody associated thrombosis, emboli from cardiac source and, rarely, vasculitis by immune complex depositions. In lupus patients, one should always look for secondary causes of the neuropsychiatric manifestation, including infection, toxic metabolic abnormalities, and hypertension.<sup>7</sup> Necropsy studies, have shown that coagulation mediated processes and infections are the most important causative agents in severe CNS pathology in systemic lupus.<sup>5,6</sup> Considering the increased risk of infections, immunosuppressive drugs should be used at the lowest possible doses.

#### The lesson

- “Neuropsychiatric lupus” is not a diagnosis.
- All neurological symptoms and signs in patients with SLE require a careful examination for infectious and vascular causes.
- In immunocompromised patients with a mass lesion in the brain, surgery can sometimes be prevented.
- When toxoplasma encephalitis is strongly suspected in lupus patients, a trial treatment under careful supervision can be safely performed.

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