Case Report

Selective Involvement of the Choroid Plexus on Cerebral Magnetic Resonance Images: A New Radiological Sign in Patients with Systemic Lupus Erythematosus with Neurological Symptoms

THIERRY DUPREZ, ADRIEN NZEUSSEU, ANDRÉ PEETERS, and FRÉDÉRIC A. HOUSSIAU

ABSTRACT. The selective involvement of the choroid plexus on brain magnetic resonance (MR) images is described in 2 patients with systemic lupus erythematosus presenting with neurological symptoms. The decrease in choroid plexus abnormalities on followup MR examination paralleled the clinical recovery with glucocorticoid therapy in both patients. Our cases indicate that selective involvement of the choroid plexus should be included in the spectrum of the radiological signs for neurological lupus. (J Rheumatol 2001;28:387–91)

Key Indexing Terms:
BRAIN
CENTRAL NERVOUS SYSTEM
MAGNETIC RESONANCE IMAGING
NEUROLOGICAL LUPUS

Focal white matter infarcts, increased T2 signal intensity of the periventricular white matter on magnetic resonance imaging (MRI), and cerebral atrophy are the common neuroimaging features in patients with systemic lupus erythematosus (SLE), who may exhibit neurological signs[1,2]. Isolated involvement of the choroid plexus has not been described on computed tomographic (CT) scans or on MR images. Others have reported a clinically silent SLE related choroidopathy that was correctly identified with In-111 labeled leukocyte imaging[3]. The choroid plexus has been shown to be a preferential target for immune complex deposition in NZB-NZW mice as well as in Wistar rats by prolonged immunization using bovine serum albumin. The resulting chronic serum sickness represents an animal model for cerebral lupus[4,5]. Similarly, the preferential involvement of the choroid plexus with immune complex deposition in human cerebral lupus has been well documented[6-8].

CASE REPORTS

Case 1. A 41-year-old woman with SLE of 6 years' duration and associated antiphospholipid antibody syndrome suddenly complained of fever, cephalalgia, neck stiffness, and photophobia. A cerebrospinal fluid (CSF) analysis 4 days after the onset of symptoms revealed pleiocytosis at 338 cells/µl (normal values < 7) with 67% lymphocytes and 33% neutrophils, elevated protein level at 192 mg/dl (normal 20–55), and low glucose level at 21 mg/dl (normal 40–80). In spite of a negative bacteriological examination, empirical treatment combining ampicillin and ceftriaxone was started. In the absence of subsequent clinical improvement, a brain MR examination was performed at Day 12 and showed normal parenchyma and meninges but swollen, contrast enhanced, and hemorrhagic choroid plexus within slightly enlarged ventricles (Figure 1A-D). Intravenous (iv) pulse therapy with methylprednisolone (1 g daily for 3 consecutive days) and cyclophosphamide (750 mg) was followed by prompt clinical recovery. Cerebrospinal fluid (CSF) analysis at 30 days showed significant improvement in laboratory variables: 74 cells/µl, proteins 71 mg/dl, and glucose 43 mg/dl. She was given monthly iv cyclophosphamide pulse therapy for 6 months. A followup MRI examination at 3 months showed significant improvement of the choroid plexus status and a decrease in size of the ventricular system (Figure 1E-F).

Case 2. A 17-year-old woman with SLE of one year duration without antiphospholipid antibodies presented with fever, cephalalgia, intermittent diplopia, and transient right hemiparesis. CSF analysis showed moderate abnormalities with a slight pleiocytosis at 10 cells/µl, a faintly elevated protein at 70 mg/dl, and normal glucose level at 46 mg/dl. Unenhanced brain MRI examination performed 3 weeks after symptoms was unremarkable, except for mild swelling of the choroid plexus (Figure 2A). Complete clinical recovery was promptly obtained after parenteral pulse therapy with methylprednisolone (1 g daily for 3 consecutive days) and cyclophosphamide (750 mg). She was given monthly iv cyclophosphamide pulse therapy for 6 months. CSF analysis was not repeated. Followup brain MRI examination at 4 months showed complete normalization of choroid plexus status (Figure 2B).

DISCUSSION

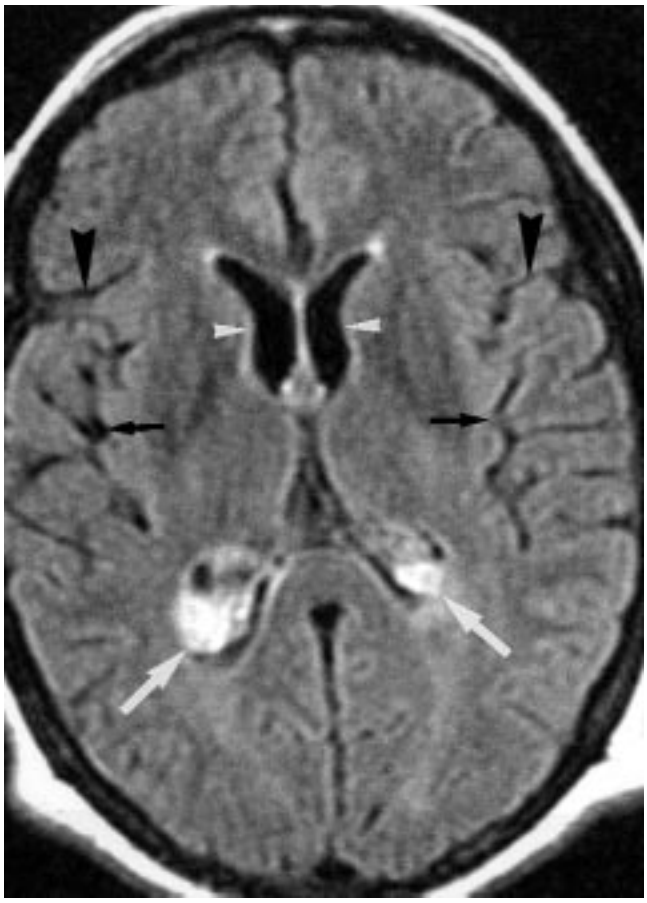
Patient 1 exhibited typical symptoms of SLE related meningitis without signs of parenchymal involvement. Patient 2 combined meningitis signs (fever, cephalalgia) with focal parenchymal sign (transient hemiparesis). In both cases,

From the Departments of Radiology and Medical Imaging, Rheumatology, and Neurology, Université Catholique de Louvain, St-Luc University Hospital, Brussels, Belgium.

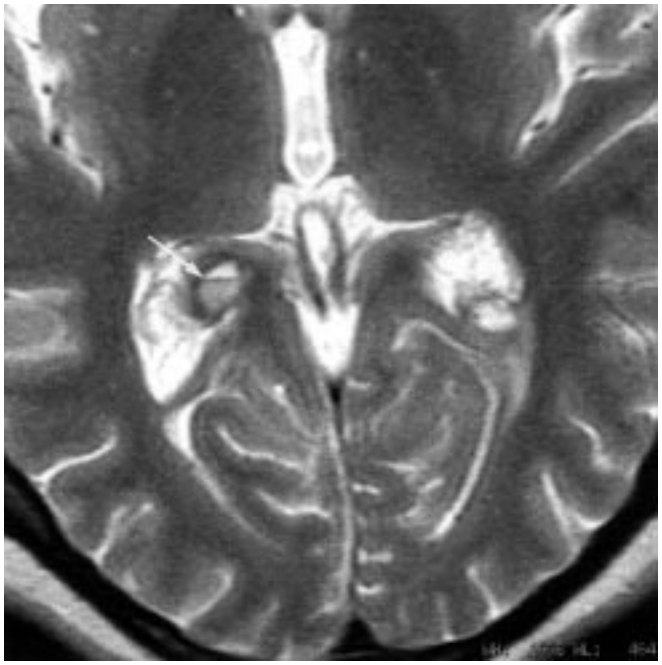
T. Duprez, MD; A. Nzeusseu, MD; A. Peeters, MD; F.A. Houssiau, MD, PhD.

Address reprint requests to Dr. T. Duprez, Department of Radiology and Medical Imaging, Université Catholique de Louvain, St-Luc University Hospital, Ave. Hippocrate 10, 1200 Brussels, Belgium. E-mail: duprez@rdgn.ucl.ac.be

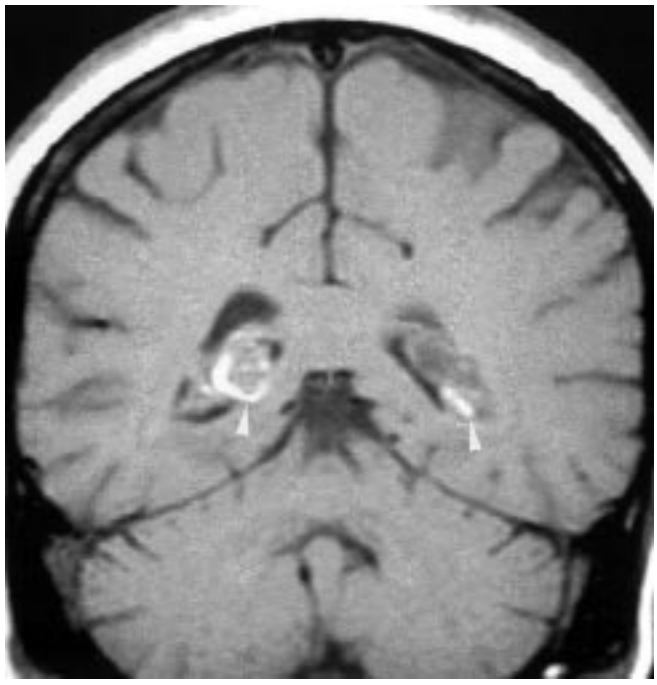
Submitted February 7, 2000 revision accepted August 22, 2000.



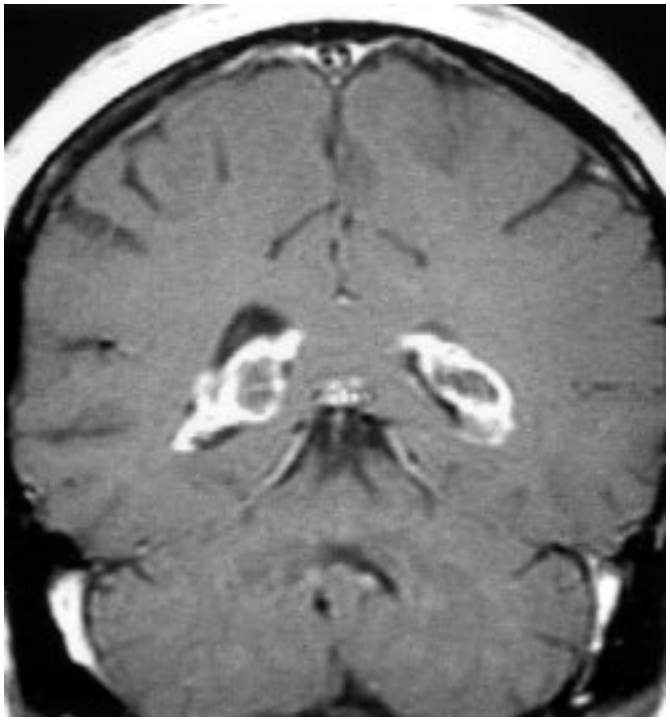
A



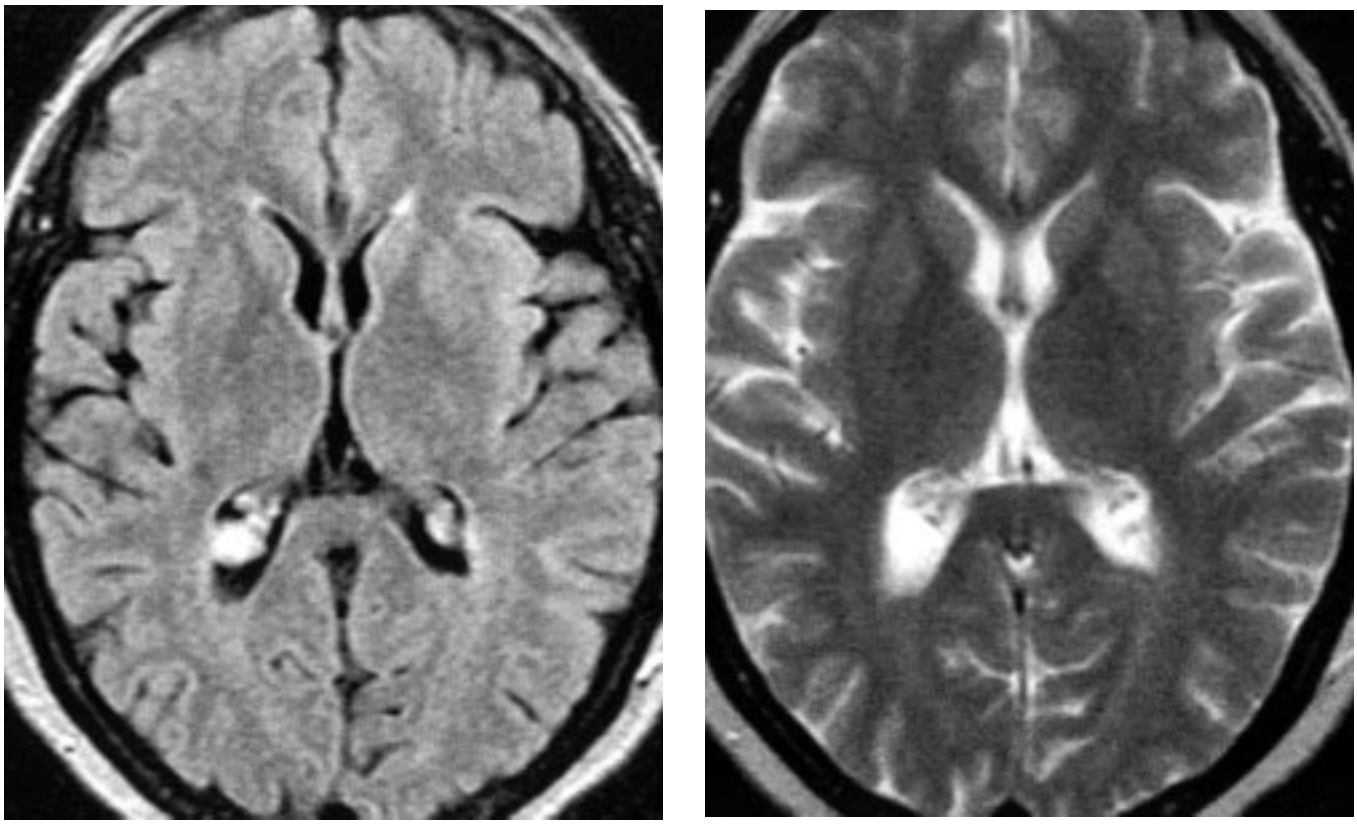
B



C



D

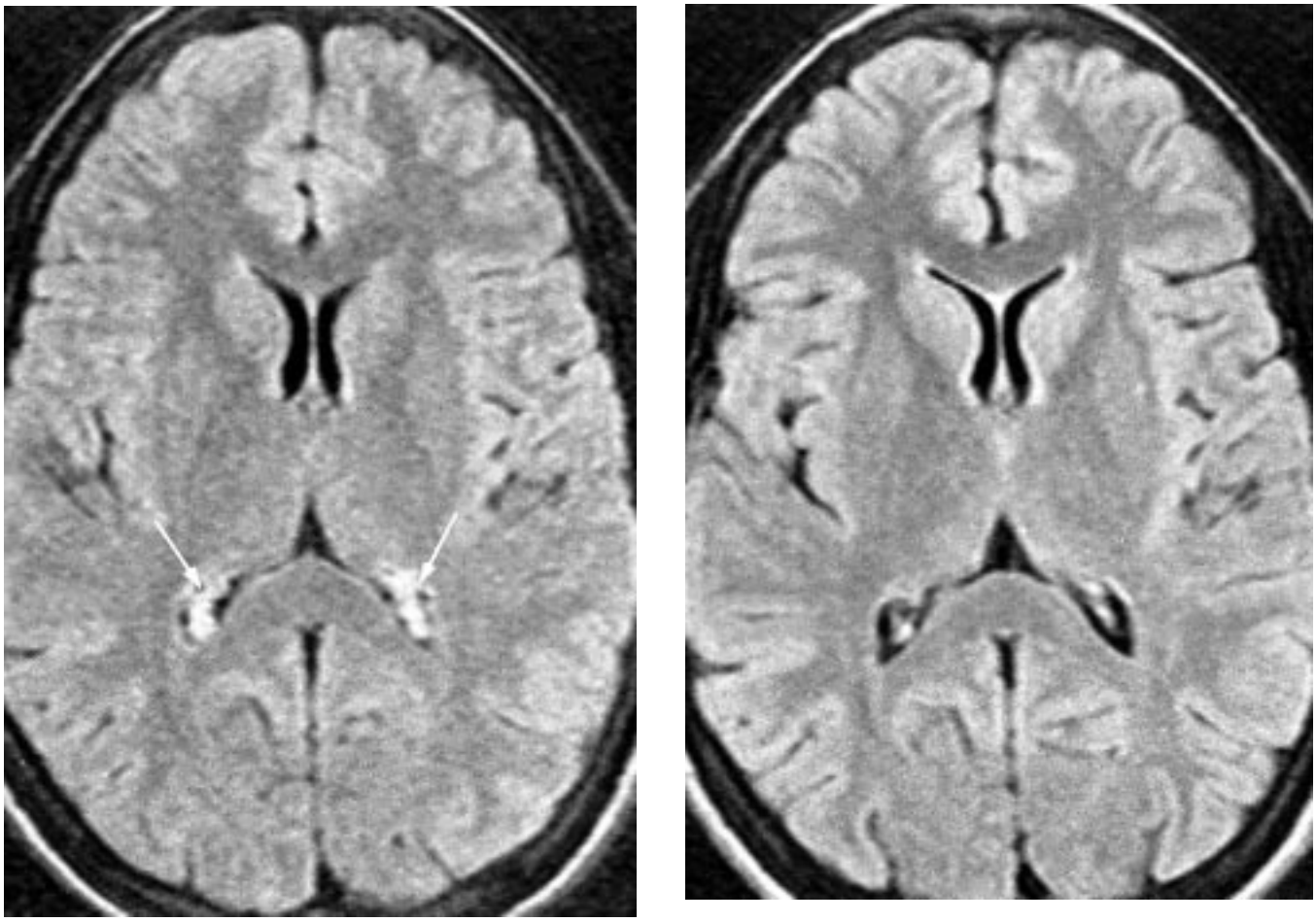


E F

Figure 1. Patient 1. A-D: initial MR examination at 12 days. E-F: followup examination at 3 months. A. Unenhanced fast spin-echo (FSE) fluid attenuated inversion recovery (FLAIR) image (TR 10,002 ms, TE_{eff} 124 ms, TI 2200 ms, ETL 18, NEX 1) in the transverse plane reveals enlarged and hyperintense choroid plexus (white arrows). Note the size of the frontal horns (between white arrowheads) and the depth of the peripheral sulci and sylvian fissures (black arrows and arrowheads). Parenchymal status is unremarkable. B. FSE T2 weighted image (TR 7600 ms, TE_{eff} 71 ms, ETL 24, NEX 2): magnified view of choroid plexus reveals a cystic area with a fluid-fluid level (white arrow) that is pathognomonic for an interface between supernatant serum and declive debris of erythrocytes containing degradation products of hemoglobin. C. Precontrast T1 weighted spin-echo image (TR 640 ms, TE 10 ms, NEX 2) in the coronal plane shows enlarged choroid plexus with aspecific low low signal intensity, except for marginal hemorrhagic areas exhibiting strong hyperintensity due to the presence of methemoglobin (arrowheads). D. Contrast enhanced T1 weighted spin-echo image (TR 640 ms, TE 10 ms, NEX 2) in a similar slice location as figure C shows strong peripheral enhancement of the enlarged choroid plexus. Edematous central areas of the choroid plexus do not enhance. Note the unexpected absence of meningeal enhancement despite clinically prominent meningeal signs. E. Followup FSE-FLAIR image (same pulse sequence data and slice location as figure A) shows the decrease in size of the choroid plexus. Frontal horns have become smaller and peripheral sulci have broadened — indirect signs of diminished intraventricular hypertension. F. Followup FSE T2 weighted image (same pulse sequence data as in D and same slice location as E) reveals diminished hemorrhagic foci within the choroid plexus. An unenhanced T1 weighted image showed a similar finding (not illustrated).

MRI examination showed the choroid plexus as the only abnormal structure of the CNS (Figures 1 and 2). A slight ventricular enlargement was additionally observed in the first patient, which resolved on followup examination (Figure 1). The degree of the choroid plexus involvement on MR images paralleled the intensity of the clinical signs and the severity of the CSF abnormalities in the acute phase. This clinical-biological-radiological correlation strongly suggested the choroid plexus involvement was the primary mechanism of both syndromes. Selective involvement of the choroid plexus has not been described before in the spectrum of the radiological signs for neurological lupus[1,2].

SLE related aseptic meningitis is a rare subentity of the disorder for which etiopathogenic factors and physiopathologic mechanisms are debated. Most reported cases are drug induced[9-11]. Neither of our patients had taken any of the implicated drugs, particularly nonsteroidal antiinflammatory drugs. Animal models of experimentally induced SLE-like syndrome[4,5] and a few human pathological observations[7,8] have revealed the choroid plexus to be a preferential site of immune complex deposition in SLE related encephalopathy as a result of the involvement of circumventricular vascular beds, which are unprotected by the blood-brain barrier. Our observations lend credence to these experimental data, as swelling, marginal ring-like contrast enhancement, and hemorrhagic foci within the choroid plexus were the only abnormal features on MR images. CSF hyperproduction is a well documented



A B

Figure 2. Patient 2. A. FSE-FLAIR transverse image (TR 10,002 ms, TE_{eff} 124 ms, TI 2200 ms, ETL 18, NEX 1) at 3 weeks shows unremarkable brain status except for a slight enlargement of the choroid plexus (arrows). B. FSE-FLAIR image (similar pulse sequence data and slice location as in A) at 4 months reveals choroid plexus shrinkage.

phenomenon in benign tumoral conditions involving the choroid plexus, such as the papilloma, which results in hypertensive hydrocephalus[12]. A similar process has been speculated in nontumoral conditions, i.e., prominence of the choroid plexus with hydrocephalus has been described in AIDS related cerebral toxoplasmosis[13]. The presence of a mild ventricular enlargement and its resolution on followup examination was observed in our first patient, who exhibited the more prominent choroid plexus involvement (Figure 1). This could theoretically result either from decreased CSF resorption due to meningitis, or from a "plexitis" induced increase in CSF production. The combination of ventricular enlargement together with the flattening of the peripheral sulci on initial examination (Figure 1A) more readily supported the second hypothesis. Benign intracranial hypertension (BIH) in patients with SLE has been speculated to result either from thrombotic obliteration of the cerebral arteriolar and venous system, or from immune complex deposition within the arachnoid villi that are responsible for CSF resorption[14-16]. Our first case raised the hypothesis of CSF hypersecretion as a third potential mechanism for BIH in SLE.

Sensitive neuroimaging modalities like CT and MRI have the potential of depicting the inflammatory swelling of the choroid plexus and the intense choroidal contrast enhancement reflecting hyperhemia and/or increased permeability of the circumventricular vascular beds. Both features reflect the immunopathological changes within the choroid plexus that have been described in human SLE[8] and in experimental chronic serum sickness[5]. MR imaging may be better suited to visualize these changes, as the technique shows greater tissue contrast and higher contrast medium sensitivity than CT scan. However, increase in choroid plexus volume and intense contrast enhancement may have low specificity because they can be encountered in other pathological conditions. In addition, significant overlapping between healthy subjects and patients can be expected since a variablility in choroid plexus size is observed in clinical

practice, and a physiological choroid plexus contrast enhancement exists in the absence of a blood-choroid barrier. Heterogeneity on T2 weighted images due to small hemorrhagic foci (Figure 1B), as well as the discrepancy between abnormally enhanced CP and normal meninges on MR images (Figure 1D) may act as additional clues for the diagnosis. However, this needs confirmation in a larger series comparing patients with SLE, patients with other choroidal pathologies, and healthy controls, with the awareness that choroid plexus abnormalities may indicate an immune disorder, without specificity for SLE or a systematic correlate to a clinical expression of CNS involvement in SLE[3,7]. Hemorrhagic foci within the choroid plexus as observed in our Patient 1 (Figures 1B, 1C) suggested severe damage to the capillary bed, resulting in blood product extravasation. The phenomenon was not observed in Patient 2, who therefore seemed to have undergone a lesser degree of capillary injury. Considering the pathological studies by Schwartz and Roberts, who identified a membranous and a vascular type of SLE related choroidopathy, one may speculate Patient 1 presented with the vascular type of SLE related choroidopathy (associated with capillary thrombi and extravasation of fibrinoid material at immunofluorescence and electron microscopy), and Patient 2 with the membranous type[8]. Brain MRI examination evaluating the choroid plexus should be performed in other manifestations of CNS lupus such as seizures and organic psychosis[17,18].

REFERENCES

1. Jacobs L, Kinkel PR, Costello PB, Alukal MK, Green FA. Central nervous system lupus erythematosus: the value of magnetic resonance imaging. J Rheumatol 1988;15:601-6.
2. Bell CL, Partington C, Robbins M, Graziano F, Turski P, Kornguth S. Magnetic resonance imaging of central nervous system lesions in patients with lupus erythematosus. Correlation with clinical remission and antineurofilament and anticardiolipin antibody titers. Arthritis Rheum 1991;34:432-41.
3. Tupler R, Madonna F, Turbinder EH. SLE-related choroidopathy depicted by In-111 leucocyte imaging. Clin Nucl Med 1991;16:680.
4. Dohrmann GJ, Herdson PB. Fine structural studies of capillaries in NZB-NZW mice. Exp Mol Pathol 1969;11:163-71.
5. Peress NS, Perillo E, Fenstermacher JD. Circumventricular organs in chronic serum sickness: a model for cerebral lupus. Biol Psychiatry 1989;26:397-407.
6. Atkins CJ, Kondon JJ, Quismorio FP, Friou GJ. The choroid plexus in systemic lupus erythematosus. Ann Intern Med 1972;76:65-72.
7. Boyer RS, Sun NC, Verity A, Nies KM, Louie JS. Immunoperoxidase staining of the choroid plexus in systemic lupus erythematosus. J Rheumatol 1980;7:645-50.
8. Schwartz MM, Roberts JL. Membranous and vascular choroidopathy: two patterns of immune deposits in systemic lupus erythematosus. Clin Immunol Immunopathol 1983:29:369-80.
9. Canoso JJ, Cohen AS. Aseptic meningitis in systemic lupus erythematosus. Report of three cases. Arthritis Rheum 1975;18:369-74.
10. Finelli PF, Yockey CC, Herbert AJ Jr. Recurrent aseptic meningitis in an elderly man. Unusual prodrome of systemic lupus erythematosus. JAMA 1976;235:1142-3.
11. Lancman ME, Mesropian H, Granillo RJ. Chronic aseptic meningitis in a patient with systemic lupus erythematosus. Can J Neurol Sci 1989;16:354-6.
12. Milhorat TH, Hammock MK, Davis DA, Fenstermacher JD. Choroid plexus papilloma. Proof of cerebrospinal fluid overproduction. Childs Brain 1976;2:273-89.
13. Bourgouin PM, Melancon D, Carpenter S, Tampieri D, Ethier R. Hydrocephalus and prominence of the choroid plexus: an unusual computed tomographic presentation of cerebral toxoplasmosis in AIDS. Can Assoc Radiol J 1992;43:55-9.
14. Carlow TJ, Glaser JS. Pseudotumor cerebri syndrome in systemic lupus erythematosus. JAMA 1974;228:197-200.
15. Green L, Vinker S, Amital H, et al. Pseudotumor cerebri in systemic lupus erythematosus.Semin Arthritis Rheum 1995;25:103-8.
16. Li EK, Chan MS. Is pseudotumor cerebri in SLE a thrombotic event? J Rheumatol 1990;17:983-4.
17. Denburg JA, Temesvari P. The pathogenesis of neuropsychiatric lupus. Can Med Assoc J 1983;128:257-60.
18. Rudin DO. The choroid plexus and system disease in mental ilness. I: a new brain attack mechanism via the second blood-brain barrier. Biol Psychiatry 1980;15:517-39.