

Benign Intracranial Hypertension and Leukoencephalopathy due to Venous Sinus Stenosis in an SLE Patient

T. Yasude MD¹, Y. Sekijima, MD, PhD^{1,2}, S. Mitsuhashi, MD, PhD¹, T. Gono, MD, PhD¹,
M. Matsuda, MD, PhD¹, S. Ikeda MD, PhD¹

¹Department of Medicine (Neurology and Rheumatology) and ²Division of Clinical and Molecular Genetics, Shinshu University School of Medicine,
3-1-1 Asahi, Matsumoto 390-8621, Japan

Address correspondence to: Yoshiki Sekijima,

Department of Medicine (Neurology and Rheumatology),

Shinshu University School of Medicine,

3-1-1 Asahi, Matsumoto 390-8621, Japan

TEL +81-263-37-2673 FAX +81-263-37-3427

E-mail sekijima@hsp.md.shinshu-u.ac.jp

Running title: BIH due to Venous Sinus Stenosis in SLE

Summary

Benign intracranial hypertension (BIH) is an uncommon syndrome of neuropsychiatric systemic lupus erythematosus (SLE) and one of the causes of intractable headache in SLE patients. We report the first SLE patient complicated by BIH and leukoencephalopathy due to venous sinus stenosis which resolved with high-dose steroids and warfarin. BIH should be included in the spectrum of neuropsychiatric manifestations during the course of SLE. MRI combined with MR venogram should be performed in SLE patients with intractable headache.

Key words: benign intracranial hypertension, SLE, venous sinus stenosis, leukoencephalopathy, magnetic resonance venography

Introduction

Involvement of the central nervous system is one of the most important complications of systemic lupus erythematosus (SLE), occurring in 14-75% of SLE patients. The common manifestations of neuropsychiatric SLE include headaches, psychosis, cognitive impairment, seizures and cerebrovascular disorders. Benign intracranial hypertension (BIH), also called pseudotumor cerebri, is an uncommon syndrome of neuropsychiatric SLE and one of the causes of intractable headache in SLE patients; the pathophysiologic mechanism in these cases is largely unknown. Here, we report an SLE patient who developed BIH and leukoencephalopathy due to venous sinus stenosis.

Case Report

The patient was a 27-year-old Japanese man. Five years earlier, he was diagnosed as having SLE based on arthralgia, alveolar hemorrhage, decreased serum complement levels, and positive results for anti-nuclear antibody (ANA), anti-dsDNA antibody, and anti-Sm antibody. In June 2005, he developed low-grade fever, headache, blurred vision, nausea, and general fatigue and was admitted to another hospital on July 16. Despite treatment with methylprednisolone (40 mg/day), the symptoms gradually deteriorated. The patient was transferred to our hospital on August 30, 2005. On physical examination, the face, neck, lung, heart, abdomen, joints and extremities were normal. Neurological examination demonstrated bilateral papilledema but visual acuity and visual field were normal. Laboratory results showed a white blood cell count of 17,710 / μ L, hemoglobin of 11.9 g/dL, and platelet count of 241,000 / μ L. Erythrocyte sedimentation rate was 20 mm/hr. Serum liver and kidney function tests were normal. PT and APTT were 10.8 sec and 23.0 sec, respectively. Complement levels were decreased: C3, 39 mg/dL (normal, 86-160) and C4, 4.7 mg/dL (normal, 17.0-45.0). Serological tests showed ANA x2,560 (normal, \leq x20), anti-dsDNA antibody 9.8 IU/mL (normal, <12.0), anti-Sm antibody 75.6 index (normal, <30), and anti-RNP antibody 120.4 index (normal, <22.0). Tests for anticardiolipin antibody and lupus anticoagulant were negative. Lumbar puncture produced clear and colorless cerebrospinal fluid (CSF) with an opening pressure of 280 mmH₂O, cell count of 2 /mm³, protein level of 61 mg/dl, and glucose level of 53 mg/dl. Brain CT and MRI demonstrated diffuse brain edema without space occupying lesion. Diffuse high-intensity signal of the cerebral white matter was observed on T2-weighted and fluid-attenuated inversion recovery MRI (Fig. 1A). MR venogram (MRV) disclosed severe stenosis of the superior sagittal sinus

and bilateral transverse sinuses (Fig. 1B). On RI cisternography, there was no delayed absorption of CSF. The patient was treated with high-dose steroids (intravenous 1000 mg methylprednisolone daily for 3 days) followed by 20 mg dexamethasone daily, glycerin and warfarin, with symptomatic improvement. Follow-up brain MRI/MRV showed marked improvement of leukoencephalopathy (Fig. 1C) and venous sinus stenosis (Fig. 1D).

Discussion

Diagnosis of BIH requires increased intracranial pressure without clinical, laboratory or radiological evidence of a space-occupying lesion or hydrocephalus. This patient fulfilled all of these criteria for BIH as well as manifesting symptoms and signs that suggested increased intracranial pressure, such as intractable headache, nausea, vomiting and bilateral papilledema. Although BIH is associated with various conditions, the etiology of the disease is incompletely understood. SLE is one of the diseases underlying BIH, albeit not common.¹⁻⁸ The pathophysiological mechanism of BIH in SLE remains to be elucidated. It is not clear whether hyperproduction of CSF, relative absorptive failure of CSF or increased cerebral blood flow are associated with the pathogenesis. However, BIH in SLE has also been attributed to sinus thrombosis in some cases.²⁻⁶ Since cerebral angiography is not routinely performed in such cases, the prevalence of sinus thrombosis in BIH remains unknown. The same pathology may in fact be present in other BIH patients with SLE. MRI combined with MRV is recommended for diagnosis of sinus thrombosis, since it allows direct visualization and accurate delineation of the thrombus.⁹

In our patient, MRV demonstrated severe venous sinus stenosis (Fig. 1B), without abnormal signal in the venous sinus on routine MRI. In combination with successful treatment using steroids and warfarin, these radiological findings suggest that venous sinus stenosis was induced by vasculitis and/or small thrombi associated with SLE in this case. The other possibility is that increases in intracranial pressure causes a secondary extrinsic compression of the venous sinus, accentuating venous hypertension and prompting the development of BIH [10]. Since sinus thrombosis/stenosis is a treatable condition¹⁰ that may be missed on routine CT and MRI, MRV should be performed under these circumstances.⁹ Another unique radiological finding in our patient was diffuse leukoencephalopathy. Although two other SLE patients demonstrating BIH and leukoencephalopathy have been reported to date [7,8], the precise mechanism of BIH and leukoencephalopathy was unclear in these cases. To our knowledge, this is the first SLE patient complicated by BIH and

leukoencephalopathy due to venous sinus stenosis, which resolved with high-dose steroids and warfarin.

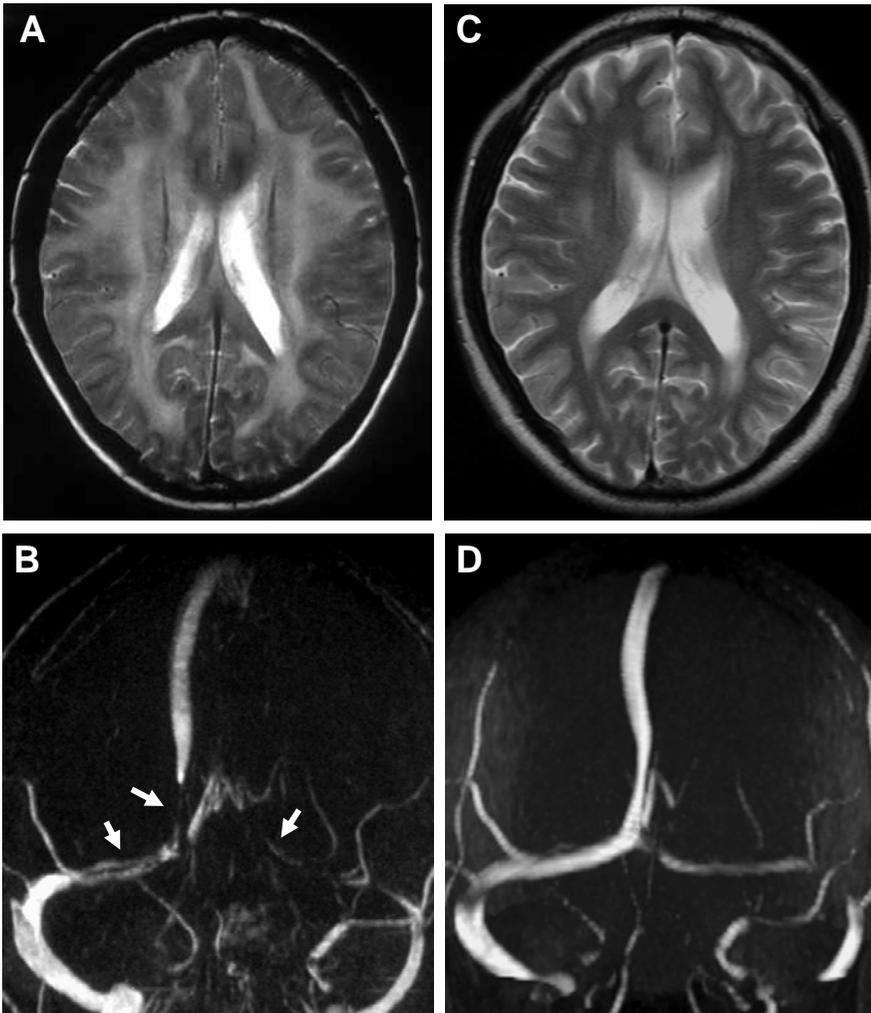
Headache is the most common neurologic symptom encountered in patients with SLE and is attributable to different syndromes. BIH should be included in the spectrum of neuropsychiatric manifestations during the course of SLE. MRV, in addition to routine MRI, should be performed in SLE patients with intractable headache.

References

1. Green L, Vinker S, Amital H, et al. Pseudotumor cerebri in systemic lupus erythematosus. *Semin Arthritis Rheum* 1995; **25**: 103-108.
2. Kaplan RE, Springate JE, Feld LG, Cohen ME. Pseudotumor cerebri associated with cerebral venous sinus thrombosis, internal jugular vein thrombosis, and systemic lupus erythematosus. *J Pediatr* 1985; **107**: 266-268.
3. Shiozawa Z, Yoshida M, Kobayashi K, Tsunoda S, Mano T. Superior sagittal sinus thrombosis and systemic lupus erythematosus. *Ann Neurol* 1986; **20**: 272.
4. Parnass SM, Goodwin JA, Patel DV, Levinson DJ, Reinhard JD. Dural sinus thrombosis: a mechanism for pseudotumor cerebri in systemic lupus erythematosus. *J Rheumatol* 1987; **14**: 152-155.
5. Li EK, Chan MS. Is pseudotumor cerebri in SLE a thrombotic event? *J Rheumatol* 1990; **17**: 983-984.
6. Flusser D, Abu-Shakra M, Baumgarten-Kleiner A, Flusser G, Sukenik S. Superior sagittal sinus thrombosis in a patient with systemic lupus erythematosus. *Lupus* 1996; **5**: 334-336.
7. Ogawa M, Ishimaru K, Shioto T, Baba M, Matsunaga M. A case of benign intracranial hypertension associated with systemic lupus erythematosus (SLE) showing diffuse white matter lesions on MRI. *Rinsho Shinkeigaku* 1994; **34**: 577-581. Japanese.
8. Chaves-Carballo E, Dabbagh O, Bahabri S. Pseudotumor cerebri and leukoencephalopathy in childhood lupus. *Lupus* 1999; **8**: 81-84.
9. Fera F, Bono F, Messina D, et al. Comparison of different MR venography techniques for detecting transverse sinus stenosis in idiopathic intracranial hypertension. *J Neurol* 2005; **252**: 1021-1025.
10. Higgins JN, Cousins C, Oowler BK, Sarkies N, Pickard JD. Idiopathic intracranial hypertension: 12 cases treated by venous sinus stenting. *J Neurol Neurosurg Psychiatry* 2003; **74**: 1662-1666.

Figure legends

Figure. (A, B) Brain MRI and MR venogram (MRV) of the patient. T2-weighted MRI showed diffuse high intensity signal of the cerebral white matter with brain edema (A). MRV showed severe stenosis of the superior sagittal sinus and bilateral transverse sinuses (arrows, B), although there was no abnormal signal in the venous sinuses on T1- or T2-weighted or fluid-attenuated inversion recovery MRI. (C) MRI performed ten months later showed marked improvement of leukoencephalopathy. (D) MRV performed one month later showed marked improvement of flow in the superior sagittal sinus and bilateral transverse sinuses.



Yasude et al. Figure 1