

The Syndrome of Bilateral Basal Ganglia Lesions in Diabetic Uremic Patients Presenting with a Relapsing and Remitting Course: A Case Report

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Abstract- The syndrome of acute bilateral basal ganglia lesions presents with parkinsonism, altered mental status, dysarthria, and dysphagia in association with specific imaging findings in the basal ganglia. It is an uncommon syndrome seen almost exclusively in patients with diabetes mellitus and renal failure. Previously reported cases have all run a monophasic course, but we report a patient with a relapsing, remitting course. This 64-year-old diabetic man with uremia on hemodialysis had an acute episode of disordered sensorium. Brain computed tomography showed the classic findings of hypointensity of bilateral basal ganglia. He recovered from the episode, but had another with parkinsonian symptoms about 18 months later. Sequential brain images demonstrated encephalomalacia of the basal ganglia. His condition waxed and waned several times, but he eventually died of unknown causes less than 2 years after the first event. This syndrome, therefore, may not be limited to just one episode.

Key Words: Diabetes mellitus, Uremia, Parkinsonism, Encephalomalasia, Basal ganglia

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INTRODUCTION

A syndrome of acute bilateral basal ganglia lesions has been reported in patients with diabetes and uremia^(1,2). The symptoms included parkinsonism, disturbance of consciousness, dysarthria, dysphagia, dyskinesia, ataxia, and seizures. As reported to this point, the syndrome has been monophasic⁽¹⁻⁷⁾. Although the neurologic symptoms usually improve, most reported patients have died soon thereafter, usually of infection. Imaging

changes are seen in the acute phase, but follow-up studies weeks or months later reportedly show resolution of the brain lesions. In a few cases, encephalomalacia or cystic lesions of the basal ganglia have been reported^(1,3). We report a patient with this syndrome who had a unique relapsing, remitting course.

CASE REPORT

A 64-year-old man with a history of hypertension

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and diabetes mellitus had diabetic nephropathy which had progressed to end-stage renal disease. He began regular hemodialysis three times a week in January 2001. In July 2003, he had an episode of disturbed sensorium that lasted for 2 weeks. Brain computed tomography (CT) obtained at that time demonstrated hypointensity of the basal ganglia bilaterally (Fig. 1A). He recovered from this episode without apparent sequelae.

In mid-December 2004, he had the acute onset of slurred speech and involuntary movements of both wrists and forearms. A brain CT revealed less degree of hypointensity affecting bilateral basal ganglia comparing with previous one (Fig. 1B). The symptoms improved without any specific treatment and he was discharged. Two days later, he was readmitted due to festinating gait and slurred speech. These symptoms worsened and he became stuporous. Neurologic examination revealed

intact cranial nerves and a plantar reflex bilaterally. The patient's muscle power was grade 3 of 5 in all extremities. There was rigidity at both wrists and symmetrically increased deep tendon reflex in all four limbs. The complete blood count and different count revealed only mild anemia (Hemoglobin 9.0) and white blood cells were within normal limits. Normal fasting sugar, serum aluminum and electrolytes were noted. The serum ammonia level was elevated at 132 $\mu\text{g/dL}$, as was the serum elevated blood urine nitrogen (84 mg/dL), and creatinine (8.6 mEq/L). A chest x-ray demonstrated pulmonary edema. On repeated brain CT, the hypointensity of the basal ganglia, especially the globus pallidus, was even more marked than on the earlier study (Fig. 1C). Brain magnetic resonance imaging (MRI) performed with fluid attenuation inversion recovery (FLAIR) imaging 12 days after the initial onset of symptoms showed bright signals

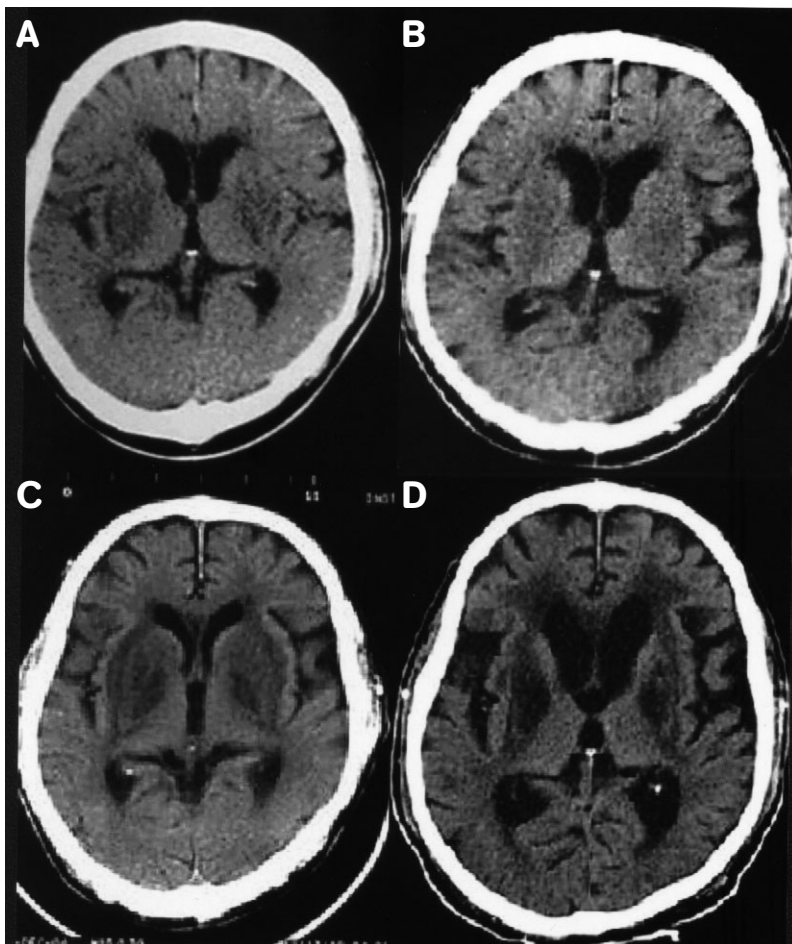


Figure 1. (A) Brain CT in July 2003, showing hypodensity of both basal ganglia. (B) Brain CT in mid-December 2004, showing less hypodensity in both basal ganglia comparing with previous imaging. (C) Brain CT in late December 2004, showing extensive and marked hypodensity in both basal ganglia, particularly in the globus pallidus and claustrum. (D) Brain CT in April 2005, showing cortical atrophy and encephalomalacia in the lenticular nuclei with relative preservation of the caudate nucleus.

in the diencephalon and cerebral peduncles bilaterally (Fig. 2A, B). T1-weighted image (Fig. 2C) showed hyperintensity in the left basal ganglia, possibly attributable to petechial hemorrhage.

Three days later, the patient developed stridor, wheezing, and respiratory failure, requiring mechanical ventilation. He was thought to have sepsis and was treated with antibiotics. In addition to the previous neurologic findings, Babinski signs developed bilaterally. Brain MRI (Fig. 3) repeated in early January 2005 showed periventricular white matter changes and encephalomalacia of the lenticular nuclei. FLAIR (Fig. 3A) and diffusion-weighted image (DWI) (Fig. 3B) showed hyperin-

tensity of the lenticular nuclei, thought perhaps to indicate petechial hemorrhaging.

The patient's course was complicated, but again he eventually recovered without obvious sequelae and was discharged. However, in April 2005, he had another acute episode of stupor, speechlessness, and inability to walk. Brain CT revealed dense hypointensity of the lenticular nuclei bilaterally, marked brain atrophy, and dilatation of the ventricles (Fig. 1D). He again recovered neurologically with only supportive treatment. He was discharged but died at home of an unknown cause in May 2005.

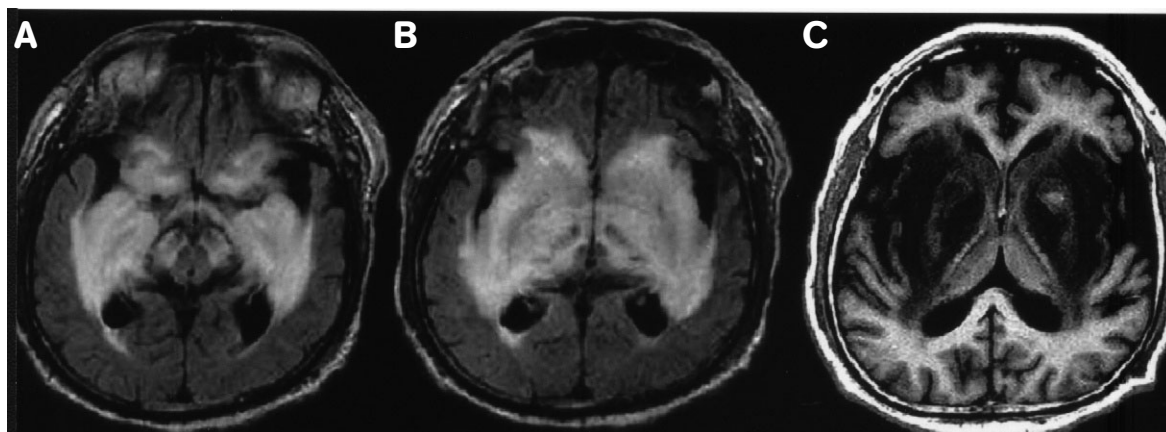


Figure 2. Brain MRI in late December 2004, twelve days after the initial onset of symptoms. FLAIR images (A, B) showing extensive hyperintensity in the basal ganglia bilaterally, extending to the neighboring white matter and cerebral peduncles. T1-weighted image (C) showed hyperintensity in the left basal ganglia.

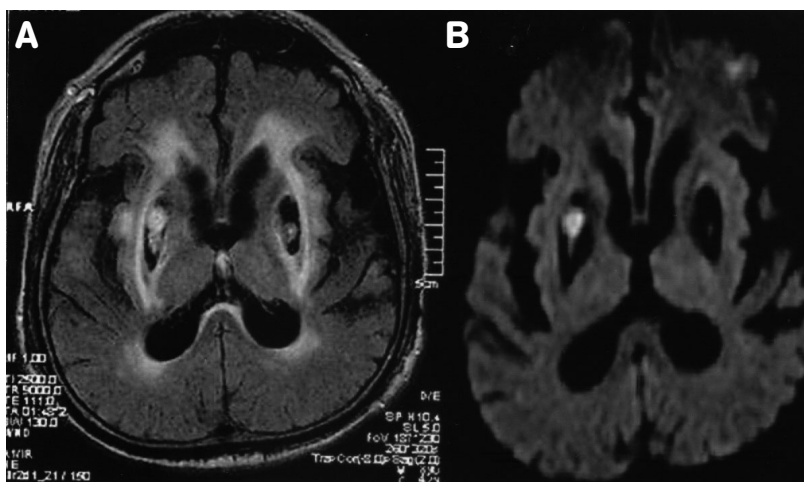


Figure 3. Second brain MRI in January 2005, 21 days after the onset of the symptoms. FLAIR image (A) shows periventricular white matter changes and encephalomalacia of both lenticular nuclei. DWI (B) and FLAIR image (A) show high signal intensity in the lenticular nuclei bilaterally.

DISCUSSION

This patient had a relapsing, remitting course of the syndrome of acute bilateral basal ganglia lesions, a previously unreported disease pattern. If the syndrome is diagnosed, it's important to be aware that more than one episode is possible. It has been reported that the abnormal basal ganglia lesions seen in imaging are mostly reversible⁽¹⁾. While our patient had some improvement after the first episode (Fig. 1B), he went on to have severe encephalomalacia both in cortical and subcortical areas, particularly in the lenticular nuclei. The head of the caudate and the thalamus were relatively intact, even in the late stage of the disease (Fig. 1D).

Lee⁽⁵⁾ and Lee et al.⁽⁶⁾ reported cases in which, in the acute stage, the lenticular nuclei lesions were bright on DWI and hypointense on apparent diffusion coefficient (ADC) mapping. This suggested that these structures were the earliest involved, perhaps by some type of cytotoxic injury⁽³⁾. This initial injury might then induce a cascade of metabolic or energy failure, causing vasogenic edema in the neighboring structures⁽⁴⁾. This theory would explain why the most severe changes are seen in the lenticular nuclei. In our patient, the resulting edema was so severe that it involved the insular cortex, diencephalon, and cerebral peduncles (Fig. 2).

The initiating event for the cytotoxic injury is still unknown. It has been attributed to hemodynamic changes occurring during hemodialysis, but the syndrome has been seen in a few patients on continuous ambulatory peritoneal dialysis or who have never been dialyzed⁽¹⁾. Another theory implicates uremic neurotoxins, which may still accumulate to some extent despite adequate dialysis. These toxins might cause the death of neurons, particularly basal ganglia cells which are easily injured by toxins and metabolic derangements. If the damage were to exceed a certain threshold level, the blood brain barrier might be broken down and vasogenic edema could ensue⁽⁵⁻¹²⁾, with full-blown expression of the syndrome. This raises the question of whether more frequent dialysis during the acute stage⁽⁶⁾ or thereafter might be considered. Similarly, kidney transplantation might also confer protection from a repeat episode. There is as

yet, however, no evidence that this works.

Lee et al.⁽⁶⁾ reported one patient with this syndrome who did not have diabetes, raising doubts as to whether diabetes is a necessary factor in provoking the injury. It has been shown that vascular autoregulatory dysfunction, such as may occur in diabetes, can interfere with dopamine metabolism in the basal ganglia⁽¹³⁾. Since most reported patients with the syndrome have had a long history of diabetes, it may be that basal ganglia injury occurs more easily when the adverse effects of diabetes and uremia on the brain are combined.

CONCLUSION

There is still much to learn about the pathophysiology of the acute bilateral basal ganglia syndrome, but our case demonstrates that it should not be assumed to be a monophasic disease. The progression of the patient's imaging abnormalities to encephalomalacia suggests that repeated attacks may cause more severe injury, especially in the lenticular nuclei. Whether more aggressive treatment of the uremia, hyperglycemia, or both can ameliorate or prevent the syndrome remains to be determined.

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