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Case report

Unstable blood sugar levels as triggers for the syndrome of acute bilateral basal ganglia lesions in diabetic uremia: Two Taiwanese patients with unusual neuroimaging findings

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ABSTRACT

The syndrome of acute bilateral basal ganglia lesions in diabetic uremia is uncommon and usually affects Asian patients. The underlying pathogenesis of this syndrome is not clear. We searched PUBMED using the keywords "bilateral basal ganglia", "diabetic", and "uremia", and found a total of 34 cases from 1998 to 2016. In most cases, blood sugar levels were normal. Here we report two Taiwanese cases presenting with dyskinesias. In one case the syndrome was triggered by hyperglycemia, and in the other by severe hypoglycemia. Their neuroimaging findings were unusual as compared with previously reported cases, presenting as mixed hypo- and hyperintensity on T1-weighted magnetic resonance imaging. We think these new finding would shed some light on the underlying pathophysiology of this syndrome. For treatment, it is advisable to keep glucose levels as stable as possible in diabetic uremic patients to prevent this syndrome. A rapid correction of hyper- or hypoglycemia after the onset may help recovery.

1. Introduction

The syndrome of acute bilateral basal ganglia lesions in diabetic uremia is a well-established but uncommon syndrome affecting mainly middle to old-aged Asian patients [1]. Typical clinical manifestations include acute involuntary movements, dysarthria, unsteady gait or parkinsonism [1–4]. Characteristic neuroimaging findings are reversible symmetrical lesions in bilateral basal ganglia with cytotoxic and/or vasogenic edema [5–8]. We conducted a computerized PUBMED literature review, using the keywords "bilateral basal ganglia", "diabetic", and "uremia". Only articles written in English with available abstracts were included. A total of 17 articles were included within the period from 1998 to 2016. The references of all those original and review articles were searched for relevant citations. After excluding one case who had no diabetic mellitus, we found a total of 34 cases reported so far. Here we report 2 new cases of acute bilateral basal ganglia lesions in diabetic uremia presenting with dyskinesias. One is associated with hyperglycemia, and the other is associated with hypoglycemia. Both of them have representative unusual brain magnetic resonance imaging (MRI) findings as compared with previously reported cases. This study was approved by Taipei City Hospital Research Ethics Committee (the approval number: TCHIRB-10701102-E).

2. Case reports

2.1. Case 1

The patient was a 32-year-old woman with a history of type II diabetic mellitus and hypertension for more than 10 years, coronary artery bypass grafting after myocardial infarction 5 years ago, and end stage renal disease under peritoneal dialysis for more than 4 years. She presented with an acute-onset right hand writing difficulty, which gradually progressed to right upper and lower limb chorea, cervical dystonia, gait disturbance, and then generalized dyskinesias within two weeks. Glucose level up to 436 mg/dl without ketone acidosis was noted. The thyroid function was within normal ranges (T3: 98 ng/dl, free-T4:1.12 ng/dl, TSH:1.08 uIU/ml). On examination, she was oriented and had no focal neurological signs other than aforementioned involuntary movements. A brain computed tomography (CT) scan showed some small calcified density in the left globus pallidus (red

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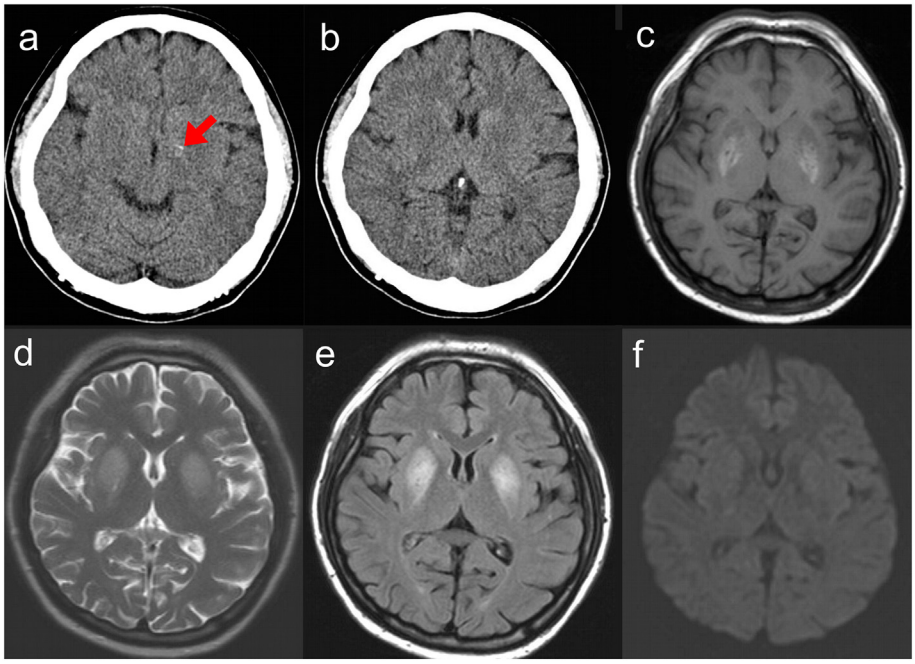

Fig. 1. Initial brain CT scan shows small calcified density in left globus pallidus (red arrow) (a) without abnormal signal in the other region (b). T1-weighted MRI axial view shows symmetric mixed hypo- and hyperintensity in bilateral basal ganglia (c). T2-weighted MRI (d) and FLAIR image (e) show hyperintensity on bilateral basal ganglia. Unenhanced DWI (f) does not demonstrate signal change in either of the basal ganglia. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

arrow) without other abnormalities (Fig. 1a, b). A brain MRI showed symmetric mixed hypo- and hyperintensity in bilateral basal ganglia on T1-weighted images (Fig. 1c), and hyperintensity on T2-weighted and fluid attenuation inversion recovery (FLAIR) images (Fig. 1d, e). Unenhanced diffusion-weighted image (DWI) did not show any signal changes in the basal ganglia (Fig. 1f).

We corrected her glucose to a level around 100–350 mg/dl within 5 days and kept regular dialysis. Besides, haloperidol and clonazepam were prescribed. However, these treatments did not stop her symptoms from progressing. Aside from the dyskinesias, her balance became poor, and she needed assistance standing up or walking in the subsequent 2 weeks.

Unfortunately, she developed acute coronary syndrome, lactic acidosis, spiking fever, and status epilepticus on the 17th day after symptom onset. A brain CT scan at the time revealed spontaneous subarachnoid hemorrhage, intraventricular hemorrhage and bilateral intracerebral hemorrhage. She expired on the 28th day.

2.2. Case 2

The patient was a 56-year-old woman with a history of type II diabetic mellitus for 10 years. She had been diagnosed with end stage renal disease and has received regular hemodialysis for 1 year. Acute generalized involuntary movements without change of consciousness developed after an episode of hypoglycemia (glucose: 23 mg/dl). Her thyrotropin level was normal (TSH:1.34 uIU/ml). There was no metabolic acidosis. The involuntary movements included bilateral limb ballism and dystonia, as well as orolingual, facial, and truncal dyskinesias. A brain CT scan showed bilateral symmetric low densities in the basal ganglia (Fig. 2a). T1-weighted brain MR image showed symmetric hypointensity of bilateral basal ganglia with faint high signal in the medial peripheral parts (Fig. 2b). T2-weighted image, FLAIR and DWI showed hyperintensity of the same regions (Fig. 2c–e). Apparent diffusion coefficient (ADC) map of those regions demonstrated isosignal intensities (Fig. 2f). Her blood sugar was corrected to the normal range along with regular hemodialysis. Haloperidol 10 mg/day was also prescribed. Her involuntary movements gradually improved over 3 weeks. However, a maintenance haloperidol of 1-2 mg per day was needed to keep the dyskinesias under reasonable control. Her blood sugar levels fluctuated in the following months, together with waxing and waning dyskinesias. Brain MRI follow-up 2 months after symptom onset revealed a regression of most of the lesions (Fig. 2h-j) except that the hyperintensity on T1-weighted image remained stationary (Fig. 2g). It showed partial regression after 6 months (Fig. 2k) and total resolution 2.5 years later (Fig. 2l).

3. Discussion

Typical brain MRI findings of the syndrome of acute bilateral symmetrical basal ganglia lesions in diabetic uremia consist of reversible bilateral symmetric basal ganglia lesions, with decreased signal intensity on T1-weighted images and increased signal intensity on T2-weighted images [6,9] with cytotoxic and/or vasogenic edema [5–8]. These changes are rather specific. In contrast to these reported typical image findings, both our cases demonstrated the unique MRI findings of mixed hypo- and hyperintensities on T1-weighted images. In most report cases, the blood sugar levels were normal. Thus an abnormal sugar level has not been considered a trigger for this syndrome. However, our experience of these 2 cases suggests that multiple trigger factors may also be involved in the occurrence of this syndrome. The basal ganglia changes triggered by hypo- or hyperglycemia in uremic patients may have a pathophysiology different from that proposed in the previously reported cases, as evidenced by their unique neuroimage changes. These changes are also distinct from those seen in another well-established entity: chorea induced by non-ketotic hyperglycemia, in which the basal ganglia lesion is usually unilateral, and shows hyperintensity change on T1-weighted MRI and variable changes on T2. [10] Although in rare cases lesions associated with chorea induced by non-ketotic hyperglycemia can also be bilateral, the signal characteristics can clearly differentiate between these two syndromes.

Possible pathogenesis of the syndrome of bilateral basal ganglia lesions in diabetic uremia may include diabetic microangiopathy, uremic toxins, and metabolic acidosis. In one FDG-PET study, markedly reduced glucose metabolism in the basal ganglia was noted [11]. Basal ganglia require high energy supplementation and blood supply for normal functioning. They are susceptible to a wide range of metabolic changes, such as dramatic change of blood sugar level, and toxins [9]. Metabolic acidosis was observed in most of the cases although was not present in some [2,12]. Multiple factors may coexist in deranging the regional cellular metabolism, as well as inducing a functional

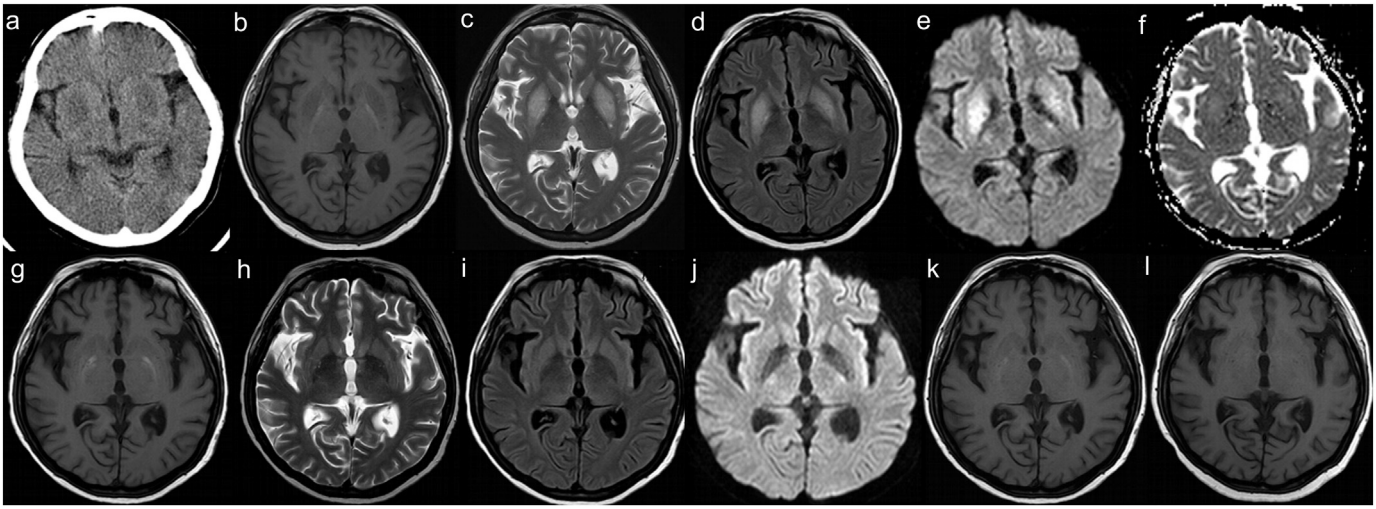

Fig. 2. Brain CT scan shows bilateral symmetric low densities in both basal ganglia (a). T1-weighted MRI axial view shows symmetric hypointensity on bilateral basal ganglia with high signal in medial peripheral part (b). T2-weighted MRI (c), FLAIR image (d) and DWI (e) show hyperintensity on bilateral basal ganglia. Apparent diffusion coefficient map does not demonstrate signal change in either of the basal ganglia (f). Repeat MRI 2 months after symptom onset shows the symmetric hyperintensity on part of bilateral basal ganglia remains stationary on T1-weighted image (g) but marked regression of most of the symmetrical basal ganglia lesions on T2-weighted image (h), FLAIR image (i) and DWI (j). Follow-up MRI 6 months later shows partial regression of the lesion on T1-weighted image (k), and total resolution 2.5 years later (l).

disturbance in smooth muscle cells of the vessel in the basal ganglia, leading to vascular autoregulatory dysfunction, vasodilatation, focal hyperaemia and basal ganglia damage [1,2]. These mechanisms can account for those typical MRI image changes [1]. In contrast to our cases, previously reported cases of acute bilateral basal ganglia lesions in diabetic uremia usually had normal blood sugar levels at syndrome onset.

Our cases had hyperintensity on T1-weighted MRI images. These changes had been reported in non-ketotic hyperglycemia [10], as well as in hypoglycemic coma [13]. One of our cases had hyperglycemia, while the other had severe hypoglycemia.

Hyperglycemia can produce impairment of the endothelium-dependent vasoreactivity of cerebral arterioles and cause blood-brain barrier breakdown and increases free radical release [6]. These mechanisms characteristically lead to hypersignal intensity on T1-weighted images. A synergistic action of poorly controlled blood sugar and vascular insufficiencies may be the possible cause of the lesions of the striatum [10]. Excessively low glucose level had been rarely cited as a possible trigger factor for this syndrome [12,14]. Diabetic uremic patients can be prone to hypoglycemic episodes due to their metabolic deficits and changes in insulin clearance [3]. Jurynczyk et al. deemed the role of hypoglycemia in the basal ganglia lesions to be cytotoxic edema manifesting as low ADC values in the central part of the involved regions [12], which was not shown in our case 2. Possible mechanisms of hypoglycemia-related brain lesions include tissue degeneration, lipid accumulation, proliferation of astrocytic glial cells, paramagnetic substance deposition, selective neuronal death, as well as a combination of these change [13]. These heterogeneous pathologic changes can explain those heterogeneous MRI changes (mixed hypo- and hyperintensities on T1-weighted image) in our case 2. The reversible T1-weighted image findings suggested that good control of blood sugar may prevent permanent brain damages. Our case 2 also presented a relapsing-remitting course in the following months in accordance with previous reports [7,15].

In conclusion, although sugar levels were normal in most cases of the syndrome of bilateral basal ganglia lesions in diabetic uremia, hyperglycemia and hypoglycemia can both trigger its occurrence. Thus it is advisable to keep glucose levels as stable as possible in diabetic uremic patients. A mixed intensity changes of the basal ganglia seem to be typical for hyperglycemia or hypoglycemia induced acute bilateral basal ganglia lesions in diabetic uremic patients. In general, only symptomatic treatment and supportive care are required in the previously reported cases. However, based on our experience of these 2 new cases, a rapid correction of hyper- or hypoglycemia (if present) after the onset may be necessary. One of our patients had poor prognosis and the other had clinical improvement and regression of most of the lesions, compatible with the variable long-term outcomes reported before.

Declarations of interest

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