Rare disease

Unusual basal ganglia lesions in a diabetic uraemic patient proven to be demyelination: first pathological observation

Yasutaka Tajima,¹ Yasunori Mito,¹ Mituru Yanai,² Yu-ichiro Fukazawa²¹Department of Neurology, Brain Health Center, Sapporo City General Hospital, Sapporo, Japan²Department of Pathology, Sapporo City General Hospital, Sapporo, Japan

Correspondence to Dr Yasutaka Tajima, yasutaka.tajima@doc.city.sapporo.jp

Summary

A 64-year-old man suffering from diabetes mellitus and chronic renal failure was admitted to our hospital because of consciousness disturbance and parkinsonism. Cranial MRI showed very characteristic features involving the bilateral basal ganglia. Subsequent postmortem examinations demonstrated demyelination in the affected areas. These myelin destruction patterns were quite similar to those of central pontine myelinolysis. However, rapid correction of hyponatraemia was ruled out in this patient. Therefore, a new demyelinating brain disease associated with diabetes mellitus and chronic renal failure was suggested.

BACKGROUND

There are reports describing unique MRI signal alterations of basal ganglia and parkinsonism in patients with diabetic uraemic encephalopathy.^{1–5} Typical radiological findings were symmetrically spreading lesions with T2 high-signal intensities in the basal ganglia. The common clinical manifestation is parkinsonism, but dyskinesia, consciousness disturbance and acute choreic movements have also been described. This rare condition is seen mostly in Asian patients and some researchers suspect a genetic background. However, the precise pathogenic mechanisms remain obscure. We present herein a patient with diabetic uraemia who developed acute basal ganglia lesions and exhibited consciousness disturbance with parkinsonism. We sequentially analysed this patient's cranial MRI findings. Despite intensive treatments, he died of sepsis 10 months after admission, and postmortem pathological examinations revealed myelinolysis in the affected areas of the brain. To the best of our knowledge, these are the first pathological observations of this peculiar form of diabetic uraemic encephalopathy.

CASE PRESENTATION

The patient was a 64-year-old man with a 30-year history of diabetes mellitus and secondary chronic renal failure. He had started haemodialysis 3 months previously, but continued to work as the president of a construction company. He had noticed gradual worsening of his motor activity for 2 weeks. Two days prior to admission, the patient's wife had found him to be slightly confused. Neurological examination revealed consciousness disturbance (Glasgow Coma Scale, E3.M5.V3), mutism, a masked face, bradykinesia, muscular rigidity and hypoactive deep tendon reflexes. Pathological reflexes were not elicited. He could not stand without assistance and his posture was stooped. Cranial nerves were not impaired. Cerebellar and sensory systems could not be tested. No involuntary movements including resting tremor were seen.

Blood chemistry examination showed elevated blood urea nitrogen (74 mg/dl) and creatinine (13.31 mg/dl) levels. Potassium was 6.7 mg/dl and sodium was 137 mg/dl. Blood glucose was 129 mg/dl. MRI demonstrated marked T2-weighted hyperintensity in the lenticular nuclei and caudate nuclei bilaterally (figure 1A). There were no abnormal findings in the pons and cerebellum (figure 1D).

Diffusion-weighted MRI demonstrated high-signal intensities in the middle of the affected areas (figure 1B) and the apparent diffusion coefficient (ADC) map showed reduced ADC values in these areas (data not shown). T1-weighted MRI demonstrated slightly low-signal alterations without gadolinium enhancement in these lesions (figure 1C). Cerebrospinal fluid examination revealed a cell count of 2/mm³ and protein level of 88 mg/dl. MR angiography showed no evidence of vascular obstruction. Proton MR-spectroscopy (MRS) showed a very low level of *N*-acetyl aspartate (NAA) in the basal ganglia lesions (data not shown). Supportive management and regular haemodialysis were continued during hospitalisation. The patient's consciousness normalised 3 days after admission and his parkinsonism gradually improved without specific medication. He could walk without assistance 2 months after admission. Masked face and muscular rigidity still remained slightly, whereas the patient was considered to be able to return to his home with minimum assistance. One month later, however, the patient suffered repeated severe infections such as pneumonia and parotitis. His clinical condition deteriorated rapidly, and he was bedridden for several months. The patient ultimately died of pneumonia following septic shock 10 months after admission. Follow-up MRI at 3 months after admission demonstrated that the bilateral T2-weighted high-signal intensity basal ganglia lesions had shrunk (figure 1E). Diffusion-weighted MRI showed resolution of the previous high signal lesions and that the central part of the putamen had a slightly lower signal. Faint

Figure 1 Temporal profile of MRI signal alterations. On admission, markedly high-signal intensities on T2-weighted MRI, the characteristic owl eye appearance, were seen in the bilateral basal ganglia (A). Diffusion-weighted MRI (the b value was 1000 s/mm²) also demonstrated very high-signal intensities inside the area of high-signal intensity on T2-weighted MRI (B). T1-weighted MRI demonstrated iso-signal and slightly low-signal changes without gadolinium enhancement (C). T2-weighted MRI did not show abnormal signal alterations in the pons and cerebellum (D). After 3 months, T2-weighted examinations showed high-signal intensity areas to be smaller (E). Diffusion-weighted MRI showed resolution of the previous high signal lesions and that the central part of the putamen had a slightly lower signal. Faint high-signal intensities persisted at the periphery (F). T1-weighted MRI showed low-signal intensities in more restricted areas of the putamen (G).

high-signal intensities persisted at the periphery (figure 1F). Additionally, low-signal intensities became more prominent on T1-weighted MRI (figure 1G). Postmortem examinations confirmed lung abscesses that could have induced septic shock. Macroscopically, lesions that had shown high-signal intensity on T2-weighted MRI in the lenticular nuclei demonstrated liquefied degenerative change with brown pigmentation (figure 2A). Microscopic examinations demonstrated areas of myelin breakdown without inflammatory changes with clear borderlines. Vascular damage such as vessel occlusion or vasculitis was not recognised. There was no evidence of infiltration of inflammatory lymphocytes (figure 2B). Serial sections with affected areas with K.B. staining indicated marked loss of myeline (figure 2D), but axons were still identifiable under Bodian staining (figure 2E). Small vessel did not show abnormal findings. Immunostaining with

anti-CD68 antibody revealed partial proliferation of macrophages in the affected areas (figure 2C).

OUTCOME AND FOLLOW-UP

The patient ultimately died of pneumonia following septic shock 10 months after admission.

DISCUSSION

Given the rarity of this condition, our presentation is of special importance because we followed temporal MRI signal alterations and conducted postmortem examinations in this case. Pathological observations were especially significant for the clarification of underlying disease mechanisms. As previously noted, the patient's MRI examinations demonstrated very characteristic appearances.^{1–4} Initially, his basal ganglia showed marked high-signal intensities on T2-weighted and diffusion-weighted MRI. The areas of T2-weighted

Figure 2 Postmortem pathological examinations. Bilaterally, the basal ganglia showed degeneration with brown pigmentation and liquefaction (A). Microscopically, these lesions had clearly visible borderline. Neither angiopathic nor inflammatory cell infiltration were recognised (B; H&E staining $\times 4$). Serial section of the affected area showed marked loss of myeline but axons still remained. Small vessel did not exhibit pathological appearances (D: K.B. staining $\times 100$, E: Bodian staining $\times 100$). In the very restricted small areas in the demyelination, proliferation of macrophages was detected (C: immunostaining with anti-CD68 antibody, $\times 200$).

high-signal intensities were broader than those of diffusion-weighted high-signals intensity. ADC values were reduced in most of the diffusion-weighted high-signal intensity areas. Follow-up T2-weighted MRI showed shrinkage of the affected lesions, while diffusion-weighted MRI showed resolution of the previous high-signal lesions. Therefore, initially, that is, in the acute stages, irreversible cytotoxic oedema occurred at the centres of the lesions, and vasogenic oedema of the peripheral areas was reversible. MRS revealed marked reductions of NAA and also indicated neuronal cell damages in the middle of the affected areas. Degenerative changes induced by cytotoxic oedema persisted, and appeared on T2-weighted images as high signal and on T1-weighted images as low-signal intensity lesions. Our pathological examinations are the first to demonstrate marked myelin breakdown in these

lesions, because pathological observations in diabetic uraemic encephalopathy have not been previously reported. Blood vessels were not damaged and no inflammatory changes were seen. Serial sections confirmed myeline loss and preserved axon. In the very small areas, macrophage could be detected using anti-CD68 antibody immunostaining. Therefore, macrophages could play some important roles in this type of demyelinating mechanism. These pathological findings were very similar to those of central pontine myelinolysis (CPM). CPM is a well-known clinical entity caused by rapid correction of hyponatraemia.⁶ Moreover, additional demyelination may occur in extrapontine areas, such as the cerebellum and basal ganglia, and was termed as extrapontine myelinolysis. Extrapontine myelinolysis occurs in about 10% of patients with CPM and their cranial MRI often show hyperintense lesions

in the striatum. Under such circumstances, the patient may be reported to exhibit reversible parkinsonism, as in our case.^{7–9} However, affected basal ganglia tend to show relatively localised appearances that involve the caudate nuclei and putamen, and differ from basal ganglia lesions in the diabetic uraemic patient with expanding lesions that have the appearance of so-called owl eyes. Moreover, some researchers have pointed out that, in the setting of extrapontine myelinolysis, the globus pallidus is typically unaffected despite involvement of the caudate nucleus and putamen (ie, there is pallidal sparing in extrapontine myelinolysis), while most diabetic uraemic encephalopathy patients have shown involvement of the pallidum as in our case. This observation would presumably be important for differential diagnosis.^{8–10} In addition, there was no history of hyponatraemia or infusion of sodium in our case. The patient was neither alcoholic nor malnourished. Therefore, other demyelinating mechanisms differing from rapid correction of hyponatraemia, one of the major causes of CPM must be considered. In diabetic uraemic patients, increased levels of uraemic molecules might induce toxic and/or metabolic injuries of the basal ganglia tissue that have been weakened by microangiopathic changes associated with long-term diabetes mellitus (1.2). In addition, basal ganglia are by nature highly vulnerable to a wide range of toxins such as mercury, carbon monoxide and probably as yet unknown molecules produced in association with chronic renal failure. Under such circumstances, homogeneous myelin destruction would presumably occur in the affected lesions, while regeneration would not. Further analyses of demyelination in cases similar to ours are needed to elucidate the primary pathogenic event triggering this disease. The findings of radiological and pathological investigations, taken together, allow us to establish this new demyelinating disorder in diabetic uraemic patients with widespread bilateral basal ganglia involvement.

Learning points

- ▶ The patient suffering from diabetes mellitus and chronic renal failure showed very characteristic MRI features involving the bilateral basal ganglia.
- ▶ The postmortem examinations demonstrated demyelination in the basal ganglia.
- ▶ Those myelin destruction patterns were quite similar to those of central pontine myelinolysis.
- ▶ We could demonstrate the new demyelinating brain disease associated with diabetes mellitus and chronic renal failure.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. Wang HC, Brown P, Lees AJ. Acute movement disorders with bilateral basal ganglia lesions in uremia. *Mov Disord* 1998;**13**:952–7.
2. Wang HC, Gheng SJ. The syndrome of acute bilateral basal ganglia lesions in diabetic-uremic patients. *J Neurol* 2003;**250**:948–55.
3. Cupidi C, Piccoli F, Bella VL. Acute reversible parkinsonism in a diabetic-uremic patient. *Clin Neurol Neurosurg* 2006;**108**:601–3.
4. Kim TK, Seo S, Kim JH, et al. Diffusion-weighted magnetic resonance imaging in the syndrome of acute bilateral basal ganglia lesions in diabetic uremia. *Mov Disord* 2006;**21**:1267–70.
5. Wang HC, Hsu JL, Shen YY. Acute bilateral basal ganglia lesions in patients with diabetic uremia: an FDG-PET study. *Clin Nucl Med* 2004;**29**:475–8.
6. Martin RJ. Central pontine and extrapontine myelinolysis: the osmotic demyelination syndromes. *J Neurol Neurosurg Psychiatry* 2004;**75**(Suppl 3):iii22–8.
7. Post B, van Gool WA, Tjissen AJ. Transient parkinsonism in isolated extrapontine myelinolysis. *Neurol Sci* 2009;**30**:325–8.
8. Sajith J, Ditchfield A, Katifi HA. Extrapontine myelinolysis presenting as acute parkinsonism. *BMC Neurol* 2006;**6**:33.
9. Tomita I, Satoh H, Satoh A, et al. Extrapontine myelinolysis presenting with parkinsonism as a sequel of rapid correction of hyponatraemia. *J Neurol Neurosurg Psychiatry* 1997;**62**:422–3.
10. Miller GM, Baler HL, Okazaki H, et al. Central pontine myelinolysis and its imitators: MR findings. *Radiology* 1998;**168**:795–802.

This pdf has been created automatically from the final edited text and images.

Copyright 2012 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.

BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Tajima Y, Mito Y, Yanai M, Fukazawa Y-ichiro. Unusual basal ganglia lesions in a diabetic uraemic patient proven to be demyelination: first pathological observation. *BMJ Case Reports* 2012;10.1136/bcr-2012-006522, Published XXX

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow