shown as target antigens for serum antibodies in patients with Guillain–Barré syndrome (GBS)[1] and Miller Fisher syndrome (MFS).[2] Gangliosides may interact with each other to form a novel epitope, which serves as a target antigen for serum antibodies.[1] In paticular, anti-GD1a/GD1b IgG is reported to be associated with severe GBS and requirement of mechanical ventilation.[1] However, there has been no previous case report describing GBS with anti-GSC antibodies in detail. In this report, we present a patient with GBS having anti-GD1a/GD1b antibody and investigated the clinical feature.

Case report

A 42-year-old man noticed weakness of the bilateral upper extremities 2 weeks after an episode of acute respiratory tract symptoms and diarrhoea. His symptoms further developed to dysarthria, dysphagia and tetraparesis, and he was admitted to the Department of Neurology, Ishikawa Prefecture Central Hospital, Kanazawa, Japan, 4 days after the onset of weakness. Neurological examination disclosed bilateral facial weakness, poor elevation of the soft palate, hoarseness, dysarthria, dysphagia, weakness of the tongue, flaccid tetraparesis (grade 4, Medical Research Council scale) and areflexia of deep tendon reflexes. He needed a wheelchair for transfer, and stomach tube for gastrogavage. Laboratory findings including cerebrospinal fluid (CSF) examination were normal, except for hypercapnia (P_{CO_2} 47.8 mm Hg) on blood gas analysis. Nerve conduction studies demonstrated a marked reduction of compound muscle action potentials (CMAP) with normal conduction velocity (CMAP was 2.87 mV and motor conduction velocity was 50.6 m/s in the right median nerve), but sensory nerves were normal. The MRI studies of the brain and spinal cord were normal. A diagnosis of GBS was made, and he was given intravenous immunoglobulin (IVIg; 400 mg/kg/day) and intravenous methylprednisolone (500 mg/day) for 5 days, according to the protocol used in the previously reported randomised trial.[3] He underwent rehabilitation, and his symptoms gradually improved 1 week after admission. He could stand by himself 2 weeks after admission, and eat by himself without a stomach tube 1 month after admission. Nerve conduction studies still showed simple reduction of CMAPs 1 month after admission (CMAP was 1.21 mV and motor conduction velocity was 53.0 m/s in the right median nerve). At 2 months after admission, he could ambulate independently. He returned to work (English teacher at a high school) 3 months after admission.

The antibodies to gangliosides (GM1, GM2, GM3, GD1a, GD1b, GD3, GT1b, GQ1b, GA1, Gal-C, and GalNac-GD1a) and GD1a/GD1b complex in the serum obtained on the first day of admission were examined by enzyme-linked immunosorbent assay, as previously described.[1 4] He was positive only to the antibody to GD1a/GD1b complex (anti-GD1a/GD1b antibody).

Comment

Our patient showed acute progressive axonal motor polyneuropathy involving the cranial nerves 2 weeks after flu-like symptoms. This condition fulfilled the established criteria of GBS, and the results of nerve conduction studies were classified as having acute motor axonal neuropathy (AMAN).[5] Anti-GD1a/GD1b antibody was detected in the acute-phase serum; however, there were no antibodies to single gangliosides, including GD1a and GD1b.

In a recent report,[1] 8 of 100 patients with GBS had anti-GD1a/GD1b antibodies, and three of these eight did not demonstrate any anti-ganglioside antibodies. These eight patients with anti-GD1a/GD1b antibody tended to have cranial nerve deficits and severe disabilities, and four of these patients required artificial ventilation.[1] Of the three anti-GD1a/GD1b antibody-positive patients with available electrophysiological data, two showed an axonal neuropathy pattern, and the remaining one showed an equivocal pattern.[1] Of the 12 patients with MFS, 7 had serum antibodies to some GSCs, and anti-GSC antibodies might influence the clinical features, as sensory signs were infrequent in patients with anti-GQ1b/GM1 antibody.[2] These findings may support the theory that anti-GSC antibodies correlate with a certain phenotype of GBS or MFS.

The clinical features of our patient were similar to those patients with anti-GD1a/GD1b antibodies,[1] such as AMAN-type GBS with cranial nerve deficits and severe disability (the Hughes Functional Grading Scale at the peak of his disability was on grade 4). Although our patient did not require artificial ventilation, his hypercapnia suggested respiratory weakness. The patient received intravenous methylpredonisolone in addition to IVIg. This combination therapy might prevent his case from being aggravated to grade 5. However, a future large-scale study will be needed to clarify this point.

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Informed consent was obtained for publication of the patient's details described in this report.

doi: 10.1136/jnnp.2006.108217

Competing interests: None declared.

References

1 **Kaida K**, Morita D, Kanzaki M, *et al*. Ganglioside complexes as new target antigens in Guillain–Barré syndrome. *Ann Neurol* 2004;**56**:567–71.
2 **Kaida K**, Kanzaki M, Morita D, *et al*. Anti-ganglioside complex antibodies in Miller Fisher syndrome. *J Neurol Neurosurg Psychiatry* 2006;**77**:1043–6.
3 **Van Koningsveld R**, Schmitz PIM, van der Meché, *et al*. Effect of methylprednisolone when added to standard treatment with intravenous immunoglobulin for Guillain–Barré syndrome: randomized trial. *Lancet* 2004;**363**:192–6.
4 **Kusunoki S**, Chiba A, Kon K, *et al*. N-acetylgalactosaminyl GD1a is a target molecule for serum antibody in Guillain–Barré syndrome. *Ann Neurol* 1994;**35**:570–6.
5 **Ho TW**, Mishu B, Li CY, *et al*. Guillain–Barré syndrome in northern China: relationship to Campylobacter jejuni infection and anti-ganglioside antibodies. *Brain* 1995;**118**:597–605.

Putaminal petechial haemorrhage as the cause of non-ketotic hyperglycaemic chorea: a neuropathological case correlated with MRI findings

Acute generalised chorea can be attributed to multiple causes, including non-ketotic hyperglycaemia. This cause has been associated with characteristic image signs of striatal hyperdensity on CT scan and hyperintensity on T1 weighted (T1W) MRI.

We report a patient presenting with this syndrome in which a postmortem study was conducted. The findings are discussed together with the neuropathological data available in the literature, contributing towards an explanation of the nature of the imaging signs that has remained elusive.

Case report

A 73-year-old woman was admitted to our neurological department for acute generalised chorea of 8 days' duration. There was no relevant personal background or family history.

On admission, the patient presented with orofacial dyskinesias and choreic movements in the neck, trunk, upper and lower limbs. The aetiological diagnostic work-up for acute chorea revealed severe hyperglycaemia on admission (>27.8 mmol/l), bicytopenia with anaemia (erythrocyte count $2.8\times10^6/mm^3$, haemoglobin 8.1 g/dl) and thrombocytopenia (104 000/μl), and an isolated antiphospholipid antibody positive titre. The remaining investigation for acute chorea was normal. The imaging studies revealed a spontaneous bilateral hyperdensity in the putamen and caudate nuclei on the admission brain CT scan. The brain MRI (1.5T; Signa Horizon, General Electrics Medical Systems, Milwaukee, Wisconsin, USA), conducted 2 weeks after admission, showed a bilateral putaminal hyperintensity in T1W images exclusively (fig 1).

Chorea persisted beyond glycaemia normalisation. The patient eventually died 32 days after admission as a result of unresolved sepsis, having begun with fever 4 days after admission. A postmortem examination was conducted.

In the neuropathological study, paraffin embedded representative sections of the left hemisphere, brainstem and cerebellum were stained with haematoxylin–eosin, Bodian–Luxol, Perls and Van Gieson stains. The basal ganglia region was studied using anterior and posterior coronal sections. Microscopic examination revealed generalised wall fibrosis of the small perforating arteries associated with dilatation of the perivascular spaces of the deep white matter. Multiple lacunes in the basal ganglia and thalamus were found in association with macrophage proliferation. Astrocytic gliosis and extravascular hemosiderin deposits together with ferruginateous deposits on perforating vessels were observed in the posterior zone of the putamen. No vascular amyloid or calcium deposits were observed.

Discussion

In our case, the triad of acute chorea, non-ketotic hyperglycaemia and a hyperdense and hyperintense putamen on CT and T1W MRI was documented. The bicytopenia and an antiphospholipid antibody positive titre could

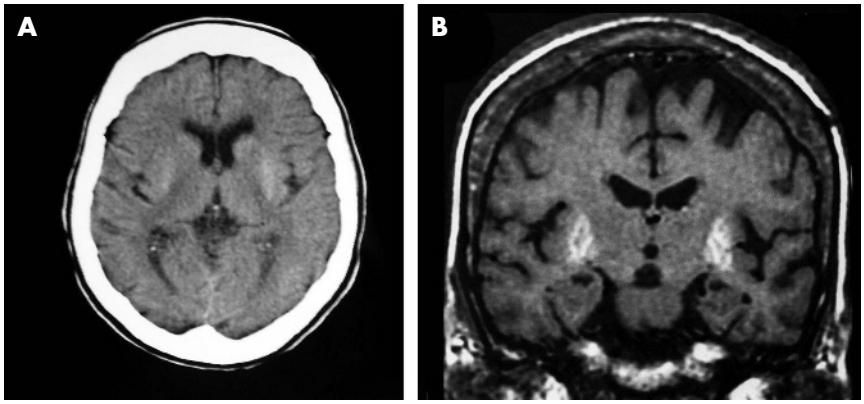

Figure 1 Image findings. (A) CT brain scan on admission—bilateral hyperdense putamen and caudate nuclei. (b) MRI brain scan conducted 2 weeks after admission—bilateral hyperintense putamen on T1W images.

support an autoimmune aetiology in the form of a secondary antiphospholipid syndrome caused by infection. However, no prothrombotic state was documented in the clinical and laboratory data and the neuropathological data provided no evidence of disseminated intravascular coagulation. In addition, patient age did not favour a primary autoimmune aetiology.

Regarding the signal changes observed on imaging studies, a critical appraisal of the published case reports with neuropathological results[3–5] emphasises the heterogeneity of the available data in terms of the time delay in neuropathological specimen collection, neuropathological findings, timing of imaging studies, characteristics of basal ganglia findings and the presence of concurrent relevant lesions. In two reported cases,[4 5] an association was postulated between the presence of reactive astrocytes and MRI changes. However, in the former case no significant hyperglycaemia was documented and an additional area of temporoparietal infarction was identified which could be associated with chorea onset. In the latter case, the findings were not observed in other regions with an identical signal alternation, namely the pallidum. In a third report,[3] calcium deposits and focal microhaemorrhages were found in the lesioned putamen and caudate where a confluent area of infarction was also observed. Although calcium was observed only on non-recent infarction areas, an association with the signal changes on CT and MRI was postulated. In addition, signal changes on MRI were localised to the anterior putamen only and did not involve the putamen more extensively, as usually observed in this syndrome.

Studies focusing on CT and MRI findings have also been inconclusive. Chu *et al*[1] conducted a gradient echo and diffusion weighted MRI study and suggested that signal changes corresponded to cytotoxic oedema. Conversely, another study[2] involving similar imaging procedures drew the same conclusions as our report. Nevertheless, both studies did not have access to neuropathology data which would confirm the accuracy of the imaging interpretation.

In our case, neuropathological findings were consistent with small previous haemorrhages in the striatum. This favours the hypothesis of petechial haemorrhages as the cause of this syndrome, suggested to be secondary to erythrocyte diapedesis due to hyperglycaemia induced blood–brain barrier dysfunction.[6] The observed vessel wall changes were consistent with a diabetes vasculopathy, which also provides an explanation for brain barrier dysfunction. Thus the initial CT changes correspond to blood and the later MRI findings to the presence of hemosiderin. Because of the transitory nature of this syndrome, a careful analysis of the reported cases, namely the timing for image and neuropathological data collection, is essential to fully understand its aetiology. Using other MRI sequences such as gradient echo or diffusion weighted imaging will further help in characterising image–neuropathology correlations.

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doi: 10.1136/jnnp.2006.105387

Competing interests : None declared.

References

1 **Chu K**, Kang DW, Kim DE, *et al*. Diffusion-weighted and gradient echo magnetic resonance findings of hemichorea–hemiballismus associated with diabetic hyperglycemia: a hyperviscosity syndrome? *Arch Neurol* 2002;**59**:448–52.
2 **Lai SL**, Tseng YL, Hsu MC, *et al*. Magnetic resonance imaging and single-photon emission computed tomography changes in hypoglycemia-induced chorea. *Mov Disord* 2004;**19**:475–8.
3 **Nath J**, Jambhekar K, Rao C, *et al*. Radiological and pathological changes in hemiballism–hemichorea with striatal hyperintensity. *J Magn Reson Imaging* 2006;**23**:564–8.
4 **Ohara S**, Nakagawa S, Tabata K, *et al*. Hemiballism with hyperglycemia and striatal T1-MRI hyperintensity: an autopsy report. *Mov Disord* 2001;**16**:521–5.
5 **Shan DE**, Ho DM, Chang C, *et al*. Hemichorea–hemiballism: an explanation for MR signal changes. *AJNR Am J Neuroradiol* 1998;**19**:863–70.
6 **Iwata A**, Koike F, Arasaki K, *et al*. Blood brain barrier destruction in hyperglycemic chorea in a patient with poorly controlled diatetes. *J Neurol Sci* 1999;**163**:90–3.