CASE REPORT

Partial interhemispheric disconnection syndrome (P-IHDS) secondary to Marchiafava-Bignami disease type B (MBD-B)

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SUMMARY

A 53-year-old man with a 35-year history of excessive alcohol intake presents to our neurology department with 4-year history of progressive neurocognitive deterioration and disconnection syndrome. MRI head demonstrates extensive demyelination of the corpus callosum (and of extracallosal sites as well), leading to a diagnosis of Marchiafava-Bignami disease. He was given treatment with vitamin B complex (including folate) and was assessed and managed by psychology, occupational therapy and physiotherapy with initial signs of improvement.

BACKGROUND

Identifying and classifying the distinct alcohol-related brain damage (ARBD) aetiologies is important because it can lead to early treatment, reduction in comorbidities and improvement of quality of life.

It is important not to group all patients with alcoholism under one diagnostic umbrella. By adequately subtyping the ARBD, it is possible to provide specific treatments, medical and non-medical (including psychological, occupational therapist and physiotherapist treatment).

Without a proper neurological assessment and diagnosis, any potential psychological intervention could have been inaccurate. By knowing the subtype of ARBD and the clinical manifestations of callosal and extracallosal lesions, cognitive-behavioural therapy can prove to be much more directed and fruitful.

A very important aspect of this case was the lack of proper management after the first evaluation. We believe that many of the patients' unfortunate problems could have potentially benefited from prompt multidisciplinary assessment and management.

CASE PRESENTATION

A 53-year-old, right-handed male patient, with a 35-year history of excessive alcohol intake (he consumed a daily average of 500 mL to 1 L of either whisky, beer, vodka or wine), mild hypertension and recurrent renal calculi, presented to our neurology clinic recently.

Approximately 4 years before his first evaluation in our neurology clinic, he had been seen in another hospital (he recently had relocated to our region) which was prompted by an insidious onset (approximately over a period of 3 weeks) of short-

term and long-term memory deterioration (to the point of having difficulty recalling the names of many close friends and even some members of his family as well), difficulties recalling and fulfilling routine activities at home, limitations to follow well-known driving routes and difficulties remembering bank codes and computer passwords. More so, almost simultaneous to his amnesia-onset, he also noted behavioural changes characterised by emotional erraticism, aggressiveness and disinterest in others. Overall, as he stated, he felt that he was 'becoming a different person'. Following this first evaluation, he had an MRI, which unfortunately was never followed-up, and the patient did not receive any formal diagnosis nor management plan. We were able to recuperate that MRI, which revealed findings characteristic of ARBD and of corpus callosum (CC) demyelination typical of Marchiafava-Bignami disease (MBD). As we can see in the figures, there was extensive hyperintense signals throughout the rostrum, genu and body of the CC, without damage of the splenium, visualised in T2 (figures 1 and 2); hypointense lesions visualised in T1, occupying the genu of the CC (figures 3 and 4) and finally, several extracallosal lesions, located in the thalamus, cortex and subcortex (figures 5 and 6).

As time progressed, he also noticed that intellectually, many things started to deteriorate. For example, after reading for a short period of time, the words gradually became 'muddled'; even more distressing, the actual meaning of the sentences was becoming progressively more difficult to interpret

Figure 1 (MRI-T2WI-sagittal) hyperintense swelling over the anterior two-thirds of corpus callosum, extending from the rostrum, genu and body. This indicates oedema and demyelination over the corpus callosum.

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Figure 2 (MRI-T2WI-axial): hyperintensities noticed in the right genu and in the splenium (central portion). Interestingly, there is also a focal extracallosal lesion in close proximity to the splenium.

Figure 5 (MRI-T2WI-sagittal): various extracallosal lesions; visualised in the subcortical parietal lobe and in the thalamus. The demyelination of the CC can also be visualised.

Figure 3 (MRI-T1-coronal): focal hypointense lesion visualised over the genu of the corpus callosum.

Figure 4 (MRI-T1-coronal): focal hypointense lesion visualised over the genu of the corpus callosum, slightly more extensive than visualised in [figure 3](#).

Figure 6 (MRI-T2WI-axial): multiple bihemispheric cortical lesions (extracallosal lesions).

In the year previous to his evaluation in our clinic, he noticed a subtle, yet progressively worsening gait, which was more obvious after walking more than 10–15 min. He felt he lacked balance on standing up and changing direction. Approximately 6 months prior to our evaluation, he noticed that his pronunciation was changing and that people had more and more difficulty understating what he was saying.

All these symptoms and the progressive nature of his disease led him to be referred to our neurology department for a second evaluation. His physical examination did not reveal any signs of malnutrition, hypovitaminosis or emaciation. His weight was 67 kg. No hepatomegaly or splenomegaly was noted; no pitting oedema or peripheral vascular disease was detected. Cardiovascular and respiratory systems were normal. The findings of neurological examination are as follows: (1) mild flaccid hypokinetic dysarthria, anterograde and retrograde amnesia, word-finding difficulties, poor verbal processing, dyslexia, left-hand and right-hand agraphia and dyscalculia; (2) strength 5/5 in four limbs and no sensory abnormalities (vibration, superficial and deep sensation) were noted; (3) no cranial nerve palsies, no nystagmus and pupils were isochoric and reactive; (4) double-hemianopia; (5) reflexes were present in all four limbs and no Babinski or frontal-reflexes (grasp or suction) were present and (6) mild ataxia gait without Romberg sign, dysmetria or adiadochokinesia was noted.

and even to remember. This, of course, caused stress, anxiety and a great deal of frustration. He described this problem as 'becoming dyslexic'. The most disabling problem was an insidious deterioration in his capacity to write, reaching the point of almost complete agraphia. Initially, he had difficulty writing certain long words, however, soon after he noticed that small three-letter words began to be difficult as well.

A detailed neurocognitive examination revealed: (1) severe left-hand agraphia and mild-to-moderate right-hand agraphia (despite retaining the ability to carry out coordinated movements with his hands), (2) unilateral anomia or severe left-hand astereognosis (with his eyes closed, he was unable to identify objects placed in his left hand); he could, on the other hand, easily name objects placed in the right hand; verbal anosmia and (3) unilateral constructional apraxia (great difficulty to copy simple geometrical figures).

Following psychological evaluation (using the Wartegg Drawing Test), it was found that he lack personal control, evasiveness of emotions, paranoid symptoms, lack of trust, fear of rejection and a feeling of social inadequacy. More so, he demonstrated signs of depression, lack of libido, sexually inhibited and verbally aggressive. Finally, he lacked personal long-term goals and felt that his intellect was practically absent.

After this evaluation, a second MRI was requested, which revealed chronic lesions pertaining to marchiafava-bignami (MFB) disease. As we can see, it revealed severe atrophy of the CC, with focal hypointense lesions in the rostrum, genu and body (figure 7), the 'sandwich' sign (classical sign of MFB) and cortical-subcortical atrophy (figure 8) and finally, numerous necrotic, cystic-like lesions in the genu and in the splenium (figures 9–12).

Figure 7 (MRI-T1WI-axial): extensive atrophy of the anterior portion of the corpus callosum, including the rostrum, genu and body (over the corresponding region visualised as demyelination and swelling in figure 1); focal hypointensities accumulated over the anterior portion.

Figure 8 (MRI-T1WI-axial): 'Sandwich sign' visualised as a diminished diameter (thickness) of the central portion of the corpus callosum; it reflects the extensive damage secondary to demyelination. There are also signs of cortical-subcortical atrophy, mainly in the posterior parietal lobe.

All other investigations were normal: lumbar puncture (oligoclonal bands, myelin-specific protein, viral-PCR, culture and neoplastic cells) was normal; vitamin B complex was normal; antibodies for vasculitis were all normal and general complete blood count was normal. Electrolytes (sodium, potassium magnesium, phosphate), calcium, thyroid hormones and C reactive protein were normal. ELISA for HIV was negative, and hepatitis B and C was negative. Protein electrophoresis in serum and

Figure 9 (MRI-T1-axial): cystic necrosis in the genu. Seen as a central hypodense lesion (corresponding to necrosis) with a hyperintense rim.

Figure 10 (MRI-T1-axial): cystic necrosis in the genu. Seen as a central hypodense lesion (corresponding to necrosis) with a hyperintense rim.

Figure 11 (MRI-T1-coronal): cystic necrosis in the genu. Seen as a central hypodense lesion (corresponding to necrosis) with a hyperintense rim.

Figure 12 (MRI-T1-axial): cystic necrosis of the splenium.

urine was normal. Albumin levels were mildly decreased; creatinine, urea and glomerulo-filtration rate glomerulo-filtration rate (GFR) were normal.

On the basis of the patients' presentation and his MRI findings, a final diagnosis of partial disconnection syndrome secondary to MBD was made.

INVESTIGATIONS

- ▶ Blood investigations (mildly deranged liver enzymes and alkaline phosphatase).
- ▶ Vitamin B₁=350 ng/g Hb (neuro-viral neuro-viral (NV) 180–550 ng/g Hb), B₂, B₆ and B₁₂, no thrombocytopenia or anaemia.
- ▶ APQ4 antibody negative (no evidence of neuromyelitis optica spectrum disorders neuromyelitis optica spectrum disorders (NMOSD)).
- ▶ Electrolytes (sodium, potassium, magnesium, phosphate), calcium, thyroid and C reactive protein normal.
- ▶ All antibodies requested (ANCA p/c, ANA, Anti-Ro/La, MPO/PR3) were normal.
- ▶ ELISA for HIV, hepatitis B and C were negative.
- ▶ Protein electrophoresis in serum and urine was normal.
- ▶ Lumbar puncture was normal (no oligoclonal bands, viral PCR, culture and cancerous cells).
- ▶ Albumin levels were mildly decreased; creatinine, urea and GFR were normal.

DIFFERENTIAL DIAGNOSIS

- ▶ Alcohol-related cognitive deterioration/dementia (ARBD).
- ▶ Wernicke encephalopathy (WE): produces lesions in the mammillary bodies, periaqueductal region and the walls of the third ventricle (not seen in our patient).
- ▶ Wernicke-Korsakoff syndrome.
- ▶ Korsakoff dementia.
- ▶ Primary demyelinating disorders (multiple sclerosis).
- ▶ Delayed or toxic-leucoencephalopathy (eg, after chemotherapy; no suspect medication use in our patient).
- ▶ Neuromyelitis optica Neuromyelitis optica (NMO) spectrum disorder.
- ▶ Paraneoplastic leucoencephalopathy.¹
- ▶ Para-infectious encephalitis (frequently with pathological cerebrovascular fluid findings and a more patchy pattern in MRI; not observed in our patient).
- ▶ HIV-related disease (immunodeficiency syndrome encephalopathy, progressive multifocal encephalopathy and cytomegalovirus cytomegalovirus (CMV) infection).
- ▶ Anterior cerebral artery ischaemic damage of CC.

TREATMENT

There is no standardised protocol for the treatment of MFB disease. Nevertheless, patients can be treated with a combination thiamine, vitamin B-complex and folate, with variable outcomes.² Patients with excessive alcohol intake are prone to vitamin deficiencies and therefore, replacement therapy might provide benefit in these cases. There is evidence that during the first 2 weeks of onset, patients with MFB may benefit from intravenous thiamine. Steroids, such as intravenous methylprednisolone (250 mg q6 hours) may also be administered. There have also been reports describing the benefits of giving amantadine together with thiamine, vitamin B₁₂ and folate. From a psychological perspective, the mainstay of treatment is cognitive-behavioural therapy (CBT).

OUTCOME AND FOLLOW-UP

Our patient is currently under the following specialties:

- ▶ Neurology.
  - ▶ Psychology (for cognitive-behavioural therapy).
  - ▶ Occupational therapy and physiotherapy.
- He is also having alcohol and nutritional counselling.

DISCUSSION

ARBD is the consequence of excessive, long-term alcohol intake. It can produce a variety of clinical syndromes: hepatic encephalopathy, Korsakoff syndrome, Marchiafava-Bignami and central pontine myelinosis (CPM). Each one has distinctive clinical and radiological features. Our patient has MBD.³

Several classifications have been proposed since its initial description. Brion was the first to do so in 1977, based on chronology of symptoms: acute, subacute and chronic.⁴ Heinrich *et al* proposed another classification, which was more complete, including radiological findings and which was summarised in types A and B.

Type A

- ▶ Altered state of level or state of consciousness.
- ▶ Cognitive deterioration and language deficiencies (dysarthria, aphasia, etc).
- ▶ Focal neurological deficiencies such as hemiparesis or hemihypoesthesia.
- ▶ T2-WI: swelling (oedema) of the entire CC on early MRI, frequently with extracallosal lesions (which are usually indicative of a poorer prognosis).⁵
- ▶ Unfavourable prognosis and evolution.

Type B

- ▶ Insidious clinical onset and progression.
- ▶ T2-WI: less frequently seen extracallosal lesions.
- ▶ More favourable prognosis.
- ▶ Less severe and disabling clinical symptoms and less long-term disabilities.⁶

Our patient, interestingly, despite lacking the typical clinical manifestations of MFB type A, he did in fact have a widespread (yet not total) involvement of the CC and also extracallosal lesions (cortical, subcortical, thalamus, etc), both of which are more commonly seen in MFB type A. His clinical progression was not as poor as would be expected from his MRI findings. Ultimately, we classified him as type B, based on his clinical manifestations rather than his MRI findings.

The symptoms that can be associated with MFB are widespread, including cognitive impairment, limb weakness and hypertonicity, language disabilities (dysarthria-aphasia) and disconnection syndromes.⁷ Our patient primarily demonstrated symptoms of partial disconnection syndrome, characterised by:

- ▶ Unilateral agraphia of the left (and right hand).
- ▶ Intermanual conflict.
- ▶ Verbal anosmia or stereognosis.
- ▶ Double hemianopia (inability to indicate the presence of a visual stimulus coming from the right or the left visual field with the contralateral hand).
- ▶ Unilateral constructional apraxia (poor performance by the right hand on task that requires special processing, such as copying geometric forms and constructional tasks).

From a radiological point of view, MBD has a particular presentation in the MRI, which is important to mention.

- ▶ Symmetric T2WI hyperintensity of the complete CC (this reflects oedema and demyelination).
- ▶ Symmetric T1WI hypointensities (reflect total loss of myelin with replacement of the region by cyst).
- ▶ Less frequently, lesions in the middle cerebellar peduncles, internal capsule and cortically.⁸
- ▶ Contrast enhancement of CC, which resolves after the post-acute stage.⁹
- ▶ Cortical and subcortical atrophy, cerebellar vermis and hemispheric atrophy (in all ARBD).¹⁰
- ▶ Symmetric atrophy of the CC with focal hypointensities on T1 and corresponding focal hyperintensities on T2 (indicate progressive demyelination, regional necrosis and cyst formation—damage to myelin at the rim with a central necrotic area).¹¹

Learning points

- ▶ Alcohol-related brain damage (ARBD), apart from generalised cortical–subcortical atrophy, can cause four distinct clinical syndromes: hepatic encephalopathy, Korsakoff syndrome (KS), Marchiafava-Bignami disease (MBD) and central pontine myelinolysis (CPM).
- ▶ Distinguishing between each one of these four entities is paramount for adequate treatment (any delay in diagnosis directly affects the patients outcome and prognosis).
- ▶ MBD is a rare condition that requires an MRI for diagnosis (therefore, MRI in patients with ARBD is important and recommended). The accepted classification was provided by Heinrich, in which MBD can be either type A or type B.
- ▶ Disconnection syndromes are very suggestive of corpus callosum pathology and in a patient with long-standing history of alcohol abuse it must guide us towards a diagnosis of MBD.
- ▶ Prompt neuropsychological assessment and management is paramount.

- ▶ ‘Sandwich sign’: lesions involving the central portion of the CC with sparing of the dorsal and ventral layer, producing the well-known ‘sandwich sign’, the characteristic diagnostic sign of MBD.¹²

It is important to mention that cognitive impairments in MBD-B may be associated with microhemorrhages. Microbleeds can worsen cognition, and there seems to be an anatomical correlation between the sites of microbleeds and the cognitive domains affected. Microbleeds are predictive of executive dysfunction, memory (short-term and long-term), language and spatial awareness (microbleeds tend to localise more commonly in the frontal–parietal lobes).^{13–15}

Contributors CC and LA involved in the clinical evaluation, investigation request, diagnosis and management of the patient. Furthermore, the patient has been followed up in our trust by a team of dedicated physiotherapists, occupational therapists, speech and language therapists and psychologists. The major contributors to the planning, conduct and reporting of the case were CC and LA.

Competing interests None declared.

Patient consent Obtained.

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