Marchiafava-Bignami Disease

Computed Tomographic Scan, 99mTc HMPAO-SPECT, and FLAIR MRI Findings in a Patient With Subcortical Aphasia, Alexia, Bilateral Agraphia, and Left-handed Deficit of Constructional Ability

Franco Ferracci, MD; Fernando Conte, MD; Manrico Gentile, MD; Rosamaria Candeago, MD; Luciano Foscolo, MD; Matteo Bendini, MD; Giuliano Fassetta, MD

Objectives: To report and discuss the neuropsychological deficits and neuroimaging findings in a patient with probable Marchiafava-Bignami disease.

Design and Method: A right-handed woman with chronic alcoholism demonstrated mutism, impaired comprehension of spoken language, alexia, and right-handed agraphia. The syndrome of interhemispheric disconnection was manifested by left-handed deficit of constructional ability and agraphia. The patient underwent brain computed tomographic scans, technetium 99m hexylmethylpropylene amineoxime–single photon emission computed tomography, and magnetic resonance imaging (MRI) that also included fluid attenuated inversion recovery images.

Setting: Clinical neurology department.

Results: The patient's symptoms were related to scattered lesions of the corpus callosum and to extensive symmetrical lesions of the centrum semiovale. Only the latter were detected by computed tomographic scans. Results of single photon emission computed tomography did not show areas of focal hypoperfusion. Results of fast spin-echo MRI showed all lesions were hyperintense in T1-weighted images and hypointense in T2-weighted images. Fluid attenuated inversion recovery images revealed that periventricular lesions had a hypointense core surrounded by a hyperintense rim; callosal lesions were still hyperintense.

Conclusions: We believe that our patient's symptoms are due to the discontinuous affection of the corpus callosum and to the bilateral cutting of the outflow from the cortex. The MRI findings may be interpreted as indicating central necrosis and peripheral demyelination of periventricular lesions and demyelination of the corpus callosum. The combined use of fast spin echo and fluid attenuated inversion recovery MRI reproduced with more accuracy than fast spin echo MRI alone some features of Marchiafava-Bignami disease known from observations at autopsy.

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Marchiafava-Bignami disease (MBD) is the symmetrical demyelination of the middle portion of the corpus callosum that can be observed in people with chronic alcoholism. Its evolution may be fatal or lead to various degrees of slowly evolving cognitive impairment. Patients with a benign course have been reported.1,2

In several reports, MBD has been shown to induce a syndrome of hemispheric disconnection,2-5 similar to the picture outlined by Gazzaniga et al7 in patients surgically deprived of cerebral commissures. The first cases of MBD diagnosed in living patients were reported after the introduction of brain computed tomography (CT) and magnetic resonance imaging (MRI); the lesions of the corpus callosum appear as areas of radiolucency or abnormal intensity signal.6,8

We report a case of MBD in a woman whose symptoms comprised mutism, alexia, bilateral agraphia, and nondominant hand deficit of constructional ability. Her symptoms will be explained by the lesions that are seen on findings from neuroimaging investigations. We shall further discuss the necrotic or demyelinating origin of such lesions by considering their different appearance on fast spin echo and fluid attenuated inversion recovery (FLAIR) MRIs.

REPORT OF A CASE

A 42-year-old, right-handed woman with confirmed alcoholism was admitted to a medical ward because of the rapid deterioration of her speech and gait. She had been abusing wine for more than 18 years. She was relatively asymptomatic...
until 2 weeks before when she had stopped eating without any apparent motive.

On admission she was drowsy and uncooperative. Results of an electroencephalogram showed diffuse theta-delta rhythms. Two weeks later, she regained normal attention and her electroencephalogram showed no abnormalities. Her gait was hesitant and wide based; it was worsened by eye closure. Her strength was normal; ankle reflexes were absent; her plantar responses were flexor. Her senses of pain and vibration were decreased distally in her lower limbs. Visual field was normal on manual examination; her optic disc appeared normal.

Spontaneous verbal production and repetition were absent; she was able to utter only the vocals a and e. She could understand simple spoken commands but not more complex ones; she nodded whenever the correct name of an object was given by the examiner. Reading was impossible in her whole visual field: only the recognition of single letters was preserved, as was that of objects. Spontaneous writing was absent. Under dictation, right agraphia consisted of a mild distortion of letters, abnormal composition of words, and occasional perseveration of graphemes; no recognizable word was written with the left hand (Figure 1). Copying of drawings was performed well with the dominant hand; with the left hand she could produce only simplified sketches. In this simplification there was no evidence of hemineglect (Figure 1). The use of actual objects such as a hammer, a lighter, and a comb was correct with both hands. Finally, no visual neglect was shown by the Albert line-crossing test performed with both hands.

Brain CT and technetium 99 hexylmethylpropylene amineoxime–single photon emission computed tomography ($^{99}$Tc HMPAO–SPECT) scans were carried out 10 days after admission. Results of CT showed diffuse cortical atrophy and 2 symmetrical areas of radio-lucency in the periventricular white matter. The $^{99}$Tc HMPAO–SPECT images indicated an irregular distribution of cortical blood flow and no selective area of hypoperfusion. Results of an MRI showed areas of abnormal signal intensity scattered in the anterior and central portions of the corpus callosum; 2 more areas of abnormal signal intensity were symmetrically distributed in the centrum semiovale surrounding the lateral ventricles from a level corresponding to the genu of the corpus callosum to the parietal lobe. All lesions were hypointense in $T_1$-weighted images and hyperintense in $T_2$-weighted images. In FLAIR images, periventricular lesions had a hypointense core surrounded by a hyperintense rim, whereas callosal lesions remained hyperintense (Figure 2). After 10 months the patient showed no improvement.

**COMMENT**

The diagnosis of MBD mainly rests on the evidence of central demyelination of the corpus callosum rather than on the variable clinical features. The symptoms of hemispheric disconnection include unilateral apraxia and agraphia without aphasia and left hemineglect in tasks carried out with the right hand. We consider this patient a case of probable MBD. After the subsidence of acute symptoms, she demonstrated a severe impairment of language functions. Mutism in the presence of extensive white matter lesions seems to represent aphemia or subcortical motor aphasia according to Benson’s definition. Patients with aphemia, however, usually fully understand written and spoken language and can communicate by writing. The lesions responsible for this clinical picture may be located in subcortical gray nuclei or along the descending pathways from cortical language areas. Mutism in MBD has also been described in 2 patients who recovered their ability to speak and were left with a residual dysarthria. There was no lesion outside the corpus callosum. Our patient had a reduced comprehension of spoken language with a perseveration of auditory semantic comprehension; she could not read or write and showed no improvement over time.

Alexia in MBD is described as the patient’s denial of visual recognition of letters and words placed in the left hemifield. This feature of hemispheric disconnection also involves the recognition of objects. In our case, alexia consisted of a complete inability to understand writ-
ten words, while the recognition of letters and objects was preserved in the whole visual field.

The severity and type of agraphia differed between the left and right hands: the words written with the right hand were mildly distorted, the succession of letters was abnormal, and sometimes they were excessively reiterated. The structure of words was unrecognizable when the left hand was used. This symptom resembles the non-dominant-handed apraxic agraphia caused by the hemispheric disconnection. Also, copying of drawings was performed with differing ability on the 2 sides: while the right hand correctly reproduced the models, the simplification shown by the patient when using her left hand suggested a constructional apraxia with no evidence of neglect, as confirmed by the Albert line-crossing test. Finally, her ability to handle some objects was bilaterally normal.

We suggest that this patient’s clinical picture may be explained by its pathologic basis: the bilateral cutting of the outflow from the cortex produced by the symmetrical lesions of the centrum semiovale plus the discontinuous interruption of callosal fibers. These features may justify the coexistence of symptoms of callosal disconnection (left-handed deficit of constructional ability and agraphia), right-handed agraphia, alexia, impaired comprehension of spoken language that might be focal symptoms of cortical damage, and mutism. Symptoms of interhemispheric disconnection associated with speech disorders and Balint syndrome were recently described in a patient with MBD with bilateral hemorrhage of parietal white matter. We would not emphasize the cortical atrophy in our patient because it had certainly been present for a long time when she could still lead a relatively normal life.

No significant data concerning the functional organization of this patient’s cortex were provided by the Tc HMPAO-SPECT. The irregular cortical perfusion is a frequent finding in the elderly. It is also an aspecific one and in our patient was probably related to the cortical atrophy.

The CT scan was of no help in providing a diagnosis in this case, the subcortical radiolucencies having no specific meaning in the absence of lesions of the corpus callosum. They might have been interpreted as subcortical strokes; however, apart from ethanol abuse, this patient had no risk factor favoring such a diagnosis.

An MRI scan eventually revealed areas of abnormal intensity signal in the corpus callosum. The quite unusual discontinuous affection of the corpus callosum might explain why symptoms of hemispheric disconnection were so poor. The same irregular succession of demyelination and normal tissue has been described in previous reports. In most cases in the literature, the anterior two thirds of the corpus callosum were lesioned.

The fast spin echo MRI confirmed the data from the literature. The hypointensities and hyperintensities observed in T1- and T2-weighted images can be interpreted as areas of cystic necrosis. The FLAIR MRI provided further information by turning the homogeneous signal intensity of periventricular areas into a hypointense core surrounded by a high-intensity signal rim; callosal lesions remained hyperintense. Although we are well aware that an MRI-based interpretation of the pathologic basis of these lesions is merely speculative without direct pathologic proof, we believe that an extrapolation is possible. To our knowledge, this is the first report of fast spin echo and FLAIR MRI used in a case of probable MBD. A rich literature exists, however, concerning the use of FLAIR MRI in cases of multiple sclerosis, where the lowering of the signal intensity of fluids enhances the hyperintense appearance of plaques. Callosal lesions in our patient behaved like multiple sclerosis–established plaques: they had well-defined margins that seem to rule out perilesional edema and showed an even higher signal intensity on FLAIR images. These features might indicate demyelination and gliosis. As to periventricular lesions, we suggest that the low-intensity nucleus might represent necrotic tissue and that the hyperintense rim might be due to gliosis or demyelination or both. We also believe that these findings represent the same disease process. Necrosis and reactive gliosis along with focal demyelination in MBD have been described, and focal symmetrical lesions of subcortical white matter have been reported as well, albeit not frequently. Although in
the cases reported by Marchiafava and Bignami the absence of perilesional astroglial reaction was considered a distinctive marker of the disease, later observations showed that gliosis is much more common than previously expected. In conclusion, we believe that in this patient, the combination of T1- and T2-weighted images and FLAIR magnetic resonance images provided some data that closely resemble those gathered from observations at autopsy.

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Reprints: Franco Ferracci, MD, Reparto di Neurologia, Ospedale Civile di Belluno, Viale Europa, 32100 Belluno, Italy.

REFERENCES