Spreading Dystonia in Probable Creutzfeldt-Jakob Disease with Serial Diffusion-Weighted Magnetic Resonance Images

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Dear Sir,

Creutzfeldt-Jakob disease (CJD) is a progressive spongiform encephalopathy that is mainly characterized by rapidly progressive dementia, myoclonus, ataxia, epilepsy partialis continua, visual disturbances and movement disorders [1–7]. Several movement disorders including myoclonus, dystonia, choreoathetosis, tremor and parkinsonism have been described in a significant number of patients with CJD [8]. However, dystonia as an early symptom is rare. We report a patient who showed generalized dystonia followed by focal dystonia in early-stage disease with concomitant lesions on diffusion-weighted MR images (DWI).

Case Report

A 64-year-old woman admitted to the hospital with a 4-week history of behavior change, emotional instability, gait disturbance and twisting of the left upper extremity. She had no history of receiving a blood transfusion or growth hormones. The patient had no history of neurosurgical or ophthalmologic surgery and no family history of neurological disease. During the initial neurological examination on admission, the patient was lethargic and showed only a withdrawal response to painful stimulation; she had synchronous contractions of the left finger, wrist and elbow muscles, which caused a dystonic pos-

turing of the left upper extremity. The dystonic posture of the left upper extremity caused levitation of the arm with flexed fingers and an extended wrist. Stimulus-sensitive generalized myoclonic jerks were

also observed. The initial DWI scans on admission showed high signal intensity at the right caudate nucleus, putamen and frontal cortex (fig. 1A). Laboratory testing included a complete blood count, blood

Fig. 1. DWI study. **A** The initial DWI shows increased signal intensities in the right striatum and in multiple cortical areas. **B** Ten-day follow-up DWI studies show increased signal intensity in both striatum and cortical areas.

chemistry, thyroid function test, venereal disease research laboratory test, vasculitis markers, HIV antibodies, vitamin B₁₂ and folate level; all were within normal limits. A spinal tap was performed; the cerebrospinal fluid had a normal opening pressure with a leukocyte count of 0/mm³, a protein level of 46 mg/dl and a glucose level of 106 mg/dl. However, the Western blot test for the 14-3-3 protein, in the cerebrospinal fluid, was positive. An initial electroencephalogram (EEG) demonstrated a diffuse slow basal rhythm and periodic asymmetrical left hemispheric sharp waves (fig. 2A). After 2 weeks, the left periodic hemispheric sharp waves evolved to periodic bilateral synchronous sharp waves (fig. 2B).

The dystonic posture and myoclonic jerks worsened even with anticonvulsive therapy (valproic acid 600 mg/day, clonazepam 0.5 mg/day). Ten days after admission to the hospital, the dystonic posture spread over the right side to include the lower extremity. The follow-up DWI scans showed high signal intensity bilaterally at the basal ganglia and cortex (fig. 1B). Five weeks after admission, the patient became comatose; the myoclonic jerks and dystonia disappeared. She died 3 months later.

Discussion

CJD belongs to a group of disorders referred to as transmissible spongiform encephalopathy. The clinical manifestations of CJD vary. Early-stage disease is characterized by behavioral change, deterioration in intellectual function and cerebellar dysfunction [9]. Approximately 90% of patients with CJD present with movement disorders; generalized myoclonus is common in advanced-stage disease [8]. However, other focal involuntary movements are rare, especially in early-stage disease. Dystonia as an early symptom of CJD is quite rare as well, but when present, it is usually unilateral with distal distribution. Several CJD cases presenting with focal dystonia have been reported [2, 3, 6]. In these reported cases, dystonia was associated with other movement disorders such as focal myoclonus, focal or generalized chorea, tremor and bradykinesia. Dystonia progressively evolved to hemidystonia or generalized dystonia with rapid deterioration in cognitive function in these patients. A few CJD cases with an atypical history of corticobasal degeneration, such as the alien hand phenomenon, apraxia and parkinsonism have also been reported

[10–12]. Our patient presented with unilateral dystonia, which evolved to generalized dystonia during the course of the disease; in addition, there were superimposed myoclonic jerks with rapid deterioration in cognitive and motor function. Parkinsonism and other clinical features of corticobasal degeneration were not observed.

In sporadic CJD, a bilateral symmetrical increased signal in the striatum on T₂-weighted MR sequences is a distinctive finding; less commonly, asymmetrical involvement of the pallidum, thalamus and cerebral (especially occipital) cortex on T₂ or proton density MR sequences is observed [13]. Some reports have shown typical MR findings of CJD [2, 6]. However, prior reports have not shown the corresponding lesion associated with focal dystonia or involuntary movement on MR images.

DWI appears to be more sensitive than the standard MR sequences; it reveals high

signal changes in the gray matter nuclei as well as the cerebral cortices [13, 14]. In our case, the initial DWI revealed a corresponding striatal lesion with contralateral focal dystonia; the follow-up DWI also revealed bilateral striatal lesions, which correlated with generalized dystonia. These DWI findings suggest that the functional changes in the basal ganglia may be related to early dystonia in patients with CJD. However, abnormalities on DWI may not closely correlate with neuropathological findings (especially early in the course of CJD), suggesting a more functional, rather than anatomical, basis to the changes identified with DWI [15]. Therefore, we thought that most CJD patients, with unilateral DWI abnormalities, do not present with focal dystonia in early-stage CJD. In our report, the initial periodic sharp waves on EEG did not correspond to the DWI findings and the unilateral dystonia. Therefore, there was no correlation between the

Fig. 2. EEG study. **A** EEG on the third hospital day shows findings typical of CJD: periodic asymmetrical sharp waves occurring at a frequency of 2 Hz. **B** EEG on the tenth hospital day shows periodic generalized sharp waves occurring at a frequency of 0.5–1 Hz.

spreading dystonia and the periodic sharp waves.

This case illustrates that focal dystonia may occur in the early stage of CJD with functional changes noted in the basal ganglia.

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