CASE REPORT

Slowly Progressive Dystonia Following Central Pontine and Extrapontine Myelinolysis

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Abstract

A 28-year-old woman was hospitalized with dysarthria and oro-mandibular and upper limb dystonia. Approximately 8 years prior to the current admission, the woman became severely hyponatremic due to traumatic subarachnoid hemorrhage-related SIADH. Brain MRIs showed a signal increase in the central pons, thalamus and striatum on T2 weighted images compatible with central pontine and extrapontine myelinolysis. From a few months after that event, dystonia progressed slowly over the subsequent 8 years. We speculate that the particular damage chiefly to the myelin structures by myelinolytic process may have caused an extremely slow plastic reorganization of the neural structures, giving rise to progressive dystonia.

(Internal Medicine 39: 956-960, 2000)

Key words: demyelination, hyponatremia, pons, basal ganglia

Introduction

Central pontine myelinolysis (CPM), first reported by Adams et al in 1959, is characterized by primary demyelination of the basis pontis, and rapid correction of hyponatremia is known to precipitate the disease. It was considered to be a disorder that progresses rapidly and often terminates in death (1). In addition to CPM, Wright et al accumulated autopsied cases with similar myelinolytic lesions in those structures outside the pons, and the term, extrapontine myelinolysis (EPM) was coined (2). With the advent of refined imaging techniques, mild and incomplete forms have been identified, and it became clear that the disorder is not necessarily incompatible with life but improves in time. However, the long-term outcome of CPM and EPM has not been well described. Here, we report a young female who has yet been showing slowly progressive dystonia long after CPM and EPM.

Case Report

A 28-year-old woman visited our hospital on December 1, 1998, because of inability to properly use her upper limbs, and difficulty in speech and swallowing. Her history dates back to March 17, 1990, when she was hit by a car while riding a bicycle and was brought to a hospital. At that time, she was rather alert, was able to answer simple questions and was without paralysis. Brain CT revealed a high density area in the left Sylvian fissure, indicating the presence of traumatic subarachnoid hemorrhage (Fig. 1). Also, a small congenital arachnoid cyst was identified in the anterior part of the left middle fossa (Fig. 2D). In a few days the high-density area disappeared, but she started to feel nauseated and frequently vomit. On March 24, she was found to be somnolent and remarkably hyponatremic at 105 mEq/l. Brain MRI T2-weighted images revealed a signal increase in the putamen, caudate nucleus and thalamus bilaterally. With water restriction and high-dose intravenous saline, her serum sodium was corrected to 135 mEq/l on March 26. She regained consciousness but nystagmus to the right and transient right hemiparesis appeared. On March 31, her consciousness was better, without nystagmus or hemiparesis, but she was unable to speak. On April 10, a high intensity area was noted in the central pons, the bilateral striatum and the intralaminar parts of the thalamus by MRI T2 sequence (Fig. 2B, D) and the perisylvian cortex of the left side was also high on T1 sequence (Fig. 2A). In a few months she became unable to close her mouth and saliva continued to dribble from the mouth corners. Five months after the traffic accident, she started to recognize difficulty in using her right hand. When discharged from hospital seven months later, she was able to walk alone and continued speech therapy. However, in the subsequent 3 years, the use of her limbs became clumsy and facial expression became progressively inappropriate due to dystonia; i.e., despite attempts to control her movement disorders by pharmacological interventions, including a large dose of trihexyphenidyl (22 mg/day) (3, 4), she remained disabled due to the problems. She had no past history of diabetes mellitus or a family history of dystonia.
Dystonia after CPM and EPM

Figure 1. On the day of head trauma, brain CT revealed a high density area in the left Sylvian fissure, indicating the presence of traumatic subarachnoid hemorrhage.

On admission to our hospital in December 1998, her general findings were marked by maxillary and foreteeth protrusion with malocclusion. She was unable to vocalize even a vowel sound, although fully alert and intelligent. She communicated with a portable computer-generated voice device. Her answers to questions were perfect with only a slight mistake in writing the characters with a pen. Visual acuity and eye movements were normal. Although facial muscle strength appeared intact, she was unable to close her lips due to facial dystonia and prognathism (Fig. 3A). No blephalospasm was noted. Her facial expression was excessive and when asked to open her mouth, her pharynx was easily inspected as her throat was extremely wide open. The temporo-mandibular joints appeared subluxated. Mastication and swallowing were sufficient but she was unable to form proper vowel sounds and was unable to vocalize even a word. Muscle strength of her tongue was normal, but it was also dystonically twisted most of the time. At rest her limbs were hypotonic and the joints appeared excessively mobile. Attempts to keep holding the upper limbs revealed a dystonic deviation of the arms and irregular flexion and extension of the fingers (Fig. 3B). The dystonia was more prominent in the right upper limb. Standing and walking were stable but her feet were inverted. Deep tendon reflexes were normoactive throughout and the plantar response was flexor bilaterally. Sensory and autonomic systems were intact.

Complete blood counts and chemistry did not show abnormalities as to liver, kidney, thyroid functions and electrolytes. Serum ceruloplasmin was normal and a battery of autoantibodies was negative. Brain MRI revealed high signal intensity areas in bilateral caudate head and putamen on T1 images (Fig. 4A, arrows), which were the same regions showing high signal intensity on T2 images eight years previously. The subthalamic nucleus also seemed high in signal intensity on coronal section T1 images. The foci of the central pons and bilateral thalamus were no longer identifiable. Single photon emission computed tomography (SPECT) showed that the blood flow of bilateral basal ganglia was decreased in the early phase, and re-distributed in the delayed phase.

When trihexyphenidyl was discontinued because of difficulty in mental concentration, the dystonia worsened and then haloperidol (2.25 mg/day) was started, which considerably improved the motility, but the speech remained unchanged.

Discussion

The dystonia of the oral-pharyngo-lingual muscles together with the involvement of the limbs are without doubt the consequence of CPM and EPM, and which appears still progressive 8 years after the event of CPM and EPM.

Central pontine myelinolysis (CPM) is a distinctive syndrome brought about by the profound derangement of electrolyte balance. Hyponatremia and its rapid correction are thought to be a common trigger to this non-inflammatory demyelination, and it progresses rapidly and in general improves incompletely. EPM, found in 10% of CPM, is characterized by symmetrical demyelinating foci in the thalamus, subthalamic nucleus, striatum, internal capsule, amygdaloid body, lateral geniculate body, cerebellar white matter and deep layers of the cortex (2). Recently, with the advent of refined imaging diagnosis, numerous reports have described a mild form and an incomplete form (5, 6). There have also been reports describing a variety of movement disorders as an outcome of this disorder (7–11).

Non-inflammatory demyelination, the cardinal pathology of CPM and EPM, is accompanied by invasion of macrophages, swelling of axons and astrocytosis, but neurons remain relatively spared. In the present case, the lesions that had been identified as T2 high lesions, were still discernible as high intensity signals on T1 images after 8 years. This gradual alteration of MRI signals may imply that the striatum is yet in the process of reorganization in terms of extremely slow plastic changes.

Why did CPM and EPM produce dystonia in this case? It is known that the pathology of bilateral striatum may give rise to a variety of movement disorders, although in many no apparent motor manifestations are identified despite the lesion. This is particularly true in patients who have had CO intoxication and pallidal necrosis. Regarding the neural structures responsible for dystonia, the thalamus, globus pallidus, putamen and mid-brain have been postulated (12). In the present case, the striatum, one of the main targets of EPM, is thought responsible for dystonia. The motor circuit model of the basal ganglia-thalamus-cortex proposed by Delong, explains that the hyperkinetic involuntary movements are a result of low activity GABA neurons projecting from the internal segment of the globus pallidus/zona reticulata of the substantia nigra to the thalamus (13). On the coronal section of T1 images, the sub-
Figure 2. MRI images a month after the trauma. The signal intensity in the striatum is low on T1 (A) and high on T2 (B). Also the intralaminar thalamic nucleus shows a high signal intensity on T2 (B). The left perisylvian cortex shows a high signal intensity on T1 (A). The central pons shows a low intensity on T1 (C) and a high intensity on T2 (D) weighted images (A and C: TR/TE=500/30, B and D: TR/TE=2,000/100).

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thalamic nucleus also appeared high in the present case. The involvement of the indirect pathway, that is the subthalamic nucleus to the internal segment of the globus pallidus and to the zona reticulata of the substantia nigra, may sustain this hypothesis. It remains to be explained, however, why it is chiefly dystonia but not chorea, athetosis or hemiballismus.

In this case, dystonia did not appear soon after the event, and progressed very slowly. The classic athetotic form of cere-
Dystonia after CPM and EPM

Figure 3. (A) When asked, she was unable to close her lips due to facial dystonia. (B) Attempts to keep holding the upper limbs revealed a dystonic deviation of the fore arms and irregular extension and flexion of her fingers.

Figure 4. After 8 years, MRI revealed high signal intensity (arrows) on T1 images (A) and low on T2 (B) in bilateral caudate nucleus and putamen, the same regions that had previously shown high intensity on T2 (A: TR/TE=540/10, B: TR/TE=4,580/117).
bral palsy is considered to result from the plastic remodeling of the residual neurons in the basal ganglia, as the insult is usually perinatal and the brain is yet premature. In our young patient, the damage might have modified the striatal functions for the proper execution of movements as the reorganization of neural networks; a slow process which has occurred over the subsequent several years (14).

Her speech problem appears chiefly due to facial dystonia with some features of severe anarthria, as laminar necrosis was identifiable near Broca’s area, and she showed slight paragraphia. Associated oro-mandibular apraxia was difficult to evaluate in this patient; as she has a profound facial dystonia. Anterior operculum syndrome, which is produced by bilateral preoperculum lesions, is unlikely in this case, as she is able to open and close her jaw and protrude her tongue.

As a long-term outcome of CPM and EPM, movement disorders that evolve extremely slowly, may be disabling to the patient. The treatment for this particular consequence is limited. However, it is well-demonstrated the CPM and EPM are preventable when one is aware of the problem of inappropriate correction of a profound electrolyte imbalance.

References

2) Wright DG, Laureno R, Victor M. Pontine and extrapontine myelinoly-

3) Fahn S. Treatment of dystonia with high dosage anticholinergic medica-
4) Hashimoto T, Shindo M, Yanagisawa N. Treatment of dystonia with high-
5) Salvesen R. Extrapontine myelinolysis after surgical removal of a pitui-

7) Seiser A, Schwarz S, Aichinger-Steiner MM, Funk G, Schnider P, Brainin M. Parkinsonism and dystonia in central pontine and extrapontine myel-
9) Sadeh M, Goldhammer Y. Extrapyramidal syndrome responsive to dopam-

10) Maraganore DM, Folger WN, Swanson JW, Ahlskog JE. Movement dis-

11) Dickoff DJ, Raps M, Yahr MD. Striatal syndrome following hyponatrem-