

Delayed-Onset Cerebellar Syndrome

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Background: Delayed-onset involuntary movements, including dystonia and myoclonus, have been reported after stroke or head trauma. Moreover, there have been reports of delayed-onset isolated intention tremor and, in several of these cases, gait ataxia.

Objective: To further define the clinical features of a delayed-onset cerebellar syndrome.

Design: Subjects with cerebellar tremor and either head trauma or stroke were identified using a computerized database, providing detailed demographic and clinical information on 4002 patients with involuntary movements other than Parkinson's disease seen at our center between 1983 and 1995. Medical records and videotaped neurological examinations were retrospectively reviewed.

Setting: The Center for Parkinson's Disease and Other Movement Disorders at Columbia-Presbyterian Medical Center, New York, NY.

Patients: Five patients with delayed-onset cerebellar syndromes.

Results: Five patients with stroke or head trauma developed a cerebellar syndrome 3 weeks to 2 years after the initial insult. The syndrome, characterized by intention tremor, ataxic dysarthria, nystagmus, dysmetria, dysdiadochokinesis, and gait ataxia, was progressive in at least one patient. In four patients, lesions were present on neuroimaging in the thalamus or brain stem (especially in the midbrain).

Conclusions: A delayed-onset cerebellar syndrome may follow head trauma or stroke. The syndrome is sometimes progressive and often disabling. The delayed onset implies that the syndrome is not caused by the initial lesion itself but may be caused by the development of post-synaptic supersensitivity or secondary reorganization of involved pathways.

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DELAYED-ONSET involuntary movements have been reported either in the setting of therapeutic use of neuroleptic agents (ie, tardive dyskinesia and tardive dystonia)^{1,2} or following stroke or head trauma (ie, palatal myoclonus, dystonia, poststroke tremor at rest).³⁻⁷ There have been reports of delayed-onset isolated intention tremor; several of these cases also exhibited gait ataxia.^{8,9} We describe five patients with stroke or head trauma who subsequently developed a delayed-onset cerebellar syndrome characterized by intention tremor as well as ataxic dysarthria, nystagmus, dysmetria, dysdiadochokinesis, and gait ataxia. The purpose of this article is to add our cases to the literature and to further define other clinical features of a delayed-onset cerebellar syndrome.

REPORT OF A CASE

A previously healthy 13-year-old right-handed boy (patient 1) sustained head trauma in a motor vehicle accident. The patient lost consciousness, and in the emergency department, he exhibited decerebrate posturing; his Glasgow Coma Scale score was 6. He required ventilator assistance. Computed tomography of the head revealed a hematoma in the left superior mesial thalamus and increased intracranial pressure without shift of midline structures. The patient was initially in a coma, but 12 days after trauma, he became responsive to verbal stimuli. Five weeks after trauma, examination dis-

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SUBJECTS AND METHODS

The study population consisted of patients with involuntary movement disorders evaluated at the Center for Parkinson's Disease and Other Movement Disorders at Columbia-Presbyterian Medical Center, New York, NY, between October 1983 and June 1995. Subjects were identified using a computerized database, providing detailed demographic and clinical information on 4002 patients with involuntary movements other than Parkinson's disease. Subjects were located by searching for the key terms *cerebellar disorder*, *cerebellar-type tremor*, *trauma*, or *stroke*. Eleven patients were identified with cerebellar syndromes following stroke or trauma. Six were excluded because we could not definitively document that cerebellar signs had a delayed onset. Five patients were included (Table). One case is described in detail.

Neurological status was assessed at three sequential intervals: time 0, the time of the initial insult (head trauma or stroke); time 1, soon after the return to baseline level of consciousness (in cases in which there was an initial reduction in level of consciousness); and time 2, the time of initial examination by a movement disorder specialist at our center (Table). In addition, four of the patients were examined by a movement disorder specialist at our center on one or more occasions after time 2. Videotaped neurological examinations (performed at time 2) and hospital records (providing clinical information about times 0 and 1) were reviewed for all five patients.

Standard definitions were used: Intention tremor was defined as oscillatory movements present on the finger-to-nose maneuver that became more apparent as fine adjustments in movement were required or as a target was approached. Dysmetria was defined as inappropriate force and timing of motion characterized by either hypermetria or hypometria and demonstrated on the finger-to-nose or heel-to-shin maneuver. Dysdiadochokinesis was defined as a disorder of rhythmicity affecting volitional rapid alternating movements of the limbs. Rebound was defined as contraction of extensor antagonists after release of the arm flexed at the elbow. Gait ataxia was defined as a poorly coordinated, unsteady, lurching, wide-based gait; and truncal ataxia was defined as poorly coordinated and unsteady truncal movements and posture. Ataxic dysarthria was defined as slow, monotonous, slurred speech with unnatural separation of syllables.¹⁰⁻¹²

closed an alert, attentive boy who had difficulty with recall and simple calculations, right trochlear nerve palsy, and mild left-sided weakness. He was ambulatory and ate pureed food. Six weeks after trauma, he first developed a mild right-handed tremor, noted with handwriting and fine finger manipulations. The tremor gradually spread to his arm and shoulder, and the severity increased markedly.

He was first evaluated at Columbia-Presbyterian Medical Center 21 months after trauma. His major complaint was right arm tremor, which made handwriting virtu-

ally impossible and significantly impaired his ability to perform activities of daily living, including eating, dressing, and bathing. On examination, he was alert and attentive but had difficulty with calculations, recall, and copying figures. Speech was fluent but characterized by ataxic dysarthria. There was horizontal nystagmus on lateral gaze, with the fast component contralateral to the direction of gaze. There was right trochlear nerve palsy, upper motor neuron facial weakness on the left side, and mild left-sided hemiparesis (Medical Research Council score, 4) with hypertonicity. On finger-to-nose testing, there was a severe, violent, right-sided intention tremor. There was dysmetria on the right side on both finger-to-nose and heel-to-shin testing. Rebound was diminished on the right side. His handwriting was almost illegible because of the severity of the tremor.

Tremor analysis (accelerometric leads and surface electromyographic electrodes positioned over proximal and distal arm muscles) was consistent with a cerebellar tremor, revealing a low-frequency (1.5 to 4 Hz) tremor with action that was characterized by a high relative amplitude on finger-to-nose testing in comparison with arm sustentation. A magnetic resonance imaging study 4 months after trauma revealed an old hematoma in the left superior mesial thalamus and ischemic changes in the right pons extending into the midbrain (Figure 1, Figure 2, and Figure 3). Botulinum toxin injections on three occasions into the right pronator muscle of the forearm and the right wrist flexors and extensors did not diminish the tremor or dysmetria.

RESULTS

Five patients developed a delayed-onset cerebellar syndrome: three after head trauma, one after intracerebral hemorrhage, and one after basilar aneurysm with midbrain compression and thalamic infarction (Table). Cerebellar signs included dysmetria (n=5), intention tremor (n=5), dysdiadochokinesis (n=4), ataxic dysarthria (n=4), ataxic gait or truncal ataxia (n=3), and nystagmus (n=3). One patient had diminished rebound; this sign was not consistently coded as present or absent in the remaining medical records. Cerebellar symptoms and signs developed between 3 weeks and 2 years after head trauma or stroke (mean, 38 weeks). In two cases (patients 2 and 3), the cerebellar syndrome was bilateral but more severe contralateral to mild weakness. In one case (patient 5), the cerebellar syndrome and corticospinal tract signs were both bilateral. In the remaining two cases (patients 1 and 4), the cerebellar syndrome was unilateral, in one case contralateral to mild weakness and in the other case ipsilateral. Three subjects initially had severe hemiparesis, but at the time of their visit to our center, all five patients had a Medical Research Council score of 4 or greater. Two of the patients had mild hemisensory abnormalities on examination; in one (patient 4), diminished light touch and pain were ipsilateral to the cerebellar signs but far too mild and patchy to account for the degree of dysmetria. The three patients with head trauma had been comatose for 2 days to 2 months (mean,

Clinical Features of Delayed-Onset Cerebellar Syndrome*

Patient No./ Age at Onset, yr/ Sex		Cause	Timing of CT and MRI‡	CT or MRI Lesions	Delay§	Neurologic Status	
Time 0	Time 1						
1/13/M	Head trauma		CT within 24 h, MRI at 4 mo	L thalamic (superior mesial) hemorrhage, R pons/midbrain (anterior) ischemic changes	6 wk	Comatose, decerebrate posturing, ventilator assistance	5 wk after insult: L-sided weakness, R cranial nerve IV palsy, mild cognitive deficit, ambulatory, pureed food
2/19/M	Head trauma		CT within 24 h, MRI at 4.5 y	L thalamic (inferior posterior/mesial) hemorrhage, L midbrain infarct (posterior), mild diffuse cortical atrophy	1 y	Comatose, ventilator assistance	4-6 mo after insult: L-sided weakness, disinhibited behavior, mild cognitive deficit, ambulatory, normal diet
3/25/M	Head trauma		CT and MRI at 5 y	Mild diffuse cortical atrophy	2 y	Comatose	2 mo after insult: L-sided weakness, L hemisensory deficit, ambulatory, normal diet
4/71/F	Stroke/hemorrhage		CT within 24 h and at 6 mo	R thalamic (superior centrolateral) hemorrhage	6 mo	L-sided weakness, L hemisensory deficit	Not applicable, patient never comatose
5/67/F	Basilar aneurysm with bilateral midbrain compression and R thalamic infarct; surgical resection 5 wk after onset of cerebellar syndrome		CT at 2 mo	R thalamic (inferior anterior-mesial) infarct and bilateral midbrain (anterior) compression	3 wk	4-Limb weakness (L>R), R cranial nerve III palsy, L cranial nerve VI palsy	Not applicable, patient never comatose

*CT indicates computed tomography; MRI, magnetic resonance imaging.

†Age at onset of cerebellar syndrome.

‡Time between insult and imaging study.

§Time between insult and onset of cerebellar syndrome.

||Time 0 was the time of initial insult; time 1, soon after return to the baseline level of consciousness; and time 2, when seen at our center.

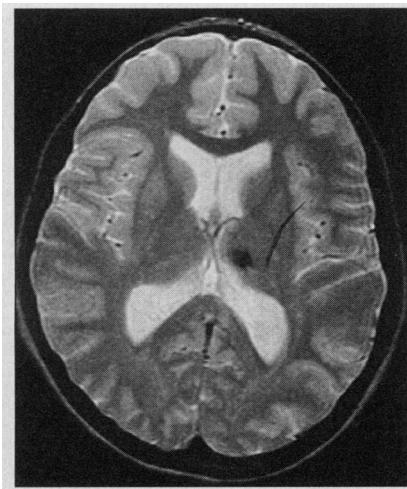


Figure 1. A follow-up T_2 -weighted head magnetic resonance image 4 months after trauma reveals an old hematoma in the left superior-mesial-central thalamus. Pencil mark indicates the left thalamus and lentiform nucleus.

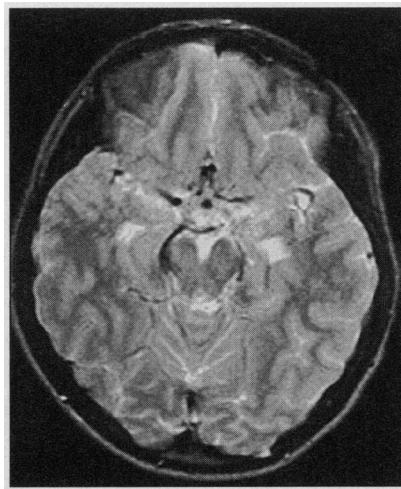


Figure 2. A follow-up T_2 -weighted head magnetic resonance image 4 months after trauma reveals ischemic changes in the right midbrain.

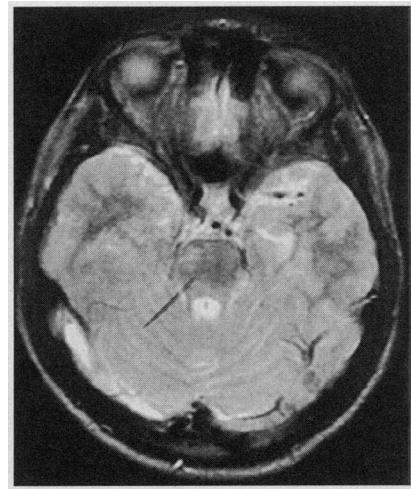


Figure 3. A follow-up T_2 -weighted head magnetic resonance image 4 months after trauma reveals ischemic changes in the right pons. Pencil mark indicates the right pons and cerebellum.

Time 2	Cerebellar Syndrome	Treatment
1 y after insult: L-sided weakness, R cranial nerve IV palsy, mild cognitive deficit, ambulatory, normal diet	Ataxic dysarthria, nystagmus, R dysmetria, R intention tremor, R diminished rebound	Three botulinum toxin injections into R forearm
4.5 y after insult: L-sided weakness, bilateral cranial nerve X palsy, mild cognitive deficit, ambulatory, normal diet	Ataxic dysarthria, nystagmus, R>L dysmetria, R>L intention tremor, R>L dysdiadochokinesis, ataxic gait	Propranolol, primidone, baclofen, clonazepam, carbamazepine, L stereotactic thalamotomy
5 y after insult: L-sided weakness, L hemisensory deficit, torticollis, ambulatory, normal diet	Ataxic dysarthria, bilateral nystagmus, R>L dysmetria, R>L intention tremor, R>L dysdiadochokinesis, ataxic gait	L stereotactic thalamotomy
6 mo after insult: L-sided weakness, L hemisensory deficit, chorea (L arm)	L dysmetria, L intention tremor, L dysdiadochokinesis, ataxic gait	Levodopa/ carbidopa, tetrabenazine
5 mo after insult: 4-limb weakness (L>R), R cranial nerve III palsy, L cranial nerve VI palsy	Ataxic dysarthria, R>L dysmetria, R>L intention tremor, R>L dysdiadochokinesis	None

24.7 days). None of the patients had a family history of cerebellar disorder.

In four cases, "tremor" was the patient's chief complaint and reason for initial evaluation at Columbia-Presbyterian Medical Center. At the point of greatest severity, all of the patients were unable to perform at least one activity of daily living (feeding, dressing, or bathing) as a result of their tremor. In two cases (patients 1 and 5), the symptoms worsened over 4 to 7 months and then reached a plateau. In one case (patient 2), symptoms worsened over 3.5 years prior to a unilateral stereotactic thalamotomy. The thalamotomy provided partial relief of the tremor, and the syndrome did not progress over the ensuing 4 months. In one case (patient 3), symptoms worsened over 3 years prior to a unilateral stereotactic thalamotomy. The thalamotomy provided partial relief of the tremor, but the dysmetria continued to progress during the ensuing 3-year period. One patient (patient 1) received botulinum toxin injections into the tremulous arm, and two others received medical treatment. There was no change in the tremor or dysmetria.

All patients had either head computed tomography or magnetic resonance imaging. Lesions were present in both the thalamus and midbrain in two patients; in the thalamus, midbrain, and pons in one patient; and in the thalamus alone in one patient. Different regions of the thalamus and midbrain were involved in each case. Two patients also had diffuse cortical atrophy. On follow-up imaging studies, no evolving changes correlated with progression of neurological deficits.

COMMENT

Delayed-onset intention tremor without other associated cerebellar signs has been reported after mild head trauma with normal findings on neuroimaging studies,¹³ after infarctions in the thalamus or frontal lobe, and after hemorrhages in the thalamus, parieto-occipital lobe, or pons.¹⁴⁻¹⁸ Ghika et al¹⁹ described three patients with delayed-onset complex hyperkinetic motor syndromes (dystonia, myoclonus, chorea, rubral tremor, and ataxia) after thalamic infarctions. Andrew et al⁸ reported eight cases of intention tremor 2.2 to 14 years after head trauma. One of these patients had gait ataxia, but head computed tomography did not reveal a focal abnormality. Iwadate et al⁹ reported eight cases of intention tremor 2 to 16 weeks after head trauma. Four of these patients had midbrain hematomas on head computed tomography; two had gait ataxia. The literature on delayed-onset intention tremor does not emphasize the presence of other cerebellar signs.¹³⁻¹⁸ We report five cases of a delayed-onset cerebellar syndrome characterized not only by intention tremor but also by other cerebellar findings, including nystagmus, ataxic dysarthria, dysmetria, and dysdiadochokinesis. The syndrome was disabling and in at least one of the cases, also progressive.

On neuroimaging, four patients had lesions in the thalamus or brain stem (especially in the midbrain), and the cerebellar syndrome was presumably caused by these lesions, although it is possible that some cases may have had additional brain-stem infarcts that were not seen. The topographic distribution of lesions within the thalamus and midbrain was not uniform, making precise clinical-anatomical correlation difficult (Table). Iwadate et al⁹ hypothesized that posttraumatic intention tremor may be caused by disruption of cerebellar outflow pathways in the brain stem, particularly the dentato-rubro-thalamic pathway. LaRochelle et al²⁰ demonstrated that intention tremor may be produced experimentally in monkeys by creating lesions in the dentato-rubro-olivary pathways.

The cerebellar syndrome was delayed and sometimes progressive, implying that it may not be attributable to the initial lesion itself. Acute cerebellar strokes and experimental ablation of areas of cerebellar cortex and deep cerebellar nuclei typically result in cerebellar signs of immediate onset that improve over days to weeks.²¹⁻²³ Occasionally, signs from cerebellar strokes develop after 2 to 5 days, possibly secondary to an evolving embolic cause.²⁴ The prolonged delay in our cases may have been caused by the development of postsynaptic supersensitivity in involved brain-stem or thalamic pathways. Delayed-onset palatal myoclonus has been attrib-

uted to the development of postsynaptic supersensitivity after decentralization of the inferior olivary nucleus by lesions in the dentato-rubro-olivary system.⁵ Alternatively, the syndrome may have been caused by secondary reorganization of cerebellar outflow or thalamic pathways.¹⁴ Ohye et al²⁵ observed changes in electrical activity in and around the thalamus (nucleus ventralis intermedius) in patients with poststroke action tremor, supporting the notion of a reorganization of thalamic nuclei following stroke. In a positron emission tomography study, Weiller et al²⁶ reported functional reorganization of the contralateral cerebellum in the recovery phase following stroke. Serial positron emission tomography studies might have helped to clarify the mechanism of delayed onset in our cases.

While some of our patients had mild weakness (Medical Research Council score ≥ 4) or sensory deficits, either cerebellar signs were present in contralateral limbs (cases 1 through 3) or the pyramidal or sensory signs (slight, patchy diminution in pain and temperature sense) were inadequate to account for the almost ballistic severity of the dysmetria (cases 4 and 5). It is unlikely that severe weakness masked early cerebellar signs, since in those with severe initial weakness (cases 1 through 3), cerebellar signs were contralateral to weak limbs. In the patients with posttraumatic syndromes, it is unlikely that earlier cerebellar signs were masked by coma, as cerebellar signs were initially noted 1 week to 22 months after return to baseline level of consciousness, while patients were ambulatory and eating normal diets. In fact, we excluded six patients because it was unclear from review of medical records whether the cerebellar signs had a delayed onset; they may have begun while consciousness was still impaired.

In summary, we report five cases of a delayed-onset cerebellar syndrome characterized by intention tremor, ataxic dysarthria, nystagmus, dysmetria, dysdiadochokinesis, and gait ataxia. The syndrome is sometimes progressive and often severely disabling. The frequency of this syndrome is difficult to estimate. While it was present in one of 800 patients with nonparkinsonian involuntary movements seen at our center, implying that it is rare, the syndrome may be more common in head injury or stroke databases. On neuroimaging, lesions are present in the thalamus or brain stem (especially in the midbrain), with possible disruption of the dentato-rubro-thalamic or dentato-rubro-olivary pathways. The delayed onset and progression imply that the syndrome is not caused by the initial lesion itself, but possibly by the development of postsynaptic supersensitivity or secondary reorganization of involved pathways.

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