Patient 1 showed onset at the age of 28 with facial and limb dystonia, pyramidal signs, and cerebellar ataxia as well as bulging eyes and ophthalmoplegia. His father was 63 at disease onset and his mother 65. Moreover, their clinical manifestations were very mild compared with those of the son. In contrast, the disease onset of the son was significantly earlier than the expected 95% confidence range lines on the correlation between the age onset and CAG repeat size. These findings strongly suggest that the differences in age at onset and clinical phenotypes between the parents and son are due to the homozygosity of the Machado-Joseph disease gene in the son. The double dose of the gene in the homozygotic son significantly enhanced the phenotypic severity of the disease. Patients with Machado-Joseph disease suspected to be homozygous were reported not to develop an elongated CAG repeat of different phenotypes than their parents. However, because the CAG repeat size is also a determinant factor for the age of onset and clinical phenotypes of patients with Machado-Joseph disease, the enhanced clinical severity in homozygous patients so far reported might have been attributed to the elongated CAG repeat size of the mutant allele. The length of the CAG repeat size of the mutant allele of the Machado-Joseph disease gene in the homozygous son and his parents in this study clearly indicates that a double dose of the gene enhanced a clinical severity. This dose effect in increasing clinical severity has been described in the PMP-22 gene of Charcot-Marie-Tooth disease type 2a and in the PLP protein gene in Pelizaeus-Merzbacher disease.

In conclusion, our results clearly indicate that a double dose of the Machado-Joseph disease gene is a determinant factor, in addition to the CAG repeat size of the gene, for the age of onset and clinical phenotypes of patients.

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Isolated body lateropulsion caused by a lesion of the cerebellar peduncles

Lateropulsion, or falling to one side, has been described in Walenberg's syndrome. It also occurs with lesions of the vestibular end organ, vestibular nerve, brainstem, cerebellum, and basal ganglia. In these cases, body lateropulsion is only one of many manifestations. Lateropulsion rarely constitutes the sole symptom and sign of a neurological disorder. Isolated lateropulsion occurred in a patient in whom MRI showed an ipsilateral lesion in the midbrain peduncle. A 32 year old woman with no history of neurological disorder developed pronounced unsteadiness within a few hours. She was unable to stand or walk and fell to the left side. She had no vertigo, nausea, or vomiting and no difficulty with vision, hearing, speech, or individual limb functions. On the next day, neurological examination showed an immediate fall to the left when standing unsupported and opened eyes. She had no body oscillations but made an attempt to correct her gait by a wide based stance. She had no cerebellar dysmetria or hypotonia in the four limbs. Eye movements were not affected. There was no ocular lateropulsion even after eyelid closure. Pupil and cranial nerve examination were normal. There were no sensory and motor disturbances. Deep tendon reflexes were normal and there was no Babinski's sign. Two days later brain CT including contrast enhancement was normal. On the third day, a brain MRI showed a high signal adjacent to the fourth ventricle at the level of thepons on T2 weighted axial sequences. The lesion included both superior and inferior peduncles but not the middle cerebellar peduncle, the brainstem, or the cerebellum (fig. 1). There was no other abnormality in the brainstem, cerebellum, or cerebrum. T1 weighted sequences with and without gadolinium injection were normal. Five days after onset, caloric irrigation produced symmetric responses. A pure tone audiogram was normal. Brainstem auditory evoked potentials after stimulation of the left ear showed no latency differences. The electroencephalogram showed waves with a slight morphological instability of waves IV and V. They were normal on the right side. Visual and somesthetic evoked potentials were normal. Cerebrospinal fluid contained 5 cells/mm3, and 0.53 g/l protein with 15.8% IgG in an oligoclonal pattern. As the CSF and MRI findings suggested an initial attack of multiple sclerosis, she was treated with steroids. She improved rapidly and was able to walk normally after 10 days. One year later brain MRI showed no abnormal signal intensity in the left cerebellar peduncles on either T1 or T2 weighted sequences. No further neurological deficit occurred during a two year follow up.

An isolated body lateropulsion is extremely rare. It has only been reported three times. In two patients, the lateropulsion was ipsilateral to a lesion located in the flocculo nodular lobe in one patient, and probably in the reticular formation of the medulla oblongata in the other. In the third patient, the side of the fall was contralateral to a lesion of the red nucleus or its environs. In our patient, body lateropulsion was the only symptom and sign. It was ipsilateral to a lesion, seen on brain MRI, adjacent to the fourth ventricle and corresponding to the topography of the superior and inferior cerebellar peduncles. The middle cerebellar peduncle, which is more lateral and not directly exposed to the cavity of the fourth ventricle, was spared. Experiments on animals support the hypothesis that the gait disturbance of our patient originated in the cerebellar peduncles. Although controversial, data suggest that unilateral section of the three cerebellar peduncles induces an ipsilateral body deviation. In monkeys, balance disorders have been seen after specific lesions of each peduncle. After lesion of the middle cerebellar peduncle, a truncal and an appendicular cerebellar ataxia occurred without reported body lateropulsion. Lesion of the superior cerebellar peduncle usually induced an ipsilateral appendicular ataxia but in at least one case, body lateropulsion occurred that overshadowed the appendicular ataxia. Section of the inferior cerebellar peduncle
produced a fall towards the side of the lesion. Although the inferior cerebellar peduncle involves the vestibulocerebellar pathways, there was no spontaneous nystagmus and a caloric test gave normal nystagmus responses, as in our patient.

Thus experimental data support the hypothesis that our patient's lateropulsion originated in a lesion of the inferior and possibly superior cerebellar peduncles, in accordance with the topography of the lesion on brain MRI.

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Progressive dysphagia due to adult Chiari I malformation mimicking amyotrophic lateral sclerosis

Chiari I malformation, characterised by caudal descent of the cerebellar tonsils, has been shown to cause progressive dysphagia, usually associated with other apparent signs and symptoms of dysfunction of lower cranial nerves, medulla, and cerebellum. Without the associated hindbrain malfunctions, however, this deformity still needs to be listed as a possible cause of neurogenic dysphagia in consideration of its readiness to be diagnosed on sagittal views of MRI and its excellent reversibility on decompression surgery. There are two reports of dysphagia as a sole manifestation of adult Chiari I malformation, in both of which the diagnosis was delayed. Presented here is a patient diagnosed as possibly having amyotrophic lateral sclerosis, who was subsequently found to have Chiari I malformation as a cause of progressive dysphagia.

A 33 year old woman had an unremarkable medical history until 1990 when she started having some difficulties in swallowing liquid, but was able to eat solid food. In 1991 she developed aspiration pneumonia, which was confirmed by an otherwise unremarkable barium swallow test. Over the next three years she was admitted to hospital four times for recurrent aspiration with increasing dysphagia. In October 1994 she was referred by a neurologist to our hospital for terminal care of her "amyotrophic lateral sclerosis." By the time of admission, she had nasal regurgitation on every liquid intake and became unable to swallow even solid foods. She required a nasogastric tube for feeding.

Physical examination showed an emaciated woman with a body weight of 30.5 kg and height of 142 cm. No physical abnormalities such as a short neck and low hairline were noted. Neck flexion was rather restricted and neck extension, although full, was associated with a dull pain in the occipital area. No papilloedema was noted. The gag reflex was bilaterally absent with moderate palatal hypoesthesia. Her voice was slightly nasal with hypomobility of the soft palate, but neither hoarseness nor dysarthria was noted. Her tongue did not show atrophy or fascicularisation. Externally ocular movements were full and there was no nystagmus. She had diffuse muscle weakness and general hyperreflexia with indifferent plantar response. There was slight impairment of coordination in the upper and lower limbs. She had mild glove and stocking type dysaesthesia with slightly decreased sensibility on all modalities. Romberg's test was equivocal. She had slight difficulties in walking straight and to one foot.

Investigations showed an unremarkable urinalysis, complete blood count, serum chemistry, and arterial blood gas analysis. Spirometry showed a percentage of the predicted value of vital capacity of 57% and a forced expiratory volume in one second of 73%. Fibreoptic laryngoscopy was essentially unremarkable except for a somewhat weak laryngeal reaction. Examination of CSF was normal with no evidence of a spinal block. Electromyography and brainstem auditory evoked responses were unremarkable. Somatosensory evoked potentials suggested bilateral peripheral neuropathy. Motor and sensory nerve conduction studies showed slightly decreased velocity in all limbs. Skull radiographs were unremarkable, without basilar impression or platybasia. The coronal views of MRI were notable for a laterocerebellar subarachnoid cyst in the left posterior fossa mildly compressing the cerebellum (fig 1), and the sagittal views showed elongation of cerebellar tonsils below the foramen magnum compared to the C2 level (fig 2). No hydrocephalus or spinal cavity was noted in the imaging studies.

She underwent suboccipital craniotomy with C1 decompression laminectomy in January 1995. One month later, she reported nearly complete resolution of dysphagia, nasal voice, and dysaesthesia of the hands. The gag reflex became weakly positive, the soft palate moved upwards well, and the palatal sensation returned. Unchanged were general hyperreflexia with indifferent plantar response and slightly impaired coordination of the extremities. This woman was first diagnosed as having amyotrophic lateral sclerosis based on the findings of progressing severe bulbar palsy, general hyperreflexia, and diffuse muscle weakness that turned out to have resulted from malnutrition. Other findings such as impairment of coordination and instability of walking were so subtle that they were attributed to muscle weakness. It was unusual for amyotrophic lateral sclerosis, however, that the patient had no apparent sign of dysfunctions of the lower cranial nerves, especially of the tongue, despite the presence of striking dysphagia. This led us to investigate the patient with MRI, which showed caudal displacement of the cerebellum.

The suggested mechanisms of dysphagia in Chiari I malformation have been stretch injury to the lower cranial nerves caused by caudal displacement of the medulla, or dysfunction of the brain stem, especially the swallowing centre itself, from compression. Pollack et al examined patients with dysphagia due to Chiari I malformation by cineoesophagograms, and found widespread impairment of all phases of swallowing, which was consistent with lesions involving the medullary swallowing centre. The uncommon manifestation of our patient—namely, prominent dysphagia without apparent involvements of other lower cranial nerves—may also be explained by rather selective impairment of a swallowing centre in the medulla.

The aetiology of adult Chiari I malformation remains obscure. Although traditionally viewed as a congenital anomaly, there is much evidence that this malformation may be an acquired deformity. Cerebellar descent occurred after repeated lumbar punctures or spinal subarachnoid shunting, which supported the hypothesis that the CSF pressure difference between the spinal and cranial compartments causes tonsillar herniation. Others suggested that a mismatch between the volume of the posterior fossa and its tissue contents may produce