Nodulus infarction mimicking acute peripheral vestibulopathy

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Abstract—The authors report two patients with cerebellar infarctions in the territory of the medial branch of the posterior inferior cerebellar artery who had vertigo, spontaneous ipsilesional nystagmus, and contralesional truncal lateropulsion. Although one of the two patients had slight dysmetria, overall signs closely mimicked those of acute peripheral vestibulopathy. The authors suggest that interruption of nodulouvular inhibitory projections to vestibular nuclei may account for the vestibular signs.

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Patients with cerebellar stroke may seek treatment for truncal lateropulsion and nystagmus. Truncal lateropulsion is a motor abnormality in which a patient cannot stand without falling to one side.^{1,2} Ordinarily, truncal lateropulsion is toward the side of a cerebellar lesion.^{1,3,4} To our knowledge, there has been one report² of truncal lateropulsion contralateral to a cerebellar lesion. In this previous report, the patient had upbeat nystagmus, a central sign. We now report two patients with medial cerebellar infarcts. Both had truncal lateropulsion, contralateral to a cerebellar lesion, and unidirectional nystagmus typical of acute peripheral vestibulopathy.

Case reports. Patient 1. A 74-year-old man developed vertigo with perceived counterclockwise rotation of the environment (i.e., from the patient's point of view), nausea, vomiting, and imbalance. He preferred to lie with the right ear uppermost because this attenuated the vertigo. On examination, he fell to the right on attempts to stand with eyes open and when sitting. He had spontaneous left-beating nystagmus with horizontal and torsional components in primary position and on gaze to the right and left. He did not have dysarthria, diplopia, ophthalmoparesis, perceived tilting of the environment, limb weakness, dysmetria, or sensory loss. Fundus photography showed no significant ocular torsion in either eve. MRI showed abnormalities consistent with a recent infarct involving the cerebellar vermis, including the nodulus and uvula bilaterally (figure 1). The flocculus and the brainstem, including vestibular nuclei, were spared. MR angiography (MRA) showed a small left vertebral artery and absent flow in the left posterior inferior cerebellar artery (PICA). A pure tone audiogram (PTA), brainstem auditory evoked potentials (BAEP), horizontal saccades, smooth pursuit, optokinetic nystagmus, and caloric responses were normal. Saccadic lateropulsion, i.e., overshoot or undershoot, on testing of saccades was not observed. On quantitative rotational testing, the vestibulo-ocular reflexes were normal, apart from increased phase lead at low frequency (0.02 Hz). Vertigo and nystagmus resolved within several days. Truncal lateropulsion improved within several weeks.

Patient 2. A 76-year-old woman developed vertigo with perceived clockwise rotation of environment and imbalance. She preferred to lie with the left ear uppermost because this attenuated

the vertigo. On examination, she fell to the left on attempting to walk and when sitting. She had spontaneous right-beating nystagmus with horizontal and torsional components in primary gaze and with gaze to either right or left. Finger-nose and heel-kneeshin tests showed minimal dysmetria on the right. There was no dysarthria, diplopia, ophthalmoparesis, visual tilting of the environment, limb weakness, or sensory loss. MRI showed abnormalities consistent with a recent infarct involving the right inferior vermis, including the right nodulouvular area (figure 2). The flocculus and the brainstem, including vestibular nuclei, were spared. MRA did not reveal a vascular lesion. PTA and BAEP were normal. Horizontal saccades, smooth pursuit, optokinetic nystagmus, and caloric responses were normal. Saccadic lateropulsion was not observed. Over several days, vertigo, nystagmus, and truncal lateropulsion subsided. At follow-up evaluation, the patient reported only mild unsteadiness when walking.

Discussion. Spontaneous unidirectional nystagmus with horizontal and torsional components, combined with falling to the side opposite the fast phase of the nystagmus, is a well-known syndrome characteristic of labyrinthine disorders.⁵ A "pseudolabyrinthine" syndrome caused by acute, medial cerebellar infarction has rarely been reported.^{1,3,4,6} In these rare cases, patients sometimes have central signs, e.g., dysarthria, gaze evoked, asymmetrical direction-changing nystagmus, asymmetrical smooth pursuit, or dysmetria.^{1,3,4,6} One of our patients did have slight dysmetria on the side of the lesion, as noted in previous reports.^{1,6,7} In our patients, however, the main features were vertigo, spontaneous unidirectional nystagmus, and truncal lateropulsion. Electronystagmogram (ENG) demonstrated normal smooth pursuit and optokinetic eye movements. Thus, the findings mimicked those of acute peripheral vestibulopathy. It was surprising that cerebellar dysmetria was not found in Patient 1, given the large MRI abnormality. However, serial neurologic examinations over several days did not find dysmetria. It

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Figure 1. Patient 1. T2-weighted axial MRI (A) showed an acute infarct in the distribution of the posterior inferior cerebellar artery (PICA), involving the nodulus (*) and uvula (**) bilaterally. MR angiography (B) showed a dominant right vertebral artery with absent flow in the left PICA (long arrow).

is interesting to compare the syndrome described in the present article with that of Wallenberg (i.e., lateral medulla) syndrome. Signs of Wallenberg syndrome include vertigo, truncal lateropulsion, and nystagmus, which were seen in our patients. However, patients with Wallenberg syndrome characteristically have additional brainstem signs, e.g., Horner syndrome, diminished gag reflex, and crossed hypalgesia, and the direction of truncal lateropulsion is ipsilesional.

Without conventional angiography, conclusions on vascular mechanism are necessarily limited. For Patient 1, MRA showed absent flow in the PICA. Apart from a dominant right vertebral artery, no vascular variants, e.g., dominant anterior inferior cerebellar artery (AICA) or AICA-PICA complex, were noted. However, AICA and PICA are not always well visualized on MRA. The clinical evidence is more consistent with PICA ischemia compared with AICA ischemia. Our patients showed neither hearing loss on audiometry nor canal paresis on caloric stimulation, both of which commonly accompany AICA stroke.⁸ Thus, our evidence suggests that the infarcted area was most likely supplied by the medial branch of PICA, the vessel that usually supplies nodulus and uvula.

Nodulus efferents project to the vestibular nuclei. Lateral nodulus projects to caudal medial vestibular nucleus; medial nodulus projects to medial part of medial vestibular nucleus; and zone III projects to the superior vestibular nucleus.^{9,10} Nodulovestibular Purkinje fibers have an inhibitory effect on ipsilateral vestibular nuclei.^{9,10} Although nodulus involvement appeared by MRI to be bilateral in Patient 1, the nystagmus suggests asymmetrical injury with greater damage on the left. We speculate that the mechanism of the spontaneous unidirectional ipsilesional nystagmus may have involved an increased tonic activity of ipsilesional medial and superior vestibular nucleus neurons caused by disconnection of inhibitory nodulovestibular Purkinje fibers from neurons in the vestibular nuclei. The nystagmus in our patients may be contrasted with that of a unilateral peripheral vestibular lesion, in which the tonic resting firing rate of semicircular canal afferents is decreased and contralesional nystagmus is the result of unopposed activity of the intact vestibular nucleus.

To put the incidence of the syndrome described in the present report into perspective, the Keimyung University Stroke Registry was reviewed. Data on MRI-confirmed posterior circulation stroke between January 1999 and September 2002 were reviewed. Among 374 patients with posterior circulation stroke, there were 155 involving PICA territory, of which 68 showed pure cerebellar involvement. However, only the two patients reported in the present article, i.e., 2 of 374 with posterior circulation stroke, showed unidirectional ipsilesional nystagmus and contralesional falling. Because the syndrome found in these two patients appears to be rare, clinicians should be cautious not to overestimate its likelihood. Nevertheless, medial cerebellar infarction may be considered in the differential diagnosis of vertigo, even if the nystagmus and lateropulsion are more typical of acute peripheral vestibulopathy.



Figure 2. Patient 2. T2-weighted axial MRI (A) showed an acute infarct in the distribution of the posterior inferior cerebellar artery, involving the right nodulus (*) and uvula (**). MR angiography (B) showed no vascular abnormalities.

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Canavan's leukodystrophy is associated with defects in cochlear neurodevelopment and deafness

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Abstract—The authors present the temporal bone histopathology of two siblings (4 months old and 6 months old at autopsy) with Canavan's disease, an autosomal recessive leukodystrophy that is variably associated with sensorineural hearing loss. The histopathology demonstrated bilateral absence of the organ of Corti throughout the apical and basal cochlea and mild secondary atrophy of the spiral ganglia neurons. The vestibular end organs and ganglia were normal. These findings implicate a role of aminoacylase II in the neurodevelopment of the organ of Corti.

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Canavan's disease is an autosomal recessive rare form of spongiform leukodystrophy caused by an inherited defect in aminoacylase II, which catalyzes the breakdown of N-acetylaspartate (NAA).¹ After a relatively normal birth, homozygous infants develop symptoms between the second and fourth months of life, including megalencephaly, severe progressive psychomotor retardation, seizures, optic atrophy, hypotonia, and early death.^{2,3} The histopathology of Canavan's disease is characterized by spongiform degeneration, demyelination, and vacuolization of the white matter and optic nerves.² There is a variable presentation of sensorineural hearing loss in Canavan's disease,⁴ but the etiology of the hearing loss has not previously been investigated. We studied the temporal bone histopathology of two siblings with Canavan's disease.

Clinical history. The parents of the patients were first cousins. The parents were of good health.

Case 1. The birth history of this 6-month-old white boy was normal. Abnormal neurologic development was first noted at 2 months of age, heralded by irritability and gradually increasing lethargy. Initially, there was generalized hypotonia and poor head control followed by hyperreflexia and spasticity. At 5 months of

age, there was no response to verbal stimuli and no tracking of objects with eye movements. The infant died at 6 months of age secondary to respiratory arrest. Autopsy of the brain revealed megalencephaly, diffuse severe spongy white matter degeneration, and no Rosenthal fibers, typical of Canavan's disease. An experienced neuropathologist reviewed the slides.

Case 2. This 4-month-old boy was the younger sibling of Case 1. He had been delivered normally. At 2 months of age, neurologic examination was notable for lack of response to verbal stimuli and poor head control. Severe psychomotor retardation and lack of tracking of objects with eye movements was noted. At 4 months of age, he died secondary to aspiration emesis. Autopsy of the brain revealed similar histopathology to the brother.

Materials and methods. The temporal bone specimens were received through the UCLA National Temporal Bone Bank. The temporal bones were obtained at autopsy, fixed in 10% formalin, decalcified in 5% trichloroacetic acid solution, and dehydrated in graded concentrations of ethyl alcohol. The specimens were embedded in celloidin and sectioned horizontally at 20 μ m. Every tenth section was stained with hematoxylin and eosin and examined under light microscopy.

 $\ensuremath{\textbf{Results.}}$ The left and right temporal bones of both patients were examined.

Auditory system. In both the 6-month-old infant (figure 1) and the 4-month-old infant (figure 2), the inner and outer hair cells of the organ of Corti were absent bilaterally at the basal and

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