

Vestibular Syndrome due to Brainstem Infarction in Swiss Mice

T. Southard, S. Trembley, T. Prezioso, K. Gabrielson, C. Morrell, C. Brayton
 Department of Molecular and Comparative Pathobiology
 Johns Hopkins University School of Medicine



Abstract

Spontaneous vestibular syndrome in mice, characterized clinically by head tilt, circling or rolling, can be attributed to otitis media, arteritis or central nervous system lesions. Post mortem examination on seven non-inbred Swiss mice (one Hsd:ND4 and six Hsd:ICR(CD-1)) submitted for pathology due to acute onset of vestibular signs revealed similar brainstem lesions. The lesions were characterized by unilateral, well-demarcated areas of necrosis, malacia and gliosis, with variable amounts of hemorrhage, in the lateral aspect of the medulla and caudal pons. The affected area includes the medial, lateral and superior vestibular nuclei, the facial nucleus and the spinal trigeminal nucleus. In one mouse, the patency of the vascular supply to the brainstem was investigated. Intracardiac injection of black ink immediately after euthanasia revealed a filling defect in the rostral segment of the vertebral artery, at the level of C1, on the side of the brainstem lesion. These findings suggest that the unilateral brainstem necrosis is secondary to occlusion or rupture of the vertebral artery. Unilateral brainstem infarction represents another potential cause of vestibular phenotype in mice and shares features with Wallenberg's Lateral Medullary Syndrome, the most common brainstem stroke in humans

Methods

Post mortem examinations were performed on seven non-inbred Swiss mice (one Hsd:ND4 and six Hsd:ICR(CD-1)) with acute vestibular signs. The mice were euthanized with CO₂, and heads were decalcified with Formical™ for 24 hours, sectioned and submitted for histology. Immediately after carbon dioxide euthanasia, the thoracic cavity was opened in one mouse and 1.5 ml of Bouin's solution was injected into the left cardiac ventricle, followed by 1.5 ml of tissue ink (PathMark™, black). To investigate the normal vasculature of the mouse brainstem, a control mouse was euthanized and 1.5 ml of yellow latex was injected into the left ventricle.

Results

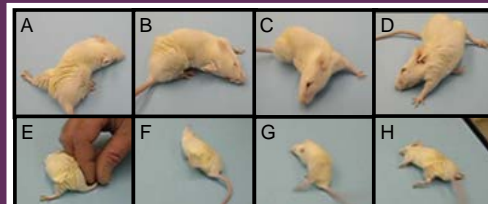


Figure 2. Affected mice show head tilt, spinning (A-D) and rolling (E-H) toward the side of the lesion.

Necropsy #	Date	Strain	Source	Lesion
56986	1/10/2006	ICR/CD1	Harlan	unilateral brainstem necrosis
58367	7/3/2006	ICR/CD1	Harlan	unilateral brainstem necrosis
58383	7/7/2006	ICR/CD1	Harlan	unilateral brainstem necrosis
58690	10/31/2006	ND4	Harlan	unilateral brainstem necrosis
58784	12/4/2006	ICR/CD1	Harlan	unilateral brainstem necrosis
58834	12/28/2006	ICR/CD1	Harlan	unilateral brainstem necrosis
59205	5/16/2007	ICR/CD1	Harlan	unilateral brainstem necrosis

Table 1. Seven non-inbred Swiss mice submitted for necropsy because of vestibular signs had unilateral brainstem necrosis. All mice were from Harlan (Frederick, MD).

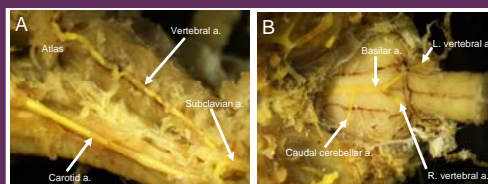


Figure 2. Intracardiac injection of yellow latex in a control mouse shows the course of the vertebral artery through the transverse foramina (opened) of the cervical vertebrae then joining contralateral artery to form the basilar artery. The first major branch of the basilar artery is the caudal cerebellar artery.

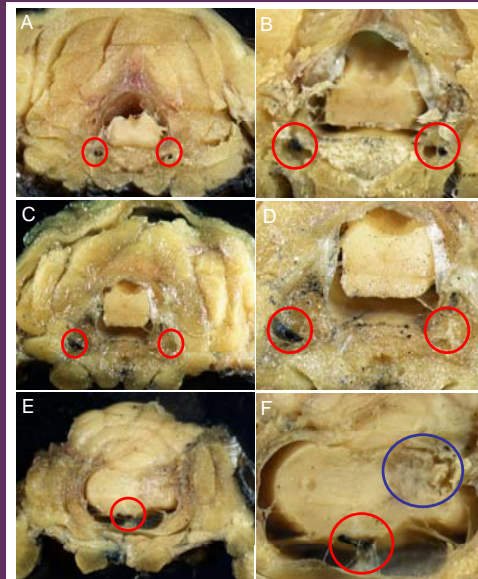


Figure 4. Postmortem intracardiac injection of ink highlights the vertebral artery. A and B. At the level of C2, both vertebral arteries contain ink. C and D. At the level of C1, there is a filling defect in the right vertebral artery. E and F. At the level of the caudal medulla, ink is visible in only the left vertebral artery as it merges with the right to form the basilar artery. There is a discrete area of malacia in the dorsolateral medulla on the right side.

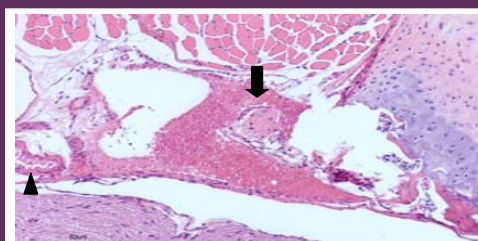


Figure 3. A putative thrombus in a branch (arrow) of the vertebral artery (arrow head) at the level of C1. There is moderate hemorrhage around the vessel.

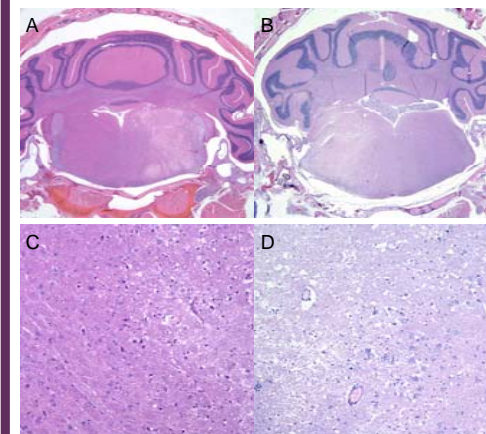


Figure 2. Brainstem lesions in two Swiss mice with vestibular syndrome. A and B. Both mice have well demarcated areas of pallor in the brainstem, near the cerebral peduncle. C and D. Lesions are characterized by neuronal loss, malacia, and gliosis with an abrupt transition to normal neuropil.

Discussion

Vestibular syndrome, characterized by head tilt, spinning and rolling, has been previously reported in mice with otitis media/interna, carotid arteritis and CNS tumors affecting the vestibular nuclei or cerebellum. The mice discussed here had lesions consistent with unilateral brainstem infarction involving the vestibular nuclei. The infarction is most likely secondary to occlusion or rupture of the vertebral artery or one of its branches. Unilateral brainstem infarction represents another potential cause of vestibular phenotype in mice and shares features with Wallenberg's Lateral Medullary Syndrome, the most common brainstem stroke in humans.

Conclusions

1. Vestibular syndrome in seven Swiss mice was associated with unilateral brainstem lesions consistent with infarcts.
2. Brainstem lesions are similar to those reported with Wallenberg's Lateral Medullary Syndrome in humans.

References

Bloom D, Hultcrantz M. (1994) Vestibular morphology in relation to age and circling behavior. *Acta Otolaryngol.* 114(4):387-92.
 Fraser H. (1996) Brain tumours in mice, with particular reference to astrocytoma. *Food Chem Toxicol* 24(2): 105-11.
 Kim JS, Lee JH, Suh DC, Lee MC (1994) Spectrum of lateral medullary syndrome. Correlation between clinical findings and magnetic resonance imaging in 33 subjects. *Stroke* 25(7):1405-10.
 Kohn, DF and MacKenzie WF (1980). Inner ear disease characterized by rolling in C3H mice. *JAVMA* 177(9): 815-7.
 Olson LD and Ediger RD (1972). Histopathologic study of the heads of circling mice infected with *Pseudomonas aeruginosa*. *Lab Anim Sci* 22(4): 522-7.

Introduction

The vestibular system provides sensory input about body position and movement. Sensory receptors are located in the inner ear and consist of specialized hair cells that detect movement and head position. Circular motion is detected by cells in the crista ampullaris of the semicircular canals, while linear motion and head position are detected by hair cells associated with calcium carbonate crystals called otoconia in the utricle and saccule. Afferent projections from the hair cells synapse on neurons in the vestibular nuclei of the brainstem or the uvula or nodulus of the cerebellum. Lesions in any of these components can cause vestibular syndrome, which in mice is characterized by head tilt, rolling, spinning and inability to eat, drink and/or groom normally. Otitis media, arteritis and CNS lesions have been reported to cause vestibular syndrome in mice.

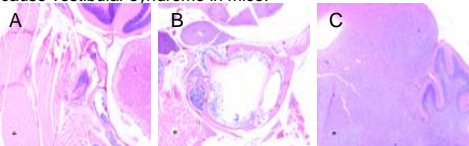


Figure 1. Some causes of vestibular syndrome in mice. A. Carotid arteritis. B. Otitis media. C. CNS tumor (astrocytoma).

Objective

To investigate the cause of vestibular syndrome in seven Swiss mice with no evidence of otitis, CNS neoplasia or vasculitis.

Acknowledgments

Thanks to Bruce Baldwin and Pat Wilcox for necropsy and histology support.
 This work funded by NIH Training Grant RR7002.