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Otopathology in Idiopathic Dandy's Syndrome

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Abstract

Background—Dandy's Syndrome, or bilateral vestibular hypofunction and oscillopsia, may cause chronic disequilibrium aggravated by head movement or in the presence of reduced light. It may be secondary to ototoxicity, central nervous system tumors, Meniere's Syndrome, infections or trauma, or may be idiopathic.

Objective—To describe the temporal bone histopathology in one individual with Idiopathic Dandy's Syndrome.

Material and Methods—Temporal bones from 1 individual were removed at autopsy and studied using light and Nomarski microscopy.

Results—In this case, the otopathology demonstrated vestibular atelectasis of the membranous labyrinth of the superior, lateral and posterior semicircular canals, but not the utricle or saccule bilaterally. The findings also included mild hair cell loss in the cristae of all semicircular canals and of the utricular and saccular maculae, and severely reduced neuronal count in Scarpa's ganglion bilaterally. There was also a scattered loss of inner and outer hair cells throughout the cochlea and moderate-to-severe loss of cochlear neurons bilaterally.

Conclusion—We have reported the histopathologic findings in a case of idiopathic Dandy's syndrome. Both temporal bones showed vestibular atelectasis of all three semicircular canals, preservation of normal saccule and utricle, and severe reduction of the neuronal population in Scarpa's ganglion bilaterally. Both ears also showed substantial degeneration of the spiral ganglion of the cochleas. Severe Scarpa's ganglion degeneration was also noted in the only other case of idiopathic Dandy's Syndrome in the literature. However, that other case had no evidence of vestibular atelectasis and had normal hearing.

Introduction

In 1941, Walter E. Dandy described a symptom complex following bilateral surgical division of the vestibular nerves for Meniere's Syndrome¹, including visual jumbling of objects occurring when the patient is in motion that disappears when at rest, and disequilibrium when walking in the dark. Both of these symptoms occurred after surgery, with subsequent gradual lessening in severity. This symptom complex of oscillopsia and/or problems while walking in the dark, now known as Dandy's Syndrome, is due to bilateral vestibular hypofunction (BVH). Ototoxicity, tumors, Meniere's syndrome, infections, and trauma have been identified as the most common causes of BVH in various studies¹⁻³. However, many cases are idiopathic.

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Only one paper has previously presented the histopathologic findings in Dandy's syndrome and of the five cases described therein, only one was idiopathic². The purpose of this study was to describe the histopathology of another patient with idiopathic Dandy's syndrome.

History

This patient first developed balance problems at the age of 59 years, which persisted throughout his subsequent life. There was a constant sense of unsteadiness aggravated by motion. He developed oscillopsia when the pavement on which he was driving or walking was uneven, which in turn caused difficulty focusing in the distance. He had difficulty in turning or during rapid motion. There was no history of oral or parenteral exposure to ototoxic substances. Medical history included a myocardial infarction at age 54 and subsequent double coronary artery bypass grafts.

Audiometry at age 60 showed bilateral high-frequency sensorineural hearing loss with normal speech discrimination in both ears. Serial audiometry at ages 61 and 62 showed no change. Auditory brainstem response (ABR) testing was normal. No hearing test was performed in the last 22 years of his life. Vestibular testing was done at age 60 and 68 and showed bilaterally absent responses to all caloric stimulation, absence of the vestibular ocular reflex (VOR) below 0.5 Hz on sinusoidal vertical axis rotation, borderline visual-vestibular ocular reflex (VVOR) gain, and absent postural stability on dynamic posturography with sway-referenced visual surround or eyes closed.

His work-up included a temporal bone CT scan, FTA-ABS, VDRL, TSH, T4, EEG, which were all normal. Brain magnetic resonance imaging (MRI) at age 60 showed multiple areas of increased signal in periventricular white matter in the centrum semiovale bilaterally. There was also suggestion of a possible small area of very mild increased signal in the mid to upper pons just to the left of midline. These findings were all non-specific in nature and consistent with microangiopathic degeneration or focal demyelination. There was mild increase in prominence of cortical sulci. There were no atrophic changes seen in the cerebellum.

The patient was found dead at home at the age of 84. Formalin was injected into the middle ears one day after death, and the temporal bones were removed 45 hours after death.

Material and Methods

The temporal bones were removed at autopsy and processed for light microscopy in the standard manner, including fixation using 10% neutral buffered formalin, decalcification using ethylenediaminetetraacetic acid, embedment in celloidin, serial sectioning in the axial plane at a thickness of 20 microns and hematoxylin and eosin staining of every tenth section⁴. All stained sections were examined by light microscopy. Graphic reconstruction of the cochlea was performed according to the method described by Schuknecht⁴ to determine loss of the neurosensory elements including hair cells, stria vascularis and cochlear neurons. Cochlear neuronal cell counts were compared with normative data reported by Schuknecht⁴. Count of vestibular neurons (Scarpa's Ganglion) was also done, using the method described by Richter⁵ and compared with normative data reported by Velasquez⁶. Evaluation of the vestibular hair cell in cristae and maculae was done using Nomarski interference contrast microscopy at 1000x magnification⁷.

Histopathologic findings

The histopathology was similar on both sides and hence is described together. The external auditory canals, tympanic membrane and ossicles were unremarkable. The mastoid was well

pneumatized. The labyrinth was fully developed. The facial nerve was normal. The trigeminal nerve was not present in these specimens. The cochleas contained 2 1/2 turns. The organ of Corti consisted of a mound of cells without hair cells in the descending part of the basal turn. There was also scattered loss of OHC and IHC throughout the cochlea. Pillar cells were preserved in all turns. There was mild patchy atrophy of the stria vascularis in all turns. There was no endolymphatic hydrops. The tectorial membrane was unremarkable in all turns. Cochlear neurons showed moderate-to-severe atrophy compared to age matched controls (see figure 1a,b).

There was partial collapse of the walls of all three ampullae but not of the saccule or utricle, bilaterally (fig.2a,b,c). In the areas of collapse there was cellular bridging at sites of infolding of the walls of the membranous labyrinth as well as mesothelial proliferation over the membranous labyrinth of the lateral semicircular canal (fig.3) and entrapment of inorganic debris in sequestered spaces associated with deformation (fig.4). Using Nomarski microscopy, the supporting cells appeared normal and there was slight loss of vestibular hair cells in the sensory epithelium of the cristae of all semicircular canals and of the utricular macula (fig.5). The epithelium of the saccular macula was unremarkable. There was severe degeneration of Scarpa's ganglion bilaterally. The neuronal count was 7065 on the right side and 8540 on the left side, compared to the expected count for this age of approximately 18,500 (fig.6).

Discussion

In this case, there was bilateral partial collapse of the three ampullae associated with cellular bridging at sites of infolding of the walls of the membranous labyrinth of the lateral semicircular canal. There was also entrapment of inorganic deposits in sequestered spaces of the membranous wall of the semicircular canals and proliferation of the mesothelial cell layer bilaterally. Additionally, there was mild hair cell loss in cristae of all semicircular canals and of the utricular macula, but not in the saccular macula. The total neuronal count was severely decreased in Scarpa's ganglion bilaterally.

This case demonstrated similar findings to that found in vestibular atelectasis described by Merchant et al⁸, which was characterized by the presence of collapse of the membranous labyrinth. They proposed a set of histologic criteria to differentiate pathologic from artifactual collapse. Collapse was considered pathologic if one or more of the following primary histologic findings were present: 1) cellular bridging at sites of infolding of the walls, 2) loss of hair cells and distortion of the neurosensory epithelium in areas where the atelectatic wall was in contact with the epithelium, and 3) entrapment of inorganic deposits in sequestered spaces associated with deformation. Confirmative findings included involvement of at least two ampullae, collapse that was partial-to-total in extent, proliferation of the mesothelial cell layer, and areas of atrophy of the walls. All these criteria were met in the present case.

The preservation of the anatomic features of the membranous labyrinth, including the inherent rigidity of the walls themselves and the protective influence of the utriculoendolymphatic valve in maintaining the volume of endolymph, is fundamental for the normal motion mechanics of the vestibular sense organs⁸. However, both theoretically and based on reports of ENG in vestibular atelectasis⁸, that condition does not cause vestibular hypofunction of the severity we observe in this case of Dandy's Syndrome.

The only previous description of histopathologic findings in idiopathic Dandy's syndrome, by Belal², also showed severe bilateral atrophy of both divisions of the vestibular nerve, including Scarpa's ganglia, as seen in this case. While the vestibular atelectasis seen in our

case would be predicted to cause or contribute to peripheral vestibular hypofunction, the dramatically reduced population of primary vestibular afferent neurons in Scarpa's ganglion bilaterally is the likely explanation for the patient's BVH and oscillopsia. Oscillopsia, the visual disturbance characterized by objects in the visual field appearing to move, is a disabling symptom that can arise from a number of causes, including damage or dysfunction of the oculomotor fixation system, the visuovestibular stabilizing system of the VOR, or the neural integrator of central visuovestibular processing⁹. This symptom is the *sine qua non* of bilateral peripheral vestibular loss and is seen most often as a consequence of ototoxic medications, such as aminoglycosides. Only a detailed and thorough history and physical exam might identify a specific cause of the symptom.

Bilateral vestibular hypofunction can also be observed in patients with cerebellar ataxia, neuropathy, and vestibular areflexia syndrome (CANVAS). Temporal bone histopathology in one case of CANVAS also showed severe loss of vestibular ganglion cells as observed in this case, but also showed atrophy of the facial nerve, particularly affecting the geniculate ganglia, and atrophy of the trigeminal ganglion. In the single reported case of CANVAS the organ of Corti and spiral ganglion was normal for age¹⁰. In the present case, the geniculate ganglion was normal and the trigeminal nerve was not present. Furthermore, cerebellar atrophy, detected by MRI is seen in most cases, but was not found in the present case.

In our case there was severe spiral ganglion cell loss bilaterally, a finding that should have significant associated hearing loss. However, the last audiogram in the case record was obtained 22 years before death and exhibited only mild hearing loss on both sides. The relationship between spiral ganglion cell degeneration and Scarpa's ganglion cell degeneration in the present case is unknown. Interestingly, the idiopathic Dandy's syndrome case reported previously by Belal² had normal hearing.

In conclusion, we have reported the histopathologic findings in a case of Idiopathic Dandy's Syndrome. Both temporal bones showed vestibular atelectasis of all three semicircular canals, preservation of normal saccule and utricle, and severe reduction of the neuronal population in Scarpa's ganglion bilaterally. Both ears also showed substantial degeneration of the spiral ganglion. Severe Scarpa's ganglion degeneration was also noted in the only other case of idiopathic Dandy's syndrome in the literature.² However, that other case had no evidence of vestibular atelectasis and had normal hearing. Clearly, more cases of idiopathic BVH must be acquired and studied to draw any conclusions concerning the range and variability of inner ear and VIIIth nerve pathology.

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Fig.1.

Audiocytocochleograms of the right (A) and left ears (B) of the individual in this report at age 62. Graphic reconstruction of the cochlea was done in each ear according to the method described by Schuknecht.⁷ Black filling represents missing or abnormal elements. Vertical axes of cytocochleogram boxes for the stria and neurons show percentage of loss. IHC = Inner Hair Cell; OHC = Outer Hair Cell.

Fig. 2.
Photomicrographs of the membranous labyrinth of the superior, lateral, and posterior semicircular canals in the right ear (A, B, C), respectively.

Fig. 3.
Photomicrograph of the superior semicircular canal in the leftside.

Fig. 4.
Photomicrograph of the posterior semicircular canal in the left side.

Fig. 5.
High power view of the vestibular neuroepithelium of the right lateral semicircular canal.
There was a mild loss of hair cells (case), compared to the control. (Nomarski 1000X)

Fig. 6.
Photomicrograph of Scarpa's ganglion on the right side. Inset shows the severe degeneration of neuronal cells.