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Review

Idiopathic bilateral vestibulopathy: an autoimmune disease?

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ABSTRACT

Bilateral vestibulopathy (BV) is the loss of function of both peripheral labyrinths or of the eighth nerves. Its etiology remains obscure in approximately 20% to 50% of cases (so-called idiopathic bilateral vestibulopathy, IBV). Alternatively, the cause could be viral or vascular; to date, causative gene mutations have not been identified.

Other potential disease mechanisms include autoimmune disorders. Antibodies have been detected against inner ear tissue (primarily against vestibular membranous labyrinth). The data suggest that the bulk of anti-labyrinthine autoantibodies may be an epiphenomenon, but a small subgroup of organ-specific autoantibodies may synergize with a cellular response to develop vestibular lesions.

The two key symptoms of BV are the following: 1. *unsteadiness of gait*, particularly in the dark or on uneven ground, and 2. *oscillopsia* associated with head movements. *Episodes of vertigo* are reported by patients with IBV, particularly early in the development of vestibular loss. Associated *hearing loss* seldom occurs in the idiopathic type of this condition. Post-mortem examinations revealed a remarkably selective loss of vestibular hair cells in the vestibular end organs but normal hair cells in the cochlea.

The diagnosis is made with a simple bedside test for defective vestibular function. The diagnosis can be confirmed by bithermal caloric testing and pendular body rotation. The therapy is based on steroid treatment, and the early initiation of immunosuppression appears to be essential for therapeutic success.

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1. Introduction

Bilateral vestibulopathy (BV) is the impairment or loss of function of both peripheral labyrinths or of the eighth nerves. This entity was first described by Dandy [1] in patients who had undergone bilateral vestibular neurectomies.

BV is rare among vestibular disorders [2,3]. In the largest cohort of patients studied, Zingler and colleagues [4] identified 255 patients with BV. Despite comprehensive investigations, the etiology of BV remains obscure in approximately 20% to 50% of cases (so-called idiopathic bilateral vestibulopathy, IBV). This frequently undetected condition is of clinical relevance not only for neurologists and otolaryngologists but also for immunologists, internists and other specialists.

2. Cause of bilateral vestibulopathy

Twenty to fifty percent of cases of bilateral vestibular failure are idiopathic [5]. The definite or probable cause of BV was determined in approximately 50% of the cohort in a study by Zingler and colleagues [4] ($n = 255$). This finding confirms that presented in a review of 52 BV patients by Vibert and colleagues [6], but contradicts that of the study by Rinne and co-workers [5], who reported that the probable cause of BV could be not determined in approximately 20% of all patients ($n = 53$). BVF is one of the rare causes of vertigo but also one with the most varied etiologies.

Ototoxic BV caused by antibiotic treatment with gentamycin alone or in combination with other ototoxic agents (e.g. diuretics) was the most frequent cause in Zingler's study [4] and other previous studies [7,8]. Streptomycin and gentamicin are known to affect peripheral vestibular sensory cells before those in the cochlea (hair cell damage of the inner ear). Zingler found Meniere's disease to be the second-most and meningoencephalitis the third-most frequent cause. Bilateral Meniere's disease may also cause BVF, and some authors stress the link between bilateral Meniere's disease and immune-mediated mechanisms [9,10]. Post-meningitic BV has been attributed mainly to bacterial agents, although viral agents have also been implicated [11,12].

Cerebellar degeneration and Friedreich's ataxia can also cause BV. Another inflammatory disorder that may also cause BV and has so far been presumably underestimated is *Creutzfeldt*–Jakob-Disease (CJD). An association of BV with this prion disease has not yet been described but is known for bovine spongiform encephalopathy [13]. The neoplastic causes of BV are bilateral acoustic neuromas in neurofibromatosis, meningeal metastasis, and infiltration of the skull base. BV was associated with cranial or peripheral neuropathies, such as vitamin B_{12} deficiency, alcohol [14], hereditary sensory and autonomic neuropathy type IV (HSAN IV) [15], and nutritional (beriberi) neuropathy [16]. Bilateral sequential vestibular neuritis [17–19] accounts for an unknown percentage of BV.

Systemic autoimmune disorders [20] are among the many causes of BV. Systemic autoimmune diseases were recently reported to coexist in 15% to 30% of patients with autoimmune inner ear diseases [21]. Auditory and vestibular disorders in autoimmune disease have been observed previously [9,22–25]. The audio-vestibular symptoms either heralded the onset of the autoimmune disease or appeared later once the diagnosis of autoimmune disease was established. Isolated bilateral auditory and vestibular failure has been reported as a presenting feature of Cogan's syndrome [26–28], polyarteritis nodosa [29] and antiphospholipid syndrome [30].

Auditory and vestibular failure has also been reported for Behcet's disease [31], systemic lupus erythematosus, rheumatoid arthritis, Wegener's granulomatosis, Harada syndrome [32], and Susac syndrome [33,34]. The other causes (Table 1) were similar to those reported in previous reviews [5,6].

3. Epidemiology

The mean age of the IBV patients varied from 38 years [6] to 57 years [35], with a range of 20 to 84 years. However, the mean age at which the diagnosis is established is near 60 years [4], as reported in previous studies [35,36]. Zingler found a preponderance of male patients, with a male/female ratio of 3:2 [4].

4. Etiopathogenesis

As an alternative to the immunologic cause, a viral or vascular cause has been hypothesized. Based on temporal bone studies, Schuknecht and Kitamura [37] have demonstrated that vestibular nerve and end organ damage, similar to that observed in viral disorders, is found in patients with so-called vestibular neuritis and that sequential bilateral vestibular neuritis could give rise to BV [18].

In the past, several suggestions have been made about possible causes, such as recurrent vestibular neuritis caused by acute or prior viral infection. A recent long-term follow-up of 103 patients with definite vestibular neuritis over a mean duration of almost 10 years did not support a viral cause of IBV because the study reported only two recurrences in the contralateral ear, neither of which caused BV [38]. Arterial obstruction to the labyrinth has been shown to give rise to isolated vestibular changes in animals [39]. Thus, vascular factors may be relevant in some cases of IBV [40].

Despite the enormous progress in dissecting the genetic basis of deafness, gene mutations that lead to bilateral vestibulopathy in humans have not yet been identified. Though a similar broad spectrum of genes may be involved in idiopathic bilateral vestibulopathy, little progress has been made in this area [41]. Other potential disease mechanisms or risk factors discussed include autoimmune disorders.

Table 1
Patients with a bilateral vestibulopathy of definite or probable cause ($n = 125$; 49% of total).

Cause of bilateral vestibulopathy	Definite cause		Probable cause		Σ	
	n	%[a]	*n*	%[a]	*n*	%[a]
Antibiotics	27	11	5	2	32	13
Meniere's disease	4	2	13	5	17	7
Miningitidis/encephalitis/cerebellitis	12	5	1	0	13	5
Two different causes	1	0	11	4	12	5
Spinocerebellar ataxia type 3 and 6/episodic ataxia type II/multiple system atrophy	0	0	9	4	9	4
Systemic autoimmune disease	2	1	6	3	8	3
Deficit of vitamin B_{12}/folic acid	3	1	1	0	4	2
Creutzfeldt–Javob disease	3	1	0	0	3	1
Cogan's syndrome	3	1	0	0	3	1
Positive family history for inner ear diseases	0	0	3	1	3	1
Miscellaneous	7	3	14	5	21	8

From: Zingler et al. [4].
[a] Frequency of each cause is given as percentage of all included patients (N = 255); some of the percentages have been rounded up, others rounded down.