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Review Article

The Molecular Biology of Vestibular Schwannomas and Its Association with Hearing Loss: A Review

Erika Celis-Aguilar,[1] Luis Lassaletta,[2] Miguel Torres-Martín,[3] F. Yuri Rodrigues,[4] Manuel Nistal,[4] Javier S. Castresana,[5] Javier Gavilan,[2] and Juan A. Rey[4]

[1] *Instituto Nacional de Neurología y Neurocirugía Manuel Velasco Suarez, 14269 Ciudad de México, DF, Mexico*
[2] *Department of Otolaryngology, "La Paz" University Hospital, 28046 Madrid, Spain*
[3] *Unidad de Investigación, Laboratorio Oncogenetica Molecular, "La Paz" University Hospital, 28046 Madrid, Spain*
[4] *Department of Pathology, "La Paz" University Hospital, 28046 Madrid, Spain*
[5] *Brain Tumor Biology Unit, CIFA, University of Navarra School of Sciences, 31009 Pamplona, Spain*

Correspondence should be addressed to Luis Lassaletta, luikilassa@yahoo.com

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Hearing loss is the most common symptom in patients with vestibular schwannoma (VS). In the past, compressive mechanisms caused by the tumoral mass and its growth have been regarded as the most likely causes of the hearing loss associated with VS. Interestingly, new evidence proposes molecular mechanisms as an explanation for such hearing loss. Among the molecular mechanisms proposed are methylation of TP73, negative expression of cyclin D1, expression of B7-H1, increased expression of the platelet-derived growth factor A, underexpression of PEX5L, RAD54B, and PSMAL, and overexpression of CEA. Many molecular mechanisms are involved in vestibular schwannoma development; we review some of these mechanisms with special emphasis on hearing loss associated with vestibular schwannoma.

1. Introduction

Vestibular schwannomas (VSs) can be classified into two broad groups: unilateral sporadic vestibular schwannoma and those associated with neurofibromatosis type 2 (NF2). VSs constitute 8% of all benign intracranial tumors, and sporadic unilateral schwannomas represent up to 95% of all VSs [1]. As new population-based studies are performed, the true incidence of VS appears to be higher than expected [2–5]. A nationwide study performed in Denmark [2] revealed that the incidence of VS had been rising from 5 cases per million population per year in 1977–1981 to 10 cases in 1992–1995. In 2004, the same research group estimated an incidence of 11.5 cases per million inhabitants per year during a 25-year period (1976–2001) [3]. Data from a US national tumor registry (2010) reported a VS incidence rate of 1.1 cases per 100,000 people per year [4]. On the other hand, Evans et al. found an incidence of 1 case in 80,000 individuals for sporadic VS, and 1 in 70,000 if NF2-related tumors were included [5]. These increasing numbers are probably due to the effect of newer and more sensitive diagnostic tests, especially magnetic resonance imaging (MRI). The age of presentation of VS is usually the fourth and fifth decades. Even though a benign tumor, if large enough, can cause neurological symptoms like hydrocephalus, brainstem compression, herniation, and ultimately death.

NF2 is an autosomal dominant disease representing 5% of all VSs. Patients with NF2 are characterized by having bilateral vestibular schwannomas. Half of these patients do not have a family history of the disease [1] and therefore represent new germline mutations. The Manchester criteria for the diagnosis of NF2 have been described elsewhere [6, 7]. These patients can also present other intracranial benign tumors. There are three types of NF2, distinguished according to clinical presentation and severity: Wishart type, Gardner type, and mosaic NF2. The Wishart type appears in childhood or late adolescence and consists of bilateral vestibular schwannomas associated with spinal tumors. The