13 The Ear and Antiphospholipid Syndrome

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Introduction

Evidence now exists that inner-ear pathology is frequently associated with immune dysfunction, including the presence of anticardiolipin antibodies (aCL) in the sera of these patients.

The pathogenesis of sensorineural hearing loss (SNHL) is still considered idiopathic, in most cases. Sudden deafness, severe hearing loss of acute onset, is usually unilateral but may also occur bilaterally as well. Patients with progressive SNHL, develop bilateral progressive hearing loss over the course of a few days to 1–2 months, although as many as 20% initially present a unilateral loss. Both disabilities occur in previously healthy subjects, with an equal preponderance among males and females.

In addition to auditory symptoms, these patients may also present vestibular complaints, such as true vertigo, lightheadedness, or ataxia. Tinnitus and aural pressure are also frequent symptoms, and may occur in one half and one third of all patients, respectively.

The potential role of autoimmunity in the pathogenesis of hearing loss was first reported by McCabe in 1979 [1], who described a pattern of bilateral SNHL characterized by rapid progression over days to months. This was based on the finding of a positive lymphocyte migration inhibition assay to cochlear antigens and the steroid responsiveness of the hearing loss in such patients. Additional support includes the following: both cellular and humoral elements of the immune system can normally be identified in inner-ear tissue; animal models demonstrate inner-ear damage after immunization with inner-ear tissue extracts; and such an injury is transferable with sensitized T cells; human SNHL can occur in the context of systemic immunological disease; and SNHL can be treated by immunosuppressive therapy [2–5]. However, the definite proof of an autoimmune etiology is still lacking because in most studies the exact nature of the immunizing antigenic epitope(s) has not yet been identified.

The Association of SNHL with Autoimmune Disease

During the last decade many reports described the association of SNHL with various autoimmune disorders such as: systemic lupus erythematosus (SLE), Sjögren syndrome, chronic ulcerative colitis, rheumatoid arthritis, polyarthritis

nodosa, polymyositis, Hashimoto's thyroiditis, and Cogan's syndrome [6–9]. The beneficial effect of immunosuppressive therapy observed in some of these patients supports the immune-mediated etiology. It was stressed that immediate treatment with corticosteroids or other immunosuppressive agents is essential because delay may lead to irreversible hearing loss [10]. The benefit of plasmapheresis in patients with suspected immune-mediated hearing loss was evaluated: improved hearing was observed in 8/16 (50%) patients and only 25% of the patients required additional immunosuppressive maintenance therapy [11]. In 1986, Bowman et al [12], prospectively tested the hearing status of 30 patients hospitalized during SLE flares and observed an 8% incidence of substantial, previously undetected hearing loss. In the same year, Caldarelli et al [13] reported profound SNHL of the right ear in a 51-year-old woman, followed 3 weeks later by a similar finding in her left ear. This was concomitant with symptoms of her newly diagnosed SLE. In 1992, Kobayashi et al [14], described bilateral SNHL in a 32-year-old woman that improved dramatically after plasmapheresis, 2 years before the diagnosis of SLE was established. They suggested that circulating immune complexes or antiphospholipid antibodies (aPL) might play a pathological role in the hearing impairment in SLE patients. In 1995, Kataoka et al [15] documented another case of intermittent bilateral SNHL in conjunction with SLE.

In the same year, Andonopoulos et al [16] reported an association between SNHL and SLE, without correlation to SLE disease activity, concluding that factors other than inflammation may be involved in the pathogenesis of this disorder. Later, Sperling et al found that out of 84 SLE patients, 31% were reported to suffer from aural symptoms, such as tinnitus and hearing loss, suggesting that these findings are also related to the immune complex nature of the disease [17].

In yet another study, the symptoms of SNHL were observed in 38% of 37 unselected systemic sclerosis (SSc) patients, suggesting that SSc may be included among the autoimmune diseases which may cause audiovestibular disturbances [18]. The association between Behcet's disease and SNHL was also reported in 1 patient who had fluctuating hearing loss, tinnitus, and dizziness, proposing a causative relationship between autoimmune vasculitis and endolymphatic hydrops [19].

Animal Models for Immune-mediated SNHL

To aid in the investigation of SNHL, several animal models were introduced. In 1983, Yoo et al [20] immunized rats with native bovine type II collagen, a major structural element of the inner ear, and induced SNHL in these animals. Ruckenstein et al [21] proposed the MRL-lpr/lpr mouse strain as a potential model of autoimmune inner-ear pathology (a strain known to develop an SLE-like disease at the age of 4–5 months) in which the authors observed cochlear pathology in 6/11 animals of this age. Based on the above, Iwai et al [22] demonstrated in severe combined immunodeficient (SCID) mice, infused with MRL-lpr/lpr spleen cells, the induction of cochlear damage which normally would not have developed in such animals. In a recent study, Billings [23] described a mouse model of CD4+ T cell–mediated autoimmune SNHL induced by immunization with peptides from the inner ear–specific proteins cochlin and β-tectorin. However, it is not yet clear how accurately this model reflects events occurring in the spontaneous idiopathic disease.