J Neurol (2013) 260:663–664
DOI 10.1007/s00415-012-6755-4

LETTER TO THE EDITORS

Steroid-responsive hearing impairment in NMO-IgG/aquaporin-4-antibody-positive neuromyelitis optica

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Received: 17 September 2012 / Revised: 2 November 2012 / Accepted: 8 November 2012 / Published online: 21 November 2012

Dear Sirs,

In 2004, Lennon et al. [7, 9] discovered a novel, pathogenic serum autoantibody reactivity [termed neuromyelitis optica (NMO)-IgG]. Aquaporin-4 (AQP4), the target antigen of NMO-IgG, is expressed in the central nervous system (CNS) as well as in numerous other tissues outside the CNS. Over the last few years an expanding spectrum of clinical syndromes associated with NMO-IgG/AQP4-IgG has been described, which includes, in addition to optic neuritis and myelitis, intractable vomiting and hiccups, oculomotor dysfunction (internuclear ophthalmoplegia, abducens nerve palsy, nystagmus), dysphagia, symptomatic narcolepsy, hyperthermia, central endocrinopathies, central hypotension, posterior reversible encephalopathy, and, in particular in children, a wide range of encephalitic manifestations including seizures [6, 11].

High levels of AQP4 are also expressed in the inner ear and the cochlear nerve, and, accordingly, deafness is a typical and consistent result of AQP4 loss as shown in transgenic mice [10, 12, 15]. Here we report on a patient with NMO-IgG/AQP4-IgG-positive NMO and hearing loss. The 51-year-old man with a 2-year history of NMO was transferred to the neurology department because of acute left-sided hearing loss; serological testing revealed antibodies to AQP4 [3, 5]. A right-sided peripheral deafness due to a non-keratinizing type II nasopharyngeal carcinoma with infiltration of the tuba auditiva had been known for 15 years. The patient had been under treatment with mycophenolate-mofetil (1,500 mg/day) for 15 months. At the ENT department, a peripheral cause was ruled out by audiometry. Physical, imaging [cranial magnetic resonance imaging (MRI), abdominal and thoracic computed tomography], blood and cerebrospinal fluid (FACS, paraneoplastic autoantibodies, neurotropic viruses) examinations did not reveal any signs of infection or tumor. Assuming a clinical attack in the context of NMO, the patient was treated with prednisolone (100 mg/day), after which he significantly improved within 10 days. Steroids were reduced to a maintenance dose of 10 mg while continuing mycophenolate-mofetil. At follow-up 4 weeks later, the patient reported left-sided hearing to be normal. This was confirmed by audiometry.

AQP4 is expressed at high levels in the central part of the cochlear nerve as well as by supporting epithelial cells (Hensen's, Claudius, and inner sulcus cells) in the organ of Corti [10, 15]. In the organ of Corti, AQP4 may facilitate rapid osmotic-driven water fluxes in the sensory epithelial cells, which are subject to large K+ fluxes during mechano-electric signal transduction and thus contribute to the volume and ion-homeostasis at these sites [10]. It was shown that transgenic mice lacking AQP4 are regularly deaf, as demonstrated by auditory brain stem response measurement [10]. Presbycusis was shown to be characterized by a decrease in AQP4 expression in an animal model [2]. In patients with NMO, AQP4 loss has been demonstrated to occur early in lesion formation, to precede astrocyte loss and to be reversible in some lesions; [4, 13, 14]

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Table 1 Clinical, radiological and serological findings

April 2009	Left-sided, isolated ON; partial recovery following treatment with IVMP
August 2009	LETM (C1–5/6) and BSTE (asymptomatic lesion in the medulla oblongata); partial recovery following IVMP
November 2009	LETM (C2–3) and BSTE with hemiparesis (MRC grades 2–4) and INO; partial recovery following IVMP and IA
March 2011	Transient hearing loss; NMO-IgG/AQP4-Ab-positive (IHC, CBA, ELISA); treatment with IVMP; complete recovery, confirmed by audiometry
September 2012	Last follow-up, under treatment with MMF: no new signs or symptoms since last visit; EDSS 5.0

BSTE brain stem encephalitis, *CBA* cell-based assay, *EDSS* expanded disability status scale, *ELISA* enzyme linked immunosorbent assay, *IA* immunoadsorption, *IHC* immunohistochemistry, *INO* internuclear ophthalmoplegia, *IVMP* intravenous methylprednisolone, *LETM* longitudinally extensive transverse myelitis, *MMF* mycophenolate mofetil, *ON* optic neuritis

accordingly, complete recovery was observed in 17 % of myelitis and 32 % of ON attacks in a recent study, mostly following steroid treatment [6]. It is therefore conceivable that AQP4-IgG might have caused reversible damage to the cochlear nerve or inner ear in our patient, all the more as other known causes of acute hearing loss were excluded. Alternatively, brain stem lesions affecting the central auditory system may have been causative in our patient; however, MRI was normal, though MRI and clinical signs of brain stem encephalitis had been noted during previous attacks (Table 1). Only one previous case of deafness in a patient with NMO has been reported in the literature; [1] however, that patient had systemic lupus erythematosus (SLE), a condition in which acute hearing impairment has been previously described [8], and NMO was not yet present at onset of the hearing impairment [1]. By contrast, no evidence for a connective tissue disorder was present in our patient. Taking into account the present report as well as the existing data suggesting a role of AQP4 in hearing, studies on the prevalence of hearing impairment in AQP4-IgG-positive patients are warranted.

Acknowledgments The work of S.J. was supported by a Fellowship from the European Committee for Treatment and Research in MS (ECTRIMS). The work of B.W. and S.J. was supported by research grants from Bayer Healthcare and from Merck Serono.

Conflicts of interest The authors declare that they have no conflict of interest.

Ethical standard For this case study, ethical standards were followed in conducting all diagnostic and therapeutic procedures.

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