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Bilateral sudden sensorineural hearing loss caused by Charcot-Marie-Tooth disease

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Abstract

Charcot-Marie-Tooth (CMT) disease or hereditary motor and sensory neuropathy (HMSN) is a relatively common neurological syndrome, which has seldom been associated with hearing dysfunction, particularly sudden sensorineural hearing loss (SNHL). Families with autosomal dominant, autosomal recessive and X-linked forms of inheritance have been described.

Sudden sensorineural hearing loss is a frustrating and frightening condition, especially if the hearing loss is bilateral. Regarding the site of the lesion, the evidence from the literature on HMSN suggests that either the VIIIth nerve or central auditory pathways are primarily involved in patients with hearing loss.

We report the first case in the English literature of a patient with Charcot-Marie-Tooth type II disease presenting bilateral SNHL in the course of his disease. The patient was hospitalized for 15 days, and undergoing treatment without any audiological improvement. Detailed clinical, audiological and laboratory examination was performed.

The aetiology and prognostic indicators of bilateral SNHL are discussed, as well as, the incidence of hearing loss in CMT patients.

Key words: Charcot-Marie-Tooth disease; Hearing Loss, Sensorineural

Introduction

Charcot-Marie-Tooth (CMT) disease, or hereditary motor and sensory neuropathy (HMSN) or peroneal muscular atrophy is a relatively common neurological syndrome, which has seldom been associated with hearing dysfunction. A chronic degenerative process of peripheral nerves and roots occurs, resulting in distal muscle atrophy of the small muscles of the hands and feet.[1] A combination of pes cavus with extreme atrophy of the anterior tibial and calf muscles and wasting of the lower thigh musculature can be observed. Deep-tendon reflexes are usually diminished to absent. The onset may occur during late childhood or adolescence, may become progressive and severe or may spontaneously arrest at any time.[2] Various conditions have been reported in association with CMT, including Friedreich's ataxia, myopathy, a combination of nephritis and sensorineural hearing loss and optic atrophy. Features of hereditary cerebellar ataxias, optic atrophy, and other cranial nerve involvement may occur in combination with the previously mentioned classic description.

Two major clinical phenotypes have been recognized: in HMSN type 1, motor nerve conduction velocity is delayed and myelin degeneration occurs; in type II, motor nerve conduction velocity is slightly reduced and axonal degeneration is a constant feature. Sensorineural hearing loss has been described as a rare occurrence in both forms.[3]

Sudden sensorineural hearing loss is a frustrating and frightening condition, especially if the hearing loss is bilateral. A universally accepted definition of SNHL does not exist. A useful definition of SNHL is a loss greater than 30 dB in three contiguous frequencies that occurs in less than three days.[4] Most SNHL, however, occur within minutes to several hours. The estimated incidence per year of SNHL ranges from five to 20 per 100 000.[5] The incidence of bilateral SNHL ranges from 0.44 per cent to 2.78 per cent of patients with SNHL.[6,7]

We report the first case in the English literature of a patient with Charcot-Marie-Tooth type II disease presenting with bilateral SNHL in the course of his disease.

Case report

A 52-year-old male, with a known history of Charcot-Marie-Tooth type II disease, was admitted due to bilateral hearing loss of sudden onset two days prior to his admission.

There was no established history of CMT disease in the family. The patient lost his mother in childhood and his sisters did not develop any abnormalities. As a child he developed pes cavus and in adult life developed wasting and weakness of the distal limb muscles, with later involvement of proximal muscles, becoming chair bound at the age of 40. The patient had no history of hearing difficulties and an audiogram 10 months prior to admission revealed a symmetrical mild hearing loss.

On neurological examination stance and gate were impossible. There was mild upper and severe lower limb weakness both distally and proximally; marked muscle wasting in the forearms, hands and lower limbs with absence of deep tendon reflexes. He had sensory loss with stocking-glove distribution. Apart from the hearing loss

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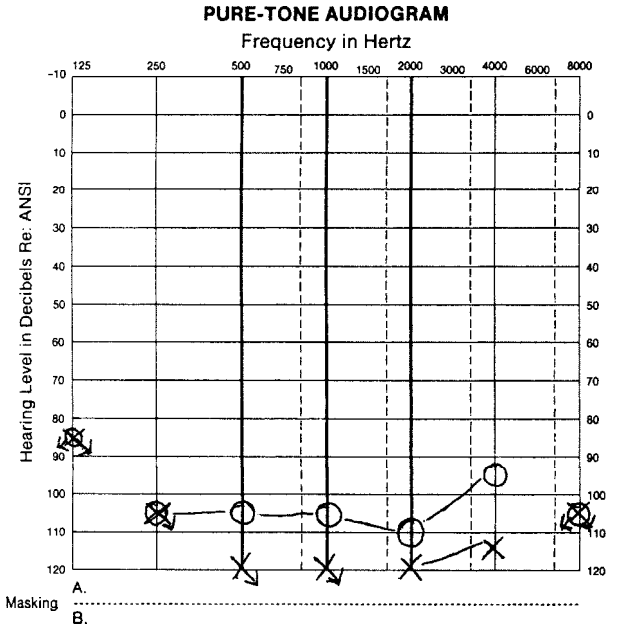

FIG. 1
Audiogram of the patient.

there was no evidence of cranial nerve involvement. Electrophysiological studies were consistent with a demyelinating neuropathy and the electrophysiological diagnosis was sensorimotor axonal polyneuropathy consistent with Charcot-Marie-Tooth (HMSN) type II.

Clinical examination showed no abnormalities and laboratory tests were within normal limits. Detailed clinical and laboratory workups excluded other possible causes for the patient's sudden sensorineural hearing loss (Table I). Standard virological tests for cytomegalovirus (CMV), hepatitis A, B, C, EB, human immunodeficiency virus (HIV) 1 and 2, fluorescent treponemal antibody absorption test, (FTA-ABS), *Treponema pallidum* haemagglutination assay (TPHA) did not reveal any recent viral infection. Posteroanterior and lateral chest X-rays, high resolution computed tomography (CT) and magnetic resonance imaging (MRI) of the head revealed no pathology and a lumbar puncture did not reveal any abnormalities.

The audiological evaluation in daily (serial) audiograms confirmed profound bilateral sensorineural hearing loss (Figure 1). Tympanograms of both ears were normal (type A). No ipsilateral or contralateral stapedial reflexes were elicited. Electronystagmography performed was within normal limits. Monaural and binaural brainstem auditory evoked potentials (BAEP) recordings were obtained using a 0.1 ms click, and no responses were detected for either ear at any of the intensity levels (up to 100 dB nHL) or repetition rates tested. The cochlear® promontory test was performed, showing wide dynamic ranges (threshold to maximum acceptable loudness – MAL) in all the frequencies tested bilaterally, as well as normal tone decay tests for both ears (Table II).

The patient was hospitalized for 15 days undergoing treatment with steroids and betahistine without any audiological improvement. He was re-evaluated after one, two and three months without any improvement of his hearing acuity.

Discussion

Many of the specific causes of bilateral SNHL that have been described encompass a broad spectrum of syndromes and diseases.[8,9] However, like unilateral SNHL, the cause of bilateral SNHL usually remains unknown. Several possible mechanisms for SNHL have been suggested, including viral infection, vascular impairment, labyrinthine membrane rupture or autoimmune mediation.[5,8] Favourable prognostic factors are absence of vertigo, the up-sloping shape of the audiogram and early treatment (within one month). Unfavourable factors are severe vertigo, the down-sloping shape of the audiogram late treatment and diabetes.[9,10]

TABLE I
LABORATORY TESTS PERFORMED IN THE PATIENT

WBC	6400/μL (72% Ne, 18% Ly)	PT	12.8 sec (control (12.3)
RBC	5.17 * 10^6/μL	APTT	32.4 sec
HCT	44.4%	INR	1.07
HGB	14.8 g/dl	Na	144 mEq/L
RBC sedimentation rate	8 mm/1sth	K	4.5 mEq/L
SGOT/AST	15 IU/L	P	3.6 mEq/dL
SGPT/ALT	8 IU/L	Ca	9.5 mg/dL
G-GT	12 IU/L	Mg	1.5 mEq/L
LDH	170 IU/L	Cholesterol	187 mg/dl
ALP	53 IU/L	Triglycerides	65 mg/dl
CRP	0.34 mg/dl	Uric acid	4.5 mg/dl
RF	9.81 IU/ml	Glu	93 mg/dl
ANA	1:80 negative	Ur	34 mg/dl
anti-DNA	1:120 negative	Cr	0.7 mg/dl
anti-centromere antibodies (AMAs)	1:80 negative		

TABLE II
COCHLEAR PROMONTORY TEST

	Frequency	50 Hz	100 Hz	200 Hz	400 Hz	800 Hz	1600 Hz
Right ear	Threshold (μA)	13	19	42	53	61	78
	MAL (μA)	68	85	92	108	140	192
Left ear	Threshold (μA)	21	39	55	68	82	97
	MAL (μA)	80	91	102	120	169	198

MAL: maximum acceptable loudness

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It is uncertain what proportion of CMT patients have auditory abnormalities. The only study in which a large number of patients was examined is by Harding and Thomas,[3] who reported that one out of 173 patients with HMSN-I and three out of 55 patients with HMSN-II complained of hearing loss. No audiometric assessment was undertaken in any of those patients. CMT disease as a possible causative factor for SNHL unilateral or bilateral has not yet been reported in the English literature.

Families with autosomal dominant, autosomal recessive and X-linked forms of inheritance have been described. The dominant form of X-linked CMT is caused by a mutation in the connexin 32 gene (C×32), mapped to the Xq13 locus.[11] Mutations in the early growth response two gene (EGR2) have been demonstrated in a very few cases of CMT type 1.[12]

Several reports have already pointed out the association between deafness and sensorimotor neuropathies. Autosomal recessive demyelinating neuropathy,[13] one form of which has been mapped to chromosome 8, autosomal dominant hereditary neuropathies type I or II, and X-linked hereditary axonal neuropathies with mental retardation[14] are all reported to be associated with deafness. The latter form has been mapped to Xq24-26, thus excluding the C×32 gene.[15]

The evidence from the literature on HMSN, particularly concerning BAEP abnormalities, suggests that either the VIIIth nerve[16,17] or central auditory pathways[2] are primarily involved in patients with hearing loss. Raglan *et al.*[18] suggested that the hearing loss in HMSN I and II is due to an affection of the VIIIth nerve fibres, comprising demyelination or loss of the ganglion cells, analogous to the abnormality found in the spinal nerves. There is no firm evidence in the literature of cochlear involvement, although some speculate that this is also involved.

We report the first case in the English literature of a patient with CMT type II disease presenting bilateral SNHL in the course of his disease. Although CMT disease cannot be definitively linked to auditory dysfunction in this patient, detailed clinical otolaryngological and neurological as well as laboratory workups have excluded other possible causes for the patient's sudden sensorineural hearing loss. Also, the preponderance of auditory nervous system involvement seems to be a logical link to a neuromuscular disease, e.g. CMT disease, in that previous reports have indicated this type of disease to be linked to various sensory and central nervous system dysfunctions.[2,3,18] The striking finding was that the promontory test was positive, indicating intact auditory nerves, and suggesting cochlear involvement. This finding suggests that patients with CMT should also be checked regularly for hearing loss. The neurologists and otolaryngologists should be aware of this entity and should always inform the patients about this potential complication of CMT.

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