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Reversible sensorineural hearing loss in Lyme disease

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Abstract
We report a case of bilateral sensorineural hearing loss of two years duration which appears to have been due to late *Borrelia burgdorferi* infection. The 39-year-old woman presented with bilateral deafness and multiple other neurological complaints some six months after developing a 'target' lesion on the lower leg after walking in the New Forest. Serology for *Borrelia burgdorferi* became positive and the patient made a complete recovery from both her deafness and her other neurological problems after a five-week course of oral antibiotic therapy.

Key words: Hearing loss, sensorineural; Lyme disease

Introduction

Lyme disease was first described following a cluster of cases in Old Lyme, Connecticut in 1975 (Steere *et al.*, 1977). It is caused by infection with the spirochaete *Borrelia burgdorferi.* The disease is carried by *Ixodes* ticks which normally live on deer, cattle, foxes, rodents and even domestic pets. The frequency of infection varies largely with geographical position, being endemic but uncommon in the United Kingdom (Muhlemann and Wright, 1987). The tick bite which leads to transfer of the spirochaete usually occurs on the legs of humans walking in woodland or scrubland areas. Once infected the human subject may develop an expanding erythematous skin lesion. As with other spirochaete infections the manifestations of disease are varied and infection may be characterized by early, intermediate and late stages. *Borrelia burgdorferi* causes disease by heterogeneous mechanisms. It is predominantly an extracellular pathogen which has the ability to invade and to persist in its human host despite the mounting of a good humoral immune response. This may be due to low or variable surface antigen presentation and to its ability to invade areas of relative immune tolerance such as connective tissue and the central nervous system (Pfister *et al.*, 1994). Live *Borrelia burgdorferi* have been shown to exert a direct toxic effect on cells. Infection excites a lymphocyte-rich inflammatory response and the inflammatory mediators released in response to infection, along with T-cell activity, cause further disease (Lim *et al.*, 1995). There is also good evidence for an auto-immune mechanism of action in Lyme disease: Lyme arthritis is more common in certain HLA phenotypes (Pfister *et al.*, 1994), anti-borrelia antibodies cross react with human axonal proteins (Sigal, 1993) and the intrathecal production of autoantibodies directed against central nervous system (CNS) proteins has been demonstrated in serologically proven neuroborreliosis (Kaiser, 1995).

Early Lyme disease is frequently, but not always, characterized by malaise, fever, myalgia, skin rash, lymphadenopathy and arthralgia. Late disease in the United Kingdom usually takes the form of various neurological manifestations, however in the United States the spectrum of late disease is different with arthritis and carditis commonly occurring. This variation in disease expression is mirrored by antigenic variants of *Borrelia burgdorferi* (Muhlemann and Wright, 1987). Facial palsy is one of the most common neurological manifestations. In one reported series of patients with facial palsy, 20 per cent were thought to be due to Lyme disease (Asbrink *et al.*, 1985). Sensorineural hearing loss has been reported to occur in 15 per cent of cases of late Lyme disease without recovery of hearing (Logigian *et al.*, 1990). However, Hanner *et al.* (1989) reported audiological evidence of partial recovery of hearing following treatment for Lyme disease. Untreated early infection may proceed to complete resolution or to late sequelae. Early treatment with antibiotics may be curative. Longer courses of antibiotic therapy are advisable in late disease. Partial early treatment may lead to the development of late Lyme disease with a reduced or even absent antibody response (Curtin and Pennington, 1995). Like syphilis, Lyme disease may mimic other diseases and a history of exposure combined with clinical evidence of infection is important in making the diagnosis of Lyme disease. Serological testing may be helpful but its value is limited by a significant rate of both false positive and false negative results. It is usual to test for infection with both immunoblot and enzyme linked immunosorbent assay (ELISA) tests. The ELISA test gives a quantitative result but is prone to a greater degree of cross-reactivity with other antigens such as syphilis, yaws, leptospirosis and rheumatoid arthritis. The Western blot test is a qualitative test for the presence of anti-*Borrelia burgdorferi* antibodies and is thought to be more specific than ELISA (Curtin and Pennington, 1995). Local microbiological advice should be sought before embarking on treatment and appropriate treatment should not be delayed for serological test results. Current recommendations are for treatment of patients with CNS manifestations with either benzylpenicillin or cefotaxime intravenously for two weeks, or cefotaxime, ceftriaxone or

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doxycycline orally for three weeks (O'Connell, 1995). Delayed or incomplete response to treatment is common (Moscatello *et al.*, 1991).

Case report

A 39-year-old woman known to suffer from insulin-dependent diabetes mellitus and autoimmune thyroid and ovarian failure was seen in the Ear, Nose and Throat Outpatients department in October 1991 complaining of a three-month history of bilateral hearing loss and intermittent bilateral tinnitus but without other ear symptoms or balance disturbance. Concurrently with the onset of deafness the woman had developed arthropathy of both knees and progressive lower motor neurone weakness of the arms and legs with sensory loss up to C3 and double incontinence. Clinical examination of the ears at this and future consultations was normal apart from a moderate to severe hearing loss. Pure tone audiometry revealed a 50 dB bilateral, symmetrical sensorineural hearing loss (Figure 1a). Brainstem evoked response audiometry using broad band click stimuli at 80 dB showed both normal wave latency and morphology. Visual evoked responses were also normal. Ipsilateral and contralateral stapedial reflexes were obtained at thresholds of between 80 and 95 dB at 500 Hz, 1 kHz, 2kHz and 4kHz in both ears. Serological testing was negative for syphilis, salmonella, streptococcal and yersinia antibodies, and for rheumatoid factor. Computerized tomography (CT) of the brain and spinal cord was normal and magnetic resonance imaging (MRI) of the brain showed minor bright spots in the frontal lobes with no evidence of demyelination or cerebellopontine abnormality. A provisional diagnosis of inflammatory myelopathy was made.

The woman became wheelchair-bound and, following continued evidence of disease progression, high-dose pulsed intravenous prednisolone was administered, with no clinical benefit. She was fitted with hearing aids and was reviewed on two further occasions in January and December 1992. On each occasion a pure tone audiogram showed a moderate to severe bilateral sensorineural deafness with thresholds of between 50 and 70 dB bilaterally and a suggestion of a slight but progressive worsening.

Further enquiry into the history of the patient's illness elicited the previously unknown information that six months prior to the onset of her neurological symptoms she had visited the New Forest for a holiday. There she had noted an insect bite on her leg which was followed by

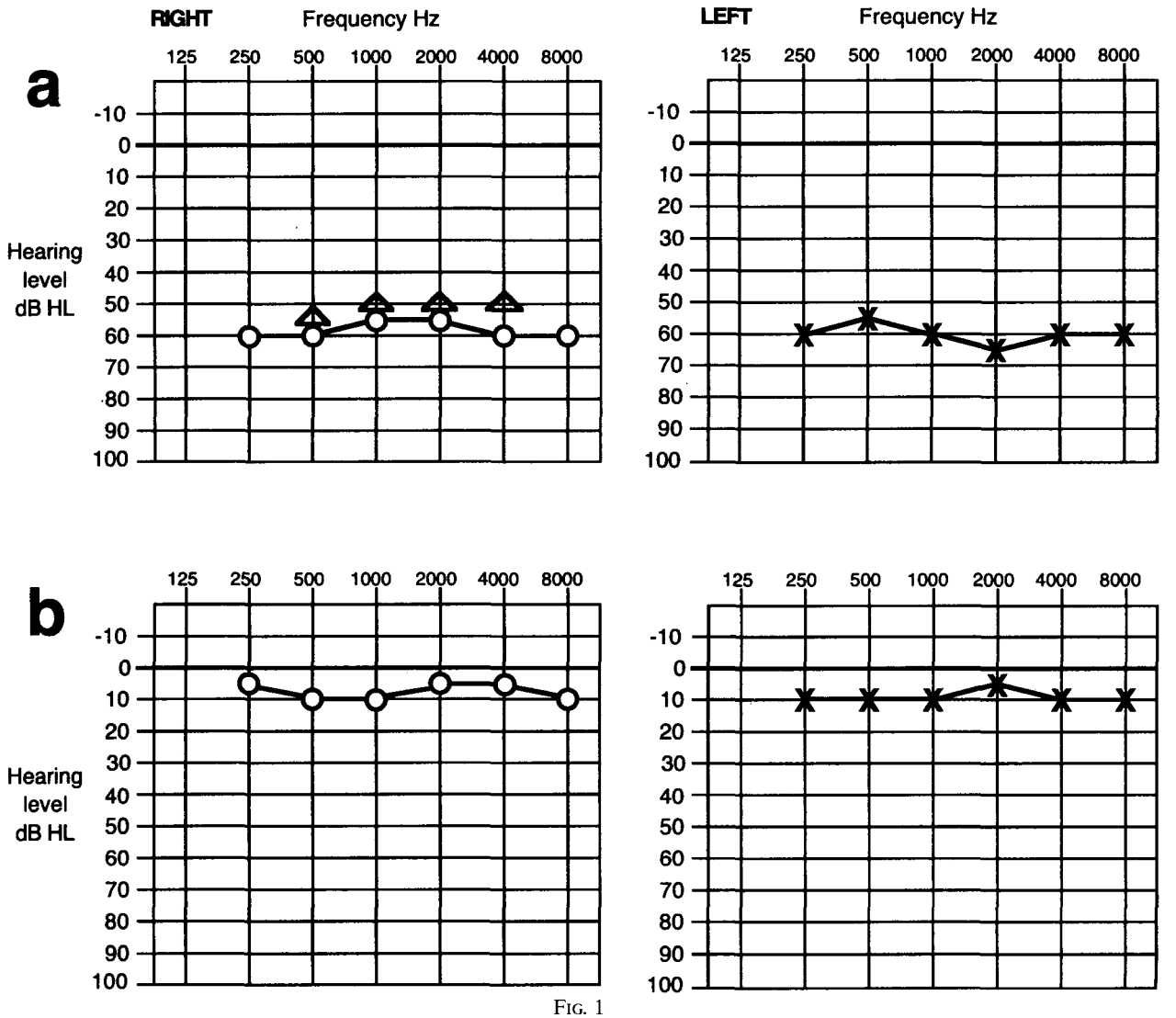

FIG. 1

Pure tone audiograms: a) shortly after onset of neurological disease in 1991; b) four months after completing antibiotic therapy for Lyme disease in 1994.

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spreading erythema and swelling 'like a dart board'. She was treated for this spreading skin lesion with a five-day course of oral amoxycillin. This history, combined with the patient's later development of multiple neurological signs and negative findings for other diseases, raised the possibility of late *Borrelia burgdorferi* infection (Lyme disease). Initial serological testing for antibodies to *Borrelia burgdorferi* was negative. Despite this it was decided to treat the patient for Lyme disease as she was severely incapacitated and steroid therapy had failed to produce any response. On microbiological advice she was treated with a two-week course of erythromycin orally followed by a three-week course of cefuroxime axetil orally. There was no immediate response but three months after completion of the antibiotics she began to regain strength, shortly afterwards discarding her wheelchair, walking sticks and hearing aids. Within six months her return to normality was virtually complete. Serological tests for Lyme disease were repeated at the start of the antibiotic therapy, when the immunoblot test was negative and the ELISA weakly positive (at a titre of 1/15), and again six months after treatment, when the immunoblot test was positive and the ELISA positive at an increased titre of 1/27. Repeat pure tone testing six months after antibiotic treatment showed normal hearing thresholds throughout the frequency range for both ears (Figure 1b). Three months later her pure tone audiogram and a speech audiogram were again normal for both ears. Two years after her recovery there has been no recurrence of either her neurological or otological symptoms.

Discussion

Reversible sensorineural hearing loss from various causes is a well recognized phenomenon, but complete recovery after more than two years of deafness is extremely rare. Sensorineural hearing loss has previously been reported in Lyme disease, although without complete recovery of hearing. Given the nature of the hearing loss and its subsequent recovery the differential diagnosis in this patient would be between autoimmune disease, multiple sclerosis, and a neuropathic infective agent such as *Treponema pallidum* (which was excluded by serological testing) or indeed *Borrelia burgdorferi.* The lack of suggestive plaques on MRI scanning of the central nervous system, normal cerebrospinal fluid examination, normal visual evoked response test and normal brainstem evoked response audiogram, obtained in the presence of hearing loss, makes multiple sclerosis extremely unlikely. The presence of stapedial reflexes at 80 to 95 dB in the presence of a 50 dB sensorineural hearing loss implies a degree of recruitment and points to the cochlea being the site of the pathology. In retrospect, electrocochleography and, had the equipment been available at the time, the recording of otoacoustic emissions would have both been of interest in looking for evidence of cochlear dysfunction. The precise pathogenesis of hearing loss in Lyme disease is, at present, unknown. The pathogenesis of disease in the peripheral and central nervous systems is better understood. In neuroborreliosis there is evidence for both direct spirochaetal invasion of the nervous system as well the presence of autoimmune mechanisms of disease (Kaiser, 1995; Pachner *et al.*, 1995). The relative significance of these mechanisms is not yet known, however, the overall impression of Lyme disease in the nervous system is of a low-grade inflammatory process with in many, but not all cases, return of function on eradication of the infecting agent.

The woman is known to have other autoimmune disorders, however, no further autoantibodies were discovered during the course of this illness and early-on she was treated with high dose corticosteroid therapy without improvement which would be unusual in pure autoimmune disease. She was known to have been in an area of infested woodland some six months before the onset of her neurological symptoms, she had developed a cutaneous lesion consistent with early *Borrelia burgdorferi* infection and she later displayed a positive antibody response to *Borrelia burgdorferi.* Furthermore she made a complete recovery from both her hearing and her other neurological defects following treatment with an antibiotic known to be effective against *Borrelia burgdorferi.* The evidence to support a diagnosis of Lyme disease in this case appears very strong. Lyme disease appears to be a rare cause of sensorineural hearing loss, but in view of the potential for reversal of the hearing loss with treatment, it should be considered in the differential diagnosis.

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