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Autoimmune sensorineural hearing loss: is it still a clinical diagnosis?

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Abstract
Inner ear involvement with sensorineural hearing loss (SNHL) has been reported in many autoimmune disorders including ulcerative colitis. The pathogenetic mechanism of hearing loss in ulcerative colitis is thought to be immune mediated. Diagnostic tests are being developed to identify inner ear autoantibodies, that may be the cause of such hearing loss. The only test that is currently available for clinical use is the Otoblot test. This, however, tests only for antibodies against bovine heat shock protein 70 which is only one of the many cross-reacting proteins against the inner ear in suspected immune-mediated hearing loss. The clinical response to steroid therapy is thus the mainstay in the diagnosis of immune-mediated hearing loss. This paper presents a series of patients with clinically suspected autoimmune hearing loss. Diagnostic assays for this condition are discussed along with a review of the recent advances in the pathogenesis and laboratory diagnosis of immune-mediated sensorineural hearing loss.

Key words: Autoimmune Diseases; Colitis, Ulcerative; Hearing Loss, Sensorineural

Introduction

Inner ear involvement with sensorineural hearing loss (SNHL) has been reported in many autoimmune connective tissue diseases, including rheumatoid arthritis, systemic lupus erythematosus, Wegener's granulomatosis and primary Sjögren's syndrome.[1–4] Sensorineural hearing loss has also been reported in association with ulcerative colitis in a small number of patients.[5–7] Most patients respond to treatment with steroids and/or immunosuppressive agents provided there is no delay in the onset of treatment.[8] The pathogenesis of the SNHL remains obscure, although T lymphocyte-mediated cytotoxicity, immune complex deposition and vasculitis affecting the inner ear have been postulated.[6,7,9,10] A presumptive clinical diagnosis of autoimmune inner ear disease is usually made as laboratory diagnosis is problematic, although recent studies have focussed on the diagnostic utility of antibodies against bovine heat shock protein (bHSP).[11] This is, however, only one of the many cross-reacting proteins that have been isolated with autoimmune inner ear disease. The purpose of this paper is to highlight cases of autoimmune sensorineural hearing loss in association with ulcerative colitis and to review the current literature on the recent advances in diagnostic tests available for autoimmune inner ear disease.

Case reports

Case 1

A 55-year-old male presented to the ENT department with a history of sudden hearing loss of two days duration. There was no history of tinnitus, vertigo, otorrhoea, trauma or recent upper respiratory tract infection. There had been no history of noise exposure or otological problems in the past. His general health was good other than for a history of ulcerative colitis for the past five years. He was not on any medication. Ear, nose and throat examination was unremarkable. An audiogram showed a bilateral sensorineural hearing loss with a pure tone average of 50 dB. His tympanograms were normal. His haematological investigations were all normal except for a raised ESR. His serum was tested for antibodies against the bHSP70 (Otoblot test) but was negative. He was started empirically on prednisolone 60 mg daily and the dose was gradually tapered down over the next two weeks. Serial audiograms were performed and his thresholds returned to normal.

Case 2

A 60-year-old lady with a 12-year history of active ulcerative colitis was referred to the ENT department with a one-week history of hearing loss. She was classed as having active disease. There were no other relevant ENT symptoms or history of recent upper respiratory tract infection or trauma. Her general health was unremarkable. ENT examination was normal. Pure tone audiometry revealed a 60 dB sensorineural hearing loss across all range of frequencies. Her haematological investigations were normal and so was the Otoblot test. She was commenced on prednisolone 60 mg/day. She was not on any 5-aminosalicylic acid (5-ASA) medication for ulcerative colitis as she could not tolerate it. Progressive improvement in hearing thresholds, were noted on serial audiometrical testing. Her hearing returned to normal in the lower frequencies and to about 20 dB at 4 kHz and 8 kHz. She was kept on low dose steroid maintenance therapy for her bowel problem and a repeat audiogram a few months later showed no further deterioration.

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Case 3

A 40-year-old male with a 10-year history of ulcerative colitis was referred to the ENT department with a progressive hearing loss of six months duration. He was in the remission phase of colitis and was on 5-ASA as maintenance therapy. He had no other ENT symptoms and there was no family history of hearing loss. There was no abnormality detected on ENT examination. On audiometric evaluation he had a 40 dB bilateral sensorineural hearing loss. He was treated with a short course of steroids without any significant improvement in hearing thresholds. His haematological investigations and Otoblot test were normal.

Immunocytochemistry

The patients' sera were tested for immuno-reactivity against the guinea-pig cochlear tissue. The guinea-pig organ of Corti was labelled with the patient's sera and then by a secondary fluorescent tagged antibody. The antibodies were found to bind specifically to the supporting cell region and to a slighter extent to the outer hair cells. This antibody binding was especially noted with the sera of the first two patients who responded to steroid therapy, unlike the last patient who was not steroid responsive and in whom antibody binding was sparse.

Discussion

In 1979, McCabe described 18 patients with suspected autoimmune sensorineural hearing loss (SNHL).[12] All patients responded well to treatment with dexamethasone and cyclophosphamide. Since 1982 there have been some case reports of SNHL associated with ulcerative colitis.[5–8] Also Kumar *et al*., have shown a subclinical hearing loss with active ulcerative colitis and Loft *et al*., have demonstrated a higher incidence of SNHL with ulcerative colitis than with Crohn's disease.[9,13] It seems that there may be two forms of hearing loss in patients with ulcerative colitis – a mild subclinical form and an occasional severe manifestation that leads to deafness. The exact pathogenetic mechanism of hearing loss in ulcerative colitis has not been established. Possible explanations for the hearing loss could be due to immune-mediated disease associated with ulcerative colitis or a non-specific effect of systemic inflammation.[9,13] Autoimmunity has been suggested in the pathogenesis of idiopathic ulcerative colitis and in its extra-intestinal manifestations. A 40 kD protein has been extracted that specifically reacts with tissue bound IgG obtained from the colon of patients with ulcerative colitis.[14] Circulating immune complexes have also been suggested to contribute to cochlear dysfunction in ulcerative colitis.[12] In ulcerative colitis antibodies to the 68 kD antigen have been identified previously.[15] All of the above studies are strongly suggestive of an autoimmune pathology for SNHL in ulcerative colitis.

Diagnosis of autoimmune inner ear disease is problematic. There is no universally accepted set of diagnostic criteria or diagnostic test for the condition. Due to the difficulty in identifying a unique cluster of symptoms associated with autoimmune inner ear disease, many objective tests have been developed with varying degrees of success. Western blot assays are currently the most widely used category of diagnostic tests for autoimmune inner ear disease. A number of recent studies have focussed on the diagnostic utility of antibodies against heat shock protein (HSP) 70, the basis of the otoblot test.[11] Hirose *et al*.,[16] evaluated assays for systemic autoimmune disease, as well as Western blotting against bovine HSP 70 (bHSP) for use in predicting corticosteroid responsiveness of rapidly progressive SNHL. The best predictor was found to be bHSP, although assay sensitivity was low (42 per cent), specificity was 90 per cent and the positive predictive value was 91 per cent. Bloch *et al*., tested the serum of 52 patients with suspected autoimmune inner ear disease or Ménière's disease using Western blot assays to recombinant bHSP 70 and recombinant HHSP 70. Reactivity was obtained against 40/52 patients with bHSP and only 12 patients' sera showed reactivity with the human HSP 70.[17] Moreover Western blot reactivity against inner ear antigens of other molecular weights have also been observed in the 42–45 kDa range and also against 35–36 and 20 kDa proteins.[18,19]

Due to the low sensitivity of the Western blot test various other assays have been used to detect antibodies in autoimmune inner ear disease. Patients' sera have been incubated against tissue sections of rat, guinea pig and human cadaveric cochlear sections to detect immunoreactivity to inner ear antigens.[15,20,21] The sera of the above reported cases showed binding to the supporting cell region and to a lesser extent to the outer hair cell region. These are similar to the pattern of binding obtained with immunofluorescent studies carried out by Disher *et al*.[22]

The above findings obtained from the immunofluorescent assays of the patients' sera support the hypothesis that the SNHL seen with ulcerative colitis is immune mediated. It also demonstrates that its presence can be established by laboratory testing. The results obtained have also correlated well with the therapeutic response obtained in the above patients. It is also clear that a negative Otoblot test is not evidence against the diagnosis of autoimmune inner ear disease. Though immunocytochemistry is a useful assay for diagnosis, it is a laborious test and at present its use is mainly as a research tool. In light of the clinical importance of accurately diagnosing treatable, potentially reversible causes of SNHL, and considering the complications associated with the use of corticosteroids, there is clearly a need for a readily available test for the diagnosis of this condition.

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