

## Research Article

# A clinical study on association between hearing loss and inflammatory bowel disease in a population attending a hospital

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## ABSTRACT

**Background:** Inflammatory bowel disease usually presents with gastrointestinal stigmata of weight loss, anaemia, and rectal bleeding, but may exhibit prominent extra-intestinal manifestations also such as joint symptoms, skin signs and some other auto-immune manifestations. During the last few years many authors have reported serious complications of IBD manifesting in the Ear-Nose-Throat (ENT) and influencing disease morbidity.

**Methods:** Twenty four patients with active ulcerative colitis (mean age 45 years) were recruited prospectively along with 24 healthy age- and sex-matched controls. Otoscopy, tympanometry and pure tone audiometry were performed. Otoscopy and tympanometry were normal in all patients and controls. Pure tone audiometry showed sensorineural hearing loss over all frequencies in patients with inflammatory bowel disease and compared with controls. The otologic data including age of onset, family history of otologic problems, exposure to noise and audiometric findings were also reviewed.

**Results:** Out of 48 patients with a history of IBD, 24 had documented SNHL, 17 of these patients had a diagnosis of ulcerative colitis and 7 had Crohn's disease. 22 patients had bilateral SNHL, and 2 patients had unilateral SNHL. Tinnitus were the most common associated aural complaint.

**Conclusion:** Sensorineural hearing loss is very unusual finding, possibly of auto-immune aetiology. We recommend steroid or immunosuppressive therapy in such a patient. Evidence for an autoimmune basis for this condition is reviewed and the potential benefit of systemic corticosteroids emphasized.

**Keywords:** Inflammatory bowel disease, Ear-nose-throat, Sensorineural hearing loss, Extraintestinal manifestations

## INTRODUCTION

Ulcerative colitis and Crohn's disease are chronic relapsing diseases of the gastrointestinal tract, widely known as Inflammatory Bowel Diseases (IBD). The basis of pathogenesis is thought to be due to inappropriate and

on-going activation of the innate immune system driven by the presence of luminal flora. The extraintestinal manifestations of IBD, however, are not of less importance. In some cases earlier presentation were extra-intestinal manifestations followed by onset of gastrointestinal symptoms by many years. As multi-

systemic diseases, IBD, have been correlated with many other organs, including the skin, eyes, joints, bone, blood, kidney, liver and biliary tract. In addition, the inner ear, should also be considered as extraintestinal involvement sites of IBD.

It was McCabe who first described autoimmune hearing loss in 1979.<sup>1</sup> Summers and Harker described the first case of dysacusis associated with ulcerative colitis in 1982.<sup>2,3</sup> Sensorineural hearing loss has frequently been described in association with variety of autoimmune diseases A<sup>3-6</sup> though the pathophysiology of sensorineural deafness remains obscure, the autoimmune nature of the disease strengthens some proposed theories that explain its appearance and progression.<sup>1,6</sup> These forms of dysacusis usually presents as a subclinical condition or as severe bilateral hearing loss, such as sudden deafness<sup>5</sup>. There are no specific tests to establish the diagnosis of autoimmune dysacusis. A Few proteins are being isolated & may have a strong connection with autoimmune condition, such as the hsp 70 although these finding are of little practical importance at present.<sup>5,6</sup> Treatment includes aggressive use of immunosuppressants, usually corticosteroids. Other immunosuppressants have also been suggested by some authors.<sup>3,5</sup> The differential diagnosis is required for cases of sensorineural dysacusis. However, examination will not necessarily confirm a specific etiology. In such cases, a treatment may be given as a test to confirm the diagnosis.<sup>7</sup> The case histories of several patients whose ulcerative colitis was preceded by partial deafness are presented. It is assumed that the partial deafness had an etiological significance leading from the communication difficulties created by the deafness to the ulcerative colitis

Sensorineural hearing loss has been described in a small number of patients with ulcerative colitis. At present, it is not known whether this is a rare & sporadic association, or whether these represent an under recognized extra-intestinal manifestation of ulcerative colitis. The aim of this study was to determine the prevalence of hearing loss in patients with ulcerative colitis.

## METHODS

This study is a prospective study conducted in the department of otorhinolaryngology in a teaching institute in Northern India. Twenty Four patients with active inflammatory disease (mean age 45 years) were recruited prospectively along with 20 healthy age- and sex-matched controls. Otoscopy, tympanometry and pure tone audiometry were performed. Otoscopy and tympanometry were normal in all patients and controls thus excluding middle ear disease and conductive hearing loss. Pure tone audiometry showed significant sensorineural hearing loss over all frequencies in patients with inflammatory bowel disease compared with controls.

## RESULTS

Out of 48 patients with a history of IBD, 24 had documented SNHL, 17 of these patients had a diagnosis of ulcerative colitis and 7 had Crohn's disease. 22 patients had bilateral SNHL, and 2 patients had unilateral SNHL. Tinnitus were the most common associated aural complaint.

**Table 1: Shows total patients (cases) with active inflammatory bowel disease.**

Total patients	Ulcerative colitis	Crohn's disease
24	17	7

**Table 2: Shows sex incidence among selected cases.**

Male	Female
5	19

**Table 3: Shows the age group mainly affected among cases.**

Age-group	Mean age	Max. No. of patients
30-55 years	39 years	10 (35-40 age group)

**Table 4: Shows lateralization of SNHL among selected cases.**

Lateralization	
Bilateral	Unilateral (right side)
22	2

**Table 5: Shows various symptoms associated with hearing loss among cases.**

Associated symptoms	
Tinnitus	8
Vertigo	3
Aural fullness	7
Autophones	1

## DISCUSSION

During the last few years many authors have reported serious complications of IBD manifesting in the Ear-Nose-Throat (ENT) and influencing disease morbidity. Sensorineural hearing loss is very unusual finding, possibly of auto-immune aetiology. Evidence for an autoimmune basis for this condition is being reviewed.

With ulcerative colitis in particular, the deterioration of systemic immunity is significantly greater & is proportional to an increase in permeability of the colic wall. Because of this, it is not unusual to find diarrhea & abdominal pain stools, symptoms more typical of distance immune-mediated mechanisms, such as reactive

arthritis & dermatitis, uveitis & vasculitis.<sup>8</sup> Sensorineural hearing loss is very unusual finding, possibly of autoimmune aetiology. We recommend steroid or immunosuppressive therapy in such a patient. Evidence for an autoimmune basis for this condition is reviewed and the potential benefit of systemic corticosteroids emphasized.

Several lines of evidence indicate that the etiology of autoimmune inner ear disease is immune mediated. First, sera from these patients frequently contain circulating immune complexes, suggesting that inner ear injury may occur via an immune complex-mediated (Type III) hypersensitivity reaction.<sup>9,10</sup> This type of reaction can be initiated by the formation of immune complexes in autoimmune disease or persistent infection.<sup>11</sup> Second, there is a nearly universal response of the disease to systemic corticosteroids & cytotoxic therapy.<sup>12</sup> These therapies are known to be effective in other diseases of inflammatory or autoimmune origin, & their efficacy in treating autoimmune inner ear disease suggests that the pathogenesis of this disease is also immune-mediated. Third, temporal bone pathology in one specimen from a patient revealed vasculitis, ghosts of blood vessels, & granulomatous tissue, all of which indicate immune injury.<sup>12</sup> Examination of more specimens is required, however, before it can be concluded that this is a uniform finding indicative of immune injury to the inner ear. Fourth, the frequent association of this disease with other known or suspected autoimmune diseases indicates that it is an autoimmune process itself or it is a result of these other systemic autoimmune processes.<sup>13,14</sup> In summary, the current facts suggest that tissue injury is mediated by immune mechanisms.

The mechanisms involved in the pathogenesis of ENT manifestations of IBD are not clear, but increased bowel permeability during active disease may cause luminal antigens to be presented to the systemic immune system. As there is already activation of the immune system and pro-inflammatory cytokines such as interleukins (IL-1, IL-12) and TNF- $\alpha$ , this may lead to significant inflammatory responses elsewhere in the body.<sup>15</sup> The inner ear, nose and throat, like other extraintestinal involvement sites in IBD, can become targets of an autoimmune attack.

It has been known that some extraintestinal manifestations may correlate with several parameters of IBD, such as extent of disease, type of disease and duration of disease. In addition, they usually parallel the activity of intestinal inflammation. These findings may need to be elucidated by further clinical and experimental studies performed with larger patient populations of IBD. An investigation of the natural course and autoimmune pathogenesis, including possible relations with autoantibodies for IBD such as pANCA (perinuclear antineutrophil cytoplasmic antibodies) and ASCA (anti-Saccharomyces cerevisiae antibodies) may also be required.

There is considerable evidence to suggest that hearing and vestibular function can be influenced by autoimmune processes. Immune mediated inner ear disease includes clinical conditions associated with rapidly progressive unilateral or bilateral forms of sensorineural hearing loss (SNHL), or even acute total deafness.<sup>16-18</sup> A systemic auto-immune disorder including IBD may present in one-third of the cases.<sup>19</sup> The clinical manifestation of the disease is most often bilateral and progressive. The hearing level often fluctuates, with periods of deterioration alternating with partial or even complete remission. The tendency is for the gradual evolution of permanent hearing loss, which usually stabilizes with some remaining auditory function but occasionally proceeds to complete deafness. Vestibular dysfunction, particularly disequilibrium and postural instability, may accompany the auditory symptoms

Many diagnostic tests have been proposed 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, specific 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.<sup>20</sup> Humoral mechanisms may also be involved in the deposition of circulating immune complexes from bacterial antibodies or viral antibody complexes. Another mechanism that has been proposed is a cell mediated immune response involving cytotoxic T cells against specific inner ear targets.<sup>21</sup> Vascular changes, i.e. the deposition of circulating immune complexes and T-cell mediated cytotoxicity,<sup>22</sup> have been described during the genesis of the bowel involvement in CD disease.

The clinical response to steroid therapy is thus the mainstay in the diagnosis of immune mediated hearing loss and therefore constitutes first-line therapy. Kuczkows-ki J. et al. report the case of a 31 year old woman with Le-sniowski-CD who presented with acute autoimmune sensorineural hearing loss of one ear and acute total deafness on the other ear after she got pregnant. Hearing level improved after treatment with steroids was initiated.<sup>16</sup> However, Kumar BN et al. reported sensorineural hearing loss and UC in a 12-year old boy which initially responded to steroid therapy, but four years later resulted in bilateral profound sensorineural hearing loss in spite of good control of his bowel disease.<sup>3</sup> Immediate treatment with steroids with or without immunosuppressive agents is essential, as delay may lead to irreversible hearing loss. TNF- $\alpha$  blockade by specific antibodies, such as infliximab, may offer an additional treatment option for these patients,<sup>23</sup> indicating that TNF- $\alpha$  may play a critical role in the pathophysiology of the disease.

Cranial neuropathies as well as typical cochlear or vestibular nerve complications can occur and are presumed to be vasculitic in etiology.

Cogan's syndrome is a rare disease found in young patients, characterized by deafness, vertigo, ocular conjunctivitis, keratitis and aortitis. Buge A et al. reported a case of this syndrome, co-existing with CD.<sup>24</sup>

In addition, Illyckyj A et al. report the case of a 30 year old woman diagnosed with CD disease and a subsequent diagnosis of Melkersson-Rosenthal syndrome (recurrent facial paralysis, recurrent and eventually permanent facial edema, placation of the tongue), with severe ear pain.<sup>25</sup>

Metastatic CD disease with involvement of the retroauricular areas has also been described by McCallum DI et al.<sup>26</sup>

Another interesting area of investigation is the presence of subclinical sensorineural hearing loss, especially in IBD patients. Akbayir N et al. investigated 39 IBD patients using otoscopy, tympanometry, and pure tone audiometry.<sup>17</sup> It was demonstrated that a subclinical sensorineural hearing loss might be associated with UC and somewhat with CD affecting mainly the high frequencies. In the light of this finding the authors suggest that all IBD patients should be investigated with labyrinth functions. Periodical follow-up is advisable in patients with positive findings.

Common ENT manifestations, usually noticed in every day's clinical practice, such as sore throat and chronic cough, apthae, hearing loss and vertigo or nasal pain may not be as innocent as they have been thought to be in the past. Especially, recurrent symptoms not responding to topical or even to oral treatment should lead the otolaryngologist to search for an underlying multisystemic disease. IBD seem to be from the most common multisystemic diseases, responsible for the former manifestations.

Some ENT clinical manifestations such as epistaxis and edema of the epiglottis and arytenoid area need urgent attention and special treatment. Protection of the air-way in such cases is mandatory.

The primary mode of treatment for moderate to severe IBD has been 5-aminosalicylic acid products, usually with steroids. In extraintestinal sites, the ulcers can be treated with topical and intralesional steroids. Topical steroids have been shown to be successful in >50% of oral ulcers. If topical treatment fails, the use of oral corticosteroids is indicated. However, because of the morbidity associated with long term steroid use, especially aseptic necrosis of the femoral head, osteoporotic fractures, diabetes mellitus, hypertension and formation of cataracts, immunosuppressive drugs such as azathioprine, methotrexate and cyclosporine have been used as well. The latter agents are well tolerated by the majority of IBD patients, with minor side effects from the ear, nose and throat. Antibodies against tumor necrosis  $\alpha$  (anti-TNF- $\alpha$ ) have shown statistically significant efficacy not only in the treatment of IBD, but

also in distinguishing immune mediated oral ulcers from sporadic aphthous ulcers. However, anti-TNF therapy can be complicated by a variety of adverse reactions, such as fever, nausea, dyspnea, headaches, rash (including a clinical lupus-like syndrome), urticaria, arthralgias and myalgias, possibly due to development of autoantibodies. Appropriate prophylaxis and therapy of these reactions will allow anti-TNF to be used safely in the vast majority of patients. In addition, patients should be screened and treated for tuberculosis before initiating anti-TNF therapy.

Finally, the potential risk for malignancies in patients with IBD has been well established previously and should also be kept in mind, especially in patients with CD. Furthermore, the high risk for cancer of the nose in patients on treatment with azathioprine has also been described.<sup>27</sup>

In conclusion, ENT manifestations should never be evaluated separately or underestimated in IBD patients. It is advisable to follow-up these patients for long periods of time, because some lesions may be manifestations of silent IBD or other multisystemic autoimmune diseases.

## CONCLUSION

Autoimmune dysacusis is one of the few sensorineural conditions in which clinical improvement may be obtained, as long as the diagnosis is promptly made and treatment is adequately employed.

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