



Clinical Manifestation of Sensorineural Hearing Loss as an Extraintestinal Complication of Inflammatory Bowel Disease

Moemi Kinoshita¹ Takayuki Okano^{1,2} Yosuke Tona¹ Hiroshi Yamazaki¹ Koichi Omori¹

¹Department of Otolaryngology, Head and Neck Surgery, Graduate School of Medicine, Kyoto University, Kyoto, Japan

²Department of Otolaryngology, Head and Neck Surgery, School of Medicine, Fujita Health University, Toyoake, Japan

Address for correspondence Moemi Kinoshita, Department of Otolaryngology, Head and Neck Surgery, Tenri Hospital, 200 Mishima-cho, Tenri-shi, Nara 632-8552, Japan (e-mail: m_kinoshita@ent.kuhp.kyoto-u.ac.jp).

Int J Pract Otolaryngol 2024;7:e38–e45.

Abstract

Inflammatory bowel disease (IBD) is an autoimmune condition often accompanied by extraintestinal manifestations including arthritis. However, hearing loss as an extraintestinal manifestation of IBD is rarely reported. This study aimed to investigate the clinical characteristics of sensorineural hearing loss associated with IBD. This study included patients with IBD and hearing loss who were registered between October 2005 and September 2022. The patients were diagnosed with ulcerative colitis (UC) or Crohn's disease (CD) by gastroenterologists in addition to sensorineural hearing loss of unknown etiology confirmed by otolaryngologists. Overall, 32 patients aged 10 to 78 years were included, consisting of 9 women, 18 patients with UC, and 14 patients with CD. Hearing loss associated with IBD was more common among men, with a median onset age of 56 years for UC and 33 years for CD. Two patients reported hearing loss in both ears before IBD onset, whereas 38 ears in 30 patients presented hearing loss after IBD onset. Various types of hearing loss were observed in the 42 affected ears. Further, hearing loss typically developed within 10 years of IBD diagnosis in approximately 63% of cases, with a median interval of 9 years among the 32 cases. In some cases, azathioprine and infliximab, therapeutic agents for IBD, were suspected to have contributed to the hearing loss. No other IBD medications were suspected to contribute to the hearing loss in any patient. The pathogenesis of hearing loss in IBD remains unclear; further large-scale investigations are warranted to elucidate the relationship between IBD and sensorineural hearing loss and to better understand the underlying pathophysiology.

Keywords

- ▶ inflammatory bowel disease
- ▶ ulcerative colitis
- ▶ Crohn's disease
- ▶ extraintestinal complications
- ▶ sensorineural hearing loss

Introduction

Inflammatory bowel disease (IBD) is a chronic inflammatory condition of the intestinal tract that is characterized by symptoms such as chronic diarrhea, abdominal pain, and

bloody stool. In the strict sense, IBD includes ulcerative colitis (UC) and Crohn's disease (CD). UC is more prevalent in individuals aged ≤ 30 years, whereas CD tends to affect younger individuals in their teens and 20s.¹ In Japan, UC is estimated to affect 200,000 individuals and CD is estimated

received
December 11, 2023
accepted after revision
July 5, 2024

DOI <https://doi.org/10.1055/s-0044-1791571>.
ISSN 2569-1783.

© 2024. The Author(s).

This is an open access article published by Thieme under the terms of the Creative Commons Attribution-NonDerivative-NonCommercial-License, permitting copying and reproduction so long as the original work is given appropriate credit. Contents may not be used for commercial purposes, or adapted, remixed, transformed or built upon. (<https://creativecommons.org/licenses/by-nc-nd/4.0/>)

Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

to affect at least 70,000 individuals, with both conditions categorized as designated intractable diseases.² The pathophysiology of IBD is presumed to involve autoimmune mechanisms that affect both innate and acquired immunity and are influenced by genetic and environmental factors.³ Notably, IBD is often treated with adrenocortical steroids (referred to as steroids hereafter) and immunosuppressants.

In addition to gastrointestinal lesions, extraintestinal complications of IBD include arthritis, skin lesions, thromboembolism, primary sclerosing cholangitis, pancreatitis, and vasculitis.⁴ Recently, hearing loss has emerged as an extraintestinal complication of IBD. However, there is a paucity of cases that report hearing loss as an extraintestinal manifestation of IBD,^{5–9} and a consensus on its pathophysiology is yet to be established. In this study, we present the clinical characteristics of 32 patients with sensorineural hearing loss hypothesized to be an extraintestinal symptom associated with IBD, along with a literature review.

Materials and Methods

This retrospective study was approved by the Ethics Committee of the Kyoto University Graduate School and Faculty of Medicine (approval number R2817). Data of patients who visited Kyoto University Hospital during the 17-year period from October 2005 to September 2022 and whose electronic medical records contained diagnoses of “IBD” and “hearing loss” were extracted. Among these, patients with confirmed clinical diagnoses of UC or CD by gastroenterologists who underwent pure-tone audiometry tests at our department of otolaryngology and were subsequently diagnosed with sensorineural hearing loss were included. Patients were considered to have hearing loss if they exhibited a threshold increase of ≥ 25 dB at one or more frequencies. Those with hearing loss of within ± 2 standard deviations of the age-specific mean for each frequency as described by Tsuiki et al¹⁰ were excluded as these cases were considered to be age-related. Patients were diagnosed with sensorineural hearing loss if the difference between bone and air conduction was < 10 dB, and other potential causes of conductive or mixed hearing loss were ruled out. Data on gender, age, age at onset of hearing loss and IBD, audiometric pattern, onset mode, presence of tinnitus and vertigo, medications used for IBD and hearing loss treatment, and history of steroid use for hearing loss were collected. In accordance with the classification of Takahashi et al,¹¹ patients' audiometric patterns were classified into eight types: low-frequency hearing loss, high-frequency hearing loss, peaked type, trough type, flat type, dip type, deaf type, and atypical. Cases with a confirmed onset of hearing loss within 72 hours were categorized as sudden-onset hearing loss, whereas those without a clear onset time or with hearing loss developing over ≥ 3 days were classified as slow-onset hearing loss. In cases with bilateral hearing loss, both ears were considered affected, and the number of ears and patients was considered for analysis. The severity of hearing loss was assessed using mean values (mean hearing acuity in five-segment testing) at 250, 500, 1,000, 2,000, and 4,000 Hz in pure-tone hearing

tests at symptom onset and cases were categorized as mild (< 40 dB), moderate (≥ 40 and < 70 dB), severe (≥ 70 and < 90 dB), and profound (≥ 90 dB).¹² Hearing recovery after steroid treatment was classified based on the hearing recovery criteria for sudden deafness established by the Ministry of Health and Welfare's Research Group for Sudden Deafness.¹³ Fisher's exact test was used for statistical analysis, with p -values < 0.05 considered statistically significant.

Results

Patient Selection

Initially, 100 patients with documented diagnoses of “IBD” and “hearing loss” in their medical records were identified. Subsequently, the medical records of the 100 patients were reviewed, and 27 patients with primary intestinal diseases other than IBD, such as intestinal Behçet's disease and lupus enteritis, were excluded. Additionally, 4 patients who had not previously visited our department and 16 patients lacking detailed records on IBD or hearing loss were excluded. Of the remaining 53 patients with confirmed IBD diagnoses and a history of visiting our department, 7 were excluded as their visits were unrelated to symptoms of hearing loss. Of the remaining 46 patients with IBD who visited our otolaryngology department with hearing loss as the primary complaint, 3 with thresholds of ≤ 25 dB at all frequencies and 2 with clear causes of sensorineural hearing loss (hearing loss after removal of an occipitotemporal tumor in one patient and posttraumatic hearing loss in the other) were excluded. Furthermore, four patients with a history of ototoxic drug use and five with age-appropriate hearing acuity, according to Tsuiki et al,¹⁰ were excluded. Ultimately, 32 patients were included in the analysis (**►Fig. 1**), all experienced sensorineural hearing loss without any conductive or mixed hearing loss. Otoscopy findings of all patients revealed no abnormalities such as tympanic membrane perforation or middle ear effusions. Moreover, interviews confirmed no history of hearing loss due to Ménière's disease or other diseases. Finally, imaging studies (computed tomography scans and magnetic resonance imaging [MRI]) were conducted to rule out other causes of hearing loss.

Gender and Age at the Onset of Hearing Loss

Of the 32 analyzed patients, 18 had UC (12 men and 6 women) and 14 had CD (11 men and 3 women). The median age at onset of hearing loss was 46 years (interquartile range [IQR], 33.75–61) for all patients, 56 years (IQR, 41–65.75) for patients with UC and 33 years (26–47.25) for patients with CD (**►Table 1**). In all cases of bilateral hearing loss, hearing loss occurred simultaneously in both ears.

Onset Modes and Audiometric Patterns

Two patients (one with UC and one with CD) developed IBD after experiencing symptoms of hearing loss, whereas 30 patients (17 with UC and 13 with CD) developed hearing loss after experiencing symptoms of IBD (**►Table 2**). The onset modes and audiometric patterns of 32 patients with 42 affected ears were analyzed. Sudden-onset hearing loss

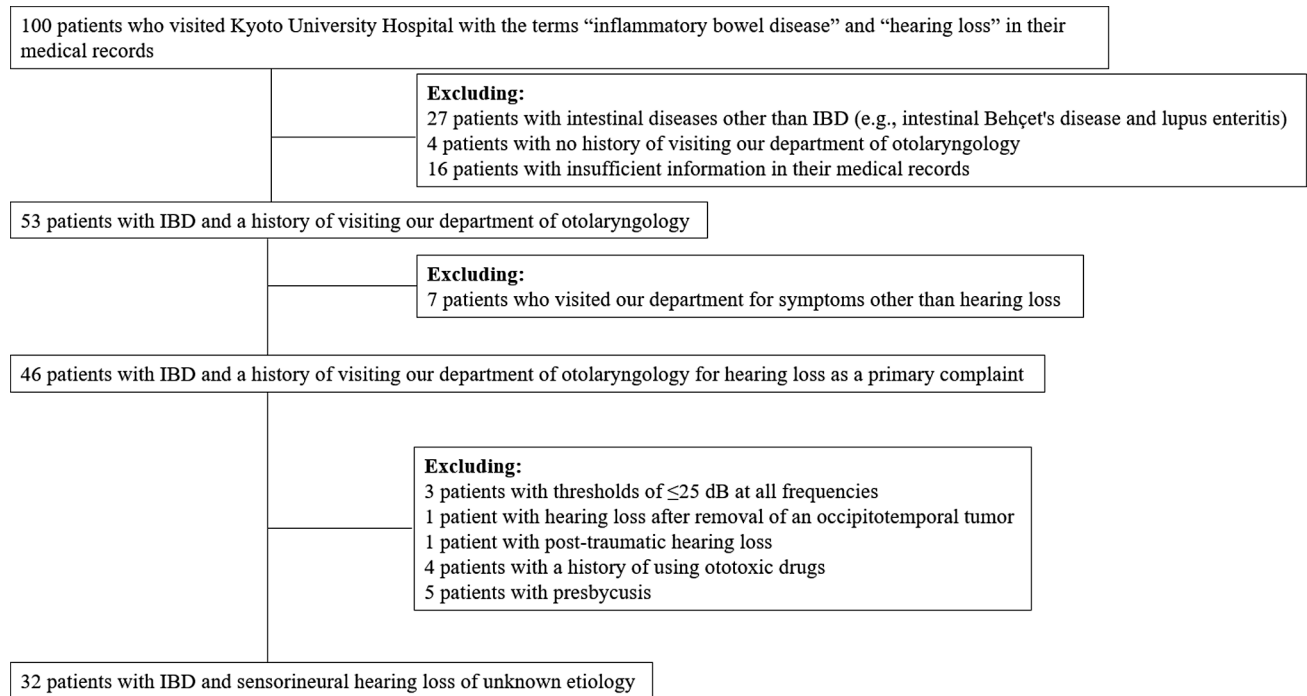


Fig. 1 Patient selection flowchart. Initially, 100 patients who visited Kyoto University Hospital between October 2005 and September 2022 and had diagnoses of “inflammatory bowel disease” and “hearing loss” in their medical records were identified. Subsequently, patients with confirmed diagnoses of ulcerative colitis (UC) or Crohn’s disease (CD) through medical chart reviews by gastroenterologists and sensorineural hearing loss based on pure-tone audiometry tests conducted by otolaryngologists were included. IBD, inflammatory bowel disease (ulcerative colitis and Crohn’s disease).

Table 1 Gender and age at onset of hearing loss

Age group	10	20	30	40	50	60	70	Total (men)
UC (men)	0	0	4 (4)	3 (1)	3 (2)	5(4)	3 (1)	18 (12)
CD (men)	1 (1)	4 (4)	3 (2)	3 (2)	2 (1)	1 (1)	0	14 (11)
Total (men)	1 (1)	4 (4)	7 (6)	6 (3)	5 (3)	6 (5)	3 (1)	32 (23)

Abbreviations: CD, Crohn’s disease; UC, ulcerative colitis.

Note: Out of the 32 analyzed patients, 18 had ulcerative colitis (UC) and 14 had Crohn’s disease (CD). The median age at onset of hearing loss was 46 years (interquartile range [IQR], 33.75–61). The median age at onset was 56 years (IQR, 41–65.75) in patients with UC and 33 years (IQR, 26–47.25) in patients with CD.

Table 2 Comparison of type of onset of hearing loss and associated symptoms of patients with ulcerative colitis (UC) and Crohn’s disease (CD)

	UC	CD	p-Value
Sudden onset (ears)	12	15	
Slow onset (ears)	12	3	0.049
Unilateral hearing loss (patients)	13	10	
Bilateral hearing loss (patients)	5	4	1.00
Vertigo (patients)	9	4	0.289
Tinnitus (patients)	7	6	1.00

Abbreviations: CD, Crohn’s disease; UC, ulcerative colitis.

Note: The percentages of sudden-onset hearing loss, bilateral hearing loss, unilateral hearing loss, vertigo, and tinnitus in patients with UC and those with CD were compared using Fisher’s exact test. The percentage of sudden-onset hearing loss differed significantly between patients with UC and those with CD ($p = 0.049$).

was observed in 27 ears (12 with UC and 15 with CD), accounting for approximately two-thirds of all the ears, and was significantly more common in patients with CD than in those with UC ($p = 0.049$; ► **Table 2**). The audiometric patterns are detailed in ► **Table 3**. In cases of unilateral hearing loss, there were no significant differences in the number of affected ears on the left and right sides. Regarding severity, mild hearing loss was observed in 14 ears of patients with UC (UC ears) and 9 ears of patients with CD (CD ears), moderate hearing loss in 6 UC ears and 6 CD ears, severe hearing loss in 4 UC ears and 2 CD ears, and profound hearing loss in 1 CD ear (► **Table 4**).

Duration of IBD and Time of Onset of Hearing Loss

The median duration between the onset of IBD and that of hearing loss was 9 years (IQR, 2.25–19), with the shortest and longest duration being concurrent onset and 33 years, respectively (► **Fig. 2**). There was no observed correlation

Table 3 Audiometric patterns at the initial visit

	UC	CD
Up-sloping	5	5
Down-sloping	11	4
Convex	1	3
U-shaped	3	0
Flat	1	0
Dip	0	2
Deaf	0	1
Atypical	3	3

Abbreviations: CD, Crohn’s disease; UC, ulcerative colitis.
 Note: The audiometric patterns at the initial visit to our department, sudden-onset hearing loss, affected ears, and associated symptoms were surveyed for 42 ears of 32 patients in whom hearing loss developed after the onset of inflammatory bowel disease.

Table 4 Classification of severity of hearing loss

	UC (ears)	CD (ears)
Mild (< 40 dB)	14	9
Moderate (≥ 40 and < 70 dB)	6	6
Severe (≥ 70 and < 90 dB)	4	2
Profound (≥ 90 dB)	0	1

Abbreviations: CD, Crohn’s disease; UC, ulcerative colitis.
 Note: The severity of hearing loss was classified based on five-segment pure-tone audiometry testing at 250, 500, 1,000, 2,000, and 4,000 Hz in 42 ears with ulcerative colitis (UC) and Crohn’s disease (CD) in which hearing loss developed after the onset of inflammatory bowel disease.

between the duration of IBD and the time of onset of hearing loss.

History of Steroid Use in IBD and Hearing Loss

Based on the diagnostic criteria and treatment guidelines for UC and CD,⁴ other than steroids, the drugs used for the treatment of IBD as identified in this study were mesalazine (Pentasa, 11 patients; Asacol, 9 patients; Lialda, 4 patients), salazosulfapyridine (7 patients), azathioprine (3 patients), 6-mercaptopurine (4 patients), tacrolimus (3 patients), infliximab (4 patients), golimumab (1 patient), vedolizumab (1 patient), betamethasone (3 patients), and cytapheresis (2 patients) for patients with UC. For patients with CD, the drugs included mesalazine (14 patients), salazosulfapyridine (2 patients), azathioprine (9 patients), 6-mercaptopurine (6 patients), infliximab (6 patients), adalimumab (3 patients), ustekinumab (3 patients), ciprofloxacin (5 patients), clarithromycin (3 patients), metronidazole (3 patients), and cytapheresis (2 patients). Among the patients included in this study, hearing acuity improved in 1 patient with CD after treatment with infliximab. However, no associations were found between other drugs and the severity of hearing loss, onset modes, or audiometric patterns.

High-dose steroid therapy was considered for the treatment of sudden sensorineural hearing loss in 7 patients. Among these, 4 patients underwent early high-dose steroid therapy; 3 of them were completely cured and 1 exhibited marked recovery (→Table 5). For the 3 patients for whom high-dose steroid therapy was considered but not administered due to past medical history or comorbidities, 1 achieved marked recovery whereas the other 2 remained unchanged. Additionally, 8 patients continued to receive oral

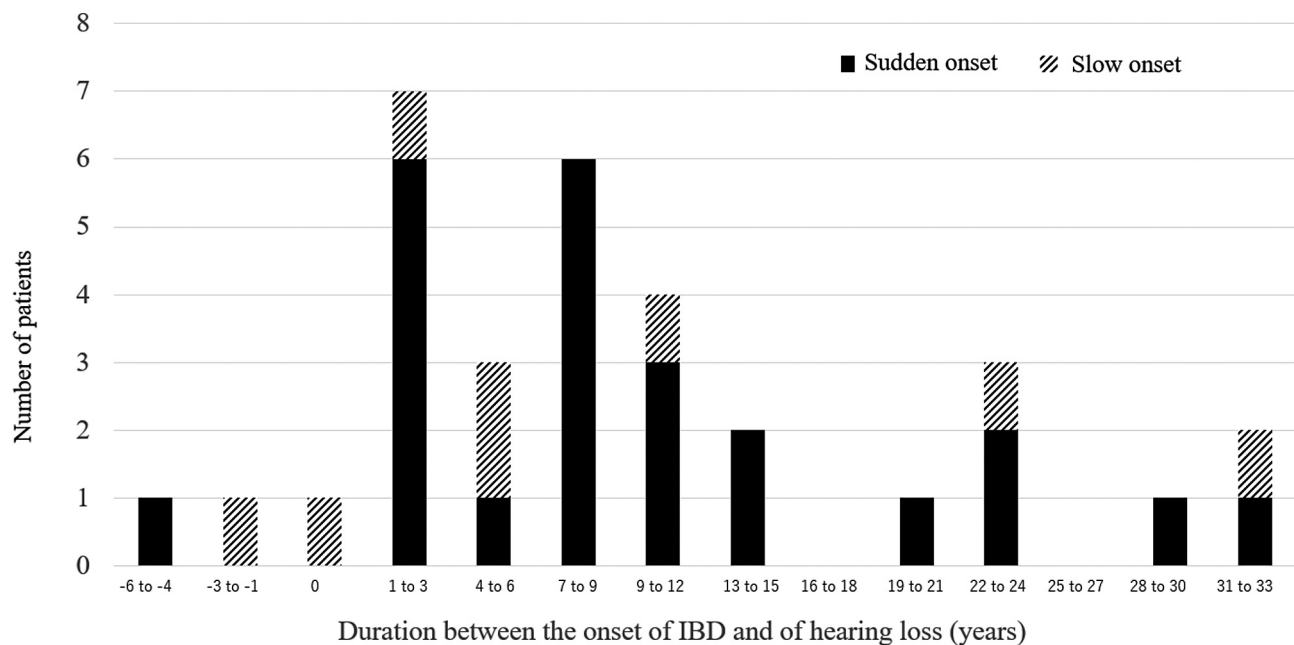


Fig. 2 Duration between the onset of inflammatory bowel disease (IBD) and of hearing loss. The shortest and longest intervals between the onset of IBD and of hearing loss were concurrent onset and 33 years, respectively, with a median duration of 9 years (interquartile range, 2.25–19). No significant correlation was observed between IBD duration and sudden onset of hearing loss.

Table 5 Hearing recovery after steroid therapy

	Cured	Marked recovery	Unchanged
Received high-dose steroid therapy	3	1	
High-dose steroid therapy considered but not received		1	2
Continued steroid therapy for IBD with comorbidities			8

Abbreviation: IBD, inflammatory bowel disease.

Note: High-dose steroid therapy was used to treat sudden sensorineural hearing loss in 7 patients. Among these, 4 underwent early high-dose steroid therapy, with 3 being cured and 1 achieving marked recovery. Further, 3 were considered for high-dose steroid therapy but did not receive it owing to medical history or comorbidities. Among these, 1 achieved marked recovery and 2 showed no improvement. Finally, 8 patients continued to receive oral prednisolone for the treatment of inflammatory bowel disease or polymyalgia rheumatica before the onset of hearing loss and their status remained unchanged.

prednisolone that was initiated before the onset of hearing loss for the treatment of IBD or other existing conditions at doses of 2.4 to 30 mg/day and they experienced no changes in hearing acuity.¹³

Discussion

The association between IBD and hearing loss was first reported by Levitan in 1973, who described 5 cases of UC accompanied by various types of hearing loss.¹⁴ Fousekis et al stated that hearing loss in patients with IBD is primarily due to autoimmune diseases of the inner ear¹⁵; further, McCabe in their study in 1979 reported that 18 patients with hearing loss and vestibular symptoms associated with autoimmune diseases responded well to steroids and immunosuppressants.¹⁶ Previous reports on IBD and hearing loss are summarized in ►Table 6.^{5-9,17-20} The studies were different in terms of the analyzed patients and methods used, and there is no consensus on the pathophysiology of hearing loss in IBD.

Our hospital's electronic medical records include data of 985 patients with UC and 348 patients with CD for the duration of the study. The incidence of sensorineural hearing loss associated with IBD in our study was <1%, indicating a relatively low occurrence rate.

Regarding the age at onset of hearing loss, Akbayir et al demonstrated that the incidence of hearing loss tends to increase with age in patients with IBD, although the differences were not statistically significant.⁶ Wengrower et al indicated that patients with IBD aged ≥ 40 years are at an increased risk of developing hearing loss.⁷ In the present study, the median age at onset of hearing loss was 56 years for patients with UC and 33 years for patients with CD, with hearing loss reported across all age groups. In terms of the age at IBD onset, UC is most commonly diagnosed in individuals aged ≤ 30 years, whereas CD predominantly affects patients in their teens and 20s.² In our study, some patients with CD developed hearing loss during their teens and 20s, aligning with the epidemiological trend that patients with CD develop sensorineural hearing loss at a younger age. Regarding gender difference in patients with IBD, the male-to-female ratio is typically 1:1 in patients with UC and 2:1 in patients with CD. Among patients with IBD and hearing loss in the present study, 66% of those with UC and 79% of those with CD were male, indicating a higher

prevalence of hearing loss in men with IBD. Akbayir et al found no significant association between hearing loss and gender.⁶ Accordingly, based on the results of the present study, we believe that the gender difference in patients with IBD and hearing loss reflects the gender difference in IBD itself.

IBD onset typically precedes the development of extra-intestinal complications in approximately 75% of cases.⁴ In the present study, hearing loss occurred after IBD onset in 94% of the cases. Regarding the audiometric patterns of hearing loss associated with IBD, Akbayir et al reported that patients with UC exhibited threshold increases at 2 to 8 kHz, whereas those with CD showed impairment at 4 kHz, indicating high-frequency hearing loss in both UC and CD.⁶ Ichihara et al observed various audiometric patterns, including low-frequency, high-frequency, and flat-type hearing loss in initial audiograms.⁵ Kumar et al reported that patients with UC without subjective hearing loss had threshold increases of approximately 10 dB across all frequency ranges compared with healthy volunteers.¹⁷ Our study revealed various audiometric patterns, including low-frequency, high-frequency, peaked, trough, flat, dip, deaf, and atypical hearing loss in patients with sensorineural hearing loss. Karmody et al reported that 84% of patients had bilateral hearing loss, with the most common symptoms including vertigo, tinnitus, and ear fullness.²⁰ In our study, 64% of patients with UC or CD with hearing loss experienced sudden-onset unilateral hearing loss, with 41% also experiencing vertigo and tinnitus. Furthermore, sudden-onset hearing loss was more common among patients with CD than among those with UC. In UC, erosions and ulcers continuously form from the rectum to the proximal side, with lesions extending to the mucosal and submucosal layers of the large intestine. Meanwhile, CD causes discontinuous lesions throughout the digestive tract from the oral cavity to the anus, with lesions affecting not only the mucosal layer but also the muscle layer.^{1-4,21,22} These pathophysiological distinctions may contribute to the higher tendency for sudden-onset hearing loss associated with CD. Patients with sudden-onset hearing loss may be more likely to recognize their hearing issues and seek early consultation with otolaryngologists. The association of CD with sudden-onset hearing loss is of clinical significance as it may prompt earlier therapeutic interventions for hearing loss. However, patients with slow-onset hearing loss may not perceive their

Table 6 Previous reports on the association between inflammatory bowel disease (IBD) and hearing loss

Study design	Patients	Endpoint	Results	Literature
Case-control study	20 patients with UC 20 controls	Pure-tone audiometry	UC patients without subjective hearing loss showed significant threshold increases at 250–8,000 Hz	Kumar et al, 2000 ¹⁷
Case-control study	39 patients with IBD (18 with UC and 21 with CD) 25 controls	Pure-tone audiometry	Patients with UC and CD showed significant threshold increases at 2,000–8,000 and 4,000 Hz, respectively	Akbayir et al, 2005 ⁶
Case-control study	24 pediatric patients with IBD (13 with UC, four with CD, and 7 with atypical-form) 20 controls	Pure-tone audiometry	No significant differences at 250–8,000 Hz	Kalyoncu et al, 2010 ¹⁸
Case-control study	33 pediatric patients with IBD (15 with UC and 18 with CD) 31 controls	Pure-tone audiometry DPOAE hearing in noise test	Children with IBD showed significant threshold increases at 8,000–16,000 Hz	Polat et al, 2020 ¹⁹
Case-control study	50 patents with UC in remission 50 controls	Pure-tone audiometry	No significant differences in mean values in the better hearing ear	Bodh et al, 2022 ⁸
Prospective comparative longitudinal study over three years	76 patients with IBD 29 controls	Pure-tone audiometry Extraintestinal manifestations	The incidence of hearing loss significantly increased in patients with IBD aged 40 years or older or having extraintestinal manifestations	Wengrower et al, 2016 ⁷
Retrospective chart review	57 patients with UC who underwent otolaryngologic investigation	Pure-tone audiometry	Only 1 out of 57 patients had hearing loss at 500–8,000 Hz	Casella et al, 2015 ⁹
Case series	19 patients with IBD and hearing loss of unknown etiology (14 with UC and 5 with CD)	Pure-tone audiometry Optimum speech level test	16 patients had bilateral hearing loss, and 3 patients had unilateral hearing loss	Karmody et al, 2009 ²¹
Case series	11 patients with IBD and ear symptoms (8 with UC and 3 with CD)	Pure-tone audiometry Psychological evaluation of hearing loss (HHIA) Vertigo symptom questionnaire (VHQ)	Clinical features in five bilateral and six unilateral patients Psychological effects of hearing loss and vertigo	Ichihara et al, 2021 ⁵

Abbreviations: CD, Crohn's disease; DPOAE, distortion product otoacoustic emission; HHIA, Hearing Handicap Inventory for Adults; IBD, inflammatory bowel disease; UC, ulcerative colitis; VHQ, Vertigo Handicap Questionnaire.

Note: Although some case reports were identified, they are not included in this table. The studies included in the table included a substantial number of cases and varied in terms of studied patients and methods, with only one 2011 report from Japan involving 11 cases. Thus, there is currently no consensus on the association between the pathophysiology of IBD and hearing loss.

hearing difficulties and may not seek medical attention from otolaryngologists. Therefore, patients with slow-onset hearing loss may not have been included in this study, representing a limitation of this study.

Regarding the time of onset of IBD and hearing loss, Ichihara et al observed that hearing loss mostly developed within 10 years after IBD diagnosis.⁵ In the present study, the median duration between the onset of IBD and that of hearing loss was 9 years, with hearing loss occurring within 10 years in 63% of

the cases. The prolonged duration of IBD in this study compared with Ichihara et al's findings may be attributed to the gradual progression of hearing loss, which often goes unnoticed by patients. Additionally, we did not find any significant association between the duration of IBD and sudden-onset hearing loss, in accordance with the study by Akbayir et al.⁶

A previous study suggested that hearing loss is a side effect of azathioprine that is used as a therapeutic agent for IBD.²³ The incidence of ototoxicity with azathioprine is reported to

be < 1% or unknown as per the package inserts for adalimumab, ciprofloxacin, and clarithromycin. However, the present study did not find a clear association between hearing loss and the drugs used. Azathioprine is also used to treat immune-mediated hearing loss,^{24,25} and it has been reported that some biological preparations might be promising as new therapeutics for autoimmune inner ear disease.²⁶ Akbayir et al noted no significant associations between hearing loss and a history of IBD treatment with azathioprine, steroids, and other drugs.⁶ In the present study, 1 patient with CD experienced hearing loss after initiating azathioprine treatment. Although detailed information on IBD activity and treatment history before the onset of hearing loss was unavailable for some patients treated at other institutions, no consistent trends were observed regarding the duration of IBD, age at onset of hearing loss, or the drugs used and their association with hearing loss as an adverse drug reaction.

The etiology and pathophysiology of hearing loss associated with IBD have not been fully understood. Previous reports suggest the potential involvement of an autoimmune disease of the inner ear.^{15,27} Kariya et al reported MRI findings of sensorineural hearing loss in patients with UC, indicating stenosis and obstruction of both cochlear ducts.²⁸ Dettmer et al observed temporal bone pathology in patients with progressive sensorineural hearing loss in CD, exhibiting granulation tissue filling the inner ear and invasion by macrophage-dominated inflammatory cells. These findings were identical to the intestinal pathology in CD and suggestive of autoimmune disease of the inner ear.²⁹ Further data from more cases are needed for better understanding the pathophysiology.

This study had several limitations. First, not all hearing loss observed in the patients could be attributed to IBD; comorbidities such as Takayasu arteritis and chronic rheumatoid arthritis may have influenced the results. Second, a selection bias was present as patients seeking treatment for hearing loss at other hospitals were not included in this study. Only patients with IBD who visited our department for hearing loss were included. Additionally, patients who were unaware of their hearing loss or had reduced hearing acuity were not included; only patients who became aware of hearing loss and were confirmed to have it through pure-tone audiometry testing were included. Third, patients did not necessarily visit otolaryngologists as soon as they noticed hearing loss, and there may have been delays between patients noticing hearing loss and when it actually occurred. To address these issues, patient screening based on medical interviews and audiometry tests may be considered for all patients with IBD aged ≥ 40 years. This comprehensive screening approach could provide more accurate insights into the patterns of hearing impairment and its association with vertigo and tinnitus symptoms in patients with IBD.

Conclusion

We investigated the clinical characteristics of sensorineural hearing loss as a potential extraintestinal symptom of IBD in a cohort of 32 patients. Further large-scale studies are

warranted to elucidate the association between IBD and sensorineural hearing loss as well as the underlying pathophysiology of sensorineural hearing loss associated with IBD.

Funding
None.

Conflict of Interest
None declared.

Acknowledgment

We would like to thank Dr. Norimitsu Uza from the Department of Gastroenterology and Hepatology at the Graduate School of Medicine, Kyoto University, for his advice in this study.

References

- 1 Japanese Society of Gastroenterology. Evidence-based clinical practice guidelines for inflammatory bowel disease (IBD). Accessed November 30, 2022 at: <https://www.jsge.or.jp/guideline/>
- 2 Japan Intractable Diseases Research Foundation/Japan Intractable Diseases Information Center. A list of disease descriptions, diagnostic criteria, and clinical survey individual forms. Accessed November 30, 2022 at: <https://www.nanbyou.or.jp/entry/>
- 3 Geremia A, Biancheri P, Allan P, Corazza GR, Di Sabatino A. Innate and adaptive immunity in inflammatory bowel disease. *Autoimmun Rev* 2014;13(01):3–10
- 4 Health and Labour Sciences Research Grant Policy Research Program on Intractable Diseases. Inflammatory bowel disease/Crohn's disease diagnostic criteria/treatment guidelines. Accessed January 4, 2023 at: <http://www.ibdjapan.org/pdf/doc15.pdf>
- 5 Ichihara H, Fujikawa T, Ito T, et al. Questionnaire-based survey of the daily-life impact of ear symptoms in patients with inflammatory bowel disease. *Nippon Jibiinkoka Gakkai Kaiho* 2021;124: 890–896
- 6 Akbayir N, Caliş AB, Alkim C, et al. Sensorineural hearing loss in patients with inflammatory bowel disease: a subclinical extra-intestinal manifestation. *Dig Dis Sci* 2005;50(10):1938–1945
- 7 Wengrower D, Koslowsky B, Peleg U, et al. Hearing loss in patients with inflammatory bowel disease. *Dig Dis Sci* 2016;61(07): 2027–2032
- 8 Bodh V, Kumar R, Sharma R, Sharma B, Sachdeva A, Azad R. Sensorineural hearing loss and ulcerative colitis in remission. *Indian J Gastroenterol* 2022;41(02):143–148
- 9 Casella G, Corbetta D, Zolezzi M, et al. Symptomatic sensorineural hearing loss in patients with ulcerative colitis. *Tech Coloproctol* 2015;19(12):729–731
- 10 Tsuiki T, Sasamori S, Minami Y, et al. Age effect on hearing: a study on Japanese. *Audiol Jpn* 2002;45:241–250
- 11 Takahashi K, Yamamoto Y, Ohshima S, et al. Audiometric patterns in acoustic neuromas: an analysis of 105 cases. *Otol Jpn* 2011; 21:23–28
- 12 Japan Audiological Society, Hearing Loss Committee. Classification of the severity of hearing loss. *Audiol Jpn* 2014;57:258–263
- 13 Nomura Y. Summary report. Ministry of Health and Welfare, Research Group on Acute Severe Hearing Loss for Specific Diseases. FY1984 Report of Research Achievements 1985:1–3
- 14 Levitan HL. The etiologic significance of deafness in ulcerative colitis. *Int J Psychiatry Med* 1973;4(04):379–387
- 15 Fousekis FS, Saridi M, Albani E, et al. Ear involvement in inflammatory bowel disease: a review of the literature. *J Clin Med Res* 2018;10(08):609–614
- 16 McCabe BF. Autoimmune sensorineural hearing loss. *Ann Otol Rhinol Laryngol* 1979;88(5 Pt 1):585–589

- 17 Kumar BN, Smith MS, Walsh RM, Green JR. Sensorineural hearing loss in ulcerative colitis. *Clin Otolaryngol Allied Sci* 2000;25(02):143–145
- 18 Kalyoncu D, Urganci N, Calis AB, Ozbal A. Sensorineural hearing loss in pediatric patients with inflammatory bowel disease. *Dig Dis Sci* 2010;55(01):150–152
- 19 Polat E, Çınar Z, Keskindemirci G, et al. Assessment of hearing function in children with inflammatory bowel disease. *J Int Adv Otol* 2020;16(03):362–366
- 20 Karmody CS, Valdez TA, Desai U, Blevins NH. Sensorineural hearing loss in patients with inflammatory bowel disease. *Am J Otolaryngol* 2009;30(03):166–170
- 21 Japan Society of Coloproctology. Inflammatory bowel disease (ulcerative colitis, Crohn's disease). Accessed March 17, 2024 at: <https://www.coloproctology.gr.jp/>
- 22 Japanese Society of Pediatric Surgeons. Diseases treated by pediatric surgeons. Accessed March 17, 2024 at: <http://www.jsps.or.jp/>
- 23 Jenkinson PW, Syed MI, McClymont L. Progressive, reversible sensorineural hearing loss caused by azathioprine. *J Laryngol Rhinol Otol* 2014;128(09):838–840
- 24 Mata-Castro N, Gavilanes-Plasencia J, Ramírez-Camacho R, García-Fernández A, García-Berrocal JR. Azathioprine reduces the risk of audiometric relapse in immune-mediated hearing loss. *Acta Otorrinolaringol Esp (Engl Ed)* 2018;69(05):260–267
- 25 Pyykkö I, Ishizaki H, Peltomaa M. Azathioprine with cortisone in treatment of hearing loss in only hearing ear. *Acta Otolaryngol (suppl)* 1997;529:83–85
- 26 Balouch B, Meehan R, Suresh A, et al. Use of biologics for treatment of autoimmune inner ear disease. *Am J Otolaryngol* 2022;43(05):103576
- 27 Hoistad DL, Schachern PA, Paparella MM. Autoimmune sensorineural hearing loss: a human temporal bone study. *Am J Otolaryngol* 1998;19(01):33–39
- 28 Kariya S, Fukushima K, Kataoka Y, Tominaga S, Nishizaki K. Inner-ear obliteration in ulcerative colitis patients with sensorineural hearing loss. *J Laryngol Rhinol Otol* 2008;122(08):871–874
- 29 Dettmer M, Hegemann I, Hegemann SC. Extraintestinal Crohn's disease mimicking autoimmune inner ear disease: a histopathological approach. *Audiol Neurootol* 2011;16(01):36–40