Received: 29 January 2021 | Revised: 25 August 2021 | Accepted: 28 August 2021

DOI: 10.1002/lio2.659

ORIGINAL RESEARCH

Laryngoscope Investigative Otolaryngology

Severe acute otitis media and mastoiditis caused by group A beta-hemolytic streptococcus

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Abstract

Objective: To describe the characteristics, diagnostics, treatment, and outcome of severe acute otitis media (AOM) and acute mastoiditis (AM) caused by group A beta-hemolytic streptococcus (GAS).

Study design: A retrospective cohort study.

Methods: The yearly incidence of inpatient care-needing GAS AOM/AM patients in our hospital catchment area between 2002 and 2018 was investigated. A detailed analysis was performed for cases treated during the last GAS epidemic in 2017-2018. Anamnesis, signs and symptoms, pure-tone audiometry results, treatment, complications, and outcome were collected from medical charts. Patients responded to an otology-specific health-related quality of life survey (EOS-16) 1.5 to 3 years after their treatment.

Results: The number of GAS infections peaks at approximately 7-year intervals. During 2017 and 2018, altogether 37 patients (29 adults and 8 children) were hospitalized due to GAS AOM/AM. AM was diagnosed in 14 (38%) patients. The disease progression was typically very rapid. At presentation, all patients had severe ear pain, 68% tympanic membrane perforation and discharge, 43% fever, and 43% vertigo. In pure-tone audiometry, there was usually a marked mixed hearing loss at presentation. There was a significant recovery in both air and bone conduction thresholds; the pure tone average improvement from presentation was 32.3 ± 14.8 dB. Rapid strep tests (RST) proved to be more sensitive than bacterial culture in identifying GAS as a cause of AOM/AM.

Conclusion: GAS AOM/AM has a rapid onset. Hearing loss usually includes a sensorineural component, which is usually reversible with adequate treatment. RST seems to be useful in detecting GAS from middle ear discharge.

Level of Evidence: 4.

KEYWORDS

acute mastoiditis, acute otitis media, group A beta-hemolytic streptococcus, health-related quality of life, *Streptococcus pyogenes*

1 | INTRODUCTION

Group A beta-hemolytic streptococcus (GAS; *Streptococcus pyogenes*) is a common pathogen, responsible for a variety of diseases.[1,2] GAS causes 5% to 10% of pharyngotonsillitis cases in adults and up to 37% in children older than 5 years; it also causes cutaneous infections.[3,4] GAS can lead to invasive infections such as bacteremia, streptococcal toxic shock syndrome, pneumonia, osteomyelitis, mastoiditis, and necrotizing fasciitis. The incidence of invasive GAS infection in developed countries is 2.3 to 6.2/100 000 and the fatality rate for streptococcal toxic shock syndrome is 30% to 60%.[2,5-12] Post-streptococcal autoimmune sequelae leading to rheumatic fever, rheumatic heart disease, arthritis, and glomerulonephritis still occur even after the discovery of penicillin.[6,13,14]

Acute otitis media (AOM) is a common reason for seeking medical attention with overall global estimated incidence rate at 10.8 out of 100 yearly[15] with 51% of these occurring in children under 5 years of age.[16] Studies of microbial etiology demonstrate that *Haemophilus influenzae*, *Streptococcus pneumoniae*, and *Moraxella catarrhalis* are significant causes of AOM, albeit the prevalence of *S. pneumoniae* has decreased since the introduction of pneumococcal conjugate vaccines.[15,17] GAS is estimated to cause 2-3% of AOM cases in children.[17] Acute mastoiditis (AM), the most common potentially serious complication of AOM, remains quite rare. Its microbial etiology is usually *S. pneumoniae* or GAS,[18,19] where GAS is the causative agent in 14% to 53% of hospitalized AOM/AM cases.[18,20,21]

The incidence of invasive GAS infections, including severe AOM and AM, has been shown to fluctuate with a cycle of approximately 7 to 8 years.[5,21-23] In Finland, the number of invasive GAS infections increased significantly in 2017 compared to previous years (Figure 1).[24] During 2017 and 2018, we also noticed a marked increase in patients with severe GAS AOM/AM needing hospital care. Since GAS and diseases caused by it are not fading away in the near future, we set out to describe the current incidence, diagnostics, disease course, and outcome of severe GAS AOM/AM in our hospital setting with special attention given to hearing outcomes. Although many GAS AOM/AM patients show marked sensorineural hearing loss (SNHL) at presentation, hearing outcomes have not been described in detail in the literature.[25-27] Also, we wanted to describe how rapid antigen detection tests (rapid strep tests [RSTs]) from middle ear secretion may be used in conjunction with the bacterial culture to expedite diagnostics.

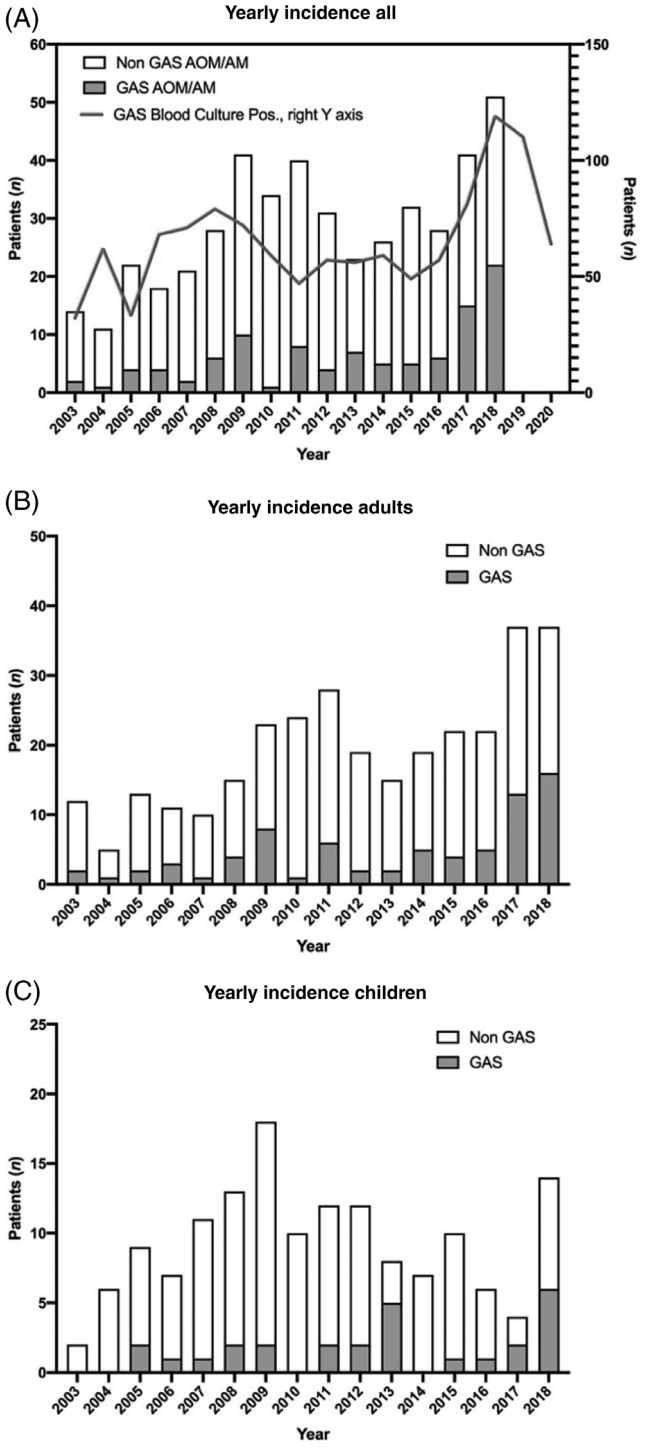

FIGURE 1 GAS bacteremia patients in Helsinki University Hospital district and GAS AOM/AM patients needing inpatient care in Helsinki University Hospital between 2003 and 2018. (A) All patients, red line indicates all GAS blood culture positive patients in Helsinki University Hospital district in 2008-2018. (B) Adult GAS AOM/AM patients. (C) Child GAS AOM/AM patients. AM, acute mastoiditis; AOM, acute otitis media; GAS, group A beta-hemolytic streptococcus

2 | MATERIALS AND METHODS

2.1 | Study design and ethics

This study was based on retrospective evaluation of patient records, with a later follow-up based on a health-related quality of life (HRQoL) survey. The study was approved by the Helsinki University Hospital Ethical committee (no 1121/2020) and had study permissions from the institutional research board (§73 HUS/66/2018 30.8.2018 and 67§ HUS/1121/2020 15.04.2020).

2.2 | Patients

This study included 206 patients requiring hospitalization at the Department of Otorhinolaryngology in Helsinki University Hospital, during 2013 and 2018 for AOM/AM and complications caused by them. The Helsinki University Hospital has 1.7 million catchment area and is the only on-call ear, nose, and throat clinic in the area meaning all ear infections that require hospitalization are treated here. The exclusion criterion was trauma as the cause of the infection and one patient was excluded on this basis. Of these 205 cases, GAS was a causative agent in 60 patients. To determine the incidence of GAS AOM/AM requiring hospitalization, we also used data from 2002 to 2012 from earlier publications.[21,28] Between 2002 and 2018, in total 314 adults and 149 children were hospitalized for AOM/AM. Of these, 76 adults (24%) and 27 (18%) children had GAS AOM/AM. For the detailed analysis part of this study, we concentrated on the 37 patients treated during the last GAS epidemic between 2017 and 2018, since the diagnostic workup and treatment protocols were uniform in our department over that period.

2.3 | Definitions and treatments

The samples for microbiological analysis were taken from every patient at presentation from the middle ear secretion after tympanocentesis, or in the case of spontaneously ruptured tympanic membrane (TM), from the external auditory canal. Usually both bacterial culture and RSTs (Quicker Dipstick Strep A test by Quidel, San Diego, California) were performed. Either positive bacterial culture (predominant or pure growth of GAS) or positive RST from middle ear secretion was considered GAS AOM/AM in this study. The diagnosis of AM was based on the clinical picture where otomicroscopy-confirmed AOM was combined with retroauricular pain, erythema and/or tenderness and/or protrusion of the auricle.[18] Chronic otitis media (COM) refers to an inflammatory condition of the middle ear and mastoid cavity that has persisted for at least 3 months. Recurrent acute otitis media (RAOM) is defined as having at least three episodes of AOM in a period of 6 months, or four or more episodes in 12 months. Fever was interpreted as axillary temperature ≥37.8°C. GAS patients were treated based on our clinical care guidelines. These included proper ventilation provided by spontaneous TM perforation, large tympanocentesis, or (in most cases) tympanostomy tube placement at presentation, intravenous antibiotics (primarily benzylpenicillin, in combination with clindamycin in more severe cases), ear drops containing ciprofloxacin and fluocinolone acetonide, and systemic methylprednisolone. Surgical treatment (tympanomastoidectomy) was performed if needed, based on individual evaluation.

2.4 | Pure tone audiometry

Of the 37 patients treated as inpatients during 2017 and 2018, 24 patients (65%) had had their hearing examined within 1 day of hospitalization and had received a second hearing examination after at least 21 days of follow-up. These patients were selected for audiologic analysis. Pure tone audiograms were extracted from a clinical audiology database (AuditBase, Auditdata, Denmark) using an SQL script (SQLTalk, Gupta Technologies, California). Air conduction (AC) thresholds were collected at 0.125, 0.25, 0.5, 1, 2, 4, 6, and 8 kHz frequencies and bone conduction (BC) thresholds for 0.25, 0.5, 1, 2, and 4 kHz frequencies. Due to difficulties in acoustic calibration, BC thresholds are typically not measured above 4 kHz. BC is not routinely measured at all in any given frequency if AC is normal (≤20 dB HL). Therefore, in a variant on analysis, we combined the audiometric information containing both the AC and BC thresholds as "minimum of AC/BC thresholds," where AC and BC thresholds were compared individually for each frequency, and if measured, the BC was chosen for further analysis. As customary to Finland, pure tone average (PTA) was computed as a mean of AC thresholds (PTA_{air}) and a mean of the minimum of AC/BC (PTA_{min}) thresholds at 0.5, 1, 2, and 4 kHz.

2.5 | HRQoL

The HRQoL was investigated using an otology-specific HRQoL instrument EOS-16[29] and a generic HRQoL survey 15D.[30] The 16-point EOS-16 covers ear symptoms, hearing, balance, psychosocial impact, and need for care. The surveys were sent to Finnish-speaking adult patients whose addresses were known (n = 22) for completion 1.5 to 3 years after the onset of infection.

2.6 | Statistics

Statistical analyses were performed using IBM SPSS Statistics for Macintosh version 25 (Armonk, New York), Microsoft Excel version 16.22 (Redmond, Washington) and Prism 8 (GraphPad, San Diego, California). Graphs were made with Prism and Matlab version R2018a (Natick, Massachusetts). The level of significance was set at $P < .05$. Two-way ANOVA with Sidak's multiple comparison test was used to analyze the audiometric data.

3 | RESULTS

3.1 | Yearly incidence of hospitalized GAS AOM/AM during 2003 and 2018

The incidences of severe AOM/AM necessitating hospitalization at our department and bacteremia caused by GAS in the Helsinki University hospital district are presented in Figure 1. The graph demonstrates fluctuations in the number of GAS infections. Between the invasive GAS epidemics, the annual average for GAS OMA/AM patients needing inpatient care is about five cases, with cases occurring more frequently during the summer months (June-August, data not shown). During the epidemic of 2017 and 2018, there was a clear correlation between incidences of GAS bacteremia in the Helsinki University hospital district and severe GAS AOM/AM treated in our

TABLE 1 Patient demographics, and clinical and laboratory findings at presentation

	All (n = 37)	Adults (n = 29)	Children (n = 8)
Age (years), mean ± SD (range)	38.8 ± 21.2 (4.1-85.9)	45.7 ± 17.9 (17.6-85.9)	12.0 ± 4.3 (4.1-15.4)
Gender: Female (%)	21 (57)	17 (59)	4 (50)
Affected ear			
Left (%)	21 (57)	18 (62)	3 (37)
Right (%)	14 (38)	9 (31)	5 (62)
Both (%)	2 (5)	2 (6)	0 (0)
Acute otitis media (%)	23 (62)	19 (66)	4 (50)
Acute mastoiditis (%)	14 (38)	10 (34)	4 (50)
Delay to GP (days), mean ± SD (range)	1.3 ± 2.0 (0–10)	1.4 ± 2.1 (0-10)	0.8 ± 1.0 (0-3)
Delay to hospital (d)	4.0 ± 4.2 (0-20)	3.9 ± 4.4 (0-20)	4.3 ± 2.9 (1-10)
Previous ear condition (%)			
RAOM	7 (19)	3 (10)	4 (50)
SOM	0 (0)	0 (0)	0 (0)
COM	0 (0)	0 (0)	0 (0)
Previously operated ear	0 (0)	0 (0)	0 (0)
Signs and symptoms (%)			
TM perforation and discharge	25 (68)	18 (62)	7 (87)
Retroauricular pain	7 (19)	3 (10)	4 (50)
Retroauricular erythema	8 (22)	0 (0)	8 (100)
Protruding ear	1 (3)	0 (0)	1 (12)
Retroauricular swelling	1 (3)	0 (0)	1 (12)
Fever	16 (43)	12 (41)	4 (50)
Vertigo	16 (43)	14 (48)	2 (25)
Nystagmus	7 (19)	7 (24)	0 (0)
Facial nerve paresis	2 (5)	2 (6)	0 (0)
Laboratory findings			
CRP (mg/L) mean ± SD (range)	117 ± 91 (3-341)	119 ± 93 (3–341)	107 ± 87 (4-234)
Leukocytes 10^9/L	11.8 ± 3.5 (5.4-19.7)	10.9 ± 3.1 (5.4-17.1)	13.2 ± 4.3 (6.1-18.7)
GAS positive ear discharge	37(100)	29 (100)	8 (100)
GAS culture pos, n = 37 taken (%)	30 (81)	22 (76)	8 (100)
RST pos, n = 30 taken (%)	29 (97)	21 (95)	8 (100)
Blood culture taken (%)	4 (11)	3 (10)	1 (12)
Blood culture positive GAS (%)	2 (5)	2 (7)	0 (0)

Note: Children 0 to <16 years old.
Abbreviations: COM, chronic otitis media; GAS, group A beta-hemolytic streptococcus; GP, general practitioner; RAOM, recurrent acute otitis media; RST, rapid strep test; SOM, serous otitis media; TM, tympanic membrane.

department, although our patients with AOM/AM only rarely had bacteremia (Figure 1 and Table 1).[31]

3.2 | Patient demographics

The cohort included 37 patients requiring inpatient care. The majority (78%) were adults (Table 1). None of the patients had COM and none had undergone previous ear surgery (except for possible grommets for treatment of earlier ear disease). Seven patients (19%; three adults and four children) had a history of RAOM.

3.3 | Findings at presentation

Time from the onset of any ear symptom suggestive of infection to the first doctor's appointment was usually short, 1.3 ± 2.0 (mean ± SD) days (Table 1). Time from the symptom onset to hospitalization was 4.0 ± 4.2 days. Ten (27%) patients were hospitalized less than 24 hours from the onset of symptoms, demonstrating the very rapid progress of the disease in many cases. The majority (68%) had TM perforation and discharge. Based on clinical judgment, 23 (62%) had AOM and 14 (38%) AM. One elderly patient had an intracranial abscess as a complication of mastoiditis.

Blood culture was taken from four (11%) patients (three adults and one children) and was GAS positive for two (5%) adult patients. Bacterial culture was taken from the ear discharge of all patients at presentation. Thirty samples (81%) were GAS positive (22/29 adults and 8/8 children). The RST was taken at presentation from 30 patients (22 adults and 8 children), and was positive in all but one adult, who had a positive GAS in bacterial culture from ear discharge (Tables 1 and 2).

3.4 | Treatment

Hospital treatment algorithm was followed (Table 3). Four adult patients had a large TM perforation as a result of the current infection, and thus did not need additional ventilation provided by the grommet. None had confirmed or suspected perforation prior to the current infection. During their hospital stay, six (16%) patients needed tympanomastoidectomy due to the infection being refractory to conservative treatment. Four of the six tympanomastoidectomies were performed within 24 hours of hospitalization. Two of the six patients experienced mastoidectomy on the third and fourth days of treatment due to increased pain. AOM patients were hospitalized on average for 3.8 ± 1.9 (range, 1-8) days. AM patients were hospitalized on average for 7.0 ± 3.4 (3-12) days (without tympanomastoidectomy) or 7.2 ± 4.8 (3-15) days (with tympanomastoidectomy). There were no differences in the length of hospital stay between adults and children.

TABLE 2 Comparison of group A beta-hemolytic streptococcus (GAS) bacterial culture and rapid strep test (RST) results from ear discharge

n = 37	Culture positive	Culture negative
RST positive	29	7
RST negative	1	0
RST not taken	7	0

Note: Bacterial culture was taken from all 37 patients.

3.5 | Audiological findings at presentation

Two patients were known to have moderate SNHL (PTA ≥ 50 dB HL) before GAS infection. The other patients' hearing had not been examined prior to infection or it was potentially tested as part of national screening studies (school, military service, and occupational), but no previous hearing loss was reported.

Audiological findings within 1 day of hospital arrival are presented in Figure 2. There was considerable variation between individuals in AC thresholds. In most cases, higher frequencies were more affected than low and mid frequencies. At presentation, the PTA_{air} was 50.3 ± 19.4 dB HL. The findings in AC thresholds are not surprising, as middle ear secretion and TM perforation are known to cause conductive hearing loss (CHL). However, our main interest was in the possible SNHL. Individual minimum AC/BC thresholds are shown in Figure 2B. At presentation, the PTA_{min} was 28.3 ± 15.4 dB

TABLE 3 Treatments given and length of hospital stay

	In total (n = 37)	Adults (n = 29)	Children (n = 8)
Intravenous antibiotics (%)	37 (100)	29 (100)	8 (100)
Benzylpenicillin and clindamycin	20 (54)	18 (62)	2 (25)
Benzylpenicillin	2 (5)	0 (0)	2 (25)
Cefuroxime	10 (27)	7 (24)	3 (36)
Cefuroxime and clindamycin	3 (8)	2 (7)	1 (13)
Ceftriaxone	1 (3)	1 (3)	0 (0)
Piperacillin/tazobactam	1 (3)	1 (3)	0 (0)
Local antibiotic/corticosteroid drops	37 (100)	29 (100)	8 (100)
Systemic corticosteroid	33 (89)	26 (89)	7 (87)
Temporal bone CT taken	13 (35)	12 (41)	1 (13)
MRI taken	1 (3)	1 (3)	0 (0)
Tympanostomy tubes at arrival	33 (89)	25 (86)	8 (100)
Mastoidectomy during hospital stay	6 (16)	5 (17)	1 (12)
Later mastoidectomy	1 (3)	1 (3)	0
Length of hospital stay (d)			
AOM, mean ± SD (range)	3.8 ± 1.9 (1–8)	3.8 ± 1.8 (1–8)	3.9 ± 2.2 (1–8)
AM without mastoidectomy	7.0 ± 3.4 (3–12)	7.0 ± 3.4 (3-12)	-
AM, with mastoidectomy	7.2 ± 4.8 (3-15)	7.5 ± 5.4 (3-15)	6 (n = 1)

Note: The presented antibiotic treatment is based on use ≥50% of the time spent on the ward. Length of hospital stay, mean ± SD (range). Children 0 to <16 years old.

Abbreviations: AOM, acute otitis media; AM, acute mastoiditis; CT, computed tomography; Mastoidectomy, tympanomastoidectomy.

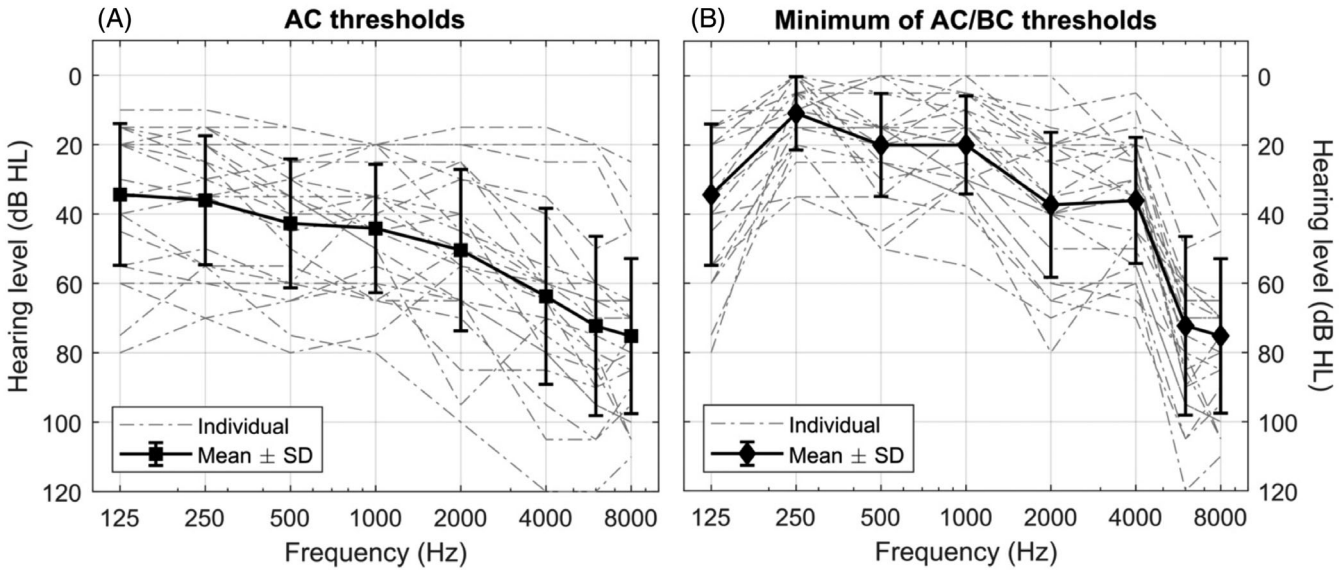

FIGURE 2 Audiological findings at presentation. (A) Air conduction. (B) Minimum of air and bone conduction thresholds

TABLE 4 Change of minimum of AC/BC thresholds at different frequencies and PTA_{min} from hospital entry to follow-up visit (% of patients)

%, n = 24 Hz	125	250	500	1000	2000	4000	6000	8000	PTA_{min}
Normal at presentation and after follow-up	46	79	58	58	33	25	8	0	42
Normalized	25	13	29	25	50	38	42	42	38
Improvement	21	0	0	4	17	21	46	50	13
No improvement	4	0	8	8	0	13	4	8	8
Worsened	4	8	4	4	0	4	0	0	0

Note: Normal threshold; ≤20 dB HL. Improvement; ≥10 dB change during follow-up (≥5 dB for PTA_{min}).

HL. Fourteen (58%) patients had SNHL within our criterion (PTA_{min} > 20 dB HL, Figure 2B, Table 4). At 4 kHz, 22 (92%) patients had elevated (>20 dB HL) AC thresholds and the mean AC threshold was 63.8 ± 25.4 dB HL. At 4 kHz, 18 (75%) patients had elevated minimum AC/BC thresholds indicating SNHL, and the mean of minimum of AC/BC thresholds was 36.0 ± 18.2. These results suggest that the conductive component of the hearing loss was on average 27.7 dB HL at 4 kHz. At 6 and 8 kHz, the BC thresholds were unavailable, but the means of AC thresholds were 72.3 ± 25.8 and 75.2 ± 22.3 dB HL, respectively. If we suggest that the CHL component stays at the same level at these higher frequencies as it does at 4 kHz, it may be assumed that BC would average 45 dB HL at these higher frequencies.

3.6 | Outcome

One patient (81 years old) died of GAS sepsis and multi-organ failure at day 3 of the treatment. All other patients survived, having a mean follow-up of 83 ± 72 (8-229) days. After follow-up, all patients had recovered from vertigo, nystagmus, facial paresis, and retroauricular pain. None of the patients had recurrent AOM/AM. One adult, who had undergone tympanomastoidectomy during the hospital stay, developed COM and needed a revision tympanomastoidectomy. One child was diagnosed with otitis media with effusion during the follow-up visit (grommet was blocked).

The audiometric results after follow-up (mean 103 ± 69 [29-229] days, n = 24) are presented in Figure 3 and Table 4. During follow-up, both AC and minimum of AC/BC thresholds recovered markedly. The positive changes were more pronounced in the higher frequencies, where the original hearing loss had been more profound. The average improvement in AC thresholds at all frequencies was 30.2 ± 13.9 dB HL ($P < .001$), where statistically significant improvement occurred in all frequencies but 125 Hz. The average improvement at all frequencies in minimum of AC/BC thresholds was 19.1 ± 10.3 dB HL ($P < .0001$), the difference being statistically significant in frequencies between 2 and 8 kHz.

After follow-up, PTA_{air} was 18.0 ± 13.6 dB HL, and the improvement from presentation was 32.3 ± 14.8 dB HL ($P < .001$; Figure 3A). After follow-up, PTA_{min} was 13.7 ± 10.8 dB HL (Figure 3C), which had improved on average by 14.6 ± 11.8 dB HL ($P < .0001$) from presentation. Altogether, these results demonstrate that the original measured 36 dB SNHL at 4 kHz as well as the estimated 45 dB SNHL at 6 and 8 Hz were in most cases reversible (Table 4).

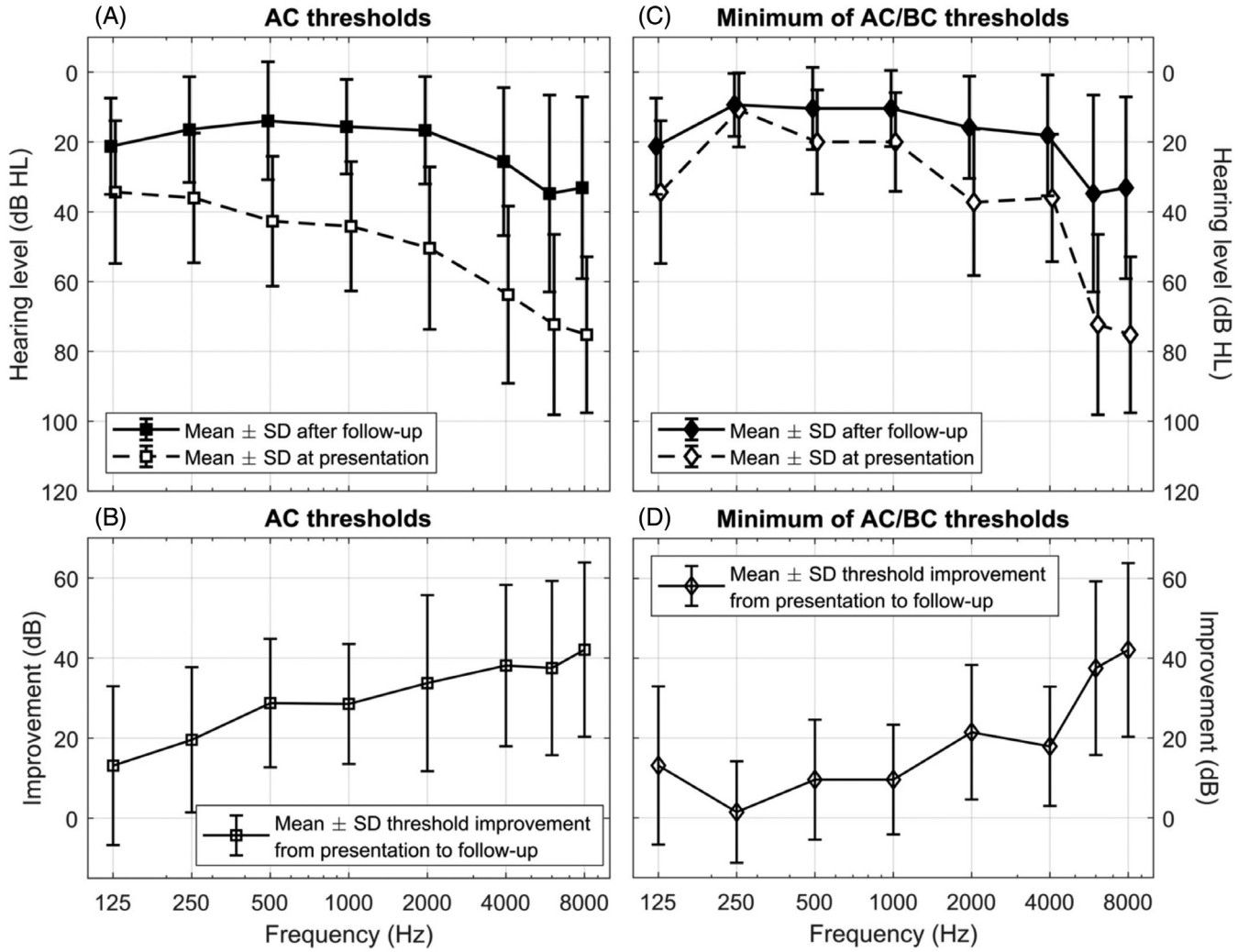

FIGURE 3 Audiological findings after follow-up. (A) Mean air conduction (AC) values at presentation and after follow-up. (B) Change in air conduction from baseline to follow-up. (C) Mean minimum of AC/BC thresholds at presentation and after follow-up. (D) Change in minimum of AC/BC thresholds from baseline to follow-up. BC, bone conduction

To find out the long-term impact of GAS AOM/AM on the HRQoL, 22 patients were sent EOS-16 and 15D questionnaires. Thirteen patients (59%) returned the questionnaires with a mean follow-up time of 2.3 ± 0.38 (1.9-3.0) years. The maximum handicap score in EOS-16 is 64. The mean score in our patients was 12.6 ± 13.7 (0-44). Three patients (23%) had EOS-16 scores 20 or above, which describes significant impairment in quality of life. One patient, who developed COM during the follow-up, scored 37 in EOS-16. Two patients with no objective residual symptoms other than SNHL, scored 44 and 20 in EOS-16. The generic 15D score was 0.94 ± 0.05 (0.83-1.0), where 1 means asymptomatic condition and 0 worst possible QoL.

4 | DISCUSSION

An exceptionally high incidence of GAS AOM/AM was observed in Finland during 2017 and 2018. At the same time, the number of GAS bacteremia cases increased significantly, as the *emm1* type emerged predominantly.[31,32] Epidemiology shows that GAS AOM/AM cases usually increase in 7 to 8-year periods[5,24] (Figure 1). The last epidemic, with 37 cases treated in a single institution with uniform clinical guidelines of care, offered an exceptional opportunity to characterize severe GAS AOM/AM and its outcome.

The leading clinical signs of GAS AOM/AM are ear pain, discharge, and rapid overall progression. This is rather atypical for AOM/AM caused by other causative agents, where the disease progression usually takes longer, with the possible exception of *S. pneumonia* infections.[21,28] In the most typical case, GAS AOM/AM presents in a previously healthy ear of a healthy person (Table 1). Although the outcomes of patients in this study were quite good, development of permanent severe SNHL or deafness remains possible, especially with insufficient treatment.

The causative agents of AOM leading to complications differ significantly between countries. In Finland, *S. pneumoniae* and GAS are

the most common findings in complicated situations,[20,21] whereas in Brazil, Pneumococcus, Haemophilus, and Staphylococcus species were the most common microorganisms in AOM with complications.[33] However, despite the health care resources in the country of residence, AOM/AM can still be disabling and fatal worldwide.[16]

We tested the use of RST to analyze samples from middle ear effusion, although the use of RST by manufacturer is limited to pharyngeal sampling. In our series, bacterial culture was taken from every inpatient. In seven cases, RST was positive despite culture resulting in "no growth." All of these seven cases had ongoing oral antibiotic treatment at the time of the microbiological sample, possibly explaining the findings. On the other hand, only one patient was RST negative, whereas the bacterial culture was positive for GAS. We consider the RST a very promising tool in rapid diagnostics.[34,35] RST is easy-to-use, non-invasive, and quick. We, however, acknowledge that more information is needed to verify the reliability of RST in the context of middle ear GAS infections. The off label use of RST has been reported in vaginal samples,[36] but to our knowledge, it has not been reported in the context of ear discharge previously.

During the GAS epidemic between 2017 and 2018, treatment algorithm was used in GAS AOM/AM: most patients received a tympanostomy tube or had large TM perforation at arrival; intravenous antimicrobial medication, primarily penicillin, when the pathogen (GAS) was confirmed and addition of clindamycin for more severe cases; systemic corticosteroid (methylprednisolone); and eardrops (corticosteroid and ciprofloxacin). The typical course of disease, with this treatment, was as follows: The infection usually started to resolve within the first couple of days; the infection subsided, the purulent secretion stopped, but abundant pulsating serous secretion continued. Next, the ear pain was reduced, vertigo reduced, and possible mastoid pain relieved. With ear secretion clearly diminishing, the patient could be discharged. However, the disease was refractory to this conservative treatment regimen in 16% of patients, who needed tympanomastoidectomy to recover. Whether or not the tympanomastoidectomy was performed had no effect on the time of hospitalization.[20,21] Patients without mastoiditis had a shorter hospitalization period. In previous publications, there are no major differences in AOM/AM hospitalization times between different pathogens, but the hospitalization for *S. pneumoniae* was the longest.[21]

The patients' hearing recovery was unexpectedly good, considering the SNHL at presentation (Figures 2 and 3; Table 4). Although most patients reported being relatively asymptomatic at their follow-up visit, they did have some residual symptoms as measured by the EOS-16 after 1.5 to 3 years. Although only two patients had no improvement at all in the 3-months follow-up, 79% of the patients had normal hearing after follow-up. One explanation of the SNHL reversibility might be vasospasm caused by inflammation. Vasospasm in turn may cause temporary hair cell dysfunction secondary to temporary ischemia instead of hair cell loss.[37] If inflammation is relieved soon enough, hair cell function may recover. Alternatively, it is possible that direct irritation of the oval and round window membrane with cytokines or other inflammation mediators leads to temporary SNHL. The fact that the higher frequencies located at the basal part of cochlea are usually the most affected supports this hypothesis of local inflammation. In this hypothesis, the transient hair cell dysfunction would be restored when inflammation is relieved.[38]

5 | CONCLUSIONS

Severe GAS AOM/AM typically has a very rapid onset with severe symptoms. Hearing loss is common and most often includes a sensorineural component. However, the hearing loss is usually reversible. RSTs seem to be useful in detecting GAS in middle ear discharge. Despite the rapid onset and initial aggressive behavior of GAS AOM/AM, its outcome with the current treatment is usually satisfactory.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

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How to cite this article: Laakso JT, Rissanen V, Ruotsalainen E, et al. Severe acute otitis media and mastoiditis caused by group A beta-hemolytic streptococcus. *Laryngoscope Investigative Otolaryngology*. 2021;6(5): 1158-1166. doi:10.1002/lio2.659