Infective Endocarditis Presenting as Endogenous Endophthalmitis Secondary to *Streptococcus agalactiae* in a Healthy Adult: Case Report and Literature Review

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Endogenous endophthalmitis secondary to group B *Streptococcus* (GBS) is extremely rare, particularly in healthy adults. However, the visual prognosis is poor. We report the first South Korean case of GBS infective endocarditis presenting as endogenous endophthalmitis and skin and soft tissue infection. Cultures of blood, vitreous humor, and pus from skin aspirates yielded a penicillin-susceptible serotype V strain of *Streptococcus agalactiae*. After 6 weeks, the patient completely recovered from GBS infective endocarditis. However, despite early antibiotic treatment and early surgical intervention, the patient’s right eye developed phthisis bulbi and was a candidate for evisceration.

Key Words: *Streptococcus agalactiae*; Endophthalmitis; Endocarditis

**Introduction**

*Streptococcus agalactiae*, a group B *Streptococcus* (GBS), is part of the normal flora of the skin, throat, lower gastrointestinal tract, and female genital tract. It is recognized as a major human pathogen in neonatal sepsis and postpartum infection. However, the incidence of invasive infection by *S. agalactiae* has increased in recent years in non-pregnant adult patients, elderly patients, and patients with chronic immunosuppressive diseases [1]. In particular, GBS endogenous endophthalmitis is an extremely rare but visually devastating disease [2-4]. The clinical profile of GBS endophthalmitis is not well characterized because little literature is available. Here, we report the first South Korean case without evidence of immunosuppression, presenting as endophthalmitis complicating GBS infective endocarditis. Furthermore, we de-
Table 1. Clinical characteristics and treatment outcomes of 22 cases of endogenous endophthalmitis due to *Streptococcus agalactiae*

| Ref | Country | Sex/age | Predisposing illness | Infection source | Other sites of infection | Time to eye signs | Laterality & visual acuity | Type of endophthalmitis | Culture (B/V) | Other culture-positive sites | Vitrectomy | Intravitreal antibiotics | Systemic antibiotics | Visual outcome | Sero-type |
|-----|---------|---------|----------------------|------------------|------------------------|-------------------|--------------------------|-------------------------|----------------|-----------------------------|------------|---------------------------|------------------|------------------|---------|
| [2] Malaysia | M/55 | None | Foot abscess | Septic arthritis | 2 weeks | OD-LP | Diffuse | +/− | Foot abscess | + | Vancomycin, gentamicin | Vancomycin, penicillin | Phthisis bulbi |
| [2] China | M/67 | None | Cervical epidural abscess | Septic arthritis | 1 week | OD-CF | Posterior | +/+ | | | | | |
| [2] China | M/53 | DM | Septic arthritis | Septic arthritis | 5 days | OD-LP | Diffuse | +/+ | Knee synovial aspirate | − | Vancomycin, ceftazidime | Penicillin, gentamicin | Evisceration |
| [2] China | M/82 | DM | Unknown | Septic arthritis | Concurrent | OD-NLP | Diffuse | +/+ | | | | | |
| [2] China | F/63 | None | Unknown | Septic arthritis | 2 days | OD-LP | Diffuse | +/+ | | | | | |
| [3] USA | M/42 | Congenital heart disease | Pharyngitis | Infective endocarditis | 10 days | OD-LP | Posterior | +/NA | | | | | |
| [4] Canada | F/80 | AE, HTN, Knee prosthesis | Unknown | Infective endocarditis, meningitis | 12 hours | OS-LP | Diffuse | +/+ | CSF | − | NA | NA | Died |
| [9] Japan | M/83 | None | Pneumonia | None | 4 days | OD-LP, OS-NLP | Posterior | −/+ | Aqueous | − | NA | Cefazidime | Enucleated |
| [10] UK | M/55 | Renal calculi, multiple myeloma | UTI | Septic arthritis | Concurrent | OD-HM, OS-6/36 | Posterior, diffuse | +/+ | Aqueous | − | Cefuroxime | Amoxicillin, gentamicin | LP, 6/6 Ib |
| [10] UK | F/76 | None | UTI | Pneumonia | 2 days | OD-LP, OS-NLP | OS-Pan | +/NA | Urine, conjunctiva | − | NA | Benzylpenicillin, gentamicin, acyclovir | LP, NLP Ib/c |
| [10] UK | M/65 | DM | Septic arthritis | Infective endocarditis | Concurrent | OD-LP, OS-6/5 | OD-Posterior diffuse, OS-Focal | +/+ | Knee aspirate | − | Cefuroxime | Amoxicillin, gentamicin, Benzylpenicillin | Phthisis bulbi, 6/5 |
| Ref | Country | Sex/age | Predisposing illness | Infection source | Other sites of infection | Time to eye signs | Laterality & visual acuity | Type of endophthalmitis | Culture (B/V) | Other culture-positive sites | Vitrectomy | Intravitreal antibiotics | Systemic antibiotics | Visual outcome | Sero-type |
|-----|---------|---------|----------------------|-----------------|-------------------------|-----------------|-------------------------|--------------------------|--------------|---------------------------|-----------|--------------------------|-------------------|----------------|---------|
| [10] | UK | M/60 | None | Pharyngitis | Septic arthritis | Concurrent | OS-6/60 | Pan | +/NA | NA | Benzylpenicillin, gentamicin | Evisceration | IA/c |
| [11] | China | F/95 | None | Pneumonia | None | 3 days | OS-NLP | Diffuse | +/NA | + | Vancomycin, cefazidime | Ampicillin / sulbactam, vancomycin | OU-NLP |
| [12] | UK | F/70 | None | Unknown | Septic arthritis | 4 days | OD-6/18, OS-6/36 | NA | +/NA | Synovial aspirate | NA | Benzylpenicillin | OU-Recovery | V |
| [13] | Canada | F/74 | None | Cellulitis, Chronic foot ulcer | None | 2 days | OS-LP | Posterior | NA/+ | Foot ulcer pus | + | Vancomycin, amikacin | Cefazolin, gentamicin | Phthisis bulbi |
| [14] | USA | F/62 | DM, HTN | Cellulitis | None | 1 week | OD-20/70, OS-LP | Diffuse | +/+ | Foot tissue | - | Vancomycin, amikacin | Penicillin G | LP, 20/100 |
| [14] | USA | M/48 | HIV, Splenectomy | Meningitis | None | 2 day | OD-CF | Pan | +/NA | CSF | Penicillin G | NLP |
| [15] | USA | F/75 | None | Septic arthritis | Infected endocarditis | 20 days | OD-20/70 | Posterior | +/NA | Urine | - | NA | Vancomycin, ceftriaxone, Clindamycin | NA |
| [16] | USA | M/56 | Leukemia | Unknown | None | 3 days | OD-LP | Diffuse | +/+ | Aqueous | + | Vancomycin, amikacin | Vancomycin, clindamycin, Cefotaxime | LP |
| [17] | USA | F/81 | HTN | UTI | None | 3 days | OD-20/400 | Diffuse | +/+ | + | Vancomycin | Vancomycin, amikacin, amphotericin | 20/200 |
| [18] | USA | F/61 | DM, HTN, MI | Endarteritis | Septic arthritis | 12 days | OD-Not stated, OD-Anterior, focal OS-Diffuse | +/+ | Synovial aspirate | + | NA | Penicillin | OS-NLP |
| Present case | Korea | F/43 | None | Cellulitis | Infected endocarditis | 2 weeks | OD-20/100 | Pan | +/+ | Pus of hip abscess | + | Vancomycin, cefazidime | Ceftriaxone, gentamicin, ampicillin | Phthisis bulbi |

Ref, reference; B, blood culture; V, vitreous culture; M, male; OS, left eye; LP, perception of light; CF, counting fingers; DM, diabetes mellitus; OD, right eye; NLP, no perception of light; F, female; NA, not applicable; AF, atrial fibrillation; HTN, hypertension; CSF, cerebrospinal fluid; UTI, urinary tract infection; HM, hand motion; OU, both eye; HIV, human immunodeficiency virus; MI, myocardial infarction.
scribe the clinical, prognostic, and therapeutic characteristics of 22 patients with this infection in the literature.

**Case Report**

A previously healthy 43-year-old woman visited our emergency room complaining of a 10-hour history of decreased visual acuity with ocular pain in the right eye. She was taking oral antibiotics (cefadroxil) for a skin abscess of the right buttock area, which developed 2 weeks earlier. She also underwent dental scaling 3 months earlier. She underwent a bilateral laser in-situ keratomileusis (LASIK) procedure 10 years earlier, and her final corrected visual acuity was 20/20 in both eyes.

On admission, she had a blood pressure of 120/60 mmHg, heart rate of 88 beats/min, body temperature of 37.9°C, and respiratory rate of 20/min. Physical examination did not reveal a cardiac murmur. No Osler’s nodes, Janeway lesions, or splinter hemorrhages were observed. There was a 3-cm skin swelling with purulent discharge on the right buttock area that was tender and erythematous. The results of the initial laboratory investigations were normal, except for a leukocyte count of 13.9 × 10^9/mm^3, with 74% neutrophils and a C-reactive protein level of 26.7 mg/dL. Ophthalmic examination revealed an initial visual acuity of 20/100 and 20/20 in the right and left eye, respectively. There was full ocular motility. Slit-lamp examination showed severe conjunctival injection and chemosis, total corneal epithelial defect, corneal edema, and keratin precipitate on the corneal endothelium. The anterior chamber was poorly visible because of keratin precipitate and intense fibrinous reaction. Intraocular pressure was 25 and 10 mmHg using Goldman applanation tonometry. The right fundus was poorly visible, and ultrasonography revealed the presence of vitritis. The results of external, slit-lamp, and fundus examinations of the left eye were normal. Clinical samples of blood, the aqueous humor of the right eye, and discharge from the buttock lesion were obtained on admission. Gram-positive cocci in chains was cultured from all of these samples, and the patient was diagnosed with endogenous endophthalmitis of the right eye as well as a skin and soft tissue infection on the right buttock secondary to streptococcal sepsis. Initial transthoracic echocardiography was normal. For the first 12 days of hospitalization, before infective endocarditis was confirmed, intravenous ceftriaxone (2 g/day) was prescribed as an empirical and definite antibiotic therapy with a regimen of intravitreal vancomycin (1 mg/0.1 mL) and ceftazidime (2.25 mg/0.1 mL).

Despite intravitreal vancomycin and ceftazidime injection, her visual acuity rapidly deteriorated to light perception within a day. On the third day of hospitalization, she underwent right core vitrectomy, which revealed a pus-filled vitreous cavity. Culture of the vitreous humor was performed. Group B β-hemolytic streptococci (S. agalactiae) was identified as the causative organism in the vitreous specimen, blood, and skin pus of the right buttock, using a VITEK II system (bioMérieux, Hazelwood, MO, USA), with a probability of 99.0%. The GBS was highly susceptible to penicillin, vancomycin, and cephalosporins according to the Clinical Laboratory Standards Institute (CLSI) guidelines. Ten days after initial transthoracic echocardiography, transesophageal echocardiography revealed a 5-mm vegetation to the anterior mitral leaflet. The patient was finally diagnosed with an invasive GBS infection with infective endocarditis presenting with endogenous endophthalmitis and a skin and soft tissue infection. A MicroScan MICROSTREP plus panel was used to determine antimicrobial susceptibility and measure minimum inhibitory concentrations. The results showed susceptibility to penicillin (0.06 μg/mL), ampicillin (0.12 μg/mL), ceftriaxone (0.25 μg/mL), ceftaxime (0.25 μg/mL), cefepime (0.25 μg/mL), meropenem (0.12 μg/mL), azithromycin (0.25 μg/mL), clindamycin (0.06 μg/mL), vancomycin (0.5 μg/mL), and levofloxacin (0.5 μg/mL). To further confirm the identity of this isolate, sequencing of a 438-base pair 16S rRNA gene fragment according to CLSI recommendations revealed a 97% identity match to S. agalactiae strain sequence type 1 (SS1) associated with serotype V (accession number: CP010867.1). According to the clinical guidelines under the clinical diagnosis of infective endocarditis, intravenous ampicillin (3 g q6 hrs) and gentamicin (5.1 mg/kg q24 hrs) were administered for 28 and 14 days, respectively, with intravitreal antibiotic therapy [5]. The patient was discharged after completing the 28-day intravenous ampicillin treatment. At the 6-month follow-up visit after the completion of antibiotic therapy, the patient remained free of complications from infective endocarditis or skin and soft tissue infection. She had no infectious signs on her right eye but had lost perception to light, and phthisis bulbi had developed.

**Discussion**

Endophthalmitis is defined as an internal infection of the eye involving the vitreous or aqueous humor that can be classified as either endogenous or exogenous depending on the route of infection. Exogenous bacterial endophthalmitis oc-
Endogenous endophthalmitis caused by GBS is very rare in non-pregnant adults, accounting for only 5.2% of bacterial endogenous endophthalmitis cases, only 21 of which have been reported in the literature worldwide [2, 9-19]. In contrast to the present case, 18 (85.7%) of these 21 cases had predisposing factors such as old age, diabetes mellitus, cardiac diseases, malignant diseases, and immunosuppression (Table 1). Including the present case, the most common septic focus was skin and soft tissue infection (n = 5, 22.7%) followed by septic arthritis (n = 3; 13.6%), urinary tract infection (n = 3; 13.6%), central nervous system infection (n = 2; 9.0%), pharyngitis (n = 2; 9.0%), pneumonia (n = 2; 9.0%), or no evident foci of infection (n = 5; 22.7%). Among them, 5 (18.1%) cases exhibited infective endocarditis, but none exhibited vegetation in the initial transthoracic echocardiography. The present case exhibited cardiac vegetation in the transesophageal echocardiography 7 days after the initial transthoracic echocardiography. Therefore, transesophageal echocardiography should be recommended for patients with endogenous endophthalmitis caused by GBS. Septic arthritis (n = 10, 45.4%) was one of the most common manifestations in previously reported cases of endophthalmitis secondary to GBS; this may be because of the role of the synovial space and vitreous humor as culture media for facilitating bacterial seeding, entrapment, and proliferation [11].

Previous cases of endophthalmitis secondary to GBS exhibited dramatic loss of vision within a few hours to a few days; this rapid progression is associated with the virulence of GBS. Hemolytin and cytolysin produced by GBS may result in the development of the necrotic vitreous cavity, total retinal detachment, and microabscesses on the choroid [2]; this eventually leads to poor visual prognosis despite prompt antibiotic therapy and surgical intervention such as in the present case. S. agalactiae is classified as serotype Ia/c, Ia/b, II, III, IV, V, VI, VII, or VIII. GBS serotypes Ia, III, and V account for more than two-thirds of cases [20]. The present patient had serotype V, which accounts for >25% of cases of invasive GBS infection [20].

The most important component in the treatment of endogenous endophthalmitis caused by GBS is prompt and appropriate systemic antibiotic therapy. Unlike exogenous endophthalmitis with a relatively intact blood–ocular barrier, endogenous endophthalmitis has a disrupted barrier due to the transmural passage of the hematogenously spreading organism [19]. Consequently, intravenous antibiotics can easily reach the ocular tissue with endogenous endophthalmitis and the primary infection site. On the contrary, intravitreal antibiotic injection has not been shown to be an effective treatment for endogenous endophthalmitis. However, it may be reasonable to select intravitreal antibiotics on a case-by-case basis, because the existing negative perception could be a consequence of selection bias [19]. Therapeutic vitrectomy can be 3 times more beneficial in retaining useful vision and decreasing the requirement of evisceration or enucleation [19]. However, the advantages of vitrectomy can be limited, because GBS causes rapid and extensive destruction of ocular structure in the early stage of infection, such as in the present case. In the literature, of the 9 eyes that underwent vitrectomy, 7 developed phthisis bulbi and loss of light perception. Although most patients recovered from GBS sepsis (except 2 cases of death; fatality rate: 9.0%), the visual outcome is poor in most patients. Among 30 cases, 22 involved the eyes, in
which only 7 eyes recovered useful vision while the others had either only light perception or no light perception and phthisis bulbi.

In conclusion, the present case suggests GBS infections should be included in the differential diagnosis of endogenous endophthalmitis in healthy adults. The present case also highlights the requirement of a high index of suspicion for infective endocarditis in patients despite normal results from initial transthoracic echocardiography. Aggressive antibiotics and surgical therapy may be needed in these cases because of rapid and extensive ocular destruction in the early stage of infection.

Conflicts of Interest
No conflicts of interest.

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