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CASE REPORT

# Diagnosis of Neurological Involvement Caused by *Streptococcus dysgalactiae*: A Case Report and Review of the Literature

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**Purpose:** This study investigated the clinical relevance, pathogenic mechanisms, and neurological involvement of *Streptococcus dysgalactiae* subspecies *equisimilis* (*SDSE*) and subspecies *dysgalactiae* (*SDSD*), with a focus on a severe case of *SDSE* meningitis complicated by septic shock.

**Patients and Methods:** A systematic review of 19 cases of neurological infections caused by *S. dysgalactiae* (*SDSE* or *SDSD*) from 1971 to 2023 was conducted, supplemented by a detailed case report. Data on patient demographics, predisposing factors, clinical manifestations, diagnostic procedures, treatment, and outcomes were analyzed.

**Results:** The reviewed cases involved 12 patients with *SDSE* and seven with *SDSD*. The median age was 53 years, and most patients had underlying conditions such as diabetes, malignancy, or cardiovascular disease. Neurological manifestations were common, with meningitis being diagnosed in 17 patients. Despite prompt antibiotic therapy, six patients (32%) died, highlighting the severe nature of these infections.

**Conclusion:** *S. dysgalactiae* can cause severe neurological infections, particularly in immunocompromised patients. Early recognition and aggressive treatment are essential to improving outcomes. Advanced molecular diagnostic techniques, such as next-generation sequencing (NGS), are crucial in identifying and managing these infections.

**Keywords:** *Streptococcus dysgalactiae*, neurological involvement, case report, review

## Introduction

*Streptococcus dysgalactiae* is a significant pathogen with a complex classification history. In 1996, attempts were made to classify *S. dysgalactiae* into two subspecies based on their host origins: those isolated from animals and those from humans. *S. dysgalactiae* subspecies *dysgalactiae* (*SDSD*) primarily colonizes the upper respiratory tract and skin of animals but can also cause infections in humans. *S. dysgalactiae* subspecies *equisimilis* (*SDSE*) is commonly found in the upper respiratory tract and skin of horses and can infect humans, often causing pharyngitis, skin infections, and other invasive diseases.[1] In 1998, it was proposed to classify αhemolytic and non-hemolytic strains as *SDSD* and β-hemolytic strains as *SDSE*.[2]

*SDSE* is a pyogenic β-hemolytic streptococcus belonging to Lancefield groups A, C, G, or L.[3] *SDSE* shares the same ecological niche as group A and C streptococci, exhibiting considerable overlap in disease profiles and sharing some pathogenic factors, including M protein and extracellular enzymes like hemolysin.[4,5] *SDSD*, however, is distinct as it is

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exclusively αhemolytic and carries the Lancefield group C antigen.[6] The disease spectrum of *SDSE* includes pharyngitis, tonsillitis, skin and soft tissue infections such as wound infections and cellulitis, necrotizing fasciitis, streptococcal toxic shock syndrome, and severe conditions like sepsis, endocarditis, and meningitis.[7–11] Immune-mediated central nervous system manifestations, such as Sydenham's chorea and pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS), have also been reported.[12] *SDSD* infections in humans are exceedingly rare, leaving the clinical characteristics largely undefined.[13] Most patients with invasive *SDSE* or *SDSD* infections have underlying conditions such as diabetes mellitus, malignancy, cardiovascular disease, bone and joint diseases, or liver cirrhosis, suggesting that *S. dysgalactiae* generally has low pathogenic potential.[14] Nevertheless, the prevalence of invasive *SDSE* and *SDSD* infections has been increasing globally.[7–9,13] This article aims to delve deeper into the evolving understanding of *S. dysgalactiae*, particularly *SDSE*, highlighting its clinical relevance and pathogenic mechanisms.

# Materials and Methods

## Study Subject

Systematic searches were independently conducted by two reviewers (JZ and XQD) across multiple databases, including EBSCO, EMBASE, MEDLINE, Scopus, and Web of Science. The search terms utilized were "Streptococcus dysgalactiae", "S. dysgalactiae", "Streptococcus equi", 'Streptococcus equisimilis', "SDSE", "SDSD", 'group C Streptococcus', "GCS", "neurological", "meningitis", "brain abscess", "ventriculitis", and "CSF". Only case reports and case series were considered, with no restriction on the start date and a cut-off date of May 1, 2024. Studies were limited to English-language publications only involving human subjects. To ensure comprehensive retrieval of relevant studies, reference lists of included studies and pertinent review articles were further examined.

Eligibility criteria for patients included: 1) presence of neurological inflammation symptoms (eg, fever, dizziness, headache, meningeal irritation, altered mental status, or sensorimotor abnormality), with cerebrospinal fluid (CSF) culture or polymerase chain reaction (PCR) positive for SDSE or SDSD; or 2) minimal or atypical neurological symptoms or inflammatory signs, but with CSF findings indicative of bacterial neurological infection, and CSF culture or PCR positive for SDSE or SDSD.

## Study Methods

For cases with neurological involvement attributed to S. dysgalactiae (SDSE and SDSD), clinical, microbiologic, histopathologic, treatment, and outcome data were extracted from medical records reviewed by two investigators (JZ and XQD). Discrepancies were resolved through consensus or, if necessary, by consulting a third reviewer (HLS). For the patient in our case report, peripheral blood and cerebrospinal fluid were collected for diagnostic evaluation of the infectious pathogen and investigation of virulence factors. The analyses included culture, smear microscopy, PCR, antibiotic susceptibility testing, and next-generation sequencing (NGS). Data were summarized using descriptive statistics, and statistical significance was determined with a $p$-value threshold of $<0.05$. All analyses were performed using R version 4.2.1.

## Patient Informed Consent

The patient provided written informed consent before participating in this study. The study was conducted following the Declaration of Helsinki and approved by the Institutional Review Board (IRB) of Peking Union Medical Hospital (ethics number: S-K653). Before enrollment, the patient received a comprehensive explanation of the purpose, procedures, potential risks, and benefits of the study. All data collected were anonymized to ensure confidentiality.

## Consent for Publication Statement

Consent to publish the case report and associated data has been obtained from the legal representative of the patient. The legal representative has been fully informed about the nature of the publication and has granted consent on behalf of the patient. This consent included permission for the use of all clinical data and diagnostic results, including next-generation sequencing findings, as presented in the manuscript. All identifying information has been anonymized to protect the patient's privacy.

# Results

## Case Report

Here, we present a case of *SDSE* in a patient with meningitis complicated by septic shock. A 68-year-old male was admitted to the emergency department with a two-week history of fatigue, two days of shortness of breath, and altered consciousness for three hours. Two weeks prior, imaging at another hospital revealed pleural effusion and ascites, but no treatment was administered. His medical history included type 2 diabetes mellitus with diabetic retinopathy and foot ulcers for 20 years, hypertension, coronary artery disease, and congestive heart failure for the past seven years. The patient was non-compliant with his medications, allergic to penicillin, had a 40-year smoking history, and his younger brother also had type 2 diabetes.

Upon admission, his Glasgow Coma Scale (GCS) score was E3V1M3, heart rate 111 bpm, blood pressure 100/60 mmHg, respiratory rate 45 breaths/min, and temperature 38.8°C. Neurological examination revealed fixed-left pupils with sluggish light reflexes. Abdominal examination showed distention and tense muscles. The skin exhibited generalized crusted lesions and an ulcer on the right knee from trauma. Diabetic foot changes included multiple ulcers. Laboratory tests revealed blood lactate 8.0 mmol/L, blood glucose 10.0 mmol/L, blood ammonia 57 μmol/L, D-Dimer 5.26 mg/L FEU, high-sensitivity C-reactive protein (hsCRP) 96.90 mg/L, total bilirubin 68.2 μmol/L, direct bilirubin 45.9 μmol/L; cardiac enzymes included creatine kinase 226 U/L, NT-proBNP >35,000 pg/mL, myoglobin 607 μg/L, and high-sensitivity cardiac troponin I (hscTnI) 487 ng/L. The WBC count was 14.44 × 10^9/L with a neutrophil percentage of 90.5%. Abdominal CT showed ascites, while head CT was unremarkable.

The patient was promptly treated with intravenous fluid resuscitation, oxygen therapy, symptomatic support, abdominal paracentesis, diuretics, coronary vasodilators, and inotropic support. Despite these interventions, he remained unconscious with no change in his GCS score. Lumbar puncture revealed an opening pressure >300 $mmH_2O$, yellow and turbid CSF with a white blood cell count of 8358 × 10^9/L, CSF protein 17.25 g/L, CSF glucose <0.20 mmol/L, and CSF lactate 20.6 mmol/L. Acute purulent meningitis was suspected, and the patient was empirically treated with meropenem and vancomycin. Unfortunately, he died from septic shock two days later. After administering empirical therapy with meropenem and vancomycin at our hospital, the fever symptoms showed improvement, leading us to believe his condition was stabilizing. Based on the suggestion of his family, the decision was made to transfer the patient to another hospital. Unfortunately, that hospital lacked the necessary facilities for advanced care. The condition of this patient worsened rapidly to septic shock after the transfer, and despite the lumbar puncture results being pending, he passed away within a day. The delay in adjusting treatment based on lumbar puncture findings was due to the urgency of his deteriorating state.

CSF culture identified *β*-hemolytic streptococci (Figure 1A), and the smear showed Gram-positive cocci (Figure 1B). Susceptibility testing demonstrated sensitivity to linezolid, vancomycin, penicillin G, ampicillin, ceftriaxone, cefotaxime, cefepime, and chloramphenicol, with high sensitivity to penicillin G, ceftriaxone, vancomycin, and linezolid. To further investigate the rapid progression of the condition, NGS was performed, revealing it to be an ST267-type *SDSE*.

This specific sequence type has been reported only once globally, with the first case identified in Beijing in 2016.[15] Phylogenetic analysis and distribution of virulence genes, antibiotic resistance genes, and plasmid replicon were shown in Figure 2.

## Demographic Characteristics and Predisposing Factors

This study identified 19 cases of neurological involvement caused by *SDSE* and *SDSD* (Table 1). The cases span from 1971 to 2023, with seven cases reported between 1971 and 2000, and 12 cases between 2000 and 2023. There was no significant trend in the number of cases over time. Of the 19 patients, seven (37%) were male, and 12 (63%) were female, with a median age of 53 years (range from newborn to 85 years). Three patients (16%) were newborns or infants; five patients (26%) were under 40 years of age; four patients (21%) were aged 40 to 64 years; and seven patients (37%) were aged 65 years or older. Seven patients (37%) were infected with *SDSD*, while 12 patients (63%) were infected with *SDSE*. There were no significant differences in age or sex distribution between the *SDSD* and *SDSE* groups.

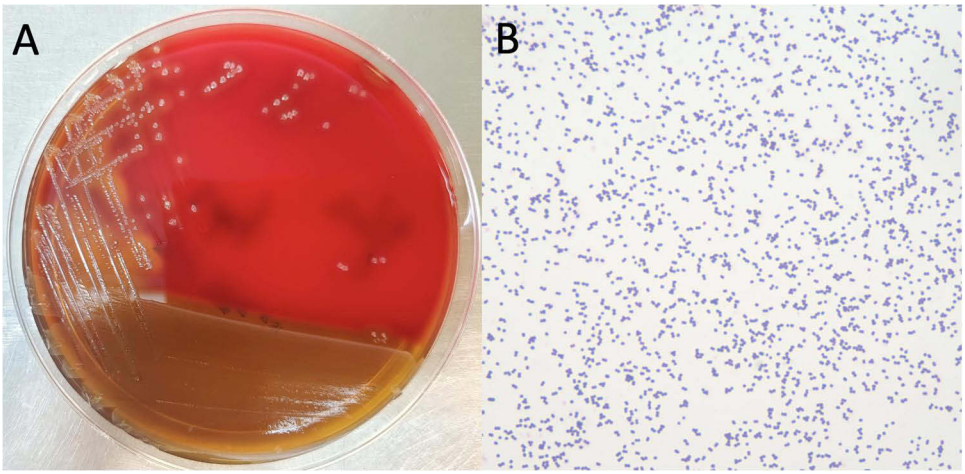


**Figure 1** The smear and culture results of the CSF of the patient. (**A**) Culture from CSF identified *β*-hemolytic streptococci. (**B**) CSF smear showed Gram-positive cocci.

Predisposing factors were reported in 18 patients (95%) (Table 1). Environmental exposure was noted in five patients: two resided in horse stables, one was a construction worker, one was a malt worker in a horse-contaminated environment, and one was a pregnant kindergarten teacher exposed to children with *SDSE* infections. Four patients had immunosuppressive conditions: two with alcoholic liver cirrhosis, one with congenital agranulocytosis, and one with chronic peripheral pancytopenia. Four patients were in the postoperative recovery period (eg, following gastrectomy), and three patients were newborns, including one premature infant, one with confirmed prenatal transmission of *SDSE*, and one healthy newborn. Two patients had implanted medical devices, with one patient having an intrathecal pump and one a pacemaker. Two patients were recovering from atrial fibrillation, and two had diabetes mellitus. Two patients had documented antecedent infections: one with streptococcal middle ear infection and one with streptococcal endocarditis. Notably, all three patients with horse-related exposure were infected with *SDSE*.

## Clinical Manifestations

Among the 16 patients who reported the time from onset to consultation, three neonates presented with symptoms immediately after birth and were referred for treatment following obstetric consultation. For the remaining patients, the median time from symptom onset to consultation was 3 days, with a range of 0 to 21 days (Table 1). Neurological or psychiatric symptoms were observed in 15 patients (79%), while signs of meningeal irritation were noted in five patients (26%). Fever was reported in 13 patients during the illness, six experienced headaches, and four presented with gastrointestinal symptoms such as nausea, abdominal pain, vomiting, diarrhea, and anorexia. The most common neurological and psychiatric symptoms included irritability, lethargy, confusion, seizures, ataxic gait, aphasia, visual or auditory disturbances, photophobia, incontinence, hemiplegia, hypoesthesia, and hyporeflexia. Meningeal signs primarily consisted of nuchal rigidity, with no patients exhibiting pathological signs such as Babinski's reflex. Ultimately, 17 patients (90%) were diagnosed with meningitis, three with brain abscess, three with ventriculitis, and one with cerebritis. Notably, four patients presented with multifocal infections. Complications were observed in eight patients (42%): four had bacteremia, one had rhabdomyolysis and endophthalmitis, one had pneumonia, one had multi-organ failure, and one presented with metabolic acidosis. In this review, we found that the initial symptoms of *SDSE* and *SDSD* are similar, with no significant differences in the incubation period or complication rates.

## Diagnostic Procedures

Most patients were diagnosed with bacterial infection upon admission. However, one patient was misdiagnosed with gastritis complicated by pneumonia, and another was initially diagnosed with urinary sepsis. Lumbar puncture was performed on all patients, whereas one had the procedure delayed due to ongoing anticoagulation therapy. Before

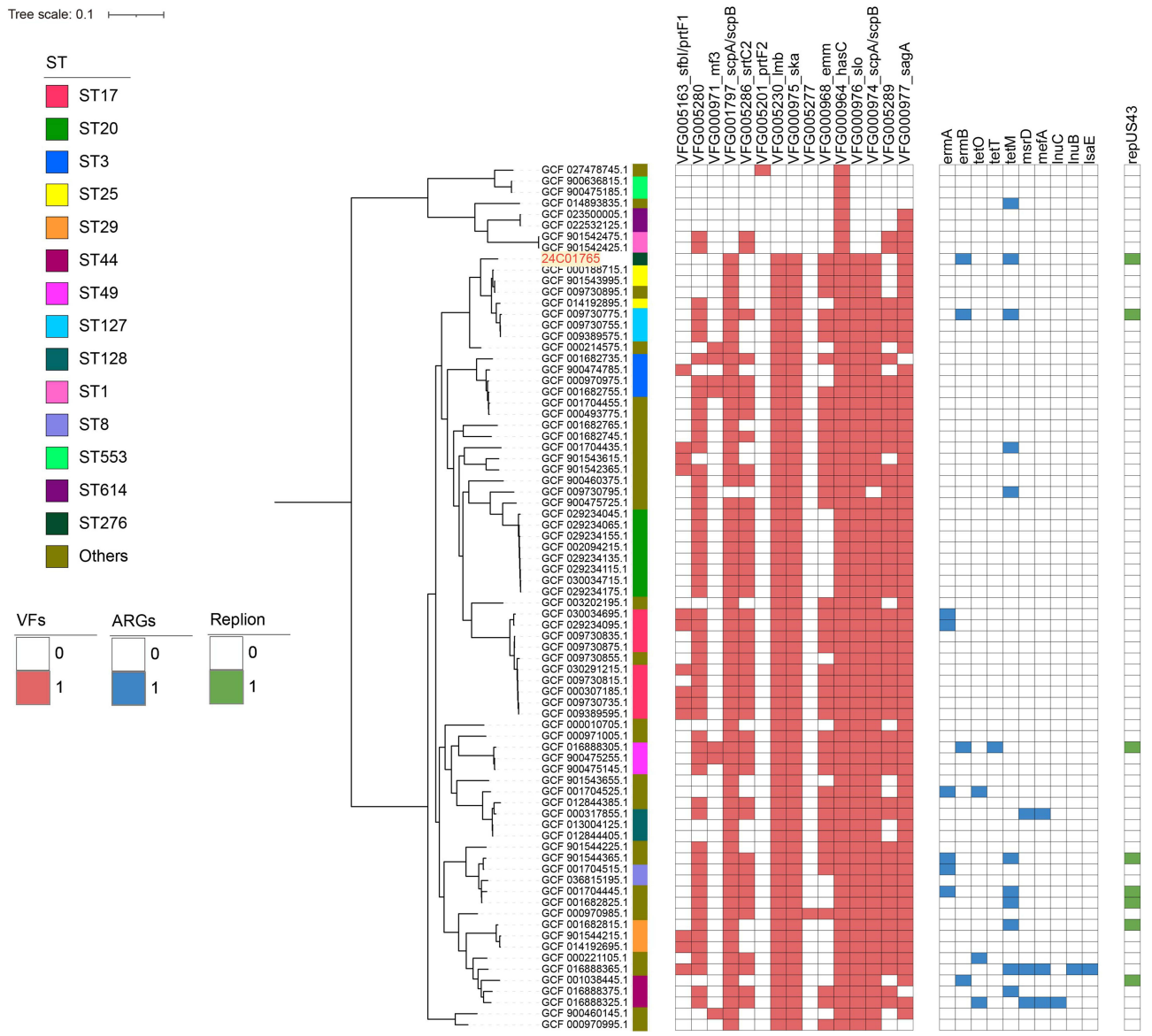


**Figure 2** Phylogenetic analysis of *SDSE* isolates based on 16S rRNA gene sequences. The tree illustrates the genetic relationships between isolates, with evolutionary relationships, virulence factors, antibiotic resistance genes, and plasmid replicon shown from left to right. Strain 24C01765, isolated from this patient, was highlighted. The tree scale was set as 0.1, indicating that a branch length of 0.1 corresponds to 0.1 substitutions per site, meaning that for every 100 nucleotide positions, one substitution is expected.

**Abbreviations**: ARGs, antibiotic resistance genes; GCF, GenBank-complete genome format; ST, sequence type; VFs, virulence factors.

definitive diagnosis, some patients received empirical treatments, including sedation, antiemetics, dehydrating agents, ibuprofen, and empirical antibiotics such as vancomycin and piperacillin/tazobactam.

Results of CSF tests were available for 14 patients, and overall, the CSF findings were consistent with bacterial infection (Table 2). CSF white blood cell counts ranged from 7 to 5200/mm³ (mean 1264/mm³), with a predominance of polymorphonuclear cells (mean 83%, range 64–100%). CSF protein levels were generally elevated (mean 1.97 g/L, range 0.37–4.31 g/L), while glucose levels were reduced (mean 28.4 mg/dL, range 0–95 mg/dL). Of the 14 patients for whom CSF culture results were available, gram-positive cocci were observed in the CSF cultures of only four patients, all of whom had not received prior empirical antibiotic therapy. Ten had negative cultures, among which one culture was negative because it followed an empirical antibiotic treatment.

**Table 1** The Demographic Characteristics, Predisposing Factors, and Clinical Manifestations of Patients with Neurological Involvement Caused by S. Dysgalactiae

| Author, Publication Year, Ref | Species | Age (y)/Sex | Predisposing factors | Diagnosis | Time from onset to consultation (d) | Signs/symptoms | Complications |
|---|---|---|---|---|---|---|---|
| Berenguer, 1992[16] | *SDSD* | 15/M | NR | Meningitis | NR | NR | Bacteraemia |
| Chung, 1982[17] | *SDSE* | 36/F | Postoperative period | Brain abscess, meningitis | 3 | Fever, lethargy, headache, diaphoresis, gastrointestinal symptoms, petechiae | Bacteraemia, pneumonia |
| Chung, 2023[18] | *SDSD* | 85/F | Postoperative period | Ventriculitis | 14 | Fever, seizure | Multiorgan dysfunction |
| Dinn, 1971[19] | *SDSE* | 48/M | Malt worker | Brain abscess | 7 | Dyspnoea, headache, haemoptysis | None |
| Doubinsky, 2018[20] | *SDSE* | 72/F | Diabetes, chronic pancytopenia | Meningitis | 3 | Seizure | None |
| Elsayed, 2003[21] | *SDSE* | 13/M | Lived on horse farm | Meningitis | 2 | Fever, photophobia, meningeal irritation, ataxia, hearing loss, gastrointestinal symptoms | None |
| Faix, 1997[22] | *SDSE* | Infant/F | Prenatal transmission | Meningitis | 0 | Fever | None |
| Guerra, 2023[23] | *SDSD* | 53/M | Construction worker | Meningitis, ventriculitis | 21 | Fever, tachycardia, meningeal irritation, diplopia, hemiparesis, hypoesthesia and hyporeflexia | None |
| Hervas, 1985[24] | *SDSE* | Infant/M | Newborn | Meningitis | 0 | Fever, irritability | None |
| Jourani, 2017[25] | *SDSE* | 57/M | Cirrhosis-related immune suppression, postoperative period | Meningitis, ventriculitis | NR | Hemiparesis, dysarthria, confusion, meningeal irritation | None |
| Khan, 2016[26] | *SDSD* | 2/F | Middle ear infection, congenital agranulocytosis | Brain abscess, meningitis, and cerebritis | 7 | Headache, visual disturbances, ataxic gait, seizure, aphasia, irritability | None |
| Larminat, 2021[27] | *SDSD* | 69/F | Intrathecal pump | Meningitis | 3 | Fever, fatigue | None |
| Luyx, 2001[28] | *SDSE* | 83/F | Heart failure status | Meningitis | 3 | Fever, tachycardia, meningeal irritation, lethargy, gastrointestinal symptoms | Metabolic acidosis |
| Mollison, 1990[29] | *SDSD* | 73/M | Cirrhosis, atrial fibrillation | Meningitis | 10 | Fever, tachycardia, tachypnea, confusion, incontinence, lethargy, gastrointestinal symptoms | Bacteraemia |
| Popescu, 2006[30] | *SDSE* | 75/F | Neighbored with horses | Meningitis | 3 | Fever, headache, lethargy | Bacteraemia |
| Quinn, 1978[31] | *SDSD* | Infant/F | Premature baby | Meningitis | 0 | Fever, tachycardia, respiratory distress syndrome, gastrointestinal symptoms | None |
| Rapoport, 2022[32] | *SDSE* | 70/F | Pacemaker implantation | Meningitis | 2 | Fever, lethargy, confusion, visual disturbances | Rhabdomyolysis, endophthalmitis |
| Saintot, 2018[33] | *SDSE* | 53/F | Streptococcus endocarditis, diabetes, postoperative period | Meningitis | NR | Walking disorders | None |
| Waltereit, 2013[34] | *SDSE* | 38/F | Pregnant women, exposure to infected persons | Meningitis | 6 | Fever, headache, fatigue, meningeal irritation | None |

**Abbreviations**: d, day; F, female; M, male; NR, not reported; Ref, reference; *SDSD*, S. *dysgalactiae* subspecies *dysgalactiae; SDSE*, S. *dysgalactiae* subspecies *equisimilis*; y, year.

**Table 2** The Laboratory Findings, Therapeutic Interventions, and Clinical Outcomes of Patients with Neurological Involvement Caused by S. Dysgalactiae

| Author, Publication Year, Ref | Species | CSF tests | Drug R/S | Treatment | Duration of Treatment (d) | Outcomes (Sequelae/ Cause of Death) |
|---|---|---|---|---|---|---|
| Berenguer, 1992[16] | *SDSD* | NR | S: PCN, EM, Vanco, Chlor, CTX, Cipro, Gent | NR | NR | Survived |
| Chung, 1982[17] | *SDSE* | WBC 7, Prot 1.25, Glu 95<br>G/S: no orgs | R: sulfisoxazole, kanamycin, Tobra, amikacin, and neomycin;<br>S: Gent, cephamandole, Amp, carbenicillin, cephalothin, Tet, Chl | Kef, Tobra | 2 | Died (septic shock) |
| Chung, 2023[18] | *SDSD* | NR | NR | CFX | NR | Survived |
| Dinn, 1971[19] | *SDSE* | WBC 400 (90% PMN), Prot 1.50, Glu 38<br>G/S: no orgs | NR | Amp, Chlor | NR | Died (septic shock) |
| Doubinsky, 2018[20] | *SDSE* | NR | NR | NR | 23 | Died (pneumonia) |
| Elsayed, 2003[21] | *SDSE* | WBC 2175 (87% PMN), Prot 1.55, Glu 22<br>G/S: no orgs | S: PCN, CTX, Vanco | CTX, Vanco, PCN, mannitol | 10 | Survived (hearing loss and ataxia) |
| Faix, 1997[22] | *SDSE* | WBC 38, Prot 1.13<br>G/S: no orgs | S: Amp, Gent | Amp, Gent | 10 | Survived |
| Guerra, 2023[23] | *SDSD* | NR | S: PCN, Vanco, FQ | CFX, Vanco | 42 | Survived |
| Hervas, 1985[24] | *SDSE* | WBC 290 (100% PMN), Prot 1.57, Glu 22<br>G/S: gram-positive cocci | S: bacitracin | PCN | 21 | Survived |
| Jourani, 2017[25] | *SDSE* | WBC 1127 (64% PMN), Prot 1.85, Glu 0<br>G/S: no orgs | NR | CFX, Amp, rifampicin | 90 | Survived |
| Khan, 2016[26] | *SDSD* | NR | S: PCN, Vanco, linezolid, and cephalosporin | CFX, metronidazole, ventricular drainage | 84 | Survived |
| Larminat, 2021[27] | *SDSD* | WBC 660 (90% PMN), Prot 4.31, Glu 14<br>G/S: gram-positive cocci | NR | Vanco, CTX | 16 | Survived |
| Luyx, 2001[28] | *SDSE* | WBC 179 (80% PMN)<br>G/S: no orgs | NR | CTX | NR | Died (septic shock) |
| Mollison, 1990[29] | *SDSD* | WBC 595 (80% PMN), Prot 3.30, Glu 27<br>G/S: no orgs | S: PCN | PCN, Chlor | 14 | Survived (hearing loss) |

(*Continued*)


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**Table 2** (Continued).

| Author, Publication Year, Ref | Species | CSF tests | Drug R/S | Treatment | Duration of Treatment (d) | Outcomes (Sequelae/ Cause of Death) |
|---|---|---|---|---|---|---|
| Popescu, 2006[30] | *SDSE* | WBC 5200 (82% PMN), Prot 0.47, Glu 6<br>G/S: no orgs | R: Tetra; S: PCN, CTX | CFX | 10 | Survived |
| Quinn, 1978[31] | *SDSD* | WBC 1010 (85% PMN), Prot 3.80, Glu 25<br>G/S: gram-positive cocci | R: sulfonamide, streptomycin, Tetra; S: Chl, PCN, methicillin | PCN, Tobra | 21 | Survived |
| Rapoport, 2022[32] | *SDSE* | WBC 3414 (88% PMN), Prot 1.60, Glu 35<br>G/S: gram-positive cocci | S: CFX, PCN, Vanco | CFX | 42 | Survived (vision loss) |
| Saintot, 2018[33] | *SDSE* | WBC 1600 (66% PMN), Prot 2.92<br>G/S: no orgs | R: aminoglycosides; S: PCN, amoxicillin, CTX, macrolides, clindamycin | CTX, Gent, dexamethasone | 9 | Died (septic shock) |
| Waltereit, 2013[34] | *SDSE* | WBC 1000, Prot 0.37<br>G/S: no orgs | NR | CFX | 14 | Survived |

**Abbreviations**: Amp, ampicillin; Chl, chloramphenicol; CFX, ceftriaxone; CTX, cefotaxime; Cip, ciprofloxacin; d, day; DIC, disseminated intravascular coagulation; EM, erythromycin; FQ, fluoroquinolones; Gent, gentamicin; G/S, Gram stain; Kef, cephalothin; NR, not reported; orgs, organisms; PCN, penicillin; PMN, polymorphonuclear cell; prot, protein; R, resistant; Ref, reference; S, sensitive; *SDSD*, S. *dysgalactiae* subspecies *dysgalactiae; SDSE*, S. *dysgalactiae* subspecies *equisimilis*; Tet, tetracycline; Tobra, tobramycin; WBC, white blood cell count.

## Treatment and Outcomes

In the 19 cases analyzed, beta-lactam antibiotics were used in 17 patients (89%), including ampicillin, penicillin, ceftriaxone, cefotaxime, and cephalothin (Table 2). Treatment duration varied widely, ranging from 2 to 90 days. Aminoglycosides were administered to four patients, including gentamicin and tobramycin. Steroids were used as adjunctive therapy in one patient (5%), who was treated with a combination of ceftriaxone, gentamicin, and dexamethasone. Out of the 19 patients, five (26%) died. The causes of death were primarily due to septic shock in four patients (21%), and one patient (5%) died from pneumonia. Among the 14 survivors, three (16%) experienced neurological sequelae. Specifically, one survivor suffered from hearing loss, one had both hearing loss and ataxia, and one experienced vision loss. The remaining 11 survivors recovered without reported sequelae. The treatment regimens for *SDSE* and *SDSD* are relatively similar, with substantial variability in treatment duration among individuals but no significant differences between the two groups. However, regarding outcomes, all seven reported *SDSD* cases achieved survival, whereas five out of 12 *SDSE* cases resulted in mortality.

# Discussion

The case we present illustrates the rapid progression and complex management of *SDSE* infection, emphasizing the critical role of pathogen-based diagnosis in guiding therapeutic decisions. While empirical treatment with meropenem and vancomycin initially led to some clinical improvement, the condition worsened due to delayed pathogen identification and lack of timely treatment adjustments, particularly during the transfer to a facility lacking an intensive care unit. This highlights the importance of continuous monitoring and early intervention, especially in high risk populations such as elderly patients with diabetes-related complications. In patients at risk of hematogenous infection, it is crucial to remain alert for septicemia and multiple organ failure, even when serum tests are inconclusive. A suggestive clinical history, such as extensive ulceration in the diabetic foot, should raise suspicion. Furthermore, the identification of the rare ST267-type *SDSE* underscores the need for vigilance regarding emerging and uncommon pathogens, which may require updated diagnostic strategies and tailored treatment plans. Additionally, this case emphasizes that symptom improvement, such as fever resolution, is not always a reliable indicator of clinical stability in severe infections, particularly in the context of septic shock, where rapid deterioration can occur. For this patient, we believe that empirical antibiotic therapy (meropenem and vancomycin) would be ineffective, as vancomycin has limited penetration across the blood-brain barrier, and although meropenem can cross the blood-brain barrier, it is not the appropriate therapy for *SDSE*. In this case, the body temperature of this patient did decrease, likely due to dysfunction of the temperature-regulating center, which resulted in a misleading improvement of symptoms and may have influenced clinical decisionmaking. Under these circumstances, we suggest measuring blood C-reactive protein and procalcitonin, which are expected to show a progressive increase. The case also calls for reconsideration of patient transfer protocols, as premature transfer to hospitals with inadequate facilities can exacerbate the outcome. However, due to the high turnover rate at this hospital and the request from his family to transfer to a more accessible facility, the patient was transferred before the blood tests and CSF analysis were available.

This case, with the review of 19 neurological cases caused by *S. dysgalactiae*, underscores the capacity of *SDSE* and *SDSD* for severe central neural system (CNS) infections, particularly in patients with underlying health conditions. The high mortality rate (32%) and prevalence of neurological sequelae in survivors emphasize the aggressive nature of these infections and the necessity for early and comprehensive treatment strategies. The incidence of *SDSE* and *SDSD* is increasing and may be higher than reported. Although considered extremely rare, recent studies have documented cases of *SDSD* infections over the years.[13,35] Meningitis caused by *S. dysgalactiae* in healthy adults may be more common than previously reported. As in immunocompetent individuals, bacterial cultures may yield negative results.[36–38] This suggests that such clinical presentations may resolve without pharmacological intervention. Moreover, due to the difficulty of lumbar puncture, many patients with mild symptoms will refuse lumbar puncture and further PCR examination. The increasing occurrence of neurological infections caused by *SDSE* and *SDSD* could be attributed to several factors. These may include an evolving pathogenicity of the bacteria, an aging population with more prevalent comorbidities, or a heightened awareness and improved diagnostic techniques that facilitate the identification of these infections.

In the reviewed cases, the presence of *SDSE* or *SDSD* in CSF cultures and PCR confirmation highlights the importance of molecular diagnostic techniques in identifying the pathogen accurately, particularly in cases with atypical presentations. In patients with *S. dysgalactiae* identified in peripheral blood or abscesses, lumbar puncture is recommended, even in the absence of overt neurological involvement. Although lumbar puncture is essential, patients undergoing empirical treatment often fail to obtain positive CSF culture or stain results. Therefore, the procedure should be performed promptly. Next-generation sequencing has emerged as a valuable tool in the diagnosis and understanding of *S. dysgalactiae* infections. Sequencing of the *emm* gene, a key marker for both *SDSE* and *SDSD*, allows for precise identification and typing of bacterial strains, aiding in epidemiological tracking and understanding the genetic basis of pathogenicity.[6,39] The ability to rapidly sequence bacterial genomes also helps assess antimicrobial resistance profiles and tailor more effective treatment strategies. Recent studies have highlighted the molecular characteristics of CNS infections caused by streptococci. Streptococcal meningitis involves bloodstream survival, adhesion to and invasion of brain microvascular endothelial cells, blood-brain barrier penetration, and immune activation. Key virulence factors include capsular polysaccharides, surface proteins (eg, M-like protein), and pore-forming toxins (eg, β-hemolysin), which vary among species.[40] Genomic analysis of *SDSE* shows shared resistance genes and virulence factors with *S. agalactiae* but lacks capsular polysaccharides and essential surface proteins, accounting for its lower pathogenicity.[41] Comparative studies may uncover diagnostic and therapeutic targets given the high prevalence of resistance genes. Moreover, virulence gene expression in *SDSE* is modulated by small noncoding RNAs, such as FasX, which regulate posttranscriptional responses to environmental signals.[42,43]

*SDSE* is generally susceptible to penicillins, cephalosporins, and vancomycin, with occasional resistance to erythromycin. For systemic infections with *SDSE*, such as pyogenic spondylodiscitis, conservative intravenous antibiotic therapy over 4–12 weeks is effective, with penicillin being the first-line therapy. Aminoglycoside combination with penicillin may be beneficial for severe infections. Combining penicillin with gentamicin or clindamycin is recommended in localized infections (eg, endocarditis and osteomyelitis).[44] Third-generation cephalosporins (3GCs) are effective for treating meningitis due to their superior CNS penetration.[4] Clindamycin can be added to inhibit toxin production for streptococcal toxic shock syndrome, and intravenous polyspecific immunoglobulins may help neutralize toxins and reduce inflammation.[45] The treatment protocol for *SDSD* remains undefined due to the limited number of documented cases; however, it is generally considered appropriate to adopt therapeutic strategies used for *SDSE*. Additionally, one review highlights vancomycin and ceftriaxone as the most commonly employed antibiotics for managing *SDSD* infections.[8,13] This review highlights the extensive usage of betalactam antibiotics in the treatment of both *SDSE* and *SDSD* infections. However, the variability in treatment duration and the adjunctive use of vancomycin and aminoglycosides suggest a lack of consensus on optimal therapy. The use of steroids in a small subset of patients points to ongoing debate about their role in treatment.[46,47]

The mortality rate associated with *SDSE* bacteremia and meningitis can reach up to 50%, particularly in cases complicated by endocarditis or brain abscesses.[25] In this review, we found that all deaths were caused by *SDSE* infection, but this does not mean that the risk of *SDSD* is less than that of *SDSE*, given the small sample size. Early intervention to prevent the spread of *S. dysgalactiae*, particularly in immunocompromised individuals, is crucial to avoiding irreversible disease progression. For atypical presentations, such as gastrointestinal symptoms like vomiting or mild alterations in consciousness, particularly in elderly patients, it is important to consider the possibility of neurological involvement. In patients with clear neurological manifestations such as meningitis, *S. dysgalactiae* should be considered a potential pathogen. This review reports a case of fetal transmission,[22] underscoring the need to consider antenatal maternal screening for *S. dysgalactiae*. Notably, any signs of visual or auditory impairment should be closely monitored. Failure to seek prompt intervention may result in irreversible vision or hearing loss.[29,32]

Several strategies should be emphasized to prevent the transmission or multisystem dissemination of *S. dysgalactiae*. These include rigorous infection control measures in healthcare settings, particularly in neonatal intensive care units, where vulnerable populations are at higher risk. Immunocompromised patients should be closely monitored, and prophylactic antibiotics may be considered in high-risk individuals following exposure. Additionally, public health initiatives should promote awareness and early diagnosis to reduce the risk of severe outcomes.

## Conclusion

This study highlights the significant pathogenic potential of *S. dysgalactiae*, particularly *SDSE*, in causing severe neurological infections. The high mortality rate and frequent neurological sequelae underscore the need for early diagnosis and comprehensive treatment strategies. We recommend a more detailed discussion of the *SDSE* versus *SDSD* distinction to enhance understanding of their respective epidemiological and clinical implications. The application of NGS and other molecular diagnostic tools is essential for accurate pathogen identification and tailoring effective therapeutic approaches. Given the increasing prevalence of *S. dysgalactiae* infections, especially in the context of an aging population with multiple comorbidities, there is a critical need for heightened clinical awareness and the development of standardized treatment protocols to improve patient outcomes.

## Ethics Statement

This retrospective cohort study was conducted following approval from the Institutional Review Board (IRB) of Peking Union Medical Hospital (ethics number: S-K653) under the ethical standards outlined in the Declaration of Helsinki.

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## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

## Disclosure

The authors report no conflicts of interest in this work.

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