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ORIGINAL ARTICLE

Serratia marcescens meningitis: Epidemiology, prognostic factors and treatment outcomes

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Background/Purpose: *Serratia marcescens* is a rare pathogen of central nervous system infections. This study was to investigate the epidemiology, prognostic factors, and treatment outcomes of *S marcescens* meningitis.
Methods: This retrospective analysis included 33 patients with culture-proven *S marcescens* meningitis hospitalized between January 2000 and June 2011.
Results: Of the 33 patients enrolled, only one did not receive neurosurgery before the onset of *S marcescens* meningitis. Patients with *S marcescens* meningitis had higher ratios of brain solid tumors (54.5%) and neurosurgery (97.0%) with a mortality rate of 15.2%. The mean interval between the first neurosurgical procedure and the diagnosis of meningitis was 17.1 days (range, 4–51 days). Only one third-generation cephalosporin-resistant *S marcescens* isolate was recovered from the patients' cerebrospinal fluid (CSF) specimens. Compared with the favorable outcome group ($n = 20$), the unfavorable outcome group ($n = 13$) had a higher percentage of brain solid tumors, more intensive care unit stays, and higher Sequential Organ Failure Assessment score, CSF lactate and serum C-reactive protein concentrations at diagnosis of meningitis. Under the multiple regression analysis, CSF lactate concentration $\geq$2-fold the upper limit of normal (ULN) was independently associated with unfavorable outcomes (odds ratio, 7.20; 95% confidence interval, 1.08–47.96; $p = 0.041$).
Conclusion: *S marcescens* meningitis is highly associated with neurosurgical procedures for brain solid tumors. CSF lactate concentration $\geq$2x ULN may predict an unfavorable outcome. Its mortality is not high and empiric treatment with parenteral third-generation cephalosporins may have a satisfactory clinical response.

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Introduction

Serratia marcescens, a species of Gram-negative bacillus of the *Enterobacteriaceae*,[1] is distributed widely in the hospital environment and has been recognized as an opportunistic pathogen causing a variety of nosocomial infections, including wound infections,[2,3] urinary tract infections,[3,4] pneumonia,[3] bacteremia,[3,5,6] endocarditis,[7] and myocarditis.[8]

However, it is a rare pathogen of central nervous system (CNS) infections. There were only case reports in patients with a history of head trauma, neurosurgical procedures, mastoiditis or chronic sinusitis.[9–13] Prosthetic devices, including external cerebrospinal fluid (CSF) drainage catheters[14] and ventriculoperitoneal (VP) shunts,[11,15] facilitate bacterial colonization and provide a potential route into the CNS, eventually causing meningitis. The use of external ventricular drains (EVDs) or VP shunts might develop an environment associated with a relatively high risk for post-neurosurgical CNS infections.

In a previous study regarding post-neurosurgical meningitis, *S marcescens* was the most common Gram-negative pathogen, accounting nearly 10% of the total 69 identified isolates.[16] However, the literature concerning the risk factors, impacts of antimicrobial therapy and clinical outcomes for *S marcescens* meningitis were limited. Hence, we conducted this retrospective study to investigate the epidemiology, prognostic factors, and treatment outcomes of *S marcescens* meningitis.

Materials and methods

Study design, patients and case definition

This retrospective study was conducted at the Chang Gung Memorial Hospital-Linkou, a 3715-bed university-affiliated hospital and tertiary referral medical center in northern Taiwan. This study has been approved by the Institutional Research Board of CGMH-Linkou (Number: 101-0477B). Through the computer-assisted microbiology databases, all patients with CSF cultures positive for *S marcescens* between January 2000 and June 2011 were reviewed.

The diagnostic criteria for *S marcescens* meningitis were based on the isolation of *S marcescens* from $\geq$1 CSF cultures with at least one of the following findings consistent with meningitis: (1) clinical manifestations, such as fever, seizure, altered consciousness, or signs of meningeal irritation; and (2) laboratory evidence, including a decreased CSF glucose concentration (CSF/serum glucose ratio $\leq$0.4 or CSF glucose $<$40 mg/dL if serum glucose was not available), increased lactate ($>$36 mg/dL) and protein ($>$32 mg/dL) concentrations, and pleocytosis ($\geq$ 10 white blood cell/μL) with neutrophil predominance.[16–18] Patients were excluded if *S marcescens* was isolated from a CSF culture without any clinical feature consistent with meningitis, or without clinical deterioration in the absence of appropriate antibiotic treatment for 3 days or more.[19] "Recurrence" was defined as a second or further meningitis episodes due to a different bacterial pathogen after the completion of therapy for the initial episode, or due to *S marcescens* 3 weeks or more after the completion of therapy for the first episode. "Relapse" of meningitis was considered if it was also caused by *S marcescens* within 3 weeks of the completion of therapy for the initial episode.[16,20]

Descriptive epidemiology

Data collected from the enrolled patients included demographics, comorbid illnesses, clinical presentations and diagnoses, neurosurgeries in recent 3 months, laboratory data, severity of illness [Glasgow Coma Scale (GCS) score and Sequential Organ Failure Assessment (SOFA) score],[21] treatment courses and outcomes. Comorbid illnesses included diabetes mellitus, hepatic dysfunction (defined as the serum total bilirubin level $\geq$2.0 mg/dL or liver cirrhosis), renal insufficiency (defined as a serum creatinine level $\geq$2.0 mg/dL or a requirement of hemodialysis), chronic lung diseases, heart failure, and hematologic or solid organ malignancies.

Microbiologic analysis

Blood cultures were processed in the clinical microbiology laboratory, using the BACTEC 9240 blood culture system (Becton Dickinson Diagnostic Instrument System, USA). *S marcescens* isolates were identified on the basis of the following properties: aerobic, Gram-negative bacilli on a Gram's stain with an indole-negative, lysine decarboxylase-positive, and ornithine decarboxylase-positive reaction.[1] Its fermentation reactions in commercial identification system were acid produced from sucrose and D-sorbital, but not from arabinose, L-rhamnose, D-xylose, cellobiose, and D-arabitol.[1] Antimicrobial susceptibility testing was performed using the disk diffusion method according to Clinical and Laboratory Standards Institute criteria.[22]

Treatment and outcomes

Appropriate antibiotic treatment was defined as the use of one or more antimicrobial agents proved to be active against *S marcescens in vitro* and capable of passing through the blood-brain barrier in adequate concentrations.[14,19] The predominant antibiotic regimen was defined as the antibiotic used for at least two-thirds of the patient's treatment course.[14]

Clinical outcomes were determined by the GCS change and mortality. A favorable outcome was considered if the GCS score was unchanged or increased at the treatment endpoint, while an unfavorable outcome was considered if there was a decreased GCS score at the treatment endpoint. Treatment endpoint was the timing of discontinuation of therapy for *S marcescens* meningitis. We defined the mortality attributable to meningitis if the patient's death was due to the meningitis or its complications.[19] Microbiologic outcomes were determined by the interval to CSF sterilization and the recurrence or relapse of *S marcescens* meningitis.

Statistical analysis

Statistical analyses were done using IBM Statistical Package for the Social Sciences version 18.0 (SPSS Inc, Somers, NY,

USA). Univariate analyses were performed with the chi-square test or Fisher's exact test for categorical variables, and the Student's *t* test or Wilcoxon test for continuous variables, as appropriate. Odds ratio (OR) and 95% confidence interval (CI) were calculated to evaluate the strength of any associations as well as the precision of the estimate of effect in the outcome analyses. Variables with a two-tailed *p* value <0.05 were entered to a backward multivariate logistic regression model to determine the factors independently associated with unfavorable outcome. A two-tailed *p* value <0.05 was considered statistically significant.

Results

Descriptive epidemiology

During the 10-year period of the study, 34 patients had *S marcescens* isolated from at least one CSF specimens. Of the 34 patients identified, 33 met the diagnostic criteria and one was contaminant. Of the 33 enrolled patients, 20 were males and 13 were females, with a mean age of 49.6 years (range, 1 month to 86 years old). Of them, 6 (18.2%) did not have any comorbid illness. The first three most common comorbid illnesses were benign or malignant brain tumors (18 patients, 54.5%), followed by diabetes mellitus (five, 15.2%) and chronic lung diseases (three, 9.1%). Only one patient did not receive neurosurgical intervention before the onset of meningitis. Patients' demographics, associated neurosurgical conditions, and comorbid illnesses are listed in Table 1. The most common neurosurgical conditions were benign or malignant brain tumors (16, 50.0%), followed by hemorrhagic cerebrovascular accidents (five, 15.6%).

The mean interval between the first neurosurgical procedure and the diagnosis of meningitis was 17.1 days (range, 4—51 days). The mean time from the diagnosis of *S marcescens* meningitis to adequate treatment was 2.8 days (range, 0—27 days), and 18 patients (54.5%) received appropriate antimicrobial therapy within 48 hours of the diagnosis of *S marcescens* meningitis. Twenty-eight patients had two or more additional CSF cultures performed after the diagnosis of *S marcescens* meningitis, and the mean interval to CSF sterilization was 15.2 days (range, 3—43 days). In this study, 20 patients (60.6%) had a favorable outcome, while 13 (39.4%) had an unfavorable outcome. Overall, five patients (15.2%) died in the hospital; one died of meningitis, and the other four died of their comorbidities (e.g., nosocomial pneumonia) or the underlying neurosurgical conditions (e.g., intracranial malignancy) despite CSF sterilization from meningitis.

Table 1 Demographic and clinical characteristics of 33 patients with *Serratia marcescens* meningitis

Characteristics	Value
Age, y	49.6 ± 24.7
Male	20 (60.6)
Comorbid illness	
Benign or malignant brain tumor	18 (54.5)
Diabetes mellitus	5 (15.2)
Chronic lung disease	3 (9.1)
Hepatic dysfunction	1 (3.0)
Heart failure	1 (3.0)
Hematologic malignancy	1 (3.0)
Renal insufficiency	0 (0.0)
Types of infections	
Spontaneous	1 (3.0)
Postneurosurgery	32 (97.0)
Neurosurgical conditions ($n = 32$)	
Tumors	16 (50.0)
Hemorrhagic cerebrovascular accident	5 (15.6)
Traumatic brain injury	5 (15.6)
Others[a]	6 (18.8)
Frequencies of neurosurgery before meningitis within 3 mos	1.6 ± 1.7
Interval between meningitis and the initial neurosurgery, d	17.1 ± 15.1

[a] Others included brain abscess, epidural abscess, hydrocephalus, ventriculitis, and subdural effusion.
Data presented as *n* (%) or mean ± standard deviation.

Clinical and laboratory characteristics of *S marcescens* meningitis

The clinical features, laboratory data and outcomes of *S marcescens* meningitis are summarized in Table 2. Two major initial clinical manifestations were fever (30 patients, 90.9%) and altered consciousness (20, 60.6%). CSF abnormalities at the onset of *S marcescens* meningitis included pleocytosis (mean, 6510 cells/μL, with 75% polymorphonuclear leukocytes), decreased CSF glucose concentration (mean, 36.8 mg/dL), elevated CSF protein concentration (mean, 534.6 mg/dL), and elevated CSF lactate concentration (mean, 107.2 mg/dL). Twenty-one patients (84.0%) had a positive Gram's staining, and two (6.1%) had polymicrobial infections, including one co-infected with *Pseudomonas aeruginosa* and the other co-infected with *Acinetobacter baumannii*. There were five patients with concomitant *S marcescens* bacteremia, two with concurrent pneumonia, and two with intra-abdominal infections. The average scores of GCS and SOFA were 13.3 and 3.5 at the diagnosis of meningitis, respectively. The overall all-cause mortality of patients in this study was 15.2% (5/33).

Twenty-eight patients had brain CT scans or magnetic resonance imaging48 hours before or after the diagnosis of *S marcescens* meningitis, and two of them had negative findings. Positive image findings were as follows: hydrocephalus (18, 64.3%), midline shift (10, 35.7%), brain abscess (5, 17.9%), infarction (4, 14.3%), and leptomeningeal enhancement (1, 3.6%).

Risk factors for unfavorable outcomes

All the 33 enrolled patients had a GCS score >3 at the onset of *S marcescens* meningitis. The analysis of potential risk factors for unfavorable outcome is listed in Table 3.

Table 2 Clinical features, laboratory data, and outcomes of patients with *S marcescens* meningitis

Variables	Value
Initial clinical presentations	
Fever	30 (90.9)
Altered consciousness	20 (60.6)
Nausea or vomiting	12 (36.4)
Seizure	9 (27.3)
Respiratory failure	7 (21.2)
Headache	6 (18.2)
Neck stiffness	3 (9.1)
Shock	2 (6.1)
Cerebrospinal fluid data	
Leukocyte count (μL)	6510.1 $\pm$ 21,600.8
Glucose level (mg/dL)	36.8 $\pm$ 32.4
Protein level (mg/dL)	534.6 $\pm$ 984.6
Lactate level (mg/dL)	107.2 $\pm$ 66.4
Positive Gram's stain result (n = 25)	21 (84.0)
Peripheral blood study	
Leukocyte count ($\times$1000/μL)	15.2 $\pm$ 6.3
C-reactive protein (mg/L)	145.3 $\pm$ 116.2
Concomitant bacteremia	5 (15.2)
Microbiologic data of cerebrospinal fluid	
Polymicrobial	2 (6.1)
Severity of illness scoring at the onset	
GCS score	13.3 $\pm$ 2.7
SOFA score	3.5 $\pm$ 2.5
Intensive care unit stay	22 (66.7)
Duration of therapy	47.6 $\pm$ 25.6
Outcome	
Attributable mortality	1 (3.0)
All-cause mortality	5 (15.2)

Data presented as n (%) or mean $\pm$ standard deviation. GCS = Glasgow Coma Scale; SOFA = Sequential Organ Failure Assessment.

According to the univariate analysis, benign or malignant brain tumors, twofold elevation of CSF lactate concentration above upper limit of normal (ULN), higher serum C-reactive protein (CRP) levels (>5 mg/L), more ICU stays, and higher SOFA score at the onset of *S marcescens* meningitis were significantly associated with unfavorable outcomes. Diabetic patients had the trend towards unfavorable outcomes, but the difference was not statistically significant.

Variables in multivariate analysis included benign or malignant brain tumors, CSF lactate $\geq$2x ULN, and SOFA score at the onset of *S marcescens* meningitis. After analysis of aforementioned variables, CSF lactate $\geq$2x ULN (odds ratio, 7.20; 95% CI, 1.08—47.96; p = 0.041) was independently associated with unfavorable outcomes for patients with *S marcescens* meningitis.

Antimicrobial therapy and outcomes

There were two patients with recurrence of meningitis, and no patient had relapsed *S marcescens* meningitis. The first patient was a 1-month-old premature female infant with spontaneous *S marcescens* meningitis and initially presenting fever and seizure. Her computed tomography (CT) revealed hydrocephalus and ventriculitis. She received patent ductus arteriosus ligation 18 days before the episode of *S marcescens* meningitis. Third-generation cephalosporins were administered intravenously 48 hours after the onset of meningitis, and had been used for 52 days in total. CSF sterilization was achieved 7 days after initiation of treatment. EVD was also performed for increased intracranial pressure. However, infection recurred 2 weeks after the completion of therapy for the initial episode, and the recurrent meningitis was caused by *Klebsiella oxytoca*. Another course of antibiotic therapy with third-generation cephalosporins was initiated, and she recovered from the recurrent meningitis.

The second patient with recurrence of *S marcescens* meningitis was a 45-year-old male receiving craniectomy for removal of brain trigeminal schwannoma 8 days before the onset of *S marcescens* meningitis. Initial presentations were fever and altered consciousness. Treatment with intravenous third-generation cephalosporin lasted for 46 days, and he also had the surgical debridement and EVD revisions twice. CSF sterilization was achieved 16 days after diagnosis. He had *S marcescens* CNS infection again around 2.5 months after the completion of therapy for the first episode. His second episode was presented as an epidural abscess. He was retreated with surgical debridement and third-generation cephalosporin, which resulted in a favorable outcome.

Of the 33 patients enrolled, only one third-generation cephalosporin-resistant *S marcescens* isolate was recovered, which was collected from subdural empyema occurring 2 months after initial craniotomy. All patients received appropriate intravenous antibiotic treatment and none of them was treated with intrathecal antibiotics. Twenty-seven patients (81.8%) received monotherapy with third-generation cephalosporins, while six patients (18.2%) received meropenem or imipenem. No seizures were observed in any of the patients who received carbapenem therapy.

Carbapenems and third-generation cephalosporins, such as ceftriaxone, ceftazidime and flomoxef, were the most frequently used antibiotics. Patients treated with third-generation cephalosporins had a shorter mean time to CSF sterilization than carbapenems (14 vs. 33 days, p = 0.021), but the duration of therapy, unfavorable outcome, and mortality had no statistical difference between these two different classes of antimicrobial agents (Table 4).

Discussion

To the best of our knowledge, this is the largest study regarding *S marcescens* meningitis in the English literature. In this study, cases occurred sporadically over a 10-year period, and all the enrolled patients were hospitalized at different wards or ICUs, so outbreak of *S marcescens* meningitis was not likely. Most of the patients in this study had neurosurgical intervention, accounting for 97.0% (32/33) of total cases. Compared with other Gram-negative meningitis, *S. marcescens* meningitis occurred more frequently in post-neurosurgical patients

Table 3 Univariate analysis of risk factors for unfavorable outcome

Outcomes	Favorable outcome[a] ($n = 20$)	Unfavorable outcome[b] ($n = 13$)	p
Age, y	43.60 ± 27.32	58.77 ± 17.18	0.085
Male	11 (55.0)	9 (69.2)	0.414
Comorbid illness			
Benign or malignant brain tumor	8 (40.0)	10 (76.9)	0.037*
Diabetes mellitus	1 (5.0)	4 (30.8)	0.066
Chronic lung disease	3 (15.0)	0 (0.0)	0.261
Hepatic dysfunction	0 (0.0)	1 (7.7)	0.394
Heart failure	1 (5.0)	0 (0.0)	>0.99
Hematologic malignancy	1 (5.0)	0 (0.0)	>0.99
Laboratory data			
CSF glucose (mg/dL)	44.63 ± 32.41	26.25 ± 30.64	0.138
CSF protein (mg/dL)	579.88 ± 1228.29	466.66 ± 464.26	0.764
CSF lactate ≥2x ULN	5 (35.7)[c]	9 (81.8)[d]	0.042*
Blood leukocyte count (×1000/μL)	15.0 ± 6.2	15.6 ± 6.6	0.778
Serum CRP (mg/L)	103.71 ± 74.47	211.96 ± 142.21	0.017*
Na (meq/L)	135.21 ± 7.04	137.69 ± 4.73	0.276
Risk factors			
Polymicrobial meningitis	1 (5.0)	1 (7.7)	>0.99
Frequencies of neurosurgery before meningitis within 3 mos	1.25 ± 1.33	2.15 ± 2.15	0.145
ICU stay	10 (50.0)	12 (92.3)	0.022*
Concomitant bacteremia	3 (15.0)	2 (15.4)	>0.99
Treatment			
CSF sterilization	17 (100.0)[f]	9 (100.0)[g]	—
Interval to CSF sterilization, d	12.29 ± 7.03	20.67 ± 13.37	0.045*
Time to adequate treatment, d	1.94 ± 2.79	4.45 ± 8.04	0.244
Adequate treatment within 72 hrs	14 (70.0)	6 (46.2)	0.171
SOFA score at the onset	2.69 ± 2.27	4.54 ± 2.47	0.048*
Catheter[e]	15 (75.0)	9 (69.2)	>0.99
Removal or revision of catheters[e]	14 (93.3)[h]	8 (88.9)[i]	0.620
Time to removal or revision of catheters, d	4.13 ± 5.03	1.90 ± 4.31	0.259
Time from diagnosed to discharge, d	51.55 ± 28.30	111.15 ± 40.43	< 0.001*
Outcome			
Alive	20	8	0.005*
Succumbed to the disease	0	1	

[a] Favorable outcome: "unchanged or increased GCS score" at the end of treatment for meningitis.
[b] Unfavorable outcome: "decreased GCS ccore" at the end of treatment for meningitis.
[c] 14 in 20 patients had such study.
[d] 11 in 13 patients had such study.
[e] Catheter: external ventricular drain or ventriculoperitoneal shunt.
[f] 17 in 20 patients had such study.
[g] 9 in 13 patients had such study.
[h] 15 in 20 patients had catheters.
[i] 9 in 13 patients had catheters.
Data presented as n (%) or mean ± standard deviation.
*Statistically significant ($p < 0.05$).
CRP = C-reactive protein; CSF = cerebrospinal fluid; ICU = intensive care unit; SOFA = sequential organ failure assessment; ULN = upper limit of normal.

(97.0% vs. 33.3–84.6%).[23–36] This result may alert neurosurgeons the bacteriology of postneurosurgical bacterial meningitis. These CNS infections due to *S marcescens* had quite variable clinical presentations ranging from surgical wound or ventricular shunt infections to deeply localized abscess formation in brain parenchyma, epidural space, or bone-flap.

The second characteristic finding distinguishing our study from previous studies for Gram-negative meningitis is the higher percentage of benign or malignant brain tumor (54.5% versus 0–26.7%).[23–26] The relationship between *S marcescens* infections and malignancy has been reported by Haddy et al.[27] They presented a study of *S marcescens*

Table 4 Antimicrobial regimens for the treatment of *S marcescens* meningitis and clinical outcomes

Predominant antimicrobial regimen (monotherapy)	Third-generation cephalosporins ($n = 27$)	Carbapenems ($n = 6$)	p
Interval to sterile CSF culture, mean d (range)	14 (4–44)	33 (4–51)	0.021*
Duration of therapy, mean d (range)	45 (5–102)	57 (31–99)	0.329
Unfavorable outcome, *n* (%)	10 (37.0)	3 (50.0)	0.659
Mortality, *n* (%)	3 (11.1)	2 (33.3)	0.216

* Statistically significant ($p < 0.05$).
CSF = cerebrospinal fluid.

bacteremia and found 20% of the patients had advanced malignancy. Besides, *S marcescens* meningitis had a lower mortality than other Gram-negative meningitis (15.2% vs. 21.0–40.0%).[23–26]

Patients' GCS scores are the important prognostic variables for bacterial meningitis.[14,28] The comparison of GCS change between the onset of *S marcescens* meningitis and at the end of treatment for meningitis could be more practical for physicians to predict the prognosis. CSF lactate is a good indicator in clinical practice to distinguish bacterial meningitis from aseptic meningitis in combination with other CSF characteristics.[18,29,30] It is also a quick, sensitive, and specific test to identify patients with post-neurosurgical bacterial meningitis.[31] Besides, from a meta-analysis of 25 previous studies, its diagnostic accuracy was higher than that of conventional markers (i.e., CSF Gram's stain, CSF leukocyte counts, CSF glucose, CSF/plasma glucose ratio, and CSF protein).[30] The role of CSF lactate level in predicting prognosis of bacterial meningitis is still conflicting.[29,32,33] In this study, CSF lactate level ≥2x ULN (cutoff, 72 mg/dL) was proved to be a valid ancillary test in predicting unfavorable outcomes for patients with *S marcescens* meningitis.

Recent epidemiologic data showed an increasing frequency of antimicrobial resistance among *S marcescens* isolates.[34–36] In this study, 32 *S marcescens* isolates from initial positive CSF sampling were all susceptible to ceftriaxone, ceftazidime, imipenem, amikacin, and gentamicin, and 31 of them were obtained from post-neurosurgical patients. Resistance to third-generation cephalosporins was only detected in one CSF isolate. Antibiotic therapy with or without neurosurgical intervention (i.e., shunt removal and/or abscess drainage) was the mainstay of treatment for our patients. Compared with carbapenems, third-generation cephalosporins had a shorter mean time to CSF sterilization (14 vs. 33 days, $p = 0.021$). Nevertheless, this phenomenon was not observed in patients with *Enterobacter* meningitis.[12] In a review of the treatment strategies for CSF shunt infections, retention of the shunt resulted in poor cure rates regardless of whether there was the use of intravenous antibiotics alone (cure rate of 24%) or with concurrent intrathecal antibiotics (cure rate 40%). In the treatment of secondary infection of an external ventricular device, removal of the device was required.[37] In this study, there was no significant difference in the outcome no matter what neurosurgeons did the removal or revision of external CSF drainage catheters or VP shunts (Table 3).

This study has limitations for its retrospective design and the small number of patients studied. However, the infrequent nature of this infection makes prospective evaluation very difficult. In addition, although this is the largest reported series of *S marcescens* meningitis to date, the single-institution setting may limit the generalizability of the findings.

In conclusion, a neurosurgical procedure for brain solid tumor has the potential for the development of *S marcescens* meningitis. The overall mortality of *S marcescens* meningitis is around 15%. CSF lactate concentration ≥2x ULN is independently associated with an unfavorable outcome. Most of the *S marcescens* CSF isolates were still susceptible in vitro to third-generation cephalosporins over a 10-year period, and the empiric therapy with parenteral third-generation cephalosporins yielded satisfactory results.

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