DOI: 10.7860/JCDR/2023/64118.18584

Case Report

Microbiology Section

Sphingobacterium multivorum Meningitis in an Immunocompetent Patient with Pituitary Macroadenoma Apoplexy: A Case Report and Review of the Literature

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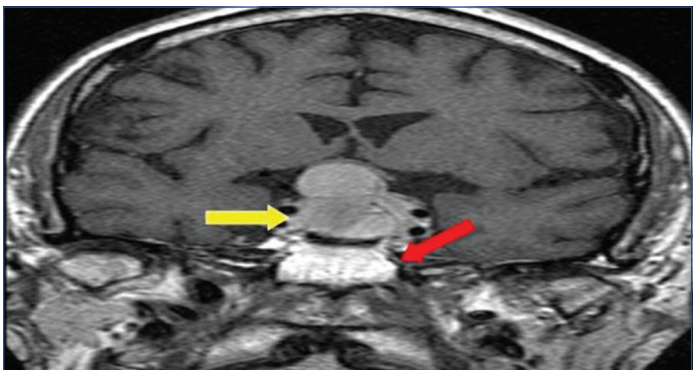
ABSTRACT

Sphingobacterium multivorum is a Gram-negative bacterium previously classified as a *Flavibacterium.* It produces non lactose fermenting colonies and is capable of producing oxidase and catalase enzymes. It is found ubiquitously in the environment and has been isolated from food, plants, soil, and aquatic environments, including hospital water supplies. Only a few cases of clinical infections caused by *Sphingobacterium multivorum* have been reported. Most cases of infection have been demonstrated in immunosuppressed patients. This case report presents the case of a 23-year-old immunocompetent woman with pituitary macroadenoma haemorrhage who developed *Sphingobacterium* meningitis following neurosurgery and subsequently died from cardiac arrest.

Keywords: Aquatic milieu, Gram-negative bacteria, Non lactose fermenting colonies, Patients, Post neurosurgery meningitis

CASE REPORT

A 23-year-old woman presented to the emergency Outpatient Department (OPD) with the chief complaints of bilateral diminished vision for the past four years, headache for the past 2.5 years, and altered sensorium for one day. On examination, she was drowsy and unresponsive to commands. Her higher mental functions could not be assessed, and speech, memory, olfaction, and comprehension could not be evaluated. Fundus examination revealed normal findings bilaterally. No facial asymmetry was observed, and assessment of other cranial nerves was not possible due to her altered sensorium. Sensory and motor examination of all four limbs showed normal nutrition, power, and tone, assessed using various physical tests commonly used in clinical examinations. The abdominal reflex was present, and the plantar reflex was bilaterally flexor. No spinal deformity was observed, but assessment of lobar signs or cerebellar signs was not possible due to the absence of neck rigidity. Upon consultation with a neuromedicine specialist, she was advised to undergo Contrast Enhanced Magnetic Resonance Imaging (CEMRI), which revealed a large, lobulated, heterogeneously enhancing soft tissue lesion in the sellar region measuring 2.7×2.4×4.1 cm^3, along with associated haemorrhage suggestive of pituitary macroadenoma with apoplexy [Table/Fig-1].

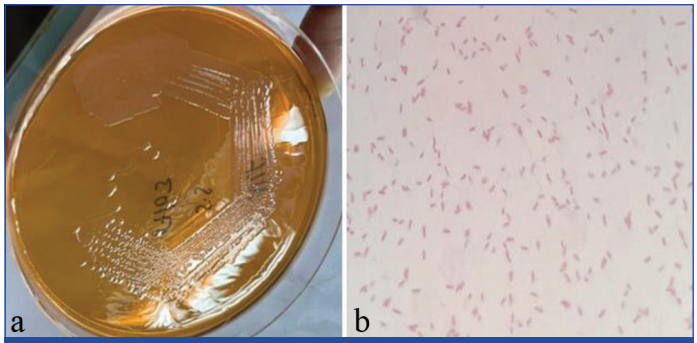


[Table/Fig-1]: CEMRI showing a large, lobulated, heterogeneously enhancing, soft tissue lesion in the sellar region associated with haemorrhage suggestive of pituitary macroadenoma (marked by yellow arrow) with apoplexy or haemorrhage (marked by red arrow).

She was referred to the Department of Neurosurgery, where she was suggested to undergo endoscopic endonasal trans-sphenoidal complete excision of the tumour. In the preoperative period, the patient experienced severe headache. After a thorough work-up and consultations with the endomedicine team, the patient was scheduled for emergency surgery. However, before being shifted to the operation theatre, the patient's condition deteriorated, and she was immediately transferred to the Intensive Care Unit (ICU). She received resuscitation measures, including intubation, ventilation, and ionotropic support, in order to stabilise her. Due to life-saving priorities, an External Ventricular Drainage (EVD) was inserted, but there was no improvement in the patient's Glasgow Coma Scale (GCS), which remained at E1V1M1, and her pupils were non-reactive, indicating a GCS score of three. Given the critical condition, the patient was promptly taken to the operation theatre for life-saving surgery.

Postoperatively, the patient arrived in the ICU in an unreversed and intubated state, with haemodynamic instability and a GCS score of three, similar to the preoperative state. Her general condition continued to deteriorate, and inotropic support was gradually increased. Despite all efforts, her condition worsened. She developed fever with chills, and her total leukocyte count was elevated to 20,800 cells/cubic mm. Cerebrospinal Fluid (CSF) obtained from the EVD was sent for body fluid analysis, which revealed 25 pus cells/cubic mm. CSF glucose was measured at 20 mg/dL, and a routine bacterial culture was sent to the bacteriology section of the Department of Microbiology due to the deteriorating condition. The CSF sample was inoculated on MacConkey agar, blood agar, and Robertson Cooked Meat broth (RCM broth). After 48 hours of incubation, growth of non lactose fermenting colonies was observed on MacConkey agar, and a smear prepared from the culture showed Gram-negative bacilli [Table/Fig-2].

The causative organism was identified as *Sphingobacterium multivorum* using Matrix-Assisted Laser Desorption/Ionisation-Time Of Flight-Mass Spectrometry (MALDI-TOF-MS). Antibiotic Sensitivity Testing (AST) was performed using the Kirby-Bauer Disc diffusion method on cation-adjusted Muller Hinton Agar (MHA), and the isolate was found susceptible to ceftazidime, ceftriaxone,



[Table/Fig-2]: Demonstration of: a) Mackonkey agar showing growth of non lactose fermenting colonies; and b) a Grams' stained smear prepared from a culture showing Gram-negative bacilli observed at 1000x magnification of the compound microscope.

levofloxacin, and Trimethoprim-Sulfamethoxazole (TMP/SMX), but resistant to aminoglycosides. Another CSF sample was sent after 72 hours of the first sample, which showed growth of the same microorganism. The patient was empirically started on intravenous ceftriaxone 4 g every 24 hours. Unfortunately, as haemorrhage from the pituitary gland was uncontrollable, the patient experienced sudden cardiopulmonary arrest and could not be revived despite multiple cycles of Cardiopulmonary Resuscitation (CPR). She was declared deceased.

DISCUSSION

Sphingobacterium multivorum is a Gram-negative bacterium previously classified as a *Flavibacterium*. It produces non lactose fermenting colonies and is capable of producing oxidase and catalase enzymes. The high concentration of sphingolipids in its cell wall is mainly responsible for its name. Common species within the *Sphingobacterium* genus include *S. thalophilum, S. multivorum, S. mizutae*, and *S. spiritorum* [1]. Initially, *Sphingobacterium multivorum* was known as CDC IIK biotype-2 strains and was found ubiquitously in the environment, isolated from food, plants, soil, and aquatic environments, including hospital water supplies [2]. Only a few cases of clinical infections caused by *Sphingobacterium multivorum* have been reported. Recent reports have observed infections in immunocompromised patients with cancer undergoing chemotherapy [3], patients with End-Stage Renal Disease (ESRD) undergoing haemodialysis, patients with Human Immunodeficiency Virus (HIV) and cystic fibrosis [4,5], and patients with diabetes mellitus [6]. The most common infections caused by this ubiquitous microorganism include bactaeremia, meningitis, spontaneous bacterial peritonitis, and lung infections.

This case involves an immunocompetent patient who presented with progressive bilateral vision loss, along with a headache and altered sensorium. She was diagnosed with pituitary macroadenoma with haemorrhage on CEMRI. She underwent endoscopic endonasal trans-sphenoidal complete excision of the tumour, after which she developed a headache. Due to a lowering GCS, an EVD was inserted, but there was no improvement. The patient experienced fever with chills, and her CSF sample from the EVD showed growth of a rare organism, *Sphingobacterium multivorum*, which was susceptible to ceftazidime, ceftriaxone, levofloxacin, and TMP/SMX. Unfortunately, she succumbed to pituitary haemorrhage and fever, and despite four cycles of CPR, she could not be revived.

To date, most isolates of *Sphingobacterium multivorum* have been identified in immunosuppressed individuals, including those with type 2 diabetes mellitus, chronic lung diseases, and underlying co-morbidities such as cystic fibrosis and chronic kidney disease. Infections caused by this bacterium can be deadly if not recognised early [7]. A case report by Abro AH et al., showed confirmed infections in immunocompetent individuals, such as the young patient in this case report with a diagnosis of pituitary macroadenoma [8].

The antibiotic susceptibility of *Sphingobacterium multivorum* consistently shows resistance to aminoglycosides, as evident in this case report and previous studies by Lambiase A et al., Abro AH et al., and Tronel H et al., [4,8,9]. *Sphingobacterium multivorum* is known to exhibit properties of Extended-Spectrum Beta-Lactamase (ESBL) resistance, Metallo-Beta-Lactamase (MBL) resistance, and resistance to third-generation cephalosporins [9]. However, the isolate identified in this case was found to be sensitive to ceftazidime, ceftriaxone, levofloxacin, and TMP/SMX, which are extensively used at this centre for suspected opportunistic infections among immunosuppressed individuals. Previous studies have also shown that most isolates of *Sphingobacterium multivorum* are susceptible to TMP/SMX [4,6,10-13], while a study by Verma RK et al., suggested sensitivity to only gatifloxacin [14]. Gatifloxacin was not tested for the isolate in this study. Other cases reported in the literature have involved immunocompromised individuals, including patients with cystic fibrosis [13], patients with End-Stage Renal Disease (ESRD) with benign prostatic hyperplasia [14], patients with multiorgan dysfunction [15], and patients with multiple myeloma [16]. This study presents a case of *Sphingobacterium multivorum* meningitis in an immunocompetent patient, which is rare. [Table/Fig-3] represents a review of infections caused by *Sphingobacterium multivorum* in recent years [3,4,6-8,10-12,14-18].

S. No.	Author(s)	Publication year	Country of study	Age/Gender	Co-morbidities	Diagnosis	Antibiotic susceptibility result	Treatment and outcome
1	Dhawan et al., [11]	1980	Chicago, Illinois, United States of America	60 years, Male	Alcoholic liver disease, esophageal stricture due to an attempt of suicide by ingestion of strong alkaline corrosive	Sepsis due to spontaneous bacterial peritonitis caused by *Pseudomonas paucimobilis*; and Aspiration pneumonia leading to acute respiratory failure	Susceptible to tetracycline, carbenicillin, TMP/SMX	Initial treatment with ampicillin and gentamicin with no improvement, followed by treatment with gentamicin and carbenicillin for 11 days. Recovered
2	Potvliege et al., [12]	1984	Brussels, Belgium	43 years, Male	Chronic renal disease maintained on hemodialysis with a history of arteriovenous fistula infection and bilateral nephrectomy	Bacteremia caused by *Flavobacterium multivorum*	Susceptible to erythromycin, tetracycline, chloramphenicol, vancomycin, gentamicin, sulfonamides, TMP/SMX	Treated with ampicillin (MIC of 8 µg/mL) for 10 days and 1 dose of tobramycin. Recovered
3	Freney et al., [3]	1987	Brussels, Belgium	57 years, Male	Non-Hodgkin lymphoma on chemotherapy complicated by bone marrow aplasia	Bacteremia caused by *Sphingobacterium multivorum*	MICs (mg/L): pefloxacin, 0.5; rifampin, 1; tetracycline, 2; erythromycin, 4; TMP/SMX, 5; chloramphenicol and ceftriaxone, 8; ceftazidime and cefotaxime, 16; carbenicillin and azlocillin, 64; Piperacillin and cephalothin, 128; gentamicin, tobramycin, vancomycin, >16; ampicillin, aztreonam and amikacin, >32; Fosfomycin, >128	Treatment with a combination of pefloxacin and TMP/SMX. Recovered

4	Reina et al., [15]	1992	Palma de Mallorca, Spain	20 month, Female	Cystic fibrosis	Sepsis with acute exacerbation of chronic bronchopathy caused by *Sphingobacterium multivorum*	Susceptible to carbenicillin, ceftazidime, ceftriaxone, cefuroxime, chloramphenicol, azlocillin, cefotaxime, ticarcillin, ciprofloxacin, imipenem, piperacillin, amikacin	Treated with ceftazidime. Recovered
5	Areekul et al., [6]	1996	Bangkok, Thailand	47 years, Male	Type 2 diabetes; HIV	Bacteremia, meningitis, liver failure caused by *Sphingobacterium multivorum*	Sensitive to TMP/SMX, chloramphenicol, tetracycline, cefotaxime, ceftazidime, ceftriaxone	Initial treatment with gentamicin and ampicillin. Then changed to ceftriaxone and TMP/SMX. Died
6	Vella et al., [13]	2001	Aranda de Duero, Burgos, Spain	74 years, Male	Chronic obstructive pulmonary disease	Sepsis due to respiratory infection caused by *Sphingobacterium multivorum*	Susceptible to TMP/SMX, tetracyclines, quinolones, aminoglycosides, β-lactams	Ceftazidime was used initially and then changed the antibiotic to cefuroxime. Recovered
7	Lambaise et al., [4]	2009	Naples, Italy	S. multivorum was isolated from 3 (2 female, 1 male) patients	Cystic fibrosis, pancreatic insufficiency	Chronic lung infection (Of 21 cases, 13 cases of *Sphingobacterium spiritovorum* and 8 cases of *Sphingobacterium multivorum*)	Susceptible to TMP/SMX and quinolones	The therapy given was not specified. The outcome of patients is not specified.
8	Grimaldi et al., [10]	2012	Paris, France	64 years, Female	Morbid obesity, coronary artery disease, type 2 diabetes, rheumatoid arthritis on long-term intermediate-dose corticosteroids	Septic shock, encephalopathy, acute kidney injury on hemodialysis, respiratory failure as a consequence of necrotising fasciitis caused by *Sphingobacterium multivorum*	Susceptible to amoxicillin-clavulanate, Ticarcillin-clavulanate, quinolones, TMP/SMX	Treated with amoxicillin-clavulanate for 10 days. Recovered
9	Nielsen et al., [16]	2014	Copenhagen, Denmark	Three cases of infection following Transrectal prostate biopsy: Case 1: 79 years, Male Case 2: 59 years, Male Case 3: 69 years, Male	Case 1: End-stage renal disease managed on hemodialysis, benign prostatic hyperplasia, and prostate cancer; Case 2 and Case 3 had benign prostatic hyperplasia	All cases were diagnosed with cystitis, while the first case also developed bacteremia caused by *Sphingobacterium multivorum*	Cases 1 and 2 both were susceptible to Ciprofloxacin and TMP/SMX. Antibiotic susceptibility testing was not available for Case 3	Case 1: Piperacillin/tazobactam was started initially and discharged on oral ciprofloxacin; Case 2: Antibiotic treatment not given; Case 3: TMP/SMX was given for 10 days. All patients recovered
10	Verma et al., [14]	2014	Uttar Pradesh, India	36 years, Male	A long history of intermittent skin lesions at multiple sites with delayed healing	Meningoencephalitis caused by *Sphingobacterium multivorum*	Sensitive to Gatifloxacin only and intermediate sensitive to piperacillin-tazobactam	Artesunate therapy in view of Malaria was started initially but later was started on Gatifloxacin. Died
11	Barahona et al., [7]	2016	New Jersey, United States of America	67 years, Female	Morbid obesity, chronic smoking, Chronic obstructive pulmonary disease, obstructive sleep apnea, severe pulmonary hypertension, atrial fibrillation, type 2 diabetes, hypertension, dyslipidemia	Sepsis and acute kidney injury in view of bacteremia caused by *Sphingobacterium multivorum*	Susceptible to amikacin, cefepime, cefotaxime, ceftriaxone, ciprofloxacin, gentamicin, imipenem, tetracycline	Cefepime and vancomycin were started initially and later switched to ciprofloxacin. Recovered
12	Abro et al., [8]	2016	Dubai, United Arab Emirates	28 years, Male	No underlying co-morbidities	Bacteremia and Meningitis caused by *Sphingobacterium multivorum*	Susceptible to ceftriaxone (MIC 8 µg/mL), cefotaxime (MIC 8 µg/mL), cefepime (MIC 2 µg/mL), ciprofloxacin (MIC 1 µg/mL), tetracycline (MIC 4 µg/mL), and trimethoprim-sulfamethoxazole (MIC <20 µg/mL)	Intravenous Acyclovir and Ceftriaxone were started initially and later Acyclovir was stopped and i.v. Ceftriaxone was continued for 10 days. Recovered
13	Pernas-Pardavila et al., [17]	2019	Santiago de Compostela, Spain	75 years, Female	Hypertension, Type 2 diabetes mellitus, Ischemic heart disease, paroxysmal atrial fibrillation, post-thyroidectomy hypothyroidism, and active seropositive rheumatoid arthritis	Pressure ulcer infected by *Sphingobacterium multivorans*	Sensitive to minocycline, levofloxacin, ciprofloxacin, and trimethoprim-sulfamethoxazole.	Ciprofloxacin therapy was started for the ulcer for 14 days. Recovered

14	Konala et al., [18]	2020	New York, United States of America	70 years, Female	Multiple myeloma in remission on steroids and lenalidomide, spinal stenosis, and osteolytic lesions from multiple myeloma, chronic obstructive pulmonary disease, hypertension, hypothyroidism, and hyperlipidemia	Cellulitis progressing to bacteremia and, eventually, sepsis caused by *Sphingobacterium multivorum*	Susceptible to ciprofloxacin (0.5 µg/mL MIC), levofloxacin (≤0.12 µg/mL MIC), and TMP/SMX (≤0.12 µg/mL MIC)	Initially was treated with vancomycin and levofloxacin but after antibiotic susceptibility testing levofloxacin was continued. Recovered
15	This case	2023	Lucknow, Uttar Pradesh, India	23 years, Female	Immunocompetent with pituitary macroadenoma apoplexy	Meningitis caused by *Sphingobacterium multivorum*	Susceptible to ceftazidime, ceftriaxzone, levofloxacin and Trimethoprim-Sulphamethoxazole (TMP/SMX)	Intravenous ceftriaxone was started empirically but due to uncontrolled pituitary hemorrhage patient died.

[Table/Fig-3]: Review of literature on infections caused by *Sphingobacterium multivorans* (N=15) [3,4,6-8,9-16].
ESRD: End stage renal disease; TMP/SMX: Trimethoprim-sulphamethoxazole; MIC: Minimum inhibitory concentration

To the best of our knowledge, this is one of the rare cases of *Sphingobacterium multivorum* reported as a causative pathogen among immunocompetent individuals. It is the fourth case of *Sphingobacterium multivorum* meningitis reported worldwide and the second case reported from India. The exact source of infection could not be determined in this study, but the repeated isolation of the microorganism suggests it as a probable cause of meningitis. The suggested source of infection could be nosocomial, as the patient developed fever after surgery and placement of the External Ventricular Drainage (EVD). Improved implementation of infection control practices may be necessary to prevent such cases in the future.

CONCLUSION(S)

This study provides an insight into the isolation of meningitis caused by *Sphingobacterium multivorum*, along with its specific antibiotic sensitivity pattern. This information can help clinicians in selecting appropriate antibiotic therapy. Additionally, it emphasises the importance of implementing strict infection control practices to prevent the nosocomial spread of infections caused by rare pathogens, which have the potential to acquire drug resistance from multidrug-resistant pathogens present in the hospital environment.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Mar 25, 2023
- Manual Googling: Jul 06, 2023
- iThenticate Software: Oct 18, 2023 (9%)

ETYMOLOGY: Author Origin

EMENDATIONS: 5

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. No

Date of Submission: **Mar 17, 2023**
Date of Peer Review: **Jun 30, 2023**
Date of Acceptance: **Jul 26, 2023**
Date of Publishing: **Oct 01, 2023**