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Multidrug-Resistant Proteus Mirabilis Meningitis in an Adolescent with Homozygous Sickle Cell Disease: Case Report

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Abstract

Background: Sickle cell disease (SCD) increases susceptibility to severe bacterial infections due to early functional asplenia. Bacterial meningitis in this population is usually caused by encapsulated organisms, while *Proteus mirabilis meningitis* is rare. Multidrug resistance further complicates management. **Case presentation**: A 17-year-old girl with homozygous SCD (HbSS), receiving hydroxyurea and folic acid therapy with up-to-date immunizations, was admitted to the intensive care unit with fever, altered consciousness, dysarthria, and paraparesis in the context of a vaso-oclusive crisis. An initial cerebral CT scan without contrast was normal. Despite empirical ceftriaxone therapy, she developed meningeal signs. Cerebrospinal fluid was turbid with neutrophilic pleocytosis, hypoglycorrhachia, and elevated protein. Culture identified a metopene—susceptible, multidrug-resistant strain *of Proteus mirabilis*. Targeted intravenous metopen (2 g every 8 hours) and supportive care for sickle cell disease, including red blood cell transfusion, led to defervescence and complete neurological recovery in less than 48 hours. **Conclusions**: This rare case underlines the need for early lumbar puncture and rapid microbiological confirmation in severe infections in patients with SCD, particularly in settings where antimicrobial resistance is increasing.

Keywords

Sickle Cell Disease, Bacterial Meningitis, *Proteus mirabilis*, Antimicrobial

Resistance, Intensive Care

1. Context

Sickle cell disease (SCD) is the most common inherited hemoglobinopathy worldwide, with a particularly high prevalence in sub-Saharan Africa [1]. Early functional asplenia predisposes affected patients to severe bacterial infections, including meningitis, which remains a major cause of morbidity and mortality in this population [2].

Bacterial meningitis in patients with SCD is classically caused by encapsulated organisms, primarily *Streptococcus pneumoniae*, *Haemophilus influenzae* type b, and *Neisseria meningitidis* [2]. In contrast, infections caused by *Proteus mirabilis* are rare and generally limited to urinary tract infections [3] [4]. Community-acquired meningitis due to *P. mirabilis* is extremely rare, particularly in adolescents without a history of neurosurgery, and the emergence of multidrug-resistant strains represents a growing therapeutic challenge [5].

2. Case Presentation

This was a 17-year-old female patient, followed for homozygous sickle cell disease (HbSS) at the Sickle Cell Disease Research and Treatment Center (CRLD), admitted to intensive care on July 22, 2025, for altered consciousness occurring in the context of a vaso-occlusive crisis associated with a suspected infectious syndrome. She was receiving treatment with hydroxyurea and folic acid, and her vaccination status was up to date, including pneumococcal, meningococcal, and *Haemophilus influenzae* type b vaccines.

The onset of symptoms dated back to July 12, 2025, marked by diffuse headaches and lower back pain initially relieved by paracetamol and tramadol. On July 19, the headaches intensified, becoming unresponsive to analgesics, accompanied by projectile vomiting and an unquantified fever. Subsequently, the patient developed dysarthria and progressive motor deficits. She was initially admitted on July 20 to a peripheral hospital where a non-contrast brain CT scan was performed, which returned normal results. Given the persistence of symptoms and her sickle cell history, she was transferred the same day to the emergency department of the Point G University Hospital. She received empirical antibiotic therapy combining ceftriaxone 1 g every 8 hours and metronidazole 500 mg every 8 hours for two days before her admission to intensive care.

Upon admission to the intensive care unit, the patient was confused, with intermittent agitation, and complained of headaches and neck pain. There was no overt meningeal rigidity, and Kernig's sign was initially negative. Neurological examination revealed a motor deficit rated 3/5 in the upper limbs and 2/5 in the lower limbs, without associated sensory disturbances. Vital signs included a blood pressure of 115/70mmHg, a heart rate of 98 beats per minute, a temperature of

38.2˚C, and an SpO_2 of 97% on room air. Diuresis was decreased, with approximately 300 mL of dark urine. The cardiopulmonary examination was unremarkable, and no organomegaly was found. Gynecological examination revealed erotematic discharge, and the urine dipstick test was positive for leukocytes.

Laboratory tests showed normocytic anemia with a hemoglobin level of 8.8 g/dL, leukocytosis of 28.5×10^9/L with a predominance of neutrophils, an elevated CRP of 225 mg/L, and a procalcitonin level of 15 ng/mL. An abdominal and pelvic ultrasound performed at the bedside revealed a moderate effusion in the pouch of Douglas, suggestive of adnexitis. Blood cultures and a urine culture were performed.

Initial management included oxygen therapy via nasal cannula, rehydration with crystalloid infusion, and multimodal analgesia combining paracetamol, nefopam, and morphine. A broad-spectrum empirical antibiotic regimen was initiated, consisting of ceftriaxone 2 g every 12 hours, metronidazole 500 mg every 8 hours, and gentamicin 480 mg daily. Thromboembolic prophylaxis with low-molecular-weight heparin was started, with continuation of maintenance therapies.

Despite this treatment, the patient's condition remained marked by persistent fever reaching 39˚C - 40˚C, worsening neurological symptoms, and increased neck pain. She experienced episodes of hemoglobinemia with severe anemia (hemoglobin 4 g/L), requiring a transfusion of packed red blood cells.

On July 23, a meningeal syndrome developed with a positive Kernig's sign. A lumbar puncture was performed, yielding cloudy cerebrospinal fluid. Analysis showed 250 leukocytes/mm^3 predominantly polymorphonuclear leukocytes, 50 erythrocytes/mm^3, hypoglycorrhachia at 1.4 mmol/L, and hyperproteinorrhachia at 1.06 g/L. Culture of the cerebrospinal fluid isolated a multidrug-resistant strain of Proteus mirabilis (Figure 1) susceptible to meropenem. It was resistant to, among others: beta-lactams (except meropenem), quinolones, aminoglycosides, tetracyclines, and phenicols. Urine culture revealed an Enterobacter cloacae infection, treated with fosfomycin, while blood cultures remained negative.

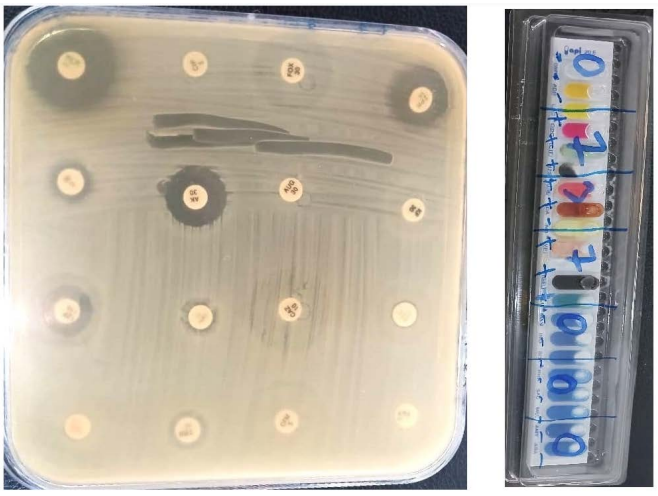

Figure 1. Identification and antibiogram.

Antibiotic therapy was adjusted with the introduction of meropenem at a dose of 2 g every eight hours by prolonged infusion for a total duration of 21 days. The clinical course was rapidly favorable, marked by the resolution of fever, a regression of pain, and complete recovery of muscle strength within 48 hours. The anemia stabilized without further hemorrhage.

Given the severity of the initial presentation and the multidrug-resistant nature of the isolated organism, the patient was kept under observation in intensive care for five days before being transferred to the sickle cell disease center for further management and follow-up. Three months after her discharge, the patient remained without sequelae and resumed her activities, including school.

3. Discussion

Bacterial meningitis remains a major medical emergency worldwide and is particularly prevalent in sub-Saharan Africa, where it continues to cause significant morbidity and mortality [6]. The clinical presentation is highly variable and depends on host factors, age, prior antibiotic exposure, and the causative pathogen. In patients with sickle cell disease (SCD), diagnosis may be delayed or complicated by overlapping symptoms of acute complications such as vaso-oclusive crises, which may initially obscure central nervous system involvement [7] [8].

Patients with SCD are at increased risk of serious infections due to early functional asplenia, impaired opsonization, and defects in innate and adaptive immunity [2]. Invasive infections are therefore classically caused by encapsulated organisms, and preventive strategies primarily focus on vaccination against these pathogens. However, this case illustrates that life-threatening infections caused by atypical and unexpected bacteria can still occur despite appropriate vaccination.

Meningitis caused by *Proteus mirabilis* is extremely rare, particularly in adolescents and in community-acquired settings. Reported cases mainly involve newborns, elderly patients, or individuals who have undergone neurosurgery or cerebrospinal fluid shunts [3] [4]. Therefore, the spontaneous occurrence of *P. mirabilis meningitis* in an immunocompromised adolescent with no history of neurosurgery is exceptional.

The pathophysiological mechanism underlying the meningitis in this patient remains unclear. Hematogenous dissemination facilitated by functional asplenia and systemic inflammation during a vaso-oclusive crisis is the most plausible explanation. Although a urinary tract infection was documented, *P. mirabilis* was not isolated from urine culture, and negative blood cultures do not rule out transient bacteremia, particularly after prior empirical antibiotic therapy.

A major clinical problem highlighted by this case is the multidrug-resistant profile of the *isolated Proteus mirabilis strain*. Resistance to third-generation cephalosporins led to empirical treatment failure. The increasing prevalence of multidrug-resistant Enterobacteriaceae in sub-Saharan Africa represents a growing public health concern and underscores the importance of early microbiological documentation with susceptibility testing [5].

Rapid cerebrospinal fluid analysis and antimicrobial susceptibility testing enabled rapid adaptation of therapy and initiation of targeted meropenem treatment. In accordance with current recommendations for Gram-negative bacillary meningitis, a prolonged 21-day course of carbapenem therapy was administered, including an initial phase of prolonged infusion in the intensive care unit to optimize pharmacokinetic and pharmacodynamic exposure [9] [10].

Although primarily targeting healthcare-associated infections, these recommendations are commonly used to inform the duration of treatment for Gram-negative bacillary meningitis. This approach has resulted in rapid clinical improvement and complete neurological recovery.

Adjuvant corticosteroids show the clearest benefit in pneumococcal meningitis, while the evidence is less established for Gram-negative bacillary meningitis [11].

Finally, this case reinforces the fact that normal neuroimaging should not delay lumbar puncture when meningitis is suspected. In febrile patients with sickle cell disease presenting with neurological symptoms, early lumbar puncture remains essential for diagnosis and prognosis.

4. Clinical Implications/Learning Points

- Atypical Gram-negative pathogens such as *Proteus mirabilis* can cause invasive meningitis in patients with sickle cell disease, even in vaccinated adolescents.
- Normal brain imaging does not rule out bacterial meningitis and should not delay lumbar puncture.
- Early microbiological documentation and susceptibility testing are essential in the context of emerging antimicrobial resistance.
- Multidrug-resistant infections require rapid adaptation of antimicrobials and access to carbapenems.
- Optimal care requires a multidisciplinary approach addressing both the complications of the infection and sickle cell disease.

5. Limitations of This Case

The case we report has several limitations that deserve to be highlighted:

- The source of the Proteus mirabilis infection remains uncertain, as this bacterium was not isolated from either blood or urine samples, which are the most common sources of dissemination.
- The antibiotic therapy administered before admission to the intensive care unit may have contributed to reducing the diagnostic yield of blood cultures and urine cultures, thereby limiting the identification of the primary infectious focus.

6. Conclusion

Community-acquired meningitis due to multidrug-resistant *Proteus mirabilis* is exceptionally rare in adolescents with sickle cell disease. Early lumbar puncture

and rapid microbiological confirmation are essential to guide effective therapy in settings where multidrug resistance is emerging.

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Ethical Approval and Consent to Participate

Not required for this case report.

Consent to Publication

Written informed consent was obtained from the patient and her legal guardians for the publication of this case report.

Availability of Data and Materials

All data generated or analyzed during this study are included in this published article.

Author Contributions

All authors contributed to patient management, data collection, manuscript writing, and approved the final version.

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Conflicts of Interest

The authors declare that they have no competing interests.

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