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Pseudomonas aeruginosa meningitis following autologous hematopoietic stem cell transplantation

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Short Report

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Abstract

Background

CNS infections caused by XDR *Pseudomonas aeruginosa* are life-threatening post-HSCT complications. The emergence of VIM-producing strains severely limits therapeutic options.

Case presentation

A 70-year-old male developed sepsis due to VIM-producing *P. aeruginosa* and subsequent meningitis on day + 7 post-autologous HSCT. Despite cefiderocol, meningitis was microbiologically confirmed. Therapy was optimized using 3-hour cefiderocol infusions plus intravenous and intrathecal colistin. The course was complicated by severe neurological decline and secondary thrombotic microangiopathy. Following intensive treatment, CSF sterilization was achieved. The patient ultimately recovered and was discharged with mild residual cognitive impairment.

Conclusion

This case highlights the efficacy of cefiderocol and dual-route colistin in treating XDR Gram-negative meningitis.

Introduction

Central nervous system (CNS) infections caused by *Pseudomonas aeruginosa* are rare but severe complications in immunocompromised patients. In the general adult population, *P. aeruginosa* meningitis is uncommon and occurs most frequently after neurosurgical procedures, whereas spontaneous cases are typically observed in patients with severe underlying diseases [1–3]. Among hematopoietic cell transplant recipients, invasive *P. aeruginosa* infections occur in approximately 1–2% of patients and are associated with high mortality rates, reaching 36% during the initial episode of infection [4].

Here, we present the case of a 70-year-old male who developed *Pseudomonas aeruginosa* sepsis and meningitis, which occurred following autologous hematopoietic stem cell transplantation.

Case presentation

A 70-year-old male with relapsed/refractory multiple myeloma underwent a second autologous hematopoietic stem cell transplantation (ASCT). Previously he was treated with multiple lines of therapy including VTD, VTD-PACE, daratumumab-based therapy, KRD, and the bispecific T-cell engager (BiTE) linvoseltamab. At the time of admission, the patient was in complete remission with ECOG performance status of 1.

On day 6 post-ASCT, the patient sustained a scalp injury following an apparent fall and neuroimaging showed no acute traumatic pathology. By day 7, he developed febrile neutropenia (CRP 314.2 mg/L). Blood and central venous catheter cultures yielded VIM-producing *Pseudomonas aeruginosa*.

Antimicrobial susceptibility testing (Table 1) demonstrated an extensively drug-resistant (XDR) phenotype, susceptible only to cefiderocol and colistin. Targeted therapy with cefiderocol (2g every 8 hours) IV was initiated.

Antibiotic	MIC [mg/L]	Interpretation[1]
Piperacillin/Tazobactam	32	R
Cefepime	>8	R
Ceftazidime	16	R
Imipenem	>8	R
Meropenem	4	I[2]
Amikacin	>16	R
Ciprofloxacin	>1	R
Colistin	2	S
Ceftazidime/Avibactam	>8	R
Aztreonam	8	R
Cefiderocol	0.5	S

Table 1. Antimicrobial susceptibility profile of the blood isolate of *Pseudomonas aeruginosa*.

[1] *Interpretations based on EUCAST clinical breakpoints.*

[2] (ATU): Susceptible, increased exposure (Area of Technical Uncertainty for *P. aeruginosa*)

Abbreviations: MIC, minimal inhibitory concentration; S, susceptible; R, resistant; I, intermediate.

Despite neutrophil engraftment on day +11, the patient developed acute delirium. CSF analysis (Table 2) confirmed meningitis with persistent growth of VIM-producing *P. aeruginosa*, despite four days of cefiderocol.

Parameter	Day 11	Day 14	Day 16	Day 22	Day 32
White cell count in CSF (x10^6/L)	60	654	1240	23	7
Polymorphonuclear neutrophil in CSF (%)	46	91	95	16	0
Lymphocytes in CSF (%)	43	7	3	68	81
CSF culture	*Pseudomonas aeruginosa*	*Pseudomonas aeruginosa*	*Pseudomonas aeruginosa*	Sterile	Sterile
Protein (g/L)	0.984	0.959	0.877	2.070	0.823
Glucose (mmol/L)	1,16	1,02	0,43	2,15	1364
Antimicrobial therapy	Cefiderocol	Cefiderocol + colistin	Cefiderocol + colistin	Cefiderocol	Meropenem

Table 2: CSF parameters and antibiotherapy received during hospitalization.

Antimicrobial therapy was escalated to prolonged 3-hour cefiderocol infusions combined with intravenous and intrathecal (IT) colistin for 3 days (Table 3). Cultures from the scalp wound also yielded *P. aeruginosa*, suggesting a possible reservoir for persistent bacteremia.

Day post-ASCT	IT colistin	IV colistin
14	0.25 MIU	8 MIU loading dose, followed by 5 MIU maintenance dose
15	-	10 MIU (5 MIU every 12 hours)
16	0.25 MIU	10 MIU (5 MIU every 12 hours)

Table 3: Colistin infusion regimen.

Abbreviations: IT, intrathecal; IV, intravenous; post-ASCT, post-autologous hematopoietic stem cell transplantation.

Following the administration of IV and IT colistin, a transient decline in renal function was observed, with serum creatinine peaking at 243 µmol/L. Consequently, doses of concomitant drugs, including cefiderocol, were adjusted. Renal function recovered rapidly with hydration.

Despite intensification of therapy, the patient's neurological status deteriorated further. While CSF cultures remained positive, inflammatory parameters increased markedly (Table 2). On day 21, the patient progressed from delirium to stupor and eventually coma, with the Glasgow Coma Scale (GCS) score of 5.

Examination showed fixed rightward gaze, horizontal nystagmus, meningismus, and myoclonic activity. Head CT remained unchanged. The patient was transferred to the intensive care unit (ICU).

By day 22, CSF pleocytosis decreased and, for the first time, CSF cultures became sterile. Cefiderocol monotherapy was continued. Subsequent workup of thrombocytopenia revealed ADAMTS-13 activity of 0,29 IU/mL, raising suspicion of secondary thrombotic microangiopathy, and therapeutic plasma exchange was initiated.

Following the combined antimicrobial and plasma exchange, the patient's condition gradually improved. As the infection and thrombotic microangiopathy resolved, the patient's neurological status steadily improved. On day 30, therapy was de-escalated to meropenem to complete the clinical course. He was eventually discharged home, microbiologically cured and hemodynamically stable, with only mild residual cognitive disorientation. The clinical course is summarized in Figure 1.

Discussion

CNS infections caused by XDR *P. aeruginosa* are rare but highly lethal in post-transplant patients, with limited evidence to guide therapy. In this case, the isolate was susceptible only to cefiderocol and colistin. Cefiderocol represents a potential therapeutic option for CNS infections caused by XDR Gram-negative pathogens. However, clinical data remain limited and largely restricted to small series and case reports. Available evidence suggests variable and often low CNS penetration, influenced by factors such as meningeal inflammation and critical illness, making pharmacokinetic optimization essential [5].

In our case, persistent CSF positivity despite early cefiderocol therapy suggests that standard dosing may be insufficient in CNS infections, likely due to pharmacokinetic constraints [6]. Escalation to prolonged 3-hour infusions was undertaken to optimize time above MIC, which may have contributed to subsequent microbiological clearance. These findings align with emerging data suggesting PK/PD optimization, rather than dose alone, is critical for efficacy in this setting [7].

The addition of intravenous and intrathecal colistin appeared decisive. Given the limited CNS penetration of systemic polymyxins, intrathecal administration likely enabled adequate bactericidal concentrations and facilitated CFS sterilization [8].

A key observation was the marked neurological deterioration occurring concurrently with microbiological response. The temporal association with neutrophil engraftment and pronounced CSF pleocytosis suggest that clinical worsening may have been driven by exaggerated inflammatory response following immune recovery rather than uncontrolled infection. This phenomenon resembles an immune reconstitution inflammatory syndrome (IRIS)-like process, which has been described in CNS infections and post-transplant settings, where paradoxical clinical deterioration occurs despite appropriate antimicrobial therapy [9].

Finally, the identification of colonized scalp wound underscores the importance of source control in preventing persistent bacteremia and CNS seeding.

Conclusion

This report contributes to the limited but growing clinical evidence supporting the potential role of cefiderocol in treating CNS infections caused by multidrug-resistant Gram-negative bacteria, particularly in situations where therapeutic options are extremely limited. Our findings also highlight the importance of treatment optimization and the potential role of inflammatory responses in clinical deterioration despite microbiological control.

Declarations

Funding

None.

Conflicts of Interest

The authors declare no conflicts of interest.

Informed Consent

Written informed consent was obtained from the patient for publication of this case report.

Author Contribution

Both authors wrote and reviewed the manuscript

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Figures

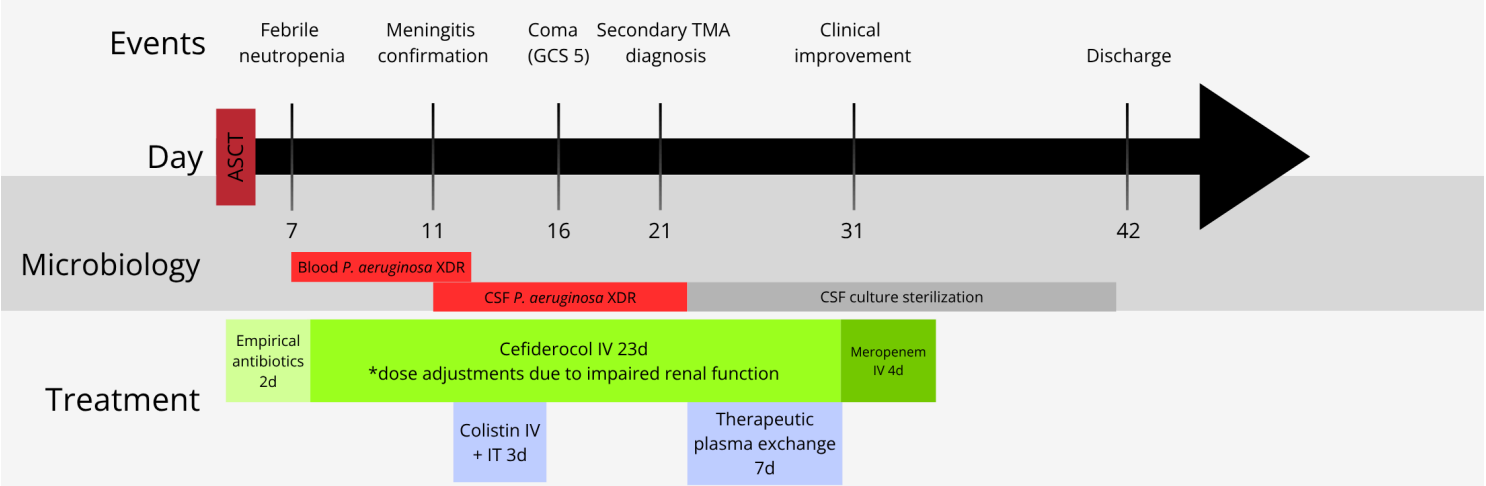


Figure 1

Clinical timeline of infection, microbiological findings, and treatment following autologous HSCT.

Abbreviations: ASCT, autologous stem cell transplantation; CSF, cerebrospinal fluid; GCS, Glasgow Coma Scale; IV, intravenous; IT, intrathecal; TMA, thrombotic microangiopathy; XDR, extensively drug-resistant.

Supplementary Files

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