Successful Non-β-lactam-based Treatment for a Case with Cefiderocol-resistant, NDM-producing *Escherichia coli* Bacteremia after Hematopoietic Stem Cell Transplantation

CAS-100

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Yoshihiro Fujiya[1], Atsuo Togashi[1], Satoshi Suzuki[1], Atsushi Saito[2], Hiroto Horiguchi[3], Satoshi Iyama[3], Yuba Inamine[4], Satowa Suzuki[4], Masayoshi Kobune[3], Koji Kuronuma[2] and Satoshi Takahashi[1]

1. Infectious disease & Laboratory Medicine, 2. Respiratory & Allergy Medicine, 3. Hematology, Sapporo Medical University, Japan
4. Antimicrobial Resistance Research Center, National Institute of Infectious Diseases, Japan Institute for Health Security

Introduction

Cefiderocol (FDC) is the only available drug for infections caused by metallo-β-lactamase (e.g., NDM) producing carbapenem-resistant Enterobacterales (CRE). Recently, resistance to FDC has emerged among NDM producers, making treatment extremely challenging. We present a successfully treated case of bacteremia due to FDC-resistant NDM-producing *E. coli*.

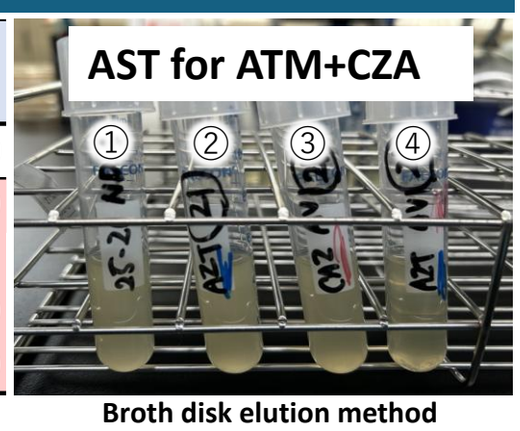
Case; 50-year-old Japanese man

- T-lymphoblastic leukemia/ lymphoma and continuous severe neutropenia
- After hematopoietic stem cell transplantation
- Diabetes mellitus
- Travel history to China 10 years earlier

Antimicrobial Susceptibility Test (AST)

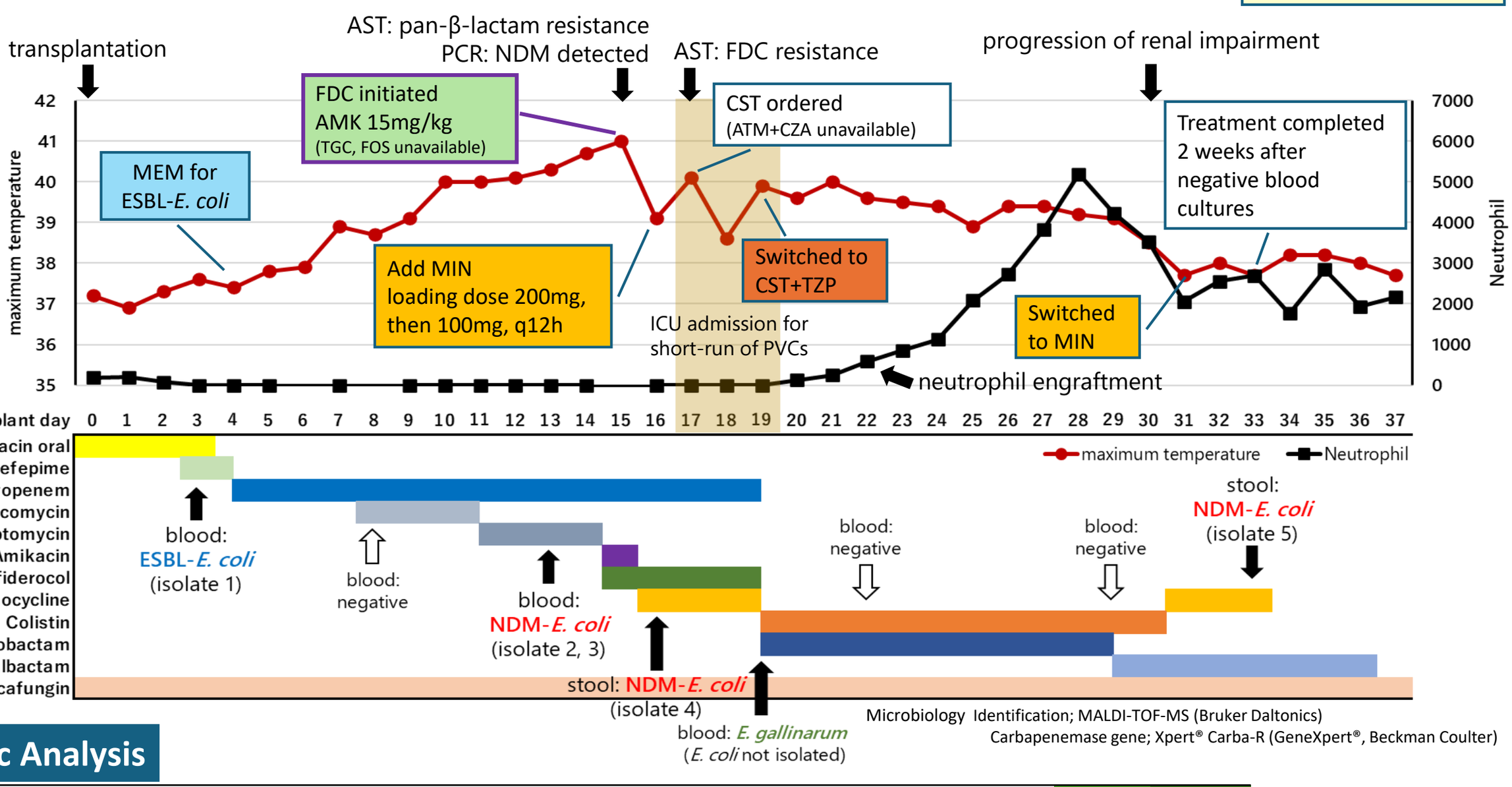
	Day of Culture	Source	BL	ATM	MEM	AMK	MIN	CIP	SXT	FOS	CST	FDC*
1	PTD3	Blood	ESBL	R (>16)	S (≤0.12)	R (>32)	I (8)	R (>2)	R (>2)	R (>16)	S (≤2)	S (0.12)
2	PTD13	Blood	NDM	R (>16)	R (>8)	S (≤16)	S (≤4)	R (>2)	R (>2)	S (≤4)	S (≤2)	R (≥64)
3	PTD13	Blood	NDM	R (>16)	R (>8)	I (32)	S (≤4)	R (>2)	R (>2)	S (≤4)	S (≤2)	R (16)
4	PTD16	Stool	NDM	R (>16)	R (>8)	S (≤16)	S (≤4)	R (>2)	R (>2)	I (16)	S (≤2)	R (≥64)
5	PTD33	Stool	NDM	R (>16)	R (>8)	S (≤16)	I (8)	R (>2)	R (>2)	S (≤4)	S (≤2)	R (≥64)

PTD, post-transplant day; BL, β-lactamase
MICs (μg/mL) were determined using the MicroScan WalkAway DxM 1096 (Beckman Coulter), and breakpoints were interpreted according to CLSI **M100-30ED**.
*FDC MICs were determined by broth microdilution (Shionogi), interpreted per CLSI M100-35ED.



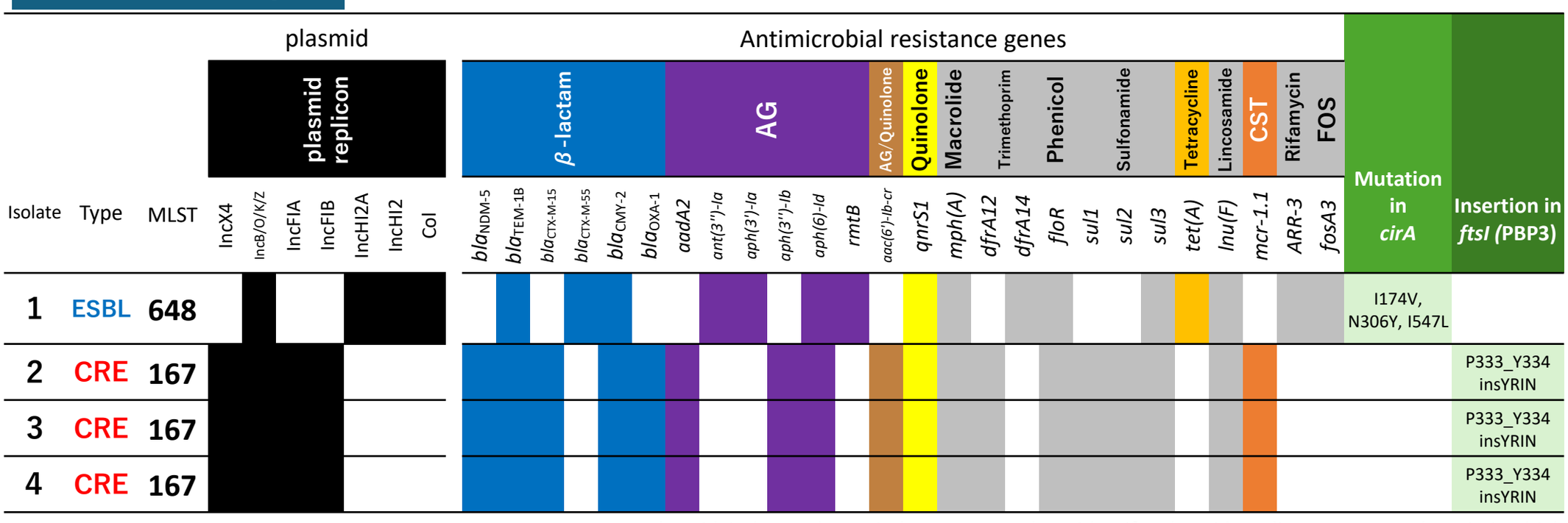
Broth disk elution method
①no disk ②ATM ③CZA ④ ATM+CZA

Resistance to ATM+CZA



Microbiology Identification; MALDI-TOF-MS (Bruker Daltonics)
Carbapenemase gene; Xpert® Carba-R (GeneXpert®, Beckman Coulter)

Genomic Analysis



PlasmidFinder and ResFinder were used to identify plasmid replicon genes and antimicrobial resistance genes, respectively, with thresholds of 95% identity and 96% coverage.

The initial ESBL-producing *E. coli* (isolate 1) differed from the later CRE isolates.

FDC resistance in *E. coli*
- **PBP3** 4-AA insertion
- **CirA** nonsense mutation
- ***bla*NDM**

PBP; penicillin-binding protein
AA; amino acid
CirA; iron-catecholate outer membrane transporter

Mutations in isolates 2–4 were consistent with those previously reported in FDC-resistant strains.

Discussion and Conclusion

- A recent study from China reported that the susceptibility rates of NDM-producing *E. coli* were **81.6% for FDC**, 100% for TGC, 95.4% for polymyxin B, and 76.1% for AMK. *(J infect 2025;91:106563)*
- **Isolate 2, 3** and **4**: **CST susceptible** by MicroScan WalkAway; ***mcr-1* positive and resistant** by Vitek2/frozen plate.
- **AMK** and **MIN** may have contributed to its effective treatment.
- Empirical use of **non-β-lactam**, though not recommended in current guidelines, may be warranted in severe infections.

Abbreviations: TZP, piperacillin-tazobactam; ATM, aztreonam; MEM, meropenem; AMK, amikacin; MIN, minocycline; TGC, tigecycline; CIP, ciprofloxacin; SXT, trimethoprim-sulfamethoxazole; FOS, fosfomycin; CST, colistin; FDC, cefiderocol; CZA, ceftazidime-avibactam; AG, aminoglycoside