

Pseudomonas Aeruginosa with Difficult-to-Treat Resistance Cases: A Single-Center Review

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Introduction

Pseudomonas aeruginosa (PA) is of particular importance among resistant Gram-negative bacteria. Recently, Difficult-to-treat resistance (DTR) has been proposed for Gram-negative infections, and the impact of DTR-PA on patients' outcomes has been alerted¹. However, the frequency of DTR in PA and the clinical features of DTR-PA-detected cases remain unknown in local general hospitals.

Methods

A retrospective observational study at a local general hospital (600 beds) in Japan. Cases with PA detected at any culture test between October 2016 and December 2024 were identified from the culture test database. DTR-PA was defined as PA with nonsusceptibility to all of anti-PA penicillins/cephalosporins, carbapenems and fluoroquinolones¹. Medical records of DTR-PA-detected cases were reviewed.

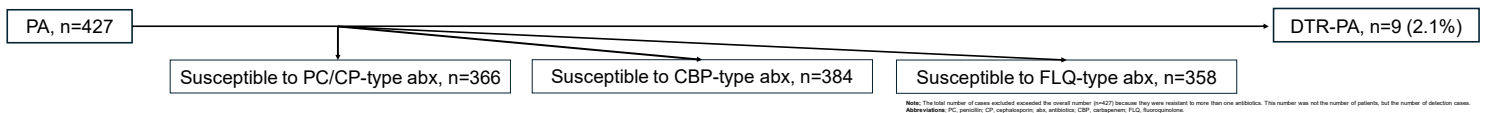
Conclusion

In a Japanese local general hospital, the **DTR-PA prevalence** was relatively **low** in cases with PA detected, while the **mortality rate** of case with DTR-PA detected was **high**.



Results

① : Figure 1: Flowchart of the Cases

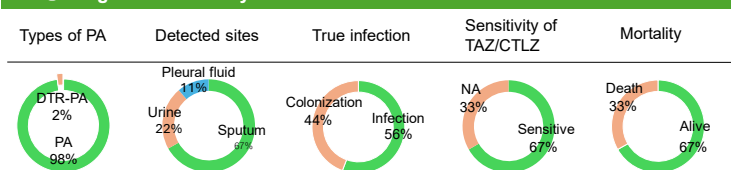


② : Table: Characteristics and Outcomes of the DTR-PA Cases

Case No.	1	2	3	4	5	6	7	8	9
Age, years old	52	60	84	79	65	52	86	71	67
Sex	M	M	M	F	M	M	M	M	M
Body mass index, kg/m ²	16.4	29.0	28.3	23.0	17.0	16.7	20.9	21.6	19.4
Comorbidities									
Bronchiectasis	(-)	(-)	(-)	(+)	(-)	(-)	(+)	(-)	(+)
Diabetes mellitus	(-)	(+)	(+)	(-)	(-)	(-)	(-)	(-)	(+)
Chronic kidney disease	(-)	(-)	(-)	(+)	(+)	(-)	(+)	(+)	(-)
Cerebrovascular disease	(+)	(-)	(-)	(-)	(-)	(+)	(-)	(+)	(-)
Case conditions									
Clinical frailty scale*	7	9	9	5	8	7	7	7	6
Serum albumin, g/dL	2.3	2.1	1.3	3.6	2.0	2.2	2.5	2.1	2.0
C-reactive protein, mg/dL	3.9	20.3	14.9	4.76	22.1	11.1	26.2	9.8	8.3
Incubation/Tracheostomy	(+)	(+)	(+)	(-)	(-)	(+)	(-)	(+)	(-)
Central venous catheter	(+)	(+)	(+)	(-)	(-)	(+)	(-)	(-)	(-)
Urinary catheter	(-)	(+)	(+)	(-)	(-)	(-)	(-)	(-)	(-)
In intensive/high care unit	(-)	(+)	(+)	(-)	(-)	(-)	(-)	(+)	(-)
PA/DTR-PA									
Cultured sites	Urn	Spt	Spt	Spt	Spt	Urn	Spt	Spt	PIF
Infection (Inf) or colonization (Col)	Inf	Inf	Inf	Inf	Inf	Col	Col	Col	Col
First detection of PA	(-)	(+)	(+)	(-)	(-)	(-)	(-)	(+)	(+)
Duration of PA to DTR-PA, months	83	NA	NA	231	5	81	186	NA	NA
Duration of admission to detection DTR-PA, days	0	25	35	0	13	0	10	246	18
MBL productive PA	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(+)	(-)
Mucoid productive PA	(-)	(-)	(-)	(+)	(-)	(-)	(-)	(-)	(-)
Antibiotics susceptibility of DTR-PA									
Susceptible to TAZ/CTLZ	(+)	(+)	(+)	UNK	(+)	(+)	UNK	UNK	(+)
Susceptible to AG-type (AMK or GM)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)
Susceptible to Colistin	(+)	(+)	(+)	(+)	(+)	(+)	(+)	UNK	(+)
Antibiotics									
Prescription of antibiotics 1 month before detection of DTR-PA	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)	(+)
Types of empirical antibiotics	CTM GM	TAZ/PIPC	LVFX LZD	MEPM AMK	TAZ/PIPC	TAZ/PIPC	CTRFX	CEZ	TAZ/PIPC
Treatment antibiotics for DTR-PA	GM	TAZ/PIPC	MEPM	MEPM AMK MFLX	MEPM AMK	(-)	(-)	(-)	(-)
Use of effective antibiotics for DTR-PA	(+)	(-)	(-)	(+)	(+)	NA	NA	NA	NA
Duration of antibiotics treatment, days	4	1	1	15	8	NA	NA	NA	NA
Reason for quitting antibiotics	cure	death	death	cure	death	NA	NA	NA	NA
Outcomes									
Length of hospital stay, days	12	28	35	22	22	25	107	357	57
OS from detection of DTR-PA, days	697	13	1	2013	22	755	211	659	142
30 days mortality	(-)	(+)	(+)	(-)	(+)	(-)	(-)	(-)	(-)
Adverse events**									
Diarrhea	(-)	(+, G1)	(-)	(-)	(-)	(+, G1)	(-)	(-)	(-)
Acute kidney injury	(-)	(-)	(-)	(+, G1)	(-)	(+, G1)	(-)	(-)	(-)

Note: Case No. 1 and 8 are same patient. *CPS is an indicator of general condition; the worse the value, the worse the condition (range 1-5). **Assessed by CTCAE v 5.0. Abbreviations: M, male; F, female; Spt, sputum; Urn, Urine; PIF, pleural fluid; NA, not available; UNK, unknown; MBL, metallo-beta lactamase; GM, meropenem; GM, Colistin.

③ : Figure 2: Summary of Outcomes



Summary of Results

- The frequency of DTR was as low as 2.1% (9/427 specimens) in the detected PA.
- Most of DTR-PA were detected in respiratory-related specimens (sputum and pleural effusion).
- All cases with DTR-PA detected had been treated with antibiotics within the past 1 month.
- Approximately a half (4/9) of detected DTR-PA were considered as colonization.
- The 30-day mortality after the first detection of DTR-PA was 33.3% (3/9).

Discussion

- The prevalence of DTR in PA in the present study was lower than previous reports (2.1-25.0%)¹⁻⁶. It may be due to differences in regions (global (geographic) or local)^{1,3}, resistance mechanism⁷, and antimicrobial stewardship.
- The 30-day mortality of cases with true infections of DTR-PA was 60% (3/5) and higher than those in previous reports (14.8-50.0%)^{5,6,8}. It may be associated with the different frequency of effective antibiotics for DTR-PA and the condition of cases.
- All DTR-PA strains with the susceptibility results obtained were susceptibility to TAZ/CTLZ. Thus, using TAZ/CTLZ in cases with DTR-PA infection may improve the outcomes.

References and COI disclosure

References can be checked here.



- Conflict of Interest Statement:** The authors have no conflicts of interest to declare.
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