

Peripheral neuropathy during long-term therapy with tedizolid

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Background

Tedizolid, the second molecule in the oxazolidinone family with linezolid, is approved for the treatment of acute bacterial skin and skin structure infections (ABSSSI). Compared to linezolid, tedizolid appears to have a better safety, especially regarding hematological and neurological tolerance. Consequently, its use has been extended to off-label indications such as bone and joint and implant-related infections. However, rare cases of tedizolid-induced optic neuritis or peripheral neuropathies have been reported. We aimed to report five cases of suspected peripheral neuropathies occurring or worsening during prolonged tedizolid therapy for complicated implant-related joint and cardiovascular infections.

Case series

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Baseline characteristics					
Sex, age (years)	Male, 72	Male, 65	Male, 65	Female, 65	Male, 75
Charlson’s comorbidity index	6	3	7	5	4
Other cause of neuropathy	-	Diabetes; other neurotoxic drug (statin)	Diabetes; chronic renal failure	-	Immune-mediated disease
Index infection	Prosthetic joint infections	Prosthetic joint infections	Cardiovascular implants	Implant-associated osteomyelitis	Prosthetic joint infections
Implicated pathogen*	<i>MRSE</i> ; <i>MSSA</i>	<i>MRSE</i>	<i>MRSE</i> ; <i>S. marcescens</i> ; <i>C. glabrata</i>	<i>K. pneumoniae</i> <i>ESBL+</i> ; <i>MRSE</i>	<i>MRSA</i>
Tedizolid therapy					
Previous therapy before tedizolid (duration of linezolid therapy, days)	Ciprofloxacin + linezolid (26)	Linezolid (15)	Levofloxacin + linezolid (25) + daptomycin + caspofungin	Piperacillin/tazobactam + linezolid (44)	Linezolid (25)
Concomitant therapy with tedizolid	No	No	Levofloxacin + caspofungin	Piperacillin/tazobactam + ciprofloxacin	No
Neuropathy description					
Time between tedizolid initiation and symptom onset or worsening (months)	13.3	2.7	12.4	8.2	25.0
Symptoms	Paresthesia	Worsening preexisting neuropathy	Worsening preexisting neuropathy	Dysesthesia	Paresthesia
Localization	Hands (bilateral)	Lower limbs	Feet (bilateral)	Feet (bilateral)	Upper and lower limbs
Time between symptom onset and electromyography (days)	92	36	81	162	42
Electromyography results	Severe sensory axonal polyneuropathy in upper and lower limbs	Axonal, sensory, length-dependent polyneuropathy	Axonal, sensory, length-dependent polyneuropathy	Normal (upper limits of the normal range)	Chronic axonal, sensory and motor peripheral polyneuropathy, predominantly in the lower limbs
Naranjo Adverse Drug Reaction Probability Scale ^o	6 (Probable)	3 (Possible)	0 (Doubtful)	3 (Possible)	3 (Possible)
Tedizolid discontinuation					
Tedizolid total duration (months)	20	2.9	16.5	8.6	25.1
Antimicrobial switch	Dalbavancin	Dalbavancin	Dalbavancin	No antibiotic	Dalbavancin
Time between discontinuation of tedizolid and first follow-up visit (days)	14	11	12	97	20
Persistence of symptoms at first follow-up visit	Yes, stable	Yes, stable	Yes, stable	Yes, stable	No, resolved
Need for neuropathy treatment	Yes	Yes	Yes	No	No
Last follow-up					
Time since discontinuation of tedizolid (years)	2.6	2.5	0.9	1	2.4
Persistence of symptoms	No, resolved	Yes, improved	Yes, stable	No, resolved	No, resolved
Need for neuropathy treatment	-	No	Yes	-	-
Electromyography control	No	Yes, improved	No	No	Yes, improved

- Time to occurrence since tedizolid initiation: 12.4 (IQR, 8,2-13,3) months
- All patients had previously been treated with a linezolid-based regimen for a median duration of 25 days, including one with linezolid-induced neuropathy (symptoms worsened under tedizolid)
- At the last follow-up (2.4 [IQR, 1-2,5] years after tedizolid discontinuation, 3 patients achieved clinical recovery from neuropathy

Conclusions

Neurological tolerance of long-term tedizolid therapy must be monitored. Preexisting neuropathy might not be a contraindication for tedizolid use, but might encourage therapeutic drug and ENMG monitorings at baseline and under treatment. The time-dependent nature of linezolid-induced neuropathy and the absence of data regarding the cumulative toxicity of both oxazolidinones advocate against the use of tedizolid in the specific case of patient experiencing linezolid-induced toxicity.