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Letter to the Editor

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Dalbavancin as long-term treatment in *Corynebacterium striatum* Infections: a literature review

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Sir,

Corynebacterium striatum is a facultative anaerobic gram-positive bacillus. Usually, it has been considered an opportunistic pathogen that colonizes skin and mucous membranes. Recent years have seen the emergence of C. striatum as a novel pathogen, particularly in those with compromised immune systems or those experiencing nosocomial outbreaks. Biofilms are a common occurrence in patients undergoing surgery or those who have received a prosthetic device, as evidenced by the presence of biofilms [1]. Its adherence to prosthetic surfaces (both hydrophobic and hydrophilic) has been attributed to the binding of fibrinogen. Recent reports of systemic infections, such as endocarditis, meningitis, osteomyelitis, and respiratory infections, as well as notable pathogens in bone and joint infections (septic arthritis), have been published [2-3]

Many laboratories do not routinely identify Corynebacterium species because they are frequently isolated as contaminants. Then their identification in culture is challenging for clinicians. New diagnostic identification technologies in clinical microbiology laboratories, such as MALDI-TOF MS, have been reported to be more accurate compared to conventional biochemical methods [2].

C. striatum exhibits limited susceptibility compared to other *Corynebacterium* species. Resistance to penicillins, cephalosporins, carbapenems, clindamycin, and fluoroquinolones is common. Susceptibility to vancomycin and linezolid is frequently found in clinical samples [3]. Then, these are the most appropriate antibiotics for *C. striatum* infections. However, both vancomycin and linezolid have significant toxicity in elderly patients. Also, vancomycin requires drug monitoring levels Therefore, the new unauthorized use of alternative medications is necessary.

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Although *C. striatum* is frequently susceptible to daptomycin, some could show daptomycin resistance or clinical failure. Chauvelot *et al.* [4] described three patients treated with daptomycin who experienced treatment failure.

Dalbavancin is a novel semisynthetic lipoglycopeptide with significant potency against a wide spectrum of Gram-positive pathogens. Its long half-life enables at least weekly administration. Rolston *et al.* [5] compared dalbavancin in vitro activity with that of vancomycin, daptomycin, linezolid, trimethoprim/sulfamethoxazole and levofloxacin against Gram-positive organisms isolated from cancer patients. Dalbavancin exhibited a more potent activity than vancomycin and daptomycin against most staphylococcal isolates, *Bacillus* spp., *Micrococcus* spp. and various streptococci. All 23 *Corynebacterium* spp. isolates were inhibited by ⩽0.03 mg/L of dalbavancin (range 0.008–0.03 mg/L). The MICs for vancomycin, daptomycin, trimethoprim/sulfamethoxazole and linezolid of these isolated were several times higher than dalbavancin.

We here present an elderly woman with an early prosthetic hip *C. striatum* infection successfully treated with debridement, antibiotics, and implant retention (DAIR), followed by long-term dalbavancin therapy.

A 91-year-old still-active female with a history of high blood pressure, moderate aortic stenosis, hypothyroidism, and severe pulmonary hypertension underwent a partially cemented left-sided total hip arthroplasty due to a sub-capital hip fracture in March 2023. Four weeks later, she consulted due to wound leakage to her general practitioner. She was immediately transferred to the orthopaedic surgery emergency department. On presentation, she was febrile at 38.5°C. The patient's left lower extremity was edematous, and examination of the left hip revealed minimal erythema, tenderness to palpation, and a decreased range of motion secondary to pain. She underwent a regimen of debridement, antibiotics, irrigation, and retention of the prosthesis (DAIR) in the operating room 24 hours after admission. Extensive necrotic tissue and pus were noted during the surgery. Thorough excision of the

Table 1 ***C. striatum*** **infections treated with dalbavancin**

Author [reference], year	Number of cases	Type of infection	Corynebacterium species	Previous therapies	Dalbavancin indication	Dalbavancin dose regimen	Adverse effects	Outcome
Molina-Collada [6], 2017	n=1	Septic native knee arthritis	*C. striatum*	Linezolid Teicoplanin	Failure (n=1)	1500 mg (one dose)	None (n=1)	Cure (n=1)
Navarro-Jiménez [7], 2022	n=7	Diabetic foot osteomyelitis	*C. striatum*	Cotrimoxazole, tedizolid, ciprofloxacin, linezolid, amoxicillin-clavulanate, clindamycin	Failure (n=3) Side effects (n=3) Failure and Side effects (n=1)	1500 mg (one dose) to 1500 mg weekly for 5 weeks	None (n=5) Nausea (n=1)	Cure (n=6) Failure (n=1)
Mansoor [8], 2023	n=6	LVAD	*C. striatum*	Vancomycin, tedizolid, daptomycin, levofloxacin, omadacycline	Convenience (n=5) Side effects (n=1)	1500 mg every two weeks	None (n=6)	Cure (n=3) Heart transplantation (n=1) Failure (n=1) LVAD thrombosis (n=1)
Soderqüist [9],2023	n=1	PJI	*C. striatum*	Vancomycin, linezolid, daptomycin	Side effects (n=1)	1500 mg every week for 12 weeks	None (n=1)	Cure (n=1)
Camara [present case], 2023	n=1	PJI	*C. striatum*	vancomycin	Convenience (n=1)	1000 mg (load dose) and 500 mg weekly for 6 weeks.	None (n=1)	Cure (n=1)

LVAD: Left Ventricular Assist Device; PJI: Periprosthetic joint infection.

necrotic tissue, rinsing and lavage, and exchange of the femoral head were performed, and six tissue biopsies were taken for culture. Empirical treatment with intravenous meropenem and vancomycin was instituted. In the biopsies, the growth of *C. striatum* was denoted. The antibiogram revealed resistance to penicillin, clindamycin, daptomycin and quinolones while being sensitive to vancomycin, linezolid, and rifampicin. Meropenem was discontinued, but a seven-day course of vancomycin was continued. Thereafter, a loading dose (1,000 mg) of dalbavancin was administered, followed by 500 mg weekly for 5 more weeks. The patient was monitored, and normal serum creatinine and GFR (83 mL/min/1.73 m^2) were noted. The local status of the soft tissue improved very slowly, with the resolution of inflammation of the hip and thigh after dalbavancin was stopped. At the follow-up in October 2023, the patient's CRP value was 0.40 mg/dL, and her extremity's inflammation had significantly declined. Her functional status was good, and she used only one walking aid outdoors.

We reviewed the scarce English literature published regarding the use of this novel antibiotic in *C. striatum* infections through a PubMed database search using the descriptors "dalbavancin", "Corynebacterium", and "infection". The main characteristics of the sixteen patients with *C. striatum* infections treated with dalbavancin are summarized in Table 1. We found four case series describing sixteen cases treated with dalbavancin (including the present case). Except for the first case reported in 2017, the remaining cases (15/16) have been recently reported between the years 2022 and 2023. Cases can be grouped into three indications: prosthetic or native osteoarticular infection (n=3), diabetic foot infections (n=7) and left ventricular assist device (LVAD; n=6). All cases received dalbavancin as at least second-line or rescue treatment (mean of 2 prior treatments). Vancomycin or linezolid were initially prescribed as treatments.

Dalbavancin indications were previous treatment failure (n=5), antibiotic side effects (n=6) and convenience (n=6). This latter indication may arouse the greatest interest in its use, as it represents an early use based on a weekly dose of the drug, as it was in our case. Dalbavancin simplifies intravenous treatment, allowing earlier patient discharge and avoiding daily venous access use, as well as vancomycin renal toxicity. In addition, linezolid poses a risk of hematological and nervous system toxicity in such an elderly patient. In contrast, dalbavancin's tolerability in the sixteen reviewed cases was excellent. No discontinuation due to adverse effects of the drug was reported.

It is noteworthy that many patients treated for diabetic foot infections (6/7) and osteoarticular infections (3/3) were cured. On the contrary, efficacy in endovascular infections was lower (3/6). These are chronic infections in which the existence of biofilm makes eradication of the microorganism difficult.

Dalbavancin has been approved for the treatment of bacterial skin and soft tissue infections as a two-dose regimen

(1,000 mg as a loading dose and one additional dose of 500 mg after 1 week) or as a single dose of 1,500 mg intravenously. However, it has also been considered for the treatment of conditions requiring prolonged antibiotic courses, such as joint and bone infections and cardiovascular infections, with or without devices. The optimal dosing and dosing interval of dalbavancin in these clinical scenarios remain to be defined. Dunne *et al.* [10] found that the steady state was reached without accumulation for 8 weeks in an extended-dosing study with 500 mg weekly administrations of dalbavancin following loading doses. However, after four weeks of use, therapeutic drug monitoring is highly recommended. Recently, some international dosing recommendations have been published based on expert panel proposals that accommodate different healthcare settings and resource availability and centre around the length of treatment duration, including up to or exceeding 6 weeks [11]. To achieve adequate dalbavancin concentrations for up to 6 weeks, 3,000 mg of dalbavancin should be given over 4 weeks for the agreed-upon complex infections requiring > 2 weeks of treatment. Therapeutic drug monitoring (TDM) is advised for longer treatment durations and in cases of renal failure.

To conclude, long-term (up to 12 weeks) dalbavancin therapy could be a successful and safe alternative for *C. striatum* infections, especially in cases of soft tissue infections such as diabetic foot and osteoarticular infections. Its role in endovascular *C. striatum* infections remains to be defined with prospective studies. Although the optimal dosing and interval of dalbavancin for extended treatment of bone and joint infections remain to be defined, therapeutic drug monitoring could help guide it.

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CONFLICTS OF INTEREST

The author declares no conflicts of interest

REFERENCES

1. Fernández-Esgueva M, et al. Infección de prótesis de rodilla por Corynebacterium striatum. Enferm Infecc Microbiol Clin.2019;37:480–491. doi: 10.1016/j.eimc.2018.05.007.
2. Streifel AC, Varley CD, Ham Y, Sikka MK, Lewis JS 2nd. The challenge of antibiotic selection in prosthetic joint infections due to Corynebacterium striatum: a case report. BMC Infect Dis. 2022;22:290. doi: 10.1186/s12879-022-07270-0.
3. Hernandez NM, Buchanan MW, Cullen MM, Crook BS, Bolognesi MP, Seidelman J, et al. Corynebacterium total hip and knee arthroplasty prosthetic joint infections. Arthroplasty Today. 2020;6:163–8. doi: 10.1016/j.artd.2020.03.008
4. Chauvelot P, Ferry T, Tafani V, Diot A, Tasse J, Conrad A, et al. Bone and joint infection involving Corynebacterium spp.: From clinical features to pathophysiological pathways. Frontiers in Medicine. 2021;7. doi: 10.3389/fmed.2020.539501.
5. Rolston KV, Wang W, Nesher L, Shelburne SA, Prince RA. In vitro activity of dalbavancin and five comparator agents against common and uncommon Gram-positive organisms isolated from cancer patients. J Antibiot (Tokyo). 2016; 69:381-7. doi: 10.1038/ja.2015.120.
6. Molina Collada J, Rico Nieto A, Díaz de Bustamante Ussia M, Balsa Criado A. Septic arthritis in a native knee due to Corynebacterium striatum. Reumatol Clin (Engl Ed). 2018;14:301-302. doi: 10.1016/j.reuma.2017.01.013.
7. Navarro-Jiménez G, Fuentes-Santos C, Moreno-Núñez L, Alfayate-García J, Campelo-Gutierrez C, Sanz-Márquez S et al. Experience in the use of dalbavancin in diabetic foot infection. Enferm Infecc Microbiol Clin (Engl Ed). 2021 Jan 12:S0213-005X(20)30416-X. doi: 10.1016/j.eimc.2020.11.013.
8. Mansoor AE, Krekel T, Cabrera NL. Experience with dalbavancin for long-term antimicrobial suppression of left ventricular assist device infections. Transpl Infect Dis. 2023;25:e14068. doi: 10.1111/tid.14068.
9. Söderquist B, Henningsson T, Stegger M. Corynebacterium striatum prosthetic joint infection successfully treated with long-term dalbavancin. Microorganisms. 2023;11:550. doi: 10.3390/microorganisms11030550.
10. Dunne MW, Puttagunta S, Sprenger CR, Rubino C, Van Wart S, Baldassarre J. Extended-duration dosing, and distribution of dalbavancin into bone and articular tissue. Antimicrob Agents Chemother. 2015 Apr;59(4):1849-55. doi: 10.1128/AAC.04550-14.
11. Senneville E, Cuervo G, Gregoire M, Hidalgo-Tenorio C, Jehl F, Miro JM et al. Expert Opinion on Dose Regimen and Therapeutic Drug Monitoring for Long-Term Use of Dalbavancin: Expert Review Panel. Int J Antimicrob Agents. 2023; 62: 106960. doi: 10.1016/j.ijantimicag.2023.106960.