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ORIGINAL RESEARCH

Molecular epidemiology and clinical significance of *Corynebacterium striatum* isolated from clinical specimens

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Purpose: This study investigated the clinical epidemiology, antimicrobial susceptibility, and molecular epidemiology of *Corynebacterium striatum* isolates.

Patients and methods: An observational study was conducted at a university hospital in the Republic of Korea from August to December 2016. All subjects were patients who tested positive for *C. striatum* clinically. Clinical data were analyzed to evaluate the microbiological and genotypic characteristics of *C. striatum* strains.

Results: Sixty-seven *C. striatum* isolates recovered from non-duplicated patients were characterized. Patients were classified into three groups according to the infection type: nosocomial infection (71.6%), health care-associated infection (8.7%), and community-acquired infection (18.8%). The most common clinical specimens were urine (35.8%) and skin abscesses (32.8%). Fifty-two (77.6%) isolates showed multidrug resistance, defined as resistance to ≥3 different antibiotic families. All strains were susceptible to vancomycin and linezolid. Resistance to other antibiotics varied: penicillin (n=65; 97.0%), ampicillin (n=63; 94.0%), cefotaxime (n=64; 95.5%), and levofloxacin (n=61; 91.0%). Phylogenetic analysis identified all 16 S rRNA gene sequences of the 67 isolates as those of *C. striatum,* where 98%–99% were homologous to *C. striatum* ATCC 6940. In multilocus sequence typing for internal transcribed spacer region, *gyrA*, and *rpoB* sequencing, the most predominant sequence types (STs) were ST2, ST3, ST6, and ST5.

Conclusion: *C. striatum* isolates may cause opportunistic infections associated with nosocomial infections through horizontal transmission. The presence of multidrug resistance and intra-hospital dissemination implicate *C. striatum* isolates as a potential target pathogen for infection control and antimicrobial stewardship programs.

Keywords: *Corynebacterium striatum*, multidrug resistant, multilocus sequence typing, opportunistic infections, nosocomial infections

Introduction

Most catalase-positive, gram-positive rods, commonly called coryneform or diphtheroid bacteria, have historically been considered simple contaminants that are unlikely to be pathogenic, when isolated from clinical specimens. Of the >80 species of *Corynebacterium* that have been reported, ~50 species rarely cause infectious diseases in humans.[1] *Corynebacterium striatum* is one of the more commonly isolated coryneform bacteria in clinical microbiology laboratories.

In the last decade, *C. striatum* has been frequently cultured from various surfaces and medical equipment in hospital settings.[2] In clinical settings, *C. striatum* is increasingly being recognized as a source of opportunistic diseases in immunocompromised

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patients suffering from malignancies, human immunodeficiency virus infection, or chronic lung diseases, and in patients wearing prosthetic devices. Furthermore, *C. striatum* is potentially pathogenic in patients with chronic diseases, who are exposed to specific circumstances, such as invasive medical procedures, prolonged use of broad-spectrum antibiotics, or long-term hospitalization.[3–5]

Occasionally, *C. striatum* strains are isolated in polymicrobial infections, where their degree of virulence remains largely undetermined. In reality, it is difficult to distinguish between a pathogen causing infection and one causing colonization. Although the clinical significance and prevalence of *C. striatum* remain unclear, this organism has been responsible for a variety of infections, such as bacteremia, arthritis, osteomyelitis, meningitis, endocarditis, breast abscess, peritonitis, wound infections, and prosthetic joint infections in both immunocompetent and immunocompromised patients.[3–6]

Infections caused by *C. striatum* are usually considered to originate endogenously. However, recent studies have documented the possibility of patient-to-patient transmission of *C. striatum*. The bacterium may cause serious nosocomial infections in intensive care unit patients and spread from patient to patient via physical contact with attending personnel or via the nosocomial environment itself.[7–9]

Despite early reports of susceptibility to a wide range of antibiotics, multidrug-resistant phenotypes have been recently reported in most *C. striatum* strains.[2,10] Moreover, multidrug-resistant *C. striatum* may cause nosocomial transmissions resulting in outbreaks in patients with specific risk factors, leading to increased mortality.[2,11]

There is limited information on the pathogenicity and clinical implications associated with *C. striatum* strains in a clinical setting. The aim of this study was to investigate the molecular characteristics, clinical significance, and antimicrobial susceptibility of *C. striatum*, with the goal of increased understanding of its pathogenicity.

Patients and methods

Study design

An observational study was conducted at the Korea University Anam Hospital, a 1,048-bed university hospital in Seoul, Republic of Korea (ROK) from August 2016 to December 2016. All subjects were adult patients (>18 years) whose clinical isolates obtained from diagnostic cultures of clinical specimens tested positive for *C. striatum*. If multiple *C. striatum* isolates were recovered from a patient, only the first isolate was included in the study.

This study was performed in compliance with the Declaration of Helsinki. The study protocol was approved by the Institutional Review Board of Korea University Anam Hospital (No. 2018AN0161). As this observational study did not entail any deviations from routine medical practice, the requirement for informed consent was waived.

Clinical data

Clinical data manually extracted from medical records included age, gender, comorbidities, clinical diagnoses, specimen categories, Charlson's comorbidity index, microbiological data, and treatment outcomes. Determination of the clinical significance of *C. striatum* isolates was based on clinical findings, such as fever, white blood cell counts, and C-reactive protein, in addition to whether the patient had or had not received antibiotics for *C. striatum*. Infections were categorized as community acquired, health care associated, or nosocomial, depending on the location that the stains were isolated from. Treatment outcomes were classified on the basis of in-hospital mortality and median length of hospitalization since *C. striatum* isolation. Additionally, demographic, clinical, and microbiological characteristics between the antibiotic treatment group and the observation group were compared.

C. striatum identification

Processing and incubation of all clinical samples was performed according to routine laboratory protocols. *C. striatum* isolates were initially identified using the MicroScan WalkAway-96 Plus system (Beckman Coulter, Inc., Brea, CA, USA) and further confirmed by sequencing of the entire 16S rRNA gene.

The *C. striatum* strains were cultured on blood agar plates for 18 hours at 37°C. The cultured colony was suspended in 200 μL of lysis buffer, incubated overnight at 37°C, and centrifuged for 5 minutes at 3,000 rpm. The pelleted bacteria were suspended in 500 μL of sterile water and boiled for 15 minutes for DNA extraction. *C. striatum* DNA was extracted using a bacterial AccuPrep Genomic DNA Extraction Kit (Bioneer, Daejeon, ROK). To amplify 16S rRNA, universal primers 16SF27 (5′-AGAGTTTGATCMTGGCTCAG) and 16SR1492 (5′-TACGGYTACCTTGTTACGACTT) were used, as previously described.[12] The purified PCR product was sequenced using primer walking with the oligonucleotides using the primers 16SF518 (5′-CCAGCAGCCGCGGTAATAC) and 16SR800 (5′- TACCAGGGTATCTAATCC).[13]

The amplified sequence was compared with those available in the GenBank database using the BLAST program.

16S rRNA sequences were aligned with Clustal W multisequence alignment program. Phylogenetic trees were constructed using the neighbor-joining genetic distance method and the MEGA 7.0 program package. The Kimura two-parameter model was chosen for all neighbor-joining tree constructions. Reliability of each tree topology was checked with 1,000 bootstrap replications.[14] Phylogenetic analysis confirmed that all 16S rRNA gene sequences of the 67 isolates were 98%–99% homologous to *C. striatum* ATCC 6940 isolates (Figure 1).

Antimicrobial susceptibility

Susceptibility to antibiotics was tested using *Streptococcus* MicroScan panel (Beckman Coulter, Inc.) and the MicroScan WalkAway-96 Plus system (Beckman Coulter, Inc.), which are considered the gold standard culture media for *Corynebacterium* as recommended by the Clinical and Laboratory Standards Institute (CLSI). The minimum inhibitory concentration (MIC) breakpoint for *Corynebacterium* (CLSI document M45-A2) was applied for the analysis of antimicrobial susceptibility.[15]

Multilocus sequence typing (MLST)

For MLST, the internally transcribed spacer 1 (ITS1) region, as well as *gyrA* and *rpoB* were amplified and sequenced for *C. striatum* strains.[2] The primers used are provided in Table S1. PCR amplification and sequence reaction were performed as previously described.[16–18]

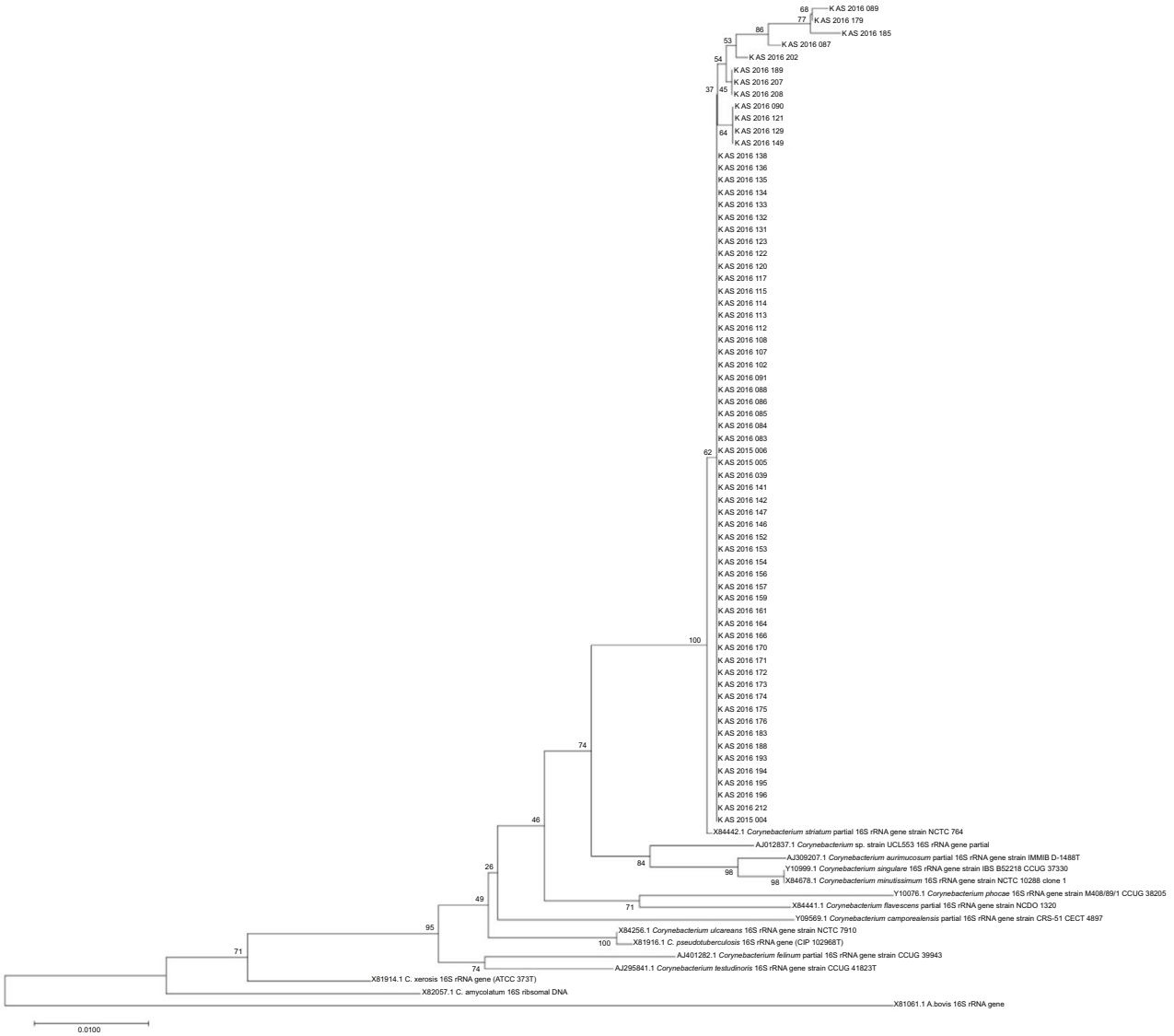


Figure 1 Phylogenetic tree based on neighbor-joining method using 16S rRNA gene sequences.
Notes: Distance estimations were calculated using the Kimura two-parameter model. Bootstrap percentages after 1,000 simulations are shown. The *Actinomyces bovis* (T) X81061 sequence was used as an outgroup.

Statistical analyses

Categorical variables are expressed as frequencies and were analyzed using Pearson's chi-squared test or Fisher's exact test. Continuous variables are expressed as medians and IQRs. The two-sample *t*-test or Mann–Whitney *U* test was used as appropriate to compare continuous variables between groups. Significance was set at $P<0.05$. SPSS Statistics, version 24.0 (IBM Corporation, Armonk, NY, USA) and SAS 9.4 (SAS Institute Inc., Cary, NC, USA) were used for data analyses.

Results

Patients and clinical characteristics

A total of 67 *C. striatum* isolates were identified in different patients. Demographic and baseline characteristics of the 67 patients are summarized in Table 1. Twenty (29.9%) patients had received antibiotics for *C. striatum* isolated from infection sites. Univariate analysis did not indicate significant differences in age, gender, category of infection, and comorbid diseases between the antibiotic treatment and the observation groups (Table 1).

C. striatum was isolated from various types of specimens (Table 2). Urine isolates (35.8%) were the most common, but only 10% of these came from those who received antibiotic therapy. Antibiotics were most commonly used in skin abscess isolates (55.0%; Table 2). Of the 67 specimens, 25 (38.8%) were polymicrobial isolates (Table 2). Among these, *Escherichia coli* (16.1%), carbapenem-resistant *Acinetobacter baumannii* (16.1%), and *Pseudomonas* species (16.1%) were the most common simultaneously isolated strains.

Antimicrobial susceptibility

All strains were susceptible to erythromycin, vancomycin, linezolid, and daptomycin (Table 3). However, intermediate

Table 1 Demographic and basic characteristics of 67 patients whose clinical specimens tested positive for *Corynebacterium striatum*

Variables	Total (N=67)	Treatment (n=20, 29.8%)	Observation (n=47, 70.1%)	*P*-value
Male, n (%)	35 (52.2)	14 (70.0)	21 (44.7)	0.058
Age (years), median (IQR)	64 (55–78)	65 (59–75)	69 (55–78)	0.564
Length from admission to *C. striatum* isolation (days), median (IQR)	15 (3–33)	12 (0–25)	20 (4–37)	0.615
Category of infection, n (%)				0.975
Community onset	13 (18.8)	4 (20.0)	9 (19.1)	
Hospital acquired	6 (8.7)	2 (1.0)	4 (8.5)	
Nosocomial	48 (71.6)	14 (70.0)	34 (72.3)	
Comorbid illness, n (%)				
Cardiovascular	22 (32.8)	6 (30.0)	16 (34.0)	0.785
Central nervous system	29 (43.3)	5 (25.0)	24 (51.0)	0.062
Malignancy	15 (22.4)	5 (25.0)	10 (21.3)	0.756
Renal	4 (6.0)	0	4 (8.5)	0.309
Hepatic	5 (7.5)	2 (10.0)	3(6.4)	0.631
Respiratory	1 (1.5)	0	1 (2.1)	1.000
Hematology	1 (1.5)	0	1 (2.1)	1.000
Transplantation	1 (1.5)	0	1 (2.1)	1.000
Diabetes mellitus	18 (26.9)	7 (35.0)	11 (23.4)	0.374
Charlson's comorbidity index, median (IQR)	2 (1–3)	2 (0–3)	2 (1–3)	0.503
Risk factors, n (%)				
Recent admission	54 (80.6)	12 (60.0)	42 (89.4)	0.392
Surgery	24 (35.8)	7 (35.0)	17 (36.2)	1.000
Prior use of antibiotics, n (%)	51 (76.1)	14 (70.0)	37 (78.7)	0.534
Steroid	8 (11.9)	3 (15.0)	5 (10.6)	0.687
Foley catheter	33 (49.3)	8 (40.0)	25 (53.2)	0.425
Mechanical ventilator	27 (40.3)	6 (30.0)	21 (44.7)	0.291
ICU care	23 (34.3)	6 (30.0)	17 (36.2)	0.780
Clinical findings				
Fever, n (%)	2 (3.0)	0	2 (4.3)	0.380
WBC ($\times 10^3/\mu L$), median (IQR)	9.8 (6.1–11.6)	12.1 (6.3–13.2)	8.9 (5.3–11.6)	0.472
CRP (mg/L), median (IQR)	75 (15–130)	109 (31–186)	59 (9–104)	0.437
Procalcitonin (ng/mL), median (IQR)	2.1 (0.1–2.9)	1.7 (0.1–1.6)	1.7 (0.1–1.6)	0.484

Abbreviations: CRP, C-reactive protein; ICU, intensive care unit; WBC, white blood cell.

Table 2 Microbiological characteristics and treatment outcomes of 67 patients whose clinical specimens tested positive for *Corynebacterium striatum*

Parameters	Total (N=67)	Treatment (n=20, 29.8%)	Observation (n=47, 70.1%)	*P*-value
Category of specimens, n (%)				0.005
Urine	24 (35.8)	2 (10.0)	22 (46.8)	
Skin abscess	22 (32.8)	11 (55.0)	11 (23.4)	
Otitis media	10 (14.9)	2 (10.0)	8 (17.0)	
Blood	6 (9.0)	1 (5.0)	5 (10.6)	
Ascites	4 (6.0)	3 (15.0)	1 (2.1)	
Pleural effusion	1 (1.5)	1 (5.0)	0	
Polymicrobial infections, n (%)	25 (38.8)	13 (65.0)	12 (25.5)	0.003
2	19 (76.0)	9 (69.2)	10 (83.3)	
≥3	6 (24)	4 (30.8	2 (16.7)	
Distribution of simultaneously isolated strain, n (%)				
Escherichia coli	5 (16.1)	3 (17.6)	2 (14.3)	0.126
Carbapenem-resistant *Acinetobacter baumannii*	5 (16.1)	4 (23.5)	1 (7.1)	0.011
Pseudomonas species	5 (16.1)	5 (29.4)	0	
Methicillin-resistant *Staphylococcus aureus*	3 (9.7)	0	3 (21.4)	0.248
Enterococcus species	3 (9.7)	0	3 (21.4)	0.248
Methicillin-susceptible *Staphylococcus aureus*	2 (6.5)	2 (11.8)	0	0.028
Methicillin-resistant coagulase-negative *S. aureus*	2 (6.5)	0	2 (14.3)	0.349
Streptococcus species	2 (6.5)	1 (5.9)	1 (7.1)	0.527
Enterobacter species	1 (3.2)	1 (5.9)	0	0.122
Proteus species	1 (3.2)	1 (5.9)	0	0.122
Klebsiella species	1 (3.2)	0	1 (7.1)	0.511
Candida species	1 (3.2)	0	1 (7.1)	0.511
Antibiotic susceptibility, n (%)				
Penicillin	2 (3.0)	0 (0)	2 (4.3)	0.525
Erythromycin	67 (100)	20 (100)	47(100)	
Levofloxacin	6 (9.0)	3 (15.0)	3 (6.4)	0.845
Vancomycin	67 (100)	20 (100)	47(100)	
Linezolid	67 (100)	20 (100)	47(100)	
Multidrug resistance, n (%)	52 (77.6)	14 (70.0)	38 (80.9)	0.106
Treatment				
In-hospital mortality, n (%)	1 (1.5)	1 (5.0)	0	0.290
Length of hospital stay since *C. striatum* isolation, median days (IQR)	35 (5–77)	31 (1–59)	31 (1–59)	0.695

Table 3 MIC_{50} and MIC_{90} values and antimicrobial susceptibility (%) of the clinical isolates of *Corynebacterium striatum*

Antibiotics	MIC (mg/L)			Percentage of susceptible isolates
	MIC_{50}	MIC_{90}	Range	
Penicillin	>4	>4	0.12–>4	3.0
Ampicillin	>4	>4	0.25–4	6.0
Cefotaxime	>2	>2	1–>2	4.5
Levofloxacin	>4	>4	≤0.5–>4	9.0
Erythromycin	>0.5	>0.5	≤0.06–>0.5	100
Linezolid	≤1	≤1	≤1	100
Vancomycin	0.5	1	≤0.25–1	100
Daptomycin	<0.25	<0.25	<0.25	100

Abbreviations: MIC, minimum inhibitory concentration; MIC_{50}, MIC for inhibition of 50% of isolates tested; MIC_{90}, MIC for inhibition of 90% of isolates tested.

to high levels of resistance to penicillin (97.0%), ampicillin (94.0%), cefotaxime (95.5%), and levofloxacin (91.0%) were observed (Table 2). Therefore, the 67 strains may be considered multidrug resistant, defined as resistance to ≥3 classes of antibiotics. There was no significant difference in the frequency of multidrug-resistant isolates between the treatment and observation groups (Table 2).

Based on resistance to penicillin, ampicillin, cefotaxime, levofloxacin, and vancomycin, the 67 *C. striatum* strains were classified into five patterns, from I to V (Table 4). Among these, pattern I, which was the multidrug-resistant phenotype susceptible to vancomycin, was the predominant in hospitalized patients (82.8%).

Table 4 Antimicrobial resistance patterns of 67 *Corynebacterium striatum* strains, categorized by susceptibility to penicillin, ampicillin, cefotaxime, levofloxacin, and vancomycin

Resistance pattern (n)	Patients (n)		Antibiotics				
	Inpatients	Outpatient	PEN	AMP	COF	LEV	VAN
I (58)	48	10	R(I)	R(I)	R(I)	R(I)	S
II (5)	1	4	R(I)	R(I)	R(I)	S	S
III (2)	1	1	S	S	S	R(I)	S
IV (1)	1	0	R(I)	S	R(I)	R(I)	S
V (1)	1	0	R(I)	S	R(I)	S	S

Abbreviations: AMP, ampicillin; COF, cefotaxime; I, intermediate; LEV, levofloxacin; PEN, penicillin; R, resistant; S, susceptible; VAN, vancomycin.

Clinical outcomes

Sepsis or septic shock was absent in all cases. Treatment outcomes of the 67 patients are shown in Table 2. Only one (1.5%) patient died during hospitalization. Death was due to a non-infectious cause. Univariate analysis showed no difference between in-hospital mortalities of the treatment and observation groups. The most commonly used therapeutic antibiotics were vancomycin, followed by tigecycline, fluoroquinolones, and piperacillin/tazobactam.

On the other hand, there were no deaths in the 42 patients who had only *C. striatum* isolated from clinical specimens. There was no difference in the length of hospital stay between the treatment and observation groups (9 [IQR, 0–15] vs 20 [IQR, 4–37] days, P=0.049).

MLST

Four genes (16S rRNA, ITS1, *gyrA,* and *rpoB*) were analyzed in all strains studied. 16S rRNA was excluded from the reinforcement analysis of MLST due to its high conservation among all strains analyzed. 16S rRNA was used to confirm the identity of *C. striatum* strains. ITS1, *gyrA,* and *rpoB* were used to discriminate among the strains, using a few nucleotide changes within sequences. Distinct allele sequences were assigned arbitrary allele numbers for each locus (Table S2).

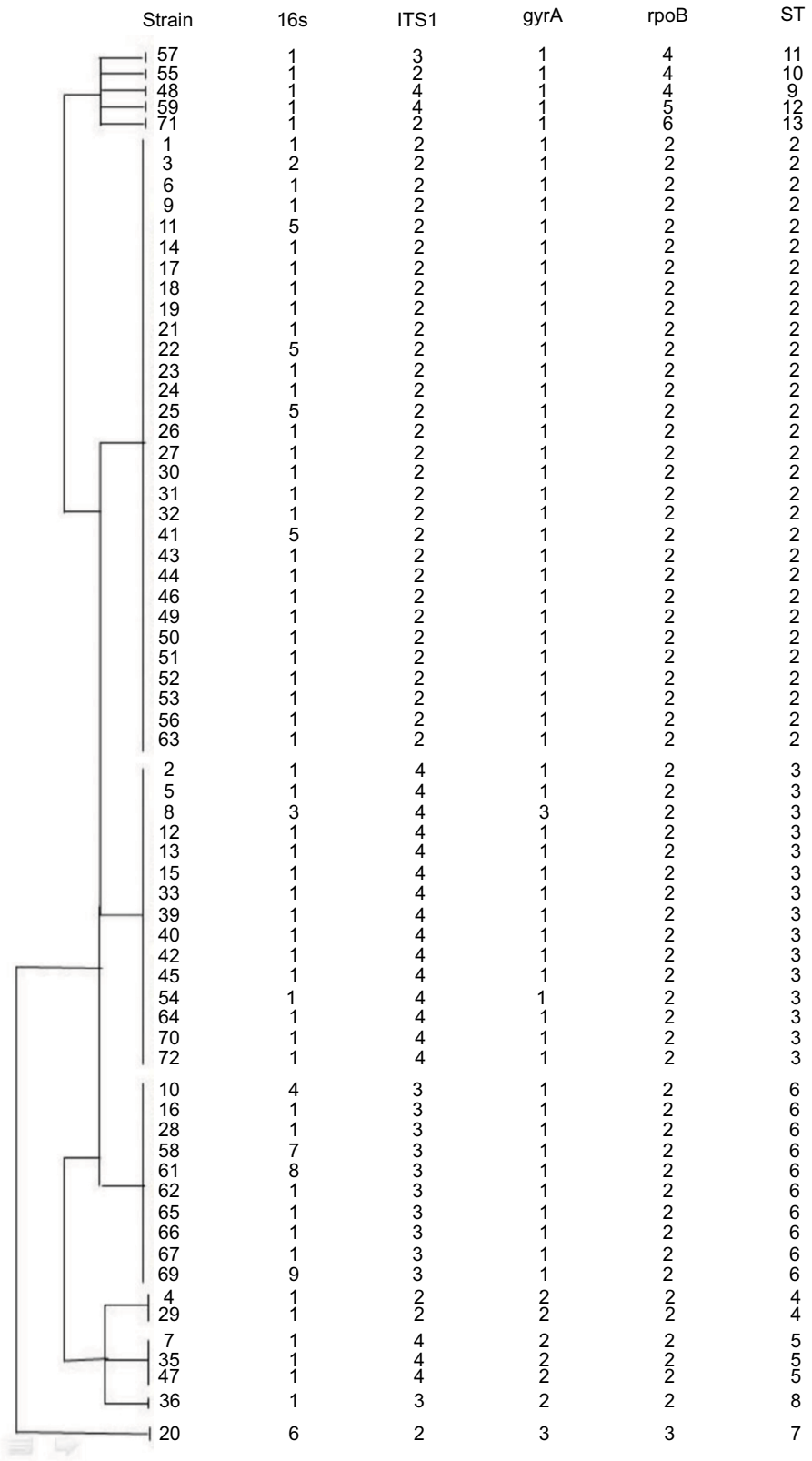
In the ITS1 region, allele 2 was the most abundant (52.2%). For *gyrA*, allele 1 was predominant (89.6%). For *rpoB*, allele 2 was the most abundant and was found in 61 strains (91.0%). Twelve sequence types (STs) were identified in these three genes. Of these, the most abundant were ST2 (44.8%), ST3 (22.4%), ST6 (14.9%), and ST5 (4.5%). Among patients with ST2, there were 24 (80.0%) nosocomial infections and 6 (20.0%) community-onset infections. Finally, each ST was grouped and schematized (Figure 2) and analyzed for antibiotic resistance (Table S2). Antibiotic resistance Pattern I occupied an overwhelming number of predominant STs: 28 (93.3%) in ST2, 13 (86.7%) in ST3, and 10 (100%) in ST6.

Discussion

This study analyzed the molecular epidemiology and clinical significance of *C. striatum* isolates recovered from clinical specimens. The data demonstrate the low virulence of *C. striatum,* reflecting its role as a colonizing opportunistic pathogen. However, the characteristics of multidrug resistance and horizontal transmission of *C. striatum* isolates suggest the possibility that it is an emerging nosocomial pathogen, which should be of interest to medical researchers.

C. striatum is reportedly susceptible to β-lactams.[19] However, presently, most strains (95.5%) display a multidrug-resistant phenotype, although all strains are susceptible to erythromycin, vancomycin, linezolid, and daptomycin. If *C. striatum* isolates are, indeed, causative agents of infections, they may require the use of broad-spectrum antibiotics such as vancomycin.[20] Antimicrobial resistance is a major global health issue. In ROK, the prevalence of vancomycin-resistant *Enterococcus faecium* has gradually increased from 22% in 2003 to 31% in 2015.[21] Since December 2010, infectious diseases caused by six types of multidrug-resistant bacteria, including vancomycin-resistant enterococci (VRE), were legally designated for surveillance as notifiable infectious microorganisms, with the enactment of the Infectious Disease Control and Prevention Act.[22] To control antimicrobial resistance, contamination and infection by *C. striatum* isolates should be accurately determined to ensure optimal use of antibiotics.

Currently, there are no guidelines for the treatment of infections caused by *C. striatum*. Optimal antimicrobial therapy is still considered controversial. Our in vitro susceptibility tests demonstrate that vancomycin and linezolid are active against *C. striatum*, indicating their potential



Strain	16s	ITS1	gyrA	rpoB	ST
57	1	3	1	4	11
55	1	2	1	4	10
48	1	4	1	4	9
59	1	4	1	5	12
71	1	2	1	6	13
1	1	2	1	2	2
3	2	2	1	2	2
6	1	2	1	2	2
9	1	2	1	2	2
11	5	2	1	2	2
14	1	2	1	2	2
17	1	2	1	2	2
18	1	2	1	2	2
19	1	2	1	2	2
21	1	2	1	2	2
22	5	2	1	2	2
23	1	2	1	2	2
24	1	2	1	2	2
25	5	2	1	2	2
26	1	2	1	2	2
27	1	2	1	2	2
30	1	2	1	2	2
31	1	2	1	2	2
32	1	2	1	2	2
41	5	2	1	2	2
43	1	2	1	2	2
44	1	2	1	2	2
46	1	2	1	2	2
49	1	2	1	2	2
50	1	2	1	2	2
51	1	2	1	2	2
52	1	2	1	2	2
53	1	2	1	2	2
56	1	2	1	2	2
63	1	2	1	2	2
2	1	4	1	2	3
5	1	4	1	2	3
8	3	4	3	2	3
12	1	4	1	2	3
13	1	4	1	2	3
15	1	4	1	2	3
33	1	4	1	2	3
39	1	4	1	2	3
40	1	4	1	2	3
42	1	4	1	2	3
45	1	4	1	2	3
54	1	4	1	2	3
64	1	4	1	2	3
70	1	4	1	2	3
72	1	4	1	2	3
10	4	3	1	2	6
16	1	3	1	2	6
28	1	3	1	2	6
58	7	3	1	2	6
61	8	3	1	2	6
62	1	3	1	2	6
65	1	3	1	2	6
66	1	3	1	2	6
67	1	3	1	2	6
69	9	3	1	2	6
4	1	2	2	2	4
29	1	2	2	2	4
7	1	4	2	2	5
35	1	4	2	2	5
47	1	4	2	2	5
36	1	3	2	2	8
20	6	2	3	3	7

Figure 2 The distribution of STs.
Abbreviation: ST, sequence type.

therapeutic value. However, in the absence of approved breakpoints for *Corynebacterium* species, those antibiotics recommended for *Staphylococcus* species have been used, except for penicillin and ampicillin, for which thresholds for *Listeria* species are used.[2,23,24]

In our study, *C. striatum* was isolated from various clinical specimens. However, only 20 (29.9%) patients received antibiotic therapy. For several decades, *C. striatum* has been considered as having limited potential for pathogenicity. The present observations confirmed its low virulence. Similar to *C. striatum* strains, VRE, which exhibit low virulence and pathogenicity, were initially considered rare opportunistic pathogens. However, in recent years, the prevalence of VRE has increased and they have joined the list of significant pathogens that frequently cause nosocomial infections with limited treatment options.[25] Although several factors contribute to virulence, such as host defense mechanisms and the expression of various microorganism traits, a higher rate of multidrug-resistant bacteria may be associated with a higher rate of infection and mortality. Therefore, efforts to contain the spread of multidrug-resistant bacteria should be given prominence by the development of antimicrobial stewardship programs.

Since the first case of *C. striatum* infection in a patient with chronic lymphocytic leukemia was published in 1980, *C. striatum* strains have been considered as emerging pathogens in clinical settings.[26,27] In recent years, they have been reported as opportunistic pathogens infecting immunocompromised patients with malignancies, COPD, cardiovascular diseases, and diabetes. Other known risk factors include long-term hospitalization, previous use of broad-spectrum antibiotics, and exposure to invasive devices.[2,9–11] In our study, 52 patients (77.6%) presented at least one predisposing condition. This suggests that *C. striatum* may have a significant clinical impact on the patients hospitalized for a long term with comorbidity, or with a history of exposure to broad-spectrum antibiotics, or those who are immunosuppressed, as well as critically ill patients with an implanted indwelling device.

In our study, *C. striatum* strains mainly caused nosocomial infections, and the four predominant STs in MLST, which accounted for 86.6% of the strains, were ST2, ST3, ST6, and ST5. The 67 strains represent distinct allele combinations (13 STs, considering only three genes: ITS1, *gyrA,* and *rpoB*). For *gyrA*, allele 1 was predominant (89.6%). For *rpoB*, allele 2 was the most abundant and was found in 61 strains (91.0%). A literature review indicates that these characteristics of *C. striatum* strains may be a major concern for global health institutions because it is an emergent Gram-positive environmental bacterium which is highly persistent, prevalent, and transmissible person to person and through caregivers, with significant multidrug resistance.[2] Furthermore, it has often caused nosocomial outbreaks.[2,7–11]

Identification of *Corynebacterium* species is challenging because there are limitations to distinguishing *Corynebacterium* species based on biochemical profiles using the Api Coryne system. Thus, as in our study, molecular methods, such as gene sequencing, are used as the complementary gold standard for bacterial identification.[28,29]

Our study had several limitations. Firstly, this study used a single-center design and included a small sample of specimens. Secondly, antibiotic treatment was decided by the treating physician based on his or her interpretation of the microbiological and clinical parameters used in general clinical practice. Finally, the antibiotic susceptibility test did not include gentamicin, as recommended by the CLSI guidelines. Therefore, the possibility that antibiotic resistance of the strains is more extensive cannot be excluded.

Conclusion

C. striatum isolates have been characterized as sources of opportunistic infections associated with nosocomial infections through horizontal transmission. They are only susceptible to a limited number of broad-spectrum antibiotics and can be isolated from clinical specimens due to colonization or contamination. Particularly, characteristics of multidrug resistance and intra-hospital dissemination indicate their potential to be considered as a target pathogen in antimicrobial stewardship programs.

Data sharing statement

Further information and requests for individual deidentified participant data sharing will be fulfilled by contacting the corresponding author YKY (young7912@korea.ac.kr) during the 5 years after publication. Clinical and molecular data and research ethics approval information can be shared.

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Disclosure

The authors report no conflicts of interest in this work.

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Supplementary materials

Table S1 Primers used in the molecular analysis of 67 *Corynebacterium striatum* strains

Gene	Primer	Sequence (5′→3′)	Function	T[a] (°C)	Length (bp)	Reference
16S rRNA	16SF27	AGAGTTTGATCMTGGCTCAG	16S rDNA	55	1,400	26
	16SR1492	TACGGYTACCTTGTTACGACTT				
16S rRNA (sequencing)	16SF518	CCAGCAGCCGCGGTAATAC	16S rDNA	–	–	27
	16SR800	TACCAGGGTATCTAATCC				
ITS1	16F945	GGGCCCGCACAAGCGGTGG	Interspacer sequence region 1	55	900	9
	23r458	CTTTCCCTCACGGTAC				
gyrA	gyrA1	GCGGCTACGTAAAGTCC	Gyrase	55	400	9
	gyrA2	CCGCCGGAGCCGTTCAT				
rpoB	C2700F	CGWATGAACATYGGBCAGGT	β-subunit of RNA polymerase enzyme	60	400	9
	C3130R	TCCATYTCRCCRAARCGCTG				

Table S2 STs at three examined loci in the *Corynebacterium striatum* strain and patterns of antimicrobial resistance

Strain	16S rRNA	ITS1	gyrA	rpoB	ST[a]	Resistance pattern
1	1	2	1	2	2	I
2	1	4	1	2	3	I
3	2	2	1	2	2	II
4	1	2	2	2	4	I
5	1	4	1	2	3	I
6	1	2	1	2	2	I
7	1	4	2	2	5	II
8	3	4	1	2	3	I
9	1	2	1	2	2	I
10	4	3	1	2	6	I
11	5	2	1	2	2	I
12	1	4	1	2	3	I
13	1	4	1	2	3	I
14	1	2	1	2	2	I
15	1	4	1	2	3	I
16	1	3	1	2	6	I
17	1	2	1	2	2	I
18	1	2	1	2	2	I
19	1	2	1	2	2	I
20	6	2	3	3	7	II
21	1	2	1	2	2	I
22	5	2	1	2	2	I
23	1	2	1	2	2	I
24	1	2	1	2	2	I
25	5	2	1	2	2	I
26	1	2	1	2	2	I
27	1	2	1	2	2	I
28	1	3	1	2	6	I
29	1	2	2	2	4	I
30	1	2	1	2	2	I
31	1	2	1	2	2	I
32	1	2	1	2	2	I
33	1	4	1	2	3	I
35	1	4	2	2	5	II
36	1	3	2	2	8	I
39	1	4	1	2	3	I
40	1	4	1	2	3	II
41	5	2	1	2	2	I
42	1	4	1	2	3	I
43	1	2	1	2	2	I
44	1	2	1	2	2	I
45	1	4	1	2	3	I
46	1	2	1	2	2	V
47	1	4	2	2	5	III
48	1	4	1	4	9	III
49	1	2	1	2	2	I
50	1	2	1	2	2	I
51	1	2	1	2	2	I
52	1	2	1	2	2	I
53	1	2	1	2	2	I
54	1	4	1	2	3	I
55	1	2	1	4	10	I
56	1	2	1	2	2	I
57	1	3	1	4	11	I
58	7	3	1	2	6	I
59	1	4	1	5	12	I
61	8	3	1	2	6	I
62	1	3	1	2	6	I
63	1	2	1	2	2	I
64	1	4	1	2	3	IV
65	1	3	1	2	6	I
66	1	3	1	2	6	I
67	1	3	1	2	6	I
69	9	3	1	2	6	I
70	1	4	1	2	3	I
71	1	2	1	6	13	I
72	1	4	1	2	3	I
ATCC 6940	1	1	1	1	1	

Note: [a]Only three of the eight loci analyzed were taken into account in obtaining ST numbers (ITS1 region, *gyrA*, and *rpoB* genes).
Abbreviations: ITS1, internal transcribed spacer 1; ST, sequence type.