Ann Clin Microbiol Vol. 19, No. 1, March, 2016
http://dx.doi.org/10.5145/ACM.2016.19.1.28
pISSN 2288-0585 · eISSN 2288-6850

Two Cases of Medical Device-Related *Corynebacterium striatum* Infection: A Meningitis and A Sepsis

Sholhui Park[1], Hae-Sun Chung[1], Eui Kyo Seo[2], Yeung Chul Mun[3], Miae Lee[1]

Departments of [1]Laboratory Medicine, [2]Neurosurgery, [3]Internal Medicine, Ewha Womans University School of Medicine, Seoul, Korea

Corynebacterium striatum is a commonly isolated contaminant in the clinical microbiology. However, it can be an opportunistic pathogen in immunocompromised and even immunocompetent hosts. The increasing prevalence of *C. striatum* infection has been associated with immunosuppression and prosthetic devices. We report a case of meningitis with cerebrospinal fluid drainage and a case of catheter-related bloodstream infection caused by *C. striatum*. The isolates were identified as nondiphtherial *Corynebacterium* species by VITEK 2 (bioMérieux, France) anaerobe and Corynebacterium card. The final identification by 16S rRNA gene sequencing analysis was *C. striatum* with 99.7% identity and 99.6% identity with *C. striatum* ATCC 6940, respectively. Both strains were sensitive to vancomycin and gentamicin, but multidrug-resistant to ciprofloxacin, penicillin, erythromycin and imipenem. **(Ann Clin Microbiol 2016;19:28-31)**

Key Words: Bloodstream infection, *Corynebacterium striatum*, Meningitis, 16S rRNA gene sequencing

INTRODUCTION

The genus *Corynebacterium* is a group of diverse organisms, which is a normal commensal of human skin and mucous membrane. Of which, *Corynebacterium striatum* is a frequently isolated species in clinical microbiology and considered as contaminant. However, it can be opportunistic pathogen in immunocompromised and immunocompetent hosts [1]. Ever since the first infection of *C. striatum*, pleuropulmonary infection, was found [2], this organism has been reported as the cause of a variety of invasive infections, including endocarditis [3], respiratory infection [4], catheter-related bloodstream infection, meningitis with cerebrospinal fluid (CSF) drain. *C. striatum* has been increasingly reported as true pathogen when patients are immunocompromised and have prosthetic devices [5]. Here, to our knowledge, we present the first case of meningitis with CSF drain in Korea and a case of catheter-related bloodstream infection caused by *C. striatum*.

CASE REPORTS

1. Case 1

A 74-year-old woman with a history of hypertension was admitted with a diagnosis of spontaneous subarachnoid hemorrhage. She had been hospitalized in neurological intensive care unit after coil embolization of aneurysm. On hospitalization day (HD) 7, she developed a fever of 38.1°C. On HD 8, she was made lumbar puncture with drain due to persistent fever with mental change. She suffered from persistent fever, but it failed to grow any microorganisms from blood, urine, CSF samples except for transtracheal aspirate; methicillin resistant *Staphylococcus aureus*. Intermittent leak was present from the spinal drain. On HD 14, CSF profile showed elevated white blood cell count 620/㎕ with 58% neutrophils, and increased protein level; 102 mg/dL. Peripheral white blood cell count was 12,860/㎕ with 87.4% neutrophils and C-reactive protein increased into 12.84 mg/dL. And then, intravenous vancomycin (750 mg per 12 hours) therapy was empirically initiated when cultures of CSF and the

Received 10 January, 2016, Revised 25 February, 2016, Accepted 7 March, 2016

Correspondence: Miae Lee, Department of Laboratory Medicine, Ewha Womans University School of Medicine, 1071, Anyangcheon-ro, Yangcheon-gu, Seoul 07985, Korea. (Tel) 82-2-2650-5222, (Fax) 82-2-2650-5091, (E-mail) miae@ewha.ac.kr

lumbar drain tip were performed. At that time, the inflammation sign of redness and swelling was noted in the lumbar drain insertion site. At the same time, gram positive rods were detected by Gram staining CSF fluid. On HD 15, parentral ceftazidime (2 g per 8 hours) was added, and diphtheroid species (strain 1) grew on blood agar plate (BAP) from the CSF culture. The overnight culture of the thioglycollate broth (NIH Thioglycollate Broth, Becton Dickinson, Sparks, MD, USA) for the lumbar drain tip was inoculated into BAP and MacConkey agar. On HD 16, the same diphtheroid species was yielded on BAP. Fever subsided after 3 days of intravenous vancomycin treatment. She was treated with vancomycin for 14 days and discharged with full recovery.

2. Case 2

A 48-year-old male patient with acute myeloid leukemia failed to achieve complete response. After fludara-busulfex conditioning via a left subclavian venous catheter, he underwent allogeneic peripheral blood stem cell transplantation (allo-PBSCT). Since then, he suffered from diarrhea and developed skin eruption on the 9th day after allo-PBSCT. On the 15th day, he developed a fever of 37.9^{o}C. The blood profile showed pancytopenia; white blood cell count 540/μL, hemoglobin 6.2 g/dL, platelet count 4,000/μL. C-reactive protein level was elevated to 2.0 mg/dL. Peripheral and central catheter blood were drawn in doublet with urine, and cultured. And then, he was empirically administered with ceftazidime (2 g per 8 hours). After 24 hours incubation, gram positive rods (strain 2) were detected in all four aerobic blood culture bottles at the same time. Subcultures on BAP agar yielded diphtheroid species. Subsequent blood cultures on the 17th day showed the same results while the culture through the catheter blood yielded the isolates 3.5 hours earlier than the peripheral blood culture. And then, additional teicoplanin (400 mg per 24 hours) was administered. Following blood cultures on the 20th day showed negative results. Even though parentral antibiotics were changed to meropenem (1 g per 8 hours) and vancomycin (500 mg per 24 hours) on the 21st day, he expired on the 22nd day after allo-PBSCT due to acute graft-versus-host disease (GVHD).

3. Identification

Colonies after 24 hours of incubation on blood agar was convex, circular, shiny, moist with entire edges, white to gray and non-hemolytic, about 1 to 1.5 mm in diameter. The results of Gram stain of the cultured bacteria were gram positive rods. Two strains were identified as *C. striatum* by VITEK 2 (bioMérieux, Marcy l'Etoile, France) anaerobe and Corynebacterium card, although strain 2 was identified as *Corynebacterium amycolatum* initially. Both strains were positive for catalase and acid productive from glucose, sucrose, galactose, and mannose. They were negative for urease, esculin hydrolysis, and maltose fermentation. To confirm the identification of the isolates, we performed 16S rRNA gene sequencing as described from the previous study [6]. Using the EzTaxon server (http://www.ezbiocloud.net/eztaxon; [7]), both strains were identified as *C. striatum* with 99.7% identity and 99.6% identity with *C. striatum* (ATCC 6940) (Table 1).

4. Antimicrobial susceptibility test

To study the antimicrobial susceptibility of the isolates, we evaluated the minimum inhibitory concentrations (MICs) by using Etest (bioMérieux) and Oxoid M.I.C. Evaluator Strip (Thermo Fisher Scientific, Basingstoke, UK). The suspensions of the isolates adjusted to 0.5 McFarland standard were inoculated onto Mueller-Hinton agar plates with 5% sheep blood (Asan Pharm, Seoul, Korea) and incubated at 37^{o}C for 20 hours. Results of antimicrobial susceptibility regarding strain 1 and strain 2 are shown in Table 2. Both strains were sensitive to vancomycin and gentamicin, but resistant to penicillin, imipenem, erythromycin, and ciprofloxacin.

DISCUSSION

C. striatum had long been considered as a contaminant from normal skin or nasopharyngeal flora. This opportunistic patho-

Table 1. Identification of the isolates

Isolate No.	Culture site	Phenotypic method (VITEK 2)	16S rRNA gene analysis
Strain 1.	CSF and drainage tip	*Corynebacterium striatum*	*Corynebacterium striatum*
Strain 2.	Catheter blood and peripheral blood	1st *Corynebacterium amycolatum* 2nd *Corynebacterium striatum*	*Corynebacterium striatum*

Abbreviation: CSF, cerebrospinal fluid.

Table 2. Antimicrobial susceptibility test of the isolates

Antibiotics	MIC (μg/mL)				
	Strain 1	Strain 2	CLSI interpretive criteria		
			S	I	R
Penicillin	>32	>32	≤1	2	≥4
Imipenem	>32	>32	≤4	8	≥16
Ciprofloxacin	>32	>32	≤1	2	≥4
Erythromycin	4	4	≤0.5	1	≥2
Gentamicin	0.06	4	≤4	8	≥16
Vancomycin	0.75	0.75	≤2		

Abbreviations: MIC, minimal inhibitory concentration; CLSI, Clinical and Laboratory Standards Institute; S, susceptible; I, intermediate; R, resistant.

gen needs to be paid attention when isolated from normally sterile body sites, purely cultured, or accompanying strong leukocyte reaction with positive Gram stain [8]. *C. striatum* have recently been reported as the pathogens of post-operative intra-abdominal infection [9], bacteremia in a patient with tracheostomy and gastrostomy tubes [10] and catheter-related bloodstream infection [11] in Korea, but not meningitis yet. To our knowledge, case 1 is the first case of *C. striatum* meningitis related with CSF drain in Korea. Laboratory tests in case 1 showed peripheral blood leukocytosis with neutrophilia, increased C-reactive protein level, CSF color change with increased white blood cell count. *C. striatum* was isolated from CSF sample and the drain tip simultaneously. In case 2, *C. striatum* was yielded from both peripheral blood and venous catheter blood, and following culture showed the same results with different time to positivity. In both cases, patients were in immunocompromised conditions having indwelling medical devices.

For more reliable identification to the species level, we performed 16S rRNA gene sequence analysis. Analysis of partial 16S rRNA gene sequence might fail to identify *Corynebacterium* to the species level, since corynebacteria show little polymophism of this gene [12]. When analyzed the whole gene sequence, most species in *Corynebacterium* can be distinguished [13]. We successfully identified two strains to the species level by analyzing the full length of 16S rRNA gene sequence.

Multidrug-resistant *C. striatum* has been implicated especially in long-term hospitalized patients [14], and the most frequent mechanism of antibiotic resistance in *Corynebacterium* species is the transmission of extrachromosomal genetic elements on large plasmids or on transposons [15]. Since the antimicrobial susceptibility of *C. striatum* is not predictable due to the emergence of multidrug resistance, antimicrobial susceptibility test should be performed for correct treatment. In these cases, both two strains were highly resistant to penicillin, imipenem, ciprofloxacin. All were resistant to erythromycin, but susceptible to gentamicin and vancomycin. As previously reported [14], we confirmed that the empirical treatment of choice for *Corynebacterium* species infection is vancomycin. Case 1 was treated with parentral vancomycin and fully recovered from the *C. striatum* infection. Case 2 expired due mainly to acute GVHD, therefore we could not assess the outcome of catheter-related bloodstream infection by *C. striatum*.

In our report, we present that *C. striatum* should be considered as pathogens in CSF and bloodstream in immunocompromised patients with medical devices. And in addition to phenotypic data, 16S rRNA gene sequencing could be a good tool for more reliable identification of genus *Corynebacterium* into species level. The *C. striatum* isolates were multidrug-resistant, but still vancomycin could be a choice of an empirical therapy.

REFERENCES

1. Lee PP, Ferguson DA Jr, Sarubbi FA. *Corynebacterium striatum*: an underappreciated community and nosocomial pathogen. J Infect 2005;50:338-43.
2. Bowstead TT and Santiago SM. Pleuropulmonary infection due to *Corynebacterium striatum*. Br J Dis Chest 1980;74:198-200.
3. Boltin D, Katzir M, Bugoslavsky V, Yalashvili I, Brosh-Nissimov T, Fried M, et al. *Corynebacterium striatum*--a classic pathogen eluding diagnosis. Eur J Intern Med 2009;20:e49-52.
4. Renom F, Gomila M, Garau M, Gallegos MD, Guerrero D, Lalucat J, et al. Respiratory infection by *Corynebacterium striatum*: epidemiological and clinical determinants. New Microbes New Infect 2014;2:106-14.
5. Reece RM, Cunha CB, Rich JD. *Corynebacterium minutissimum* vascular graft infection: case report and review of 281 cases of prosthetic device-related *Corynebacterium* infection. Scand J Infect Dis 2014;46:609-16.
6. Schuurman T, de Boer RF, Kooistra-Smid AM, van Zwet AA. Prospective study of use of PCR amplification and sequencing of 16S ribosomal DNA from cerebrospinal fluid for diagnosis of bacterial meningitis in a clinical setting. J Clin Microbiol 2004;42:734-40.
7. Kim OS, Cho YJ, Lee K, Yoon SH, Kim M, Na H, et al. Introducing EzTaxon-e: a prokaryotic 16S rRNA gene sequence database with phylotypes that represent uncultured species. Int J Syst Evol Microbiol 2012;62:716-21.
8. Funke G, von Graevenitz A, Clarridge JE 3rd, Bernard KA. Clinical microbiology of coryneform bacteria. Clin Microbiol Rev 1997;10:125-59.
9. Choi HS, Kim JS, Jung ES, Kim AJ, Jung H, Park YS, et al. A case of post-operative intra-abdominal infection caused by *Corynebacterium striatum*. Korean J Med 2012;82:516-9.
10. Yoo G, Kim J, Uh Y, Lee HG, Hwang GY, Yoon KJ. Multidrug-

resistant *Corynebacterium striatum* bacteremia: first case in Korea. Ann Lab Med 2015;35:472-3.
11. Yang HS, Kim YJ, Cho SY, Shin E, Lee HJ. Central venous catheter-related bloodstream infection by *Corynebacterium striatum* identified by 16S rRNA and rpoB gene sequencing. Ann Lab Med 2015;35:548-50.
12. Khamis A, Raoult D, La Scola B. rpoB gene sequencing for identification of *Corynebacterium* species. J Clin Microbiol 2004; 42:3925-31.
13. Bernard K. The genus corynebacterium and other medically relevant coryneform-like bacteria. J Clin Microbiol 2012;50:3152-8.
14. Otsuka Y, Ohkusu K, Kawamura Y, Baba S, Ezaki T, Kimura S. Emergence of multidrug-resistant *Corynebacterium striatum* as a nosocomial pathogen in long-term hospitalized patients with underlying diseases. Diagn Microbiol Infect Dis 2006;54:109-14.
15. Olender A. Mechanisms of antibiotic resistance in *Corynebacterium* spp. causing infections in people. In: Pana M, ed. Antibiotic resistant bacteria - A continuous challenge in the new millennium. 1st ed; InTech, 2012:387-402.

=국문초록=

의료기구를 통한 *Corynebacterium striatum* 감염: 뇌수막염 1예와 균혈증 1예

이화여자대학교 의학전문대학원 [1]진단검사의학교실, [2]신경외과학교실, [3]내과학교실

박설희[1], 정혜선[1], 서의교[2], 문영철[3], 이미애[1]

*Corynebacterium striatum*은 임상 미생물에서 흔히 동정되는 오염균 중 하나이다. 하지만 면역이 저하된 환자나 정상면역인 환자에서 기회감염의 원인이 될 수 있다. *C. straitum* 감염의 증가는 면역저하와 의료기구 사용과 관련이 있다고 보고된 바 있다. 저자들은 *C. striatum*에 의한 뇌척수액 배액관 감염과 관련한 뇌수막염 1예와 카테터 관련 균혈증 1예를 보고하고자 한다. 균주는 VITEK 2 (bioMérieux, France) ANC 카드로 *Corynebacterim*으로 동정되었다. 16S rRNA 유전자 염기서열 분석으로 모두 *C. striatum* (*C. striatum* ATCC 6940과의 일치율 99.7%와 99.6%)으로 동정되었다. 두 균주는 vancomycin과 gentamicin에 감수성, ciprofloxacin, penicillin, erythromycin 그리고 imipenem에 모두 내성을 보였다. [Ann Clin Microbiol 2016;19:28-31]

교신저자 : 이미애, 07985, 서울시 양천구 안양천로 1071
이화여자대학교 의학전문대학원 진단검사의학교실
Tel: 02-2650-5222, Fax: 02-2650-5091
E-mail: miae@ewha.ac.kr