



## LETTER TO THE EDITOR

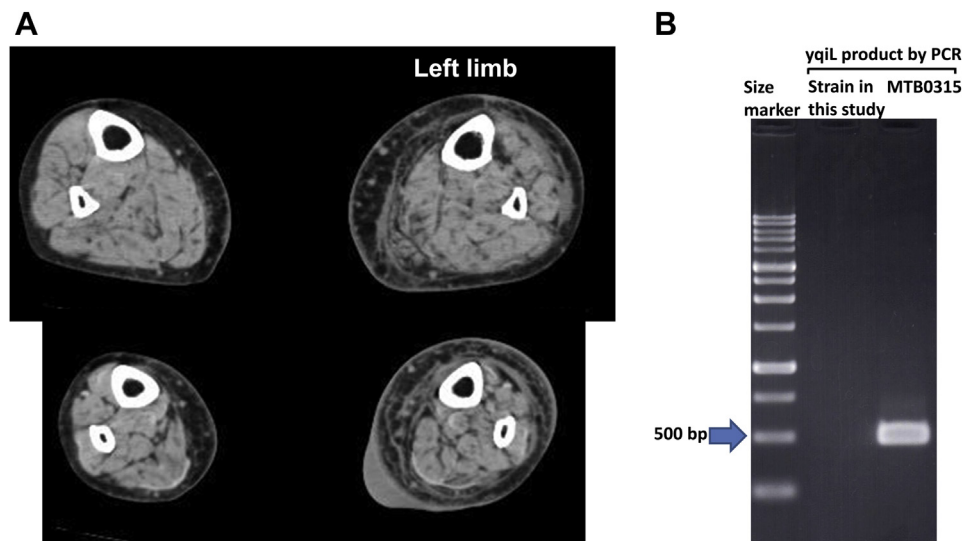
## Necrotizing Fasciitis Caused by Infection with *Streptococcus pyogenes* Harboring *emm* Genotype 11 and Sequence Type 403



Necrotizing fasciitis (NF) is one of the manifestations concerning severe streptococcal infections. In addition to virulence factors in *Streptococcus pyogenes* (group A streptococci, GAS), host cell damage is induced by the immune responses of macrophages to GAS exposure.<sup>1</sup> Analysis of the *emm* gene coding N-terminal end of GAS M protein<sup>2</sup> and multilocus sequence typing (MLST) based on nucleotide sequences of internal fragments of seven housekeeping loci (*gki*, *gtr*, *murI*, *mutS*, *recP*, *xpt*, and *yqiL*)<sup>3</sup> are applied for molecular epidemiology. We report a case of NF caused by infection with GAS harboring *emm11* and sequence type (ST) 403 in an elderly patient with diabetes mellitus and a previous artificial joint replacement for the left knee.

A 75-year-old female with diabetes mellitus presented with fever in 2014. She had received an artificial joint replacement

for the left knee. Physical examination revealed no abnormal findings including skin abnormality. Biochemical and serologic tests on admission indicated mild elevation of aspartate aminotransferase (60 IU/L), alanine aminotransferase (61 IU/L), and C-reactive protein level (0.53 mg/dL), together with a negative result for rapid influenza test using a nasal swab. On the 2<sup>nd</sup> hospitalization day, erythema, swelling, heat, and spontaneous pain developed in the left lower limb (below the artificial joint), and intravenous treatment with cefazolin (4 g/day) was started. On the 3<sup>rd</sup> hospitalization day, the cutaneous lesions progressed to blister and fragile conditions. Computed tomography images (Figure 1A) of the lower limb indicated extension of low density areas along the fascia and regions with increased density in the subcutaneous tissue, as well as the swollen appearance: these



**Figure 1** (A) Computed tomography images of the lower limb indicated extension of low-density areas along the fascia and regions with increased density in the subcutaneous tissue as well as the swollen appearance; these findings were compatible with necrotizing fasciitis. (B) The *emm* typing and multilocus sequence typing (MLST) for the *Streptococcus pyogenes* isolate revealed *emm11* and sequence type (ST) 403 having allele profile [*gki3-gtr4-mur16-mutS5-recP1-xpt5-yqiL* (acetyl-CoA acetyltransferase) 67]. The *yqiL67* indicated a null allele: the internal fragment (434 bp) for MLST and the full-length (1185 bp) could not be amplified using the polymerase chain reaction (PCR) assay in duplicate. MTB0315 strain harboring *emm1* (accession number AB738042) and ST28 was used as positive control of *S. pyogenes*.

Conflicts of interest: The authors have no conflicts of interest to declare in relation to this article.

<http://dx.doi.org/10.1016/j.jecm.2014.07.001>

1878-3317/Copyright © 2014, Taipei Medical University. Published by Elsevier Taiwan LLC. All rights reserved.

findings were compatible with NF. Since Gram-positive cocci in chains were detected through blood culture obtained on admission, antimicrobial treatment was changed to combined administration of ampicillin (6 g/day) and clindamycin (1.8 g/day). On the 4<sup>th</sup> hospitalization day, she was transferred to another medical center to receive surgical procedures (drainage and debridement) for the NF. The lesions improved, and she was discharged approximately 1 month later.

GAS grew on a blood agar plate. This isolate was identified as *S. pyogenes* based on nucleotide sequences (1427 bp) in 16S rRNA, which showed 100% similarity to the type strain. Antimicrobial susceptibility showed the isolate to be susceptible to selected agents. The *emm* typing and MLST revealed *emm11* and ST403 having the allele profile (*gki3-gtr4-murI6-mutS5-recP1-xpt5-yqiL67*). The *yqiL67* indicated a null allele: the internal fragment (434 bp, Figure 1B) for MLST and the full length (1185 bp) could not be amplified using polymerase chain reaction assay in duplicate.

Emergence of uncommon *emm* types among 334 isolates was reported among adult patients from 1997 through 2008 in Southern Taiwan.<sup>4</sup> Formerly rare *emm* types including *emm11* emerged dramatically after 2004. The *emm11* was associated with both superficial infections and cellulitis. Molecular characteristics of GAS skin and soft tissue infections ( $n = 73$ ) were described from 2005 to 2007 in Taiwan; one of the most prevalent *emm* types was *emm11* (12.3%).<sup>5</sup> Among the macrolide-resistant strains, the most prevalent clone was *emm11*/ST403 in 2004 and 2005 in Spain.<sup>6</sup> The molecular epidemiology should be monitored for the streptococcal infections in different countries.

#### Acknowledgments

This work was supported in part by JSPS KAKENHI grant number 25670469 (to T. Takahashi).

#### References

1. Matoba T, Nakatani Y, Arai K, Matsui H, Yoshida H, Takahashi T. Interleukin-1 $\beta$  response of peritoneal macrophages to *Streptococcus pyogenes* exposure: differential response to living and heat-killed bacteria. *J Exp Clin Med* 2013;**5**: 227–30.
2. Takahashi T, Sunaoshi K, Sunakawa K, Fujishima S, Watanabe H, Ubukata K, Invasive Streptococcal Disease Working Group. Clinical aspects of invasive infections with *Streptococcus dysgalactiae* ssp. *equisimilis* in Japan: differences with respect

to *Streptococcus pyogenes* and *Streptococcus agalactiae* infections. *Clin Microbiol Infect* 2010;**16**:1097–103.

3. Enright MC, Spratt BG, Kalia A, Cross JH, Bessen DE. Multilocus sequence typing of *Streptococcus pyogenes* and the relationships between *emm* type and clone. *Infect Immun* 2001;**69**:2416–27.
4. Chiang-Ni C, Wu AB, Liu CC, Chen KT, Lin YS, Chuang WJ, Fang HY, et al. Emergence of uncommon *emm* types of *Streptococcus pyogenes* among adult patients in southern Taiwan. *J Microbiol Immunol Infect* 2011;**44**:424–9.
5. Lin JN, Chang LL, Lai CH, Lin HH, Chen YH. Clinical and molecular characteristics of invasive and noninvasive skin and soft tissue infections caused by group A *Streptococcus*. *J Clin Microbiol* 2011;**49**:3632–7.
6. Pérez-Trallero E, Montes M, Orden B, Tamayo E, García-Arenzana JM, Marimón JM. Phenotypic and genotypic characterization of *Streptococcus pyogenes* isolates displaying the MLS<sub>B</sub> phenotype of macrolide resistance in Spain, 1999 to 2005. *Antimicrob Agents Chemother* 2007;**51**:1228–33.

Akiyoshi Shibayama\*, Mitsugu Tamaki, Haruyuki Nagasawa  
Department of Clinical Laboratory, Mishuku Hospital,  
Federation of National Public Service and  
Personnel Mutual Aid Associations,  
Tokyo, Japan

Susumu Nakamata  
Department of Gastroenterology, Mishuku Hospital,  
Federation of National Public Service and  
Personnel Mutual Aid Associations,  
Tokyo, Japan

Yoshitaka Nakamori  
Department of Respiratory Medicine, Mishuku Hospital,  
Federation of National Public Service and  
Personnel Mutual Aid Associations,  
Tokyo, Japan

Haruno Yoshida, Takashi Takahashi\*\*  
Laboratory of Infectious Diseases, Graduate School of Infection Control  
Sciences, Kitasato University, Tokyo, Japan

\* Corresponding author.

\*\* Corresponding author.

E-mail: A. Shibayama <akiyoshi0930@kxf.biglobe.ne.jp>;  
T. Takahashi <taka2si@lisci.kitasato-u.ac.jp>

Jun 9, 2014