Septic arthritis caused by an emerging ST121 methicillin-susceptible, PVL-negative *Staphylococcus aureus* harbouring a variant of bone sialoprotein-binding protein gene

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Abstract

ST121/*agr*-IV methicillin-susceptible *Staphylococcus aureus* was isolated from a patient of septic arthritis (synovial fluid, blood, skin and nasal cavity). Although the Panton-Valentine leukocidin (PVL) gene was negative, this isolate harboured a gene encoding a variant of bone sialoprotein-binding protein with a shortened SD-repeat region.

Keywords: Bone sialoprotein-binding protein, septic arthritis, ST121, *Staphylococcus aureus*

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ST121 *S. aureus,* which mostly harbours Panton-Valentine leucocidin (PVL), is a highly virulent clone and is distributed globally [1,2]. However, PVL-negative ST121 isolate is also considered an emerging cause of severe diseases [3]. Here we report isolation of ST121 PVL-negative methicillin-susceptible *S. aureus* (MSSA) from septic arthritis, and identification of a novel variant of bone sialoprotein-binding protein (Bbp) [4].

A 12-year-old Japanese boy abruptly developed severe right shoulder pain and high-grade fever, and was brought to our hospital for care. At the age of 4 he had been diagnosed as having polyarticular juvenile idiopathic arthritis, and contracture of his systemic joints had progressed. He had recently been treated with prednisolone, methotrexate, and human monoclonal anti–tumor necrosis factor alpha antibody. On admission, his temperature was 39.9°C and systolic blood pressure was 92 mm Hg. The right shoulder joint was warm, swollen and tender with a restricted range of movement. Head and neck examination revealed postauricular eczema with bleeding. Blood test revealed increased white blood cell count (11 600/mm^3, 77% neutrophils) and C-reactive protein (15.54 mg/dL). Magnetic resonance imaging of the right shoulder revealed a moderate effusion in the right shoulder joint and external to the joint. Aspiration of the shoulder joint yielded purulent synovial fluid containing 160 000 leukocytes/mm^3 and Gram-positive cocci. Acute septic arthritis of the right shoulder was diagnosed. Arthroscopic lavage of the joint was performed. Cefazolin and vancomycin were administrated as the initial therapy; thereafter, cefazolin was administered for 6 weeks according to the antibiotic sensitivity of the bacteria isolated from synovial fluid and venous blood. There was no evidence of infective endocarditis. He fully recovered, without recurrence for a year.

From synovial fluid, venous blood, exudate of postauricular eczema and swabs of nasal cavity of the patient, MSSA was isolated and designated YM514-j/v/e/n, respectively. They were classified into ST121, *spa*-t5072, *agr*-IV, *coa*-Va and showed identical genetic traits, having *bbp* which encodes Bbp, an Sdr family adhesin [4] (Tables 1 and 2), while findings were negative for the PVL gene. These findings indicated that the four isolates were of the same clone, suggesting occurrence of endogenous infection in the patient. Nucleotide sequences of *bbp* determined for YM514-j and YM514-v were identical, encoding a 1088 aa protein (GenBank accession no. KY095832), which is 83 aa shorter than the prototype Bbp [4]. Alignment of the Bbp revealed that YM514 Bbp has an SD-repeat region comprising 92 aa, which is shorter than other reported Bbp by 62 to 84 aa (Supplementary Fig. 1). This repeat region spans the bacterium's cell wall and acts as a stalk connecting with ligand-binding region of this protein by analogy with other Sdr proteins [5,6].

TABLE 1. Genotype of *Staphylococcus aureus* isolated from patient with septic arthritis

Isolate	Specimen	Genotype (ST, *spa, agr, coa*)
YM514-j	Synovial fluid	ST121, *spa*-t5072, *agr*-IV, *coa*-Va
YM514-v	Blood	ST121, *spa*-t5072, *agr*-IV, *coa*-Va
YM514-e	Postauricular eczema	ST121, *spa*-t5072, *agr*-IV, *coa*-Va
YM514-n	Nasal cavity	ST121, *spa*-t5072, *agr*-IV, *coa*-Va

ST, sequence type.

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TABLE 2. Molecular characteristics of *Staphylococcus aureus* isolated from patient with septic arthritis

Characteristic	Value
Detected genes	
Leukocidin	*lukDE*
Haemolysin	*hla, hlb, hld, hlg, hlg2*
Enterotoxin(-like)	*seg, sei, sem, sen, seo, selu, selx, sely, selw*
Adhesin	*icaA, icaD, cna, eno, fnbA, fnbB, ebpS-v,*[a] *clfA, clfB, fib, sdrC, sdrE, bbp*
Exoenzyme	*V8* (*sspA*), *sspB, aur, acpA, sak, efb, splA, splB, splC*
Other virulence factors	*isaA, isaB, vWbp*[b]
Regulatory elements	*agrA, cvfA, mgr, rot, sarA, saeR-saeS, trap, vraR,* DeoR family, GntR family, LysR family, MarR family
Aminoglycoside resistance	*aac(6′)-Ie-aph(2″)-Ia*
Mutation in quinolone resistance–determining region	*gyrA*: Ser 84 Leu; *grlA*: Ser 80 Phe
Drug resistance	Gentamicin, levofloxacin

[a]Variant of elastin-binding protein with internal deletion [9].
[b]Von Willebrand factor binding protein gene.

Although its relation to virulence is not clear, the SD-region variant possibly could affect the stability of Bbp on the bacterial cell surface. Despite the low prevalence in *S. aureus, bbp* is often associated with bloodstream infections and osteomyelitis [7,8]. However, *bbp*-positive ST121/*agr*-IV *S. aureus* has been mostly PVL positive and/or methicillin resistant [1,3,9,10]. Accordingly, PVL-negative MSSA (ST121/*agr*-IV) harbouring *bbp*, as detected in the present study, may be an emerging virulent clone to be noted.

Conflict of Interest

None declared.

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.nmni.2017.05.010.

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