Table 5 Antibacterial susceptibility of *Moraxella catarrhalis*

Antibacterial agent	MIC (μg/ml)		
	50 %	90 %	Range
PCG	16	32	≤0.06 to 64
ABPC	8	16	≤0.06 to 32
SBT/ABPC	0.125	0.25	≤0.06 to 0.5
CVA/AMPC	0.25	0.25	≤0.06 to 0.5
PIPC	2	16	≤0.06 to 32
TAZ/PIPC-1	≤0.06	≤0.06	≤0.06
TAZ/PIPC-2	0.125	0.125	≤0.06 to 0.125
CCL	2	8	0.125 to 32
CFDN	0.25	0.5	≤0.06 to 1
CFPN	0.5	1	≤0.06 to 4
CDTR	0.5	1	≤0.06 to 2
CEZ	4	16	0.125 to 64
CMZ	0.5	1	≤0.06 to 4
CTM	1	2	0.25 to 4
CAZ	0.25	0.5	≤0.06 to 2
CTRX	1	2	≤0.06 to 4
CFPM	1	4	≤0.06 to 8
CZOP	2	8	≤0.06 to 8
IPM	≤0.06	0.125	≤0.06 to 0.25
PAPM	≤0.06	≤0.06	≤0.06 to 0.125
MEPM	≤0.06	≤0.06	≤0.06
BIPM	≤0.06	≤0.06	≤0.06 to 0.125
DRPM	≤0.06	≤0.06	≤0.06
FRPM	0.5	0.5	≤0.06 to 1
AZT	2	4	0.125 to 8
GM	0.125	0.125	≤0.06 to 0.25
TOB	0.25	0.25	≤0.06 to 0.5
AMK	0.5	1	≤0.06 to 2
ABK	0.125	0.25	≤0.06 to 0.5
EM	0.125	0.25	≤0.06 to 0.5
CAM	0.125	0.25	≤0.06 to 0.5
AZM	≤0.06	≤0.06	≤0.06
TEL	0.125	0.25	≤0.06 to 0.25
CPFX	≤0.06	≤0.06	≤0.06 to 0.125
LVFX	≤0.06	≤0.06	≤0.06 to 2
TFLX	≤0.06	≤0.06	≤0.06
MFLX	≤0.06	≤0.06	≤0.06 to 0.5
PZFX	≤0.06	≤0.06	≤0.06 to 2
GRNX	≤0.06	≤0.06	≤0.06 to 0.25
MINO	0.125	0.25	≤0.06 to 1
CLDM	2	4	0.5 to 8
VCM	64	128	32 to 128
TEIC	16	32	8 to 32
LZD	8	8	2 to 16

Susceptibilities of the 70 strains of *M. catarrhalis* to 40 antimicrobial agents were studied

Table 6 Antibacterial susceptibility of *Klebsiella pneumoniae*

Antibacterial agent	MIC (μg/ml)		
	50 %	90 %	Range
ABPC	32	128	8 to ≥256
SBT/ABPC	4	8	2 to 32
CVA/AMPC	2	4	0.5 to 16
PIPC	4	8	0.5 to ≥256
TAZ/PIPC-1	2	4	≤0.06 to 32
TAZ/PIPC-2	2	4	0.25 to 32
CCL	0.5	1	0.125 to ≥256
CFDN	0.125	0.25	≤0.06 to ≥128
CFPN	0.5	1	≤0.06 to 32
CDTR	0.125	0.5	≤0.06 to ≥128
CEZ	1	2	0.5 to ≥256
CMZ	0.5	1	0.25 to 64
CTM	0.125	0.25	≤0.06 to ≥256
CAZ	0.125	0.25	≤0.06 to 64
CTRX	≤0.06	0.125	≤0.06 to 64
CFPM	≤0.06	0.125	≤0.06 to 8
CZOP	≤0.06	≤0.06	≤0.06 to 32
IPM	0.125	0.5	≤0.06 to 1
PAPM	0.125	0.5	≤0.06 to 0.5
MEPM	≤0.06	≤0.06	≤0.06 to 0.125
BIPM	0.125	0.5	≤0.06 to 1
DRPM	≤0.06	≤0.06	≤0.06 to 0.125
FRPM	0.5	0.5	0.125 to 32
AZT	≤0.06	0.125	≤0.06 to 4
GM	0.25	0.25	≤0.06 to 0.5
TOB	0.5	0.5	≤0.06 to 8
AMK	1	1	0.125 to 2
ABK	0.5	0.5	≤0.06 to 0.5
AZM	8	16	1 to 64
CPFX	≤0.06	≤0.06	≤0.06 to 4
LVFX	≤0.06	0.25	≤0.06 to 4
TFLX	≤0.06	≤0.06	≤0.06 to 8
MFLX	0.125	0.5	≤0.06 to 8
PZFX	≤0.06	≤0.06	≤0.06 to 2
GRNX	≤0.06	0.25	≤0.06 to 8
MINO	2	4	0.25 to 64

Susceptibilities of the 78 strains of *K. pneumoniae* to 35 antimicrobial agents were studied

The incidence of MRSA was as high as 58.5 %, which is similar to the data reported by Mochizuki et al. [6] under the analyses via WHONET 5. These MRSA strains are susceptible to ABK, VCM, TEIC, and LZD, except that a few strains which are somewhat less susceptible (MIC 8.0 μg/ml) to ABK may possess both *aph(3′)-III* and *aac(6′)/aph(2″)* genes, as reported recently [5]. Although

Table 7 Antibacterial susceptibility of *Pseudomonas aeruginosa*

Antibacterial agent	MIC (μg/ml)		
	50 %	90 %	Range
PIPC	4	≥256	0.5 to ≥256
TAZ/PIPC-1	4	128	0.125 to ≥256
TAZ/PIPC-2	4	128	0.25 to ≥256
CAZ	2	32	0.5 to ≥128
CTRX	32	≥256	1 to ≥256
CFPM	4	32	0.25 to ≥256
CZOP	2	32	0.125 to ≥256
IPM	1	16	≤0.06 to 64
PAPM	4	32	0.25 to 128
MEPM	0.5	16	≤0.06 to ≥256
BIPM	0.25	16	≤0.06 to 128
DRPM	0.25	8	≤0.06 to ≥128
AZT	4	32	0.125 to ≥256
GM	1	8	≤0.06 to ≥256
TOB	0.5	2	≤0.06 to ≥256
AMK	2	8	0.125 to 64
ABK	1	8	0.125 to 32
CPFX	0.25	8	≤0.06 to 128
LVFX	1	16	≤0.06 to ≥256
TFLX	0.5	≥32	≤0.06 to ≥32
MFLX	4	16	≤0.06 to ≥256
PZFX	0.5	8	≤0.06 to ≥256
GRNX	2	32	≤0.06 to ≥256
MINO	16	64	0.5 to ≥256

Susceptibilities of the 103 strains of *P. aeruginosa* to 23 antimicrobial agents were analyzed

the emergence of resistant MRSA against VCM, TEIC, or LZD has already been reported in Japan, such a resistant strain was not detected in this surveillance.

In the previous criteria, the concentration at which *S. pneumoniae* is considered to be susceptible to penicillin for the treatment of pneumonia was determined by reference to the susceptibility breakpoint for meningitis (0.06 μg/ml). In this surveillance, the susceptibility of *S. pneumoniae* to PCG was categorized with the new criteria of breakpoint MICs (MIC of PCG: PSSP ≤2, PISP 4, PRSP ≥8), and the proportion of PSSP/PISP/PRSP was found to be 94:6:0. These results suggest that penicillin is still effective against community-acquired pneumonia caused by *S. pneumoniae* but that some penicillin-intermediate strains are present. Among PSSP, more than 85 % are thought to be *ermB*-harboring strains because of their resistance to macrolides (EM, CAM, and AZM) and CLDM and susceptibility to the ketolide TEL.

To understand the trend of the susceptibility of *S. pneumoniae* to PCG, we also compared the incidence of the *S. pneumoniae* isolation in each year with the previous criteria (MIC of PCG: PSSP ≤0.06, PISP 0.125–1, PRSP ≥2). Although the proportions of PSSP/PISP/PRSP of 2006 and 2007 were at a similar level (61:35:4 and 65:30:5, respectively), the susceptibility of *S. pneumoniae* to PCG seems to have decreased in 2008 and 2009 (53:35:12 and 56:27:17, respectively). In particular, the frequency of PRSP, increased from 11.8 % in 2008 to 17.3 % in 2009. In comparison to 2006, the statistical difference of the frequency of PRSP in 2008 and in 2009 was at $P = 0.006$ and at $P = 0.0001$, respectively. Because it is difficult to detect these alarming trends by the new criteria of breakpoint MICs, careful watching using the previous criteria is continuously needed.

Concerning *H. influenzae*, half the strains in the present survey showed decreased susceptibility to ABPC without production of β-lactamase; i.e., BLNAI (21.1 %) and BLNAR (18.7 %). The incidence of BLNAI in adults is thought to be somewhat lower (30.4 %) than that in children [7]. All six fluoroquinolones demonstrated extremely strong activity (MIC_{90} ≤0.06 μg/ml) against *H. influenzae* strains, regardless of their ABPC susceptibility. Among the other agents, PIPC, TAZ/PIPC, CDTR, CTRX, and MEPM showed strong activities (MIC_{90}s of 0.125–0.25 μg/ml) against BLNAS, BLNAI, and BLNAR strains. TAZ markedly restored the activity of PIPC against BLPAR (MIC_{90} decreased from ≥256 μg/ml to 0.125 μg/ml).

The susceptibilities of *M. catarrhalis* in the present survey showed that β-lactamase inhibitors restored the activities of penicillins against these strains: SBT decreased the MIC_{90} of ABPC from 16 to 0.25 μg/ml. The data suggest that most of the strains were resistant to penicillins because of β-lactamase production. For the treatment of *M. catarrhalis* infections, carbapenems, macrolides, and fluoroquinolones may be recommended because these drugs showed strong activities, with MIC_{90}s ≤0.06–0.25 μg/ml.

The prevalence of ESBL strains has become a concern in recent years. Yagi et al. [8] conducted a survey of ESBLs among 9,794 *K. pneumoniae* clinical isolates in Japan during the period January 1997 to January 1998, and they reported that 34 isolates (0.3 %) had been found to produce ESBLs. However, an increase in the number of ESBL-producing strains has been suggested; Yamaguchi et al. [9] reported the results of a nationwide surveillance of antibacterial activity of clinical isolates in 2009, and 3.3 % (3 of 91 strains) of *K. pneumoniae* were found to be ESBL-producing strains. In our study, 1 of 78 strains (1.3 %) of *K. pneumoniae* were found to be ESBL-producing strains, and the results were consistent with previous reports.

In the present survey, 2 (1.9 %) metallo-β-lactamase (MBL)-producing strains and 3 (2.9 %) multidrug-resistant strains were found in 103 *P. aeruginosa* isolates. Yamaguchi et al. compared the frequencies of multidrug-resistant strains of *P. aeruginosa* between isolates from the urinary

tract infections and those of RTIs; they reported 5.6 % and 1.8 % of multidrug-resistant strains were found from the urinary isolates and the respiratory isolates, respectively. Therefore, a low incidence of multidrug-resistant *P. aeruginosa* may be limited to respiratory infections [10].

We think our surveillance data will be a useful reference for the treatment of respiratory infections in our country. There is substantial evidence that the overuse of antibiotics is a major cause for the emergence of resistance in respiratory pathogens. To prevent the further spread of antimicrobial resistance in respiratory pathogens, proper antibiotic use is necessary. We should also continue the surveillance to determine the actual situation of the resistance shown by bacterial respiratory pathogens to antimicrobial agents.

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〈報　告〉

インフルエンザ(H1N1) 2009 流行期間中の施設内感染対策

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Infection Control Measures in Medical Facilities for Influenza (H1N1) 2009 Pandemic Period

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要　　旨

2009年のインフルエンザパンデミックでは，当初感染性・病原性が不明確な中，各医療機関では国の施策をふまえさまざまな感染対策が講じられたが，それらを比較・検討するため本調査を計画した．米国疾病予防管理センター(CDC)より公表された医療機関におけるパンデミック(H1N1) 2009の感染対策に関する暫定ガイドラインを参考にアンケートを作成し，平成22年度厚生労働科学研究費補助金による新興・再興感染症研究事業　新型インフルエンザ等の院内感染制御に関する研究会に所属する施設に対し調査を行った．25施設中17施設より回答が得られ，病床平均は610床(0～1300床)で，ほぼ全て(88%)の施設でインフルエンザ対応の専門部署の設置や情報提供，サーベイランスなどの対策がとられていた．トリアージによる患者の動線分離(82%)や患者に対するマスク着用(94%)もよく実践されていたが，施設毎に実施期間のばらつきがみられた．個人防護具の使用も同様に内容や期間にばらつきがみられたが，サージカルマスクは一貫して用いられていた．全体的にはパンデミック(H1N1) 2009流行初期は厳密な感染対策を採用し，感染性・病原性が明らかになるにつれ季節性インフルエンザに準じた対策に変化する様子がうかがえた．特に各施設が実際に患者を経験した後に現実的な対応に移行したと考えられた．今後の施設内感染対策を考えるうえで，対策の妥当性や効果，情報共有などの問題について継続して検討すべきと考えられた．

Key words：インフルエンザ(H1N1) 2009，感染制御，感染対策委員会，個人防護具

はじめに

2009年，新型インフルエンザ(以下パンデミック(H1N1) 2009とする)が出現し，人類は約40年ぶりにインフルエンザパンデミックに直面した．当初は感染性・病原性が不明確な中，国の方針に基づき，各医療施設ではさまざまな感染対策が講じられた．その後，感染性・病原性が明らかになるにつれ感染対策は適宜変更されたが，それに伴う医療現場での混乱も多かった．

パンデミック(H1N1) 2009流行期間中，各施設で行われた感染対策をあらためて振り返り，対策実施上の問題点や今後の課題等を検討することは重要と思われる．そこで我々は，パンデミック(H1N1) 2009流行期間中に，各医療施設でどのような感染対策がとられ，時間経過でどのように変化したか，アンケート方式による調査を行ったので報告する．

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材料と方法

対象は，「平成22年度厚生労働科学研究費補助金による新興・再興感染症研究事業　新型インフルエンザ等の院内感染制御に関する研究会(代表研究者　切替照雄)」に所属する25の医療機関とし，これらに「パンデミック(H1N1) 2009流行期間中の施設内感染対策」という題目でアンケート方式による調査を行った．

本アンケートでは，パンデミック(H1N1) 2009 流行期間を 2009 年 5 月 1 日～2010 年 3 月 31 日として，その期間中に各々の医療機関でとられた施設内感染対策に対する項目について調査した．質問項目は病床数，パンデミック(H1N1) 2009 症例の経験時期といった情報に加え，1) 感染対策活動の強化・充実，2) 患者の受け入れ体制，3) 外来診療体制，4) 病棟診療体制，5) 個人防護具の使用状況と感染対策，6) 職員に対する対応，7) 感染対策用器材の制限・備蓄の 7 項目で構成され，その内容と期間について記載する形式とした．質問の具体的内容は結果であわせて示す．パンデミック(H1N1) 2009 に対する施設内感染対策については CDC(Centers for Disease Control and Prevention)よりガイドライン[1]が公表されており，今回のアンケート内容の一部はそれを参考に作成した．

アンケートの集計において，日付を記載するものについては全回答の中央値，期間を記載するものについては開始日と終了日それぞれの中央値を示した．

結　　果

アンケートの返信は 25 施設中 17 施設(68%)であった．17 施設のうち 1 施設は診療所からの回答であった．回答施設は北海道，宮城，東京，埼玉，長野，愛知，大阪，兵庫，山口，香川，佐賀，熊本の各都道府県に分布し，診療所を除いた病院の規模は 200 以上 500 床未満が 8 病院で 500 床以上が 8 病院となっており，病床平均は 610 床(300～1300 床)であった．

各施設においてパンデミック(H1N1) 2009 症例を最初に経験した日の分布を図 1 に示す．中央値は 2009 年 7 月 27 日であった．

次に，アンケートの各項目に対する回答を図 2 に示す．それぞれの設問に対し，該当した施設の割合を示した．

感染対策活動を強化・充実するにあたり，インフルエンザ対策を統括する部署を設けた施設(88.2%)では，具体的にはインフルエンザ対策室を新たに設置(46.7%)や感染対策委員会内に特別委員会を設置(33.3%)した施設がみられた．その他，委員会に並行して医療現場での実務者協議を行った施設もあった．インフルエンザ対策を統括する部署では，各種の方法で，インフルエンザに対する感染対策の情報発信を行っており(94.1%)，情報をホームページ上に掲載(56.3%)，感染対策マニュアルの改定(87.5%)，教育活動(87.5%)といった方法が採られていた．

外来診療においては，全ての病院において，病院建物の外ないしは中に何らかの形で新たにインフルエンザ専用の診察エリアが設置された．病院建物の外に診療エリアを設けた施設では，テント(46.7%)やプレハブ建物(13.3%)や敷地内の別の建物(26.7%)を用いていた．これら病院建物の外で診療を行っていた期間の中央値は，2009 年 5 月 9 日～7 月 29 日であった．一方，病院建物の中では救急外来の一部(42.9%)や外来ブースの一部(50.0%)を専用にするなどして診療を行っていた．これら病院建物の中で診療を行っていた期間の中央値は 2009 年 7 月 2 日～2010 年 3 月 31 日であった．また，予めインフルエンザ様症状のスクリーニングを行い患者の動線を分離する手段をとった施設(82.4%)では，ポスター掲示(92.9%)，予診カード(21.4%)，職員による振

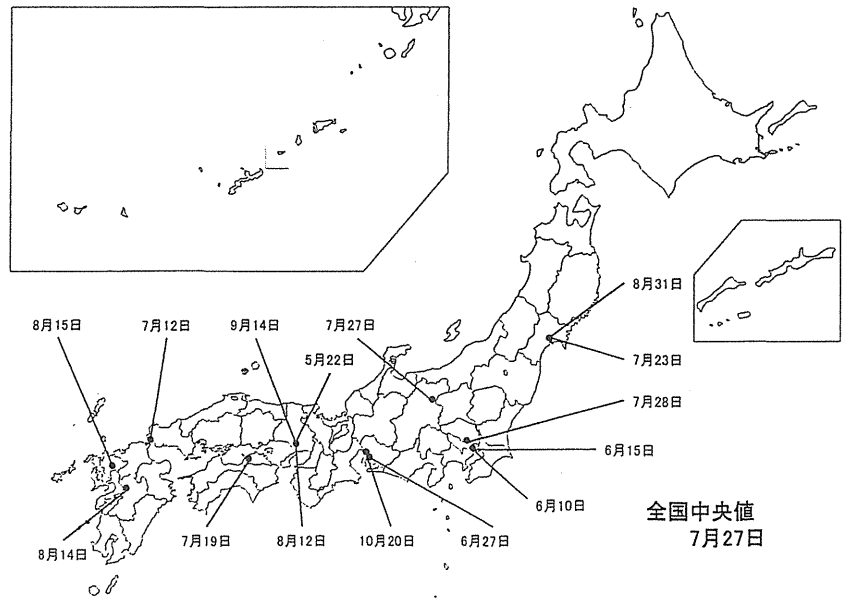

図 1　パンデミック(H1N1) 2009 を初めて経験した日の国内比較

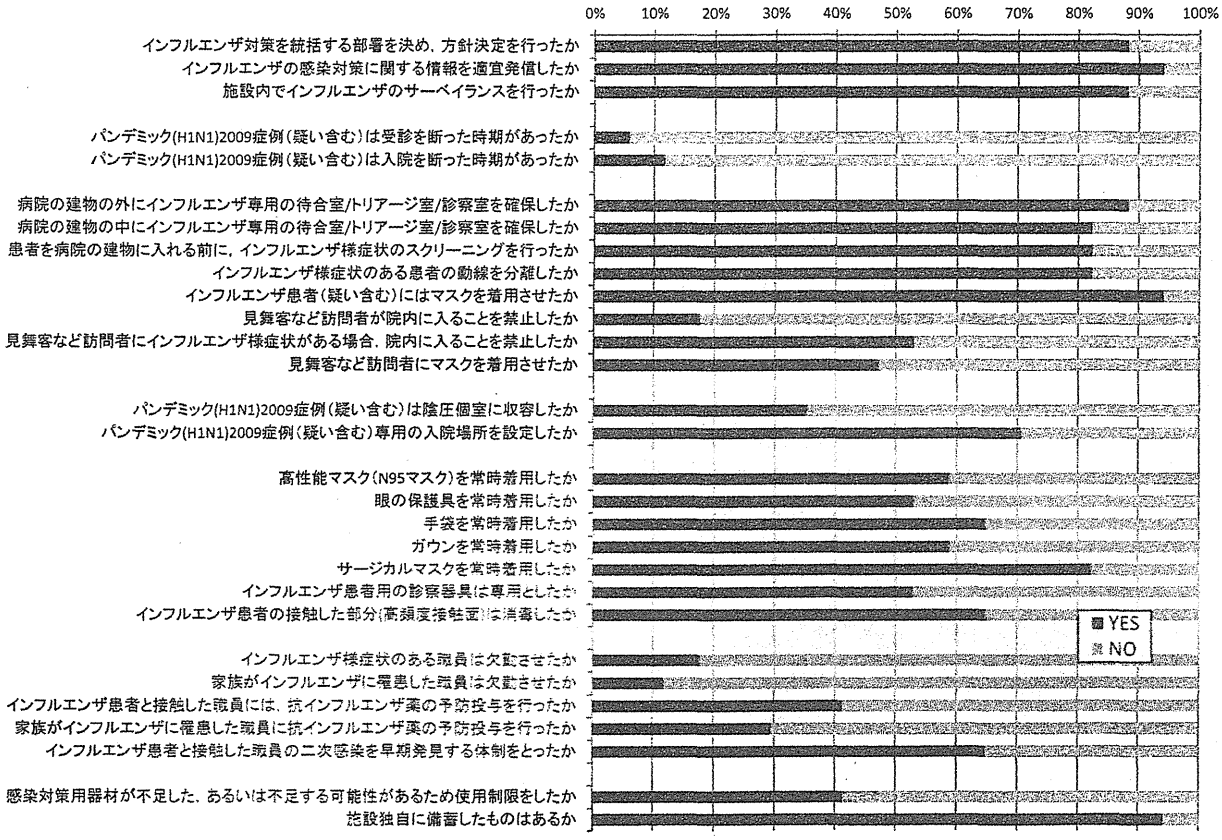

図2　アンケートに対してYESと回答した割合

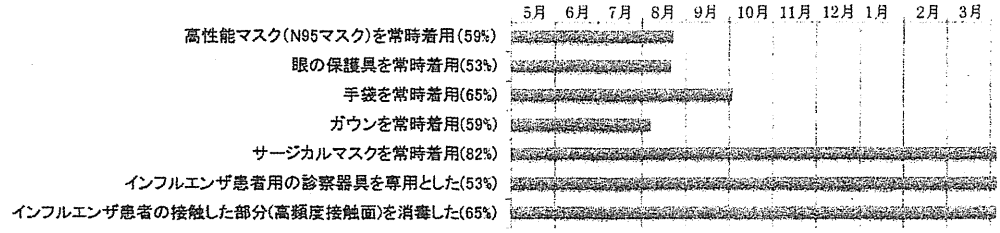

図3　個人防護具の使用と消毒の実施期間

り分け(28.6%)や，院内放送，インターフォンの利用などが行われた．なお，診療にあたり，外来玄関口などには速乾性手指消毒剤を設置し，手指消毒を徹底している施設もみられた．

入院診療では6施設(35.3%)で陰圧個室を使用しており，その期間は中央値で2009年5月1日～11月6日であった．その後は病棟全体をインフルエンザ患者専用にする(25.0%)，あるいはその一部のみを専用にする(58.3%)，通常の個室対応(25.0%)といった通常の季節性インフルエンザと同様の対策に変更された．

また，個人防護具の使用や消毒をした場合の各々の実施期間を図3に示した．

今回のインフルエンザ流行に際し，感染対策用器材が不足するおそれがあるためにその使用を制限した施設は7施設(41.1%)であり，サージカルマスクが6施設(85.7%)と最も多く，その他，擦込式アルコール消毒薬1施設(14.3%)，インフルエンザ迅速診断キット1施設(14.3%)であった．また，独自に器材の備蓄を行っていた施設は16施設(94.1%)あり，内訳としてはサージカルマスク11施設(68.8%)，N95マスク9施設(56.3%)，アルコール消毒薬7施設(43.8%)，抗インフルエンザウイルス薬9施設(56.3%)，迅速診断キット8施設(50%)，その他ガウンなど3施設(18.8%)であった．

考　察

今回のパンデミックを経験するまで，国は高病原性鳥インフルエンザA/H5N1ウイルス由来の株がパンデミ

ックを引き起こす場合を想定し，新型インフルエンザ対策行動計画などの策定を行ってきた[2]が，予想に反して2009年4月にブタ由来のH1N1の発生が確認されパンデミックを引き起こした．

流行当初は詳細なウイルスの特徴や臨床・疫学的特徴などが不明ではあったものの，この「新型」インフルエンザの高い死亡率が報道されていたこともあり，当時考えうる最大限の対策が講じられることになった．2009年4月28日には政府より基本的対処方針が発表され，感染症法に規定する新型インフルエンザ等感染症とし，発熱相談センターや発熱外来などの設置準備が開始された．その後2009年5月9日に初の症例が検疫で捕捉され，5月16日には国内の初発例が報告された[3]．

今回の調査では，各医療施設において流行初期からインフルエンザ専用の対策委員会が設置され，積極的にサーベイランスが行われており，また診療においては病院建物の外にテントやプレハブなどを設けること，個人防護具としてN95マスクやゴーグルを用いるなど厳重な感染対策がとられている例が多くみられた．

2009年5月下旬にはある程度病原性や感染性に対する知見が蓄積されたこともあり，国立感染症研究所感染症情報センターより5月31日付で暫定的な手引きとして「医療機関における新型インフルエンザ感染対策」が公表された．この中には，医療施設においては外来患者を含むすべての来訪者に対し，インフルエンザ様症状をスクリーニングし，有症状者を別に誘導すること，入院が必要な場合でも通常の個室でよいこと，診療スタッフは常時サージカルマスクを着用し，検体採取時にはゴーグルや手袋を着用し，気管支鏡などエアロゾル産生リスクのある手技に限ってN95マスクやゴーグル，手袋の着用を行うことが示された[4]．

また，国内での患者の増加を反映し，2009年6月19日には政府より「医療の確保，検疫，学校・保育施設等の臨時休業の要請等に関する運用指針」が改定され，一律入院措置が中止され，通常医療機関での診療に移行するに至った[5]．

このように政府の指針は5月下旬から6月中旬にかけて，流行初期のような厳重な感染対策から，次第に季節性インフルエンザと同様の対策へと変更されていった．今回の調査を見る限り診療エリアを病院建物の外に設けたり，個人防護具としてN95マスクやゴーグルを用いるなどの厳重な感染対策は7月下旬～8月中旬頃(中央値)まで実施されていたことがわかる．これは各施設で初めてインフルエンザ患者を診断した時期である2009年7月27日(中央値)に近いものであった．このことは，国からの通知がでても各医療機関がすぐには感染対策を変更していないことを示しているとともに，患者の診療を経験した後により現実的な感染対策に変更された可能性が考えられる．

新型インフルエンザのような未経験の感染症が出現した場合，その当初においてはやや過剰ともいえるほどの厳密な感染対策が採られることはやむを得ない．わが国のパンデミックプランにおいても当初は致死率の高いインフルエンザウイルスが想定されていたし，それは賢明なことだったと思われる．しかし，ウイルスの病原性解明等に伴い，政府がその感染対策を緩和した指針を発表しても，医療現場ではそれに迅速に追随することが困難であったことが今回の調査からうかがえる．多くの医療機関は，自施設でパンデミック(H1N1) 2009感染者の診療を経験した後に感染対策方法を緩和したと推察できた．これはパンデミックの初期において疾患の臨床像や感染対策に関する情報が医療の現場に浸透するのに時間がかかることを示唆している．今後このような情報共有をどうすべきか検討が必要と考える．

一方，感染対策器材についてみるとN95マスクやゴーグル，ガウンなどといった飛沫，空気感染予防などの器具は流行の拡大とともに用いられなくなる傾向がみられたものの，サージカルマスクなどの日常よく用いられる防護具に関しては流行期間中一貫して用いた施設がほとんどであった．しかし，各種感染対策器材の品不足が問題になったため，約半数の施設では感染対策器材の使用制限を設けることとなり，その中で最も制限されたのはサージカルマスクであった．感染対策器材の備蓄はほとんどすべての施設で行われており，マスクや迅速診断キット，治療薬など幅広く備蓄を行っていたことがわかった．なお，備蓄を予定していたものの，サージカルマスクが品薄で入手できなかったという回答もみられた．

CDCは，流行終息後に新型インフルエンザ発生時の感染対策として，図4に示すようなガイドラインを発表した．今回調査した医療機関の多くにおいて，後にCDCが示した感染対策がすでに実施されていたことが分かる．

CDCのガイドラインと対比するとインフルエンザ症状を有する外来者の訪問は原則禁止している施設は9施設(約50%)にとどまっており，「曝露リスクの除去」の観点からは問題となる可能性が考えられた．また，外

曝露リスクの除去 Elimination of potential exposure
(例)インフルエンザ症状のある外来者の訪問を禁止する
ハード面(物理面・技術面)の対策 Engineering control
(例)パーティションなどによりトリアージエリアをつくる(患者飛沫から職員を守る)
(例)エアロゾル産生手技を行う際には換気に配慮する
ソフト面(管理面)の対策 Administrative control
(例)職員には可能な限りワクチン接種を行う
(例)トリアージエリアを作り患者の導線を管理する
(例)患者や外来者のスクリーニングを行う
(例)高頻度接触面の消毒
(例)患者にマスクを着けさせる
個人防護具 Personal protective equipment(PPE)
(例)手袋，ガウン，フェイスマスク，眼の防護具などを適切に使用する

図4　CDCガイドラインによる施設内感染対策の概要

来・入院ともに診療場所を限定することにより，Engineering control(技術面・物理面の対策)を行うこと，さらに，トリアージを行い患者の動線を分離することや，有症状者のスクリーニング，患者に対するマスク着用などといった，Administrative control(管理面の対策)においても多くの施設で実践されていた．個人防護具の使用は初期の時点ではさまざまな防護具が用いられており，施設によりその種類や期間に大きなばらつきがみられたものの，サージカルマスクは最も頻用されており，かつ長期間用いられていた．

パンデミック(H1N1) 2009流行から約2年が経過した現在，あらためて各施設で行われた感染対策を振り返ると，施設内感染の予防として行われた対策は概ね流行終息後に発表されたCDCのガイドラインと比較しても矛盾はないと考えられた．今後再び起こる可能性のあるパンデミックに対し，時流に合わせ，かつ効果的な感染対策を講じることができるように，国から各自治体・施設への連絡体制の強化や情報の共有を行うことができるよう整備する必要があると考えられた．

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利益相反について：利益相反はない．

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Infection Control Measures in Medical Facilities for Influenza (H1N1) 2009 Pandemic Period

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Abstract

At the time of the 2009 influenza pandemic, the pathogenicity in the early stage was indefinite, but individual medical facilities took infection control measures according to guidance from central government. Here the infection control measures adopted by these medical facilities during the pandemic period are evaluated. Referring to the interim guidance from the centers for disease control and prevention on infection control measures for the 2009 H1N1 influenza in healthcare settings, we created and distributed a questionnaire on infection control to 25 medical facilities belonging to the Research Group of Emerging and Re-emerging Infectious Diseases (H22-SHINKO-IPPAN-003). Almost all (88%) of the 17 responding medical facilities, with an average number of hospital beds of 610 (range 0-1300), took measures against influenza by establishing special units, sharing information, and performing influenza surveillance. Measures such as setting up triage areas to separate influenza patients (82%) and making influenza patients wear facemasks (94%) were also generally taken, but the period of implementation differed in each facility. Differences were also apparent in the implementation period and the content of personal protective equipment measures, but the wearing of facemasks was consistently adopted. In general, strict infection control measures were taken in the early stage of the pandemic, and as the pathogenicity was clarified, these measures were revised to those implemented for seasonal influenza, especially after the facility had actually encountered influenza cases. The validity and efficacy of infection control measures for pandemics as well as information sharing procedures should be evaluated to provide better central guidance to facilities nationwide in the future.

Key words : Influenza (H1N1) 2009, infection control, infection control committee, personal protective equipment

Trial to control an outbreak of Panton-Valentine leukocidin–positive methicillin-resistant *Staphylococcus aureus* at a boarding school in Japan

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Background: Our retrospective investigation of methicillin-resistant *Staphylococcus aureus* (MRSA) infection at a hospital in Japan around 2007 suggested dissemination of community-associated MRSA (CA-MRSA) strains among healthy students in a Japanese boarding school, which frequently caused skin disease and exhibited the same antibiogram patterns.

Methods: Active surveillance of skin diseases for 6 months after May 2008, examination of MRSA carriage in selected high-risk groups, and investigation of their life circumstances, including environmental cultures, were conducted in the school. Furthermore, we strengthened hygiene practices and improved recognized risk factors from November 2008 and observed the occurrence of skin diseases and MRSA carriage rate for the evaluation of infection controls.

Results: We identified 21 patients with skin diseases in whom MRSA strains were isolated. MRSA colonization rates in 3 selected groups ranged from 7.6% to 36.6%. The rates of both skin disease and MRSA carriage decreased significantly after infection controls were introduced. Genetic analysis revealed a main dissemination of a PVL-positive SCC*mec* IVc clone (41/47 isolates in total), presenting as a different pulsed-field type than USA300.

Conclusion: This first report of a PVL-positive CA-MRSA outbreak in Japan demonstrates systematic management of dissemination by conducting surveillance in a closed community.

Key Words: Closed community; surveillance; outbreak; skin and soft tissue infection; colonization.

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Methicillin-resistant *Staphylococcus aureus* (MRSA) has emerged as a cause of infection in community settings, known as community-associated MRSA (CA-MRSA). CA-MRSA can cause severe and even life-threatening infections even in otherwise healthy patients, with virulence frequently depending on the carriage of Panton-Valentine leukocidin (PVL).[1] Many community outbreaks caused by these virulent strains have been reported in the United States.[2,3] They are classified mainly as the USA300 strain,[4] sporadic infections of which were also recently detected in Japanese communities.[5,6] However, most prevailing CA-MRSA strains in Japan do not carry PVL genes,[7,8] and no outbreak in Japanese community settings has been reported to date.

This retrospective investigation, conducted at one of our affiliated hospitals in Japan between October 2006 and April 2008, identified 17 young male patients with skin and soft tissue infection (SSTI) caused by MRSA, presenting with almost the same antibiogram: resistant to oxacillin (OXA) and some cephems but susceptible to imipenem/cilastatin (IPM/CS), gentamicin (GM), clindamycin (CLDM), minocyclin (MINO), levofloxacin (LVFX) and

vancomycin (VCM). All patients were otherwise healthy students attending the same boarding high school. These successive MRSA occurrences implied an ongoing outbreak of CA-MRSA strains with some virulent factors. The present study aimed to clarify the dissemination of CA-MRSA by a survey of the school, including MRSA carriage examinations; investigate the genotypic characteristics of isolated MRSA strains; and control MRSA prevalence in a closed school community.

MATERIALS AND METHODS

Population characteristics

We surveyed a 3-year boarding high school in Japan, attended by approximately 700 healthy students aged 15-19 years and staffed by approximately 300 teachers and other staff members. The students live and work closely together, and sometimes experience skin abrasions from participating in regular training and sports clubs, such as rugby, martial arts, and baseball. Students or staff who become ill usually visit a clinic within the school. But because the clinic does not provide detailed examinations (eg, cultures of pus discharge), patients with serious clinical symptoms are usually transferred to one of our affiliated hospitals near the school.

Active surveillance and clinical definition of CA-MRSA

In our hospital's outpatient clinic, we conducted active surveillance of SSTI cases, including cellulitis and subcutaneous abscess, from the school between May and October 2008. We obtained samples from SSTI lesions regardless of clinical severity, to detect causal agents. Samples were incubated using capenic cultivation with the candle jar method on a Trypticase Soy Agar II with 5% sheep's blood (TSA II) plate, a Chocolate II agar plate, or aerobically on a modified Drigalski agar plate (all from Nippon BD, Tokyo, Japan) for 24-48 hours at 37°C. The susceptibility of isolated *S aureus* was examined using a Micro Scan autoSCAN-4 system (Siemens Healthcare Diagnostics, Tokyo, Japan) in accordance with guidelines of the Clinical and Laboratory Standards Institute.[9] The following antibiotics were tested: OXA, penicillin G, ampicillin, cefazolin (CEZ), cefozoplan, cefdinir, IPM/CS, meropenem, amikacin (AMK), arbekacin, GM, erythromycin, clarithromycin, azithromycin, CLDM, MINO, LVFX, sulfamethoxazole/trimethoprim, VCM, teicoplanin, and linezolid. We diagnosed the isolated agents as CA-MRSA if they were *S aureus*–resistant to oxacillin and cultured from patients within 48 hours of consultation with no history of recent hospitalization.

Examination of nasal and pharyngeal colonization in 3 high-risk groups

We performed carriage examinations in 3 selected groups. Group 1 (performed in May 2008) included 11 of 17 students with SSTIs caused by MRSA between October 2006 and April 2008 (6 had already graduated). Group 2 (performed between July and September 2008) comprised 35 students from the rugby club, 32 from the judo club, and 12 from the kendo club (n = 79) who were considered high-risk subjects because group 1 included some members belonging to these clubs. Group 3 comprised 41 freshmen with a previous history of suspected staphylococcal infections (including suppurative wound, skin abscess, cellulitis, infected eczema, hordeolum, conjunctivitis, and infected atheroma) between April (at entry) and November 2008, who were selected based on school clinical records and examined twice, in January 2009 and January 2010. In all 3 groups, samples were obtained from both the nares and pharynx using a sterile dry cotton swab and cultured to detect *S aureus* on TSA II plates as described earlier. Colonization of *S aureus* was judged to be positive when isolated from at least one sample from either the nares or pharynx.

Investigation of life circumstances and environmental cultures

We investigated the students' life circumstances by evaluating their life at the boarding school, especially regarding their participation in sports clubs and their dormitory rooms and hygiene practices. We also obtained environmental cultures of 50 frequent contact points, including sports equipment, gym floors, items in bathrooms, and toilet seats. We also examined ointment tubes repeatedly used in the clinic.

Changes over time in students with SSTIs

SSTI patients who visited the clinic and were subsequently hospitalized were investigated during 2 periods, January 2007 to November 2008 and November 2008 (when infection control commenced) to June 2010.

Molecular typing

Detection of the *mecA* gene, PVL genes, and the *arcA* gene in arginine catabolic mobile element (ACME), and typing of staphylococcal cassette chromosome *mec* (SCC*mec*) elements and *spa* (staphylococcal protein A gene) were carried out as described previously.[7,8,10]

Multilocus sequence typing

The multilocus sequence typing of MRSA strains representing each pulsotype was determined as described

previously,[7] and standard nomenclature was applied (http://www.mlst.net).

Pulsed-field gel electrophoresis

Chromosomal DNA of the MRSA strains was digested with *Sma*I and separated by pulsed-field gel electrophoresis (PFGE) as reported previously.[7] USA300-0114 and USA500, kindly provided by Fred C. Tenover (Centers for Disease Control and Prevention; currently at Cephied, Sunnyvale, CA), were used as references.

Statistical analysis

In the carriage examination of group 3, data were analyzed using the paired *t* test. For the evaluation of SSTI occurrences, data were analyzed using the Student *t* test. All results are expressed as mean ± standard error. A significant difference was defined as $P < .05$.

The study was designed to conform to the Helsinki Declaration, and it was approved by the hospital's Ethics Committee.

RESULTS

Active surveillance and clinical features of SSTI patients at the boarding school

During active surveillance of the school between May and October 2008, we identified 21 individuals with an SSTI (all males, with no past history of recent hospitalization), including 19 students, 1 teacher (case 8), and 1 other staff member (case 16). MRSA strains were isolated from all 21 individuals. The incidence of MRSA causing SSTIs was calculated as 32.4 per 1,000 outpatients during the period (21 MRSA cases per 649 outpatients from the school) and was considered an outbreak. The incidence of MRSA infections in communities surrounding our hospital was 0.36 per 1,000 outpatients during the same period. Table 1 summarizes the clinical features of 21 cases. Many cases occurred in the hot, humid season of July and August. Thirteen cases presented with fever. Many cases had abnormal laboratory findings. Incision and drainage was performed in 18 cases. The average duration of therapy 10 ± 0.84 days (range, 5-12 days). Fifteen patients were hospitalized. An alternative antibiotic was used in 5 cases because of resistance to the first antibiotic administered. Case 5 was rehospitalized 4 days after discharge because of relapse, and debridement was performed. Cases 7, 9, and 19 developed SSTI a few days after scratching insect bites. Figure 1A shows cellulitis on the left sole of case 1, who belonged to the kendo club and suffered from periodic skin abrasions on the soles of his feet. He had the same lesion in October 2006 when MRSA was already isolated. Figure 1B shows an abscess on the right buttock of case 6. Cases 2 and 15 also had buttocks abscesses. Figure 1C is a computed tomography image of a perineal abscess in case 21, who experienced itching in the pubic region, which later became swollen, red, and painful with abscess formation.

Genotypic characterizations of CA-MRSA strains isolated from patients with SSTI

We analyzed 18 CA-MRSA strains isolated from 18 of 21 cases (strains of cases 2, 5, and 18 were not preserved due to technical problems). All 18 strains were identical PVL-positive SCC*mec* IVc clones with identical PFGE banding patterns (lane A-1 in Figure 1D), which belonged to the multilocus sequence type (ST) 8, *spa* type 8, and coagulase type III. The PFGE banding patterns of our isolates differed from those of ST8 strains USA300 and USA500 isolated from the United States (lanes 1 and 2 in Figure 1D, respectively). Carriage of the *arcA* gene in ACME, which enhances virulence and fitness and is frequently identified in USA300 clones,[1] was negative. The isolated strains were resistant to OXA, penicillin G, ampicillin, and cefdinir and susceptible to CEZ, cefozoplan, IPM/CS, meropenem, AMK, arbekacin, GM, erythromycin, clarithromycin, azithromycin, CLDM, MINO, LVFX, sulfamethoxazole/trimethoprim, VCM, teicoplanin, and linezolid.

Carriage examinations in groups 1 and 2

Positive rates of MRSA carriage were 18.2% in group 1 and 7.6% in group 2, and methicillin-sensitive *S aureus* (MSSA) carriage rates were 63.6% in group 1 and 29.1% in group 2. All MRSA isolates were PVL-positive SCC*mec* IVc strains with the same PFGE banding patterns as shown in lane A-1 in Figure 1D. In group 2, there were 3 MRSA carriages in both the rugby club and judo club (positive rate of 8.6% and 9.4%, respectively), but no carriage in the kendo club. Thus, attendance of frequent-contact sports clubs was considered a possible risk factor for MRSA infection in the school.

Primary and secondary carriage examination in group 3

Table 2 compares the first and second carriage examinations in group 3. In 2009, there were 12 PVL-positive SCC*mec* IVc MRSA carriers (29.3%) and 3 PVL-negative MRSA carriers (7.3%), for a total of 15 MRSA carriers (36.6%) among 41 students. Of the 12 PVL-positive MRSA isolates, 11 had identical PFGE banding patterns to those isolated during the active surveillance period (lane A-1 in Figure 1D), and 1 showed an almost identical banding pattern with the exception of one band (lane A-2 in Figure 1D;

Table 1. Clinical features of 21 SSTI patients between May and October 2008

Patient/age, years	SSTI/site	Month	BT, °C	Laboratory values		Incision and drainage	Duration of therapy, days	Admission, days	Antibiotics		Sports club
				WBC, μL	CRP, mg/dL				First	Second	
1/17	Cellulitis/left sole	May	37.1	9,520	0.42	+	10	–	CCL	–	Kendo
2/17	Abscess/left hip	May	36.9	9,050	0.37	+	8	7	PIPC	–	Tennis
3/18	Cellulitis/left thigh	May	38.5	10,120	3.69	–	10	5	PIPC	LVFX	Tennis
4/16	Cellulitis/left sole	May	37.3	5,580	1.35	+	11	6	PIPC	LVFX	Kendo
5/17	Cellulitis/left sole	June	38.3	11,940	4.01	+	13	9	CEZ	LVFX	Judo
	(relapse)	June	36.8	7,800	1.88	Debridement	18	18	CLDM + LVFX	–	
6/17	Abscess/right hip	June	38.1	9,030	2.94	+	20	9	CLDM	–	Tennis
7/17	Cellulitis/right arm	July	37.8	12,680	6.05	+	12	10	CLDM	–	ND
8/38	Abscess/right axilla	July	37.4	9,070	2.36	+	11	7	CLDM	–	Soccer (coach)
9/17	Cellulitis/left thigh	July	36.8	9,050	3.18	+	10	6	CLDM	–	Archery
10/16	Abscess/right elbow	July	36.6	ND	ND	+	5	–	CCL	–	Ping pong
11/15	Cellulitis/lower thigh	July	37.3	11,210	3.11	–	9	5	CLDM	–	Baseball
12/17	Cellulitis/right sole	August	37.1	ND	ND	+	5	–	CFPN-PI	–	ND
13/16	Cellulitis/left thigh	August	36.9	9,660	7.52	+	13	4	CLDM	–	ND
14/17	Abscess/mandible	August	ND	ND	ND	+	11	–	CFPN-PI	–	ND
15/16	Abscess/left hip	August	ND	ND	ND	+	5	–	CFPN-PI	–	Handball
16/40	Abscess/abdominal wall	August	ND	ND	ND	+	5	–	CFPN-PI	–	–
17/16	Abscess/left middle finger	August	36.0	6,100	0.78	+	17	12	PIPC	MINO	Canoe
18/16	Abscess/right index finger	September	37.4	9,260	1.98	+	8	5	LVFX	–	Wrestling
19/17	Abscess/left knee	September	37.9	7,970	2.08	+	10	7	CEZ	–	Gymnastics
20/15	Abscess/right knee	September	39.1	14,160	2.37	–	9	6	CLDM	–	Rugby
21/16	Abscess/pubic region	October	38.9	11,820	6.88	+	14	8	CEZ	CLDM	Tennis

BT, body temperature; *CCL*, cefaclole; *CEZ*, cefazolin; *CFPN-PI*, cefcapene pivoxil; *CLDM*, clindamycin; *CRP*, C-reactive protein (normal range, <0.3 mg/dL); *LVFX*, levofloxacin; *MINO*, minocycline; *ND*, no data; *PIPC*, piperacillin; *WBC*, white blood cell (normal range, 4,000-8,000/μL).

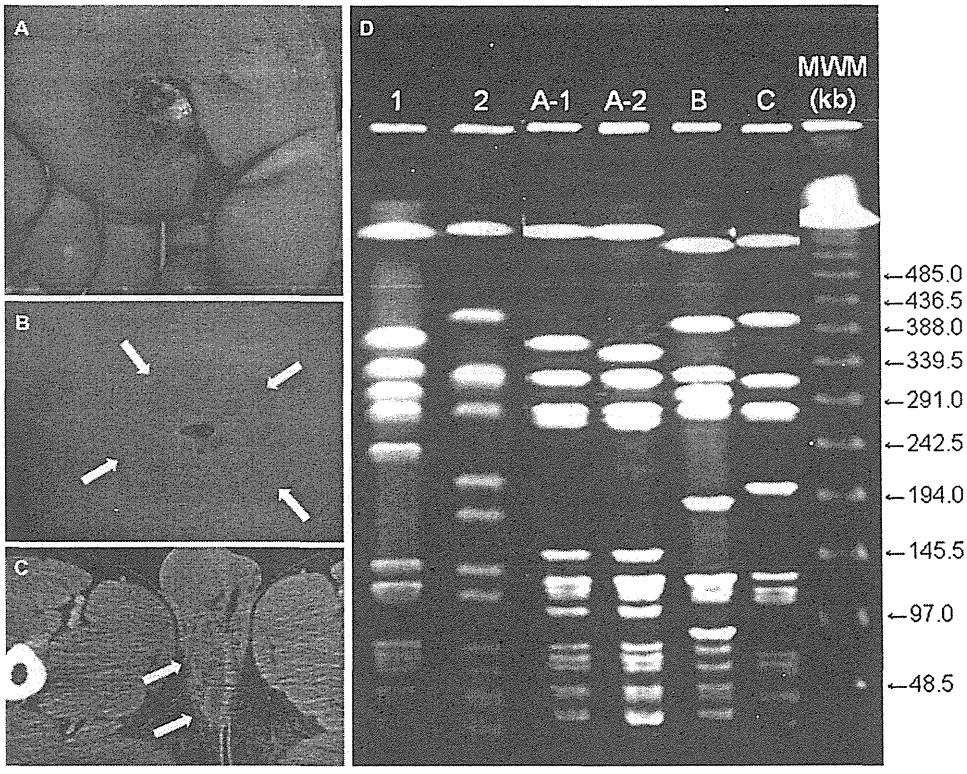

Fig 1. Representative lesional findings of SSTIs caused by MRSA strains (A-C) and PFGE patterns of *Sma*I-digested DNA from MRSA isolates in the school (D). (A) Cellulitis on the left sole in case 1, who belongs to a kendo club and sometimes suffers from skin abrasions on the soles of his feet. (B) Abscess (arrow) on the right buttock in case 6. Similar lesions were also observed in cases 2 and 15. (C) Computed tomography image of perineal abscess (arrow) in case 21, who experienced itching in the pubic region, which later became swollen, red, and painful. Incision and drainage was performed, and a large volume of abscess fluid was released. (D) Lane 1, USA300-0114. Lane 2, USA500. Lane A-1, predominant PVL-positive SCC*mec* IVc MRSA strains isolated from SSTI cases and carriage examinations. Lane A-2, isolated from one student on primary examination with similar banding patterns to lane A-1. Lane B, PVL-negative SCC*mec* V strains isolated from 2 students on primary examination, absent on secondary examination. Lane C, PVL-negative SCC*mec* IV strains isolated from 1 student on primary examination and 3 students on secondary examination. MWM, molecular weight marker.

Table 2. Results of the first and second examinations in group 3

	Second exam, January 2010, n (%) [SSTI cases in 2009]*			
First exam, January 2009 41 cases examined	**PVL-positive MRSA**	**PVL-negative MRSA**	**MSSA**	**No *S aureus***
PVL-positive MRSA, 12 cases	1 (8.3)	1 (8.3) [1]	4 (33.3) [1]	6 (50) [2]
PVL-negative MRSA, 3 cases	0	0	2 (66.7)	1 (33.3) [1]
MSSA, 5 cases	1 (20)	0	3 (60)	1 (20) [1]
No *S aureus*, 21 cases	0	2 (9.5)	7 (33.3)	12 (57.1) [3]

*SSTI cases between the first and second examinations.

SCC*mec* IVc, ST8, *spa* type 1767, coagulase type III). The 3 PVL-negative MRSA isolates consisted of 2 SCC*mec* V strains (lane B in Figure 1D; ST1715, *spa* type 127, coagulase type VII, with susceptibility differing from lane A-1 only in GM resistance), and 1 SCC*mec* IV strain (lane C in Figure 1D; ST8, *spa* type 5071, coagulase type III, with susceptibility differing from lane A-1 in intermediate susceptibility to

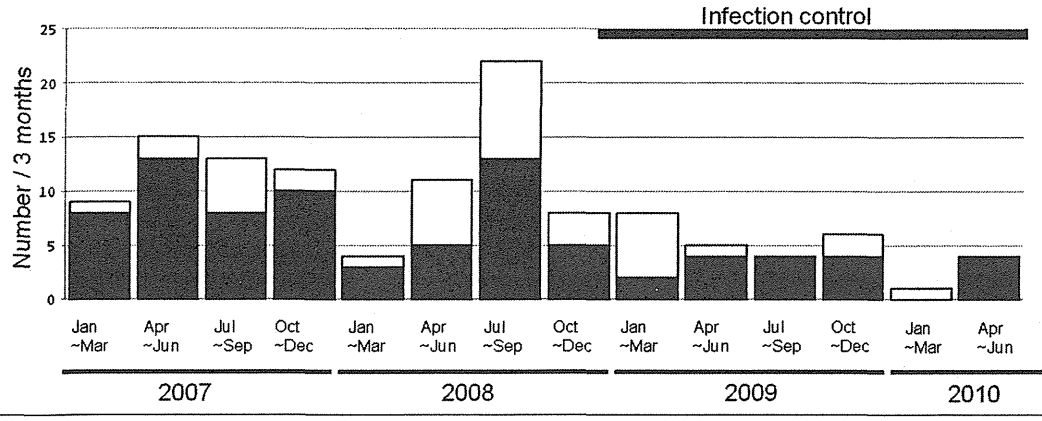

Fig 2. Chronological changes in the number of SSTI cases between January 2007 and June 2010, including cases with proven and nonproven causal agents. The black bar indicates the students who visited only the clinic for treatment of SSTI in each 3-month period. The white bar indicates the students hospitalized due to SSTI in each 3-month period. After combined measurements for infection control were implemented in November 2008, the number of those who visited only the clinic with an SSTI decreased significantly, from 2.70 ± 0.38/month to 1.11 ± 0.30/month ($P = .001$). The number of those hospitalized also decreased significantly, from 1.21 ± 0.27/month to 0.53 ± 0.22/month ($P = .03$). The total rate of SSTI cases decreased significantly, from 3.91 ± 0.51/month to 1.63 ± 0.37/month ($P < .001$), suggesting that the horizontal infection was suppressed.

AMK). At the follow-up examination in 2010, only 5 MRSA carriers were detected. Two of these carried the same strains as lane A-1, and 3 carried the same strains as lane C. Carriage of all MRSA strains was significantly reduced, from 36.6% to 12.2%, over the course of 1 year ($P = .005$). Nine of the 41 students received antibiotic therapy for SSTI during 2009. Focusing on the 32 SSTI-free students, the number of MRSA carriers was spontaneously and significantly reduced from 10 (31.3%) to 4 (12.5%) over the course of 1 year under strengthened infection control measurements ($P = .04$).

Environmental cultures in the school

Among the 50 contact points, one PVL-positive MRSA strain isolated from a toilet seat exhibited identical PFGE banding patterns to lane A-1 in Figure 1D. MSSA strains were also isolated from tatami mats in the judo facility, mats from the wrestling club, and a strength-training machine. All ointment tubes in the clinic were free of *S aureus*.

Overall genotypic character of MRSA isolates in the school

In a series of surveys, we isolated and examined a total of 47 MRSA strains, 41 of which were PVL-positive SCC*mec* IVc strains of the same pulsed-field type (87.2%), including 18 from SSTI cases, 22 from carriage examinations, and 1 from a toilet seat. The 6 PVL-negative isolates included 4 SCC*mec* IV clones and 2 SCC*mec* V clones, isolated from carriage examinations.

Changes in SSTI cases before and after infection control

Figure 2 shows the occurrence of SSTI cases. After nurses and staff implemented systematic management of infection control in November 2008, the rate of clinic visitation in individuals with an SSTI decreased significantly, from 2.70 ± 0.38/month to 1.11 ± 0.30/month ($P = .001$). The rate of hospitalization also decreased significantly, from 1.21 ± 0.27/month to 0.53 ± 0.22/month ($P = .03$), as did the total number of SSTI cases, from 3.91 ± 0.51/month to 1.63 ± 0.37/month ($P < .001$).

DISCUSSION

We report an outbreak of a PVL-positive MRSA clone in a boarding school and a prospective follow-up study aimed at reducing the prevalence. Our original hypothesis, based on retrospective investigation of MRSA strain antibiograms, suggested dissemination of the same CA-MRSA strains. Active surveillance and examination of MRSA carriage in the school proved this dissemination. Systematic measures were then implemented to suppress the outbreak. This is a first report of systematic management of a CA-MRSA outbreak in a closed community setting in Japan.

During the 6-month active surveillance period, the incidence of MRSA infection increased up to 32.4 per 1,000 visits, approximately 5.5 times higher than the reported incidence of 5.9 per 1,000 visits in 2005 in the United States in 2005,[11] where PVL-positive CA-MRSA

is much more prevalent compared with Japan. Surprisingly, all MRSA strains isolated from SSTI cases were the same single PVL-positive clone suspected to be horizontally transmitted, despite the other PVL-negative strains detected in carriage examinations. Some risk factors for CA-MRSA infection have been identified,[1] and our investigation identified similar risk factors in the school, including skin damage, frequent-contact sports, inadequate hygiene, sharing of equipment or clothing, scratching insect bites, hot and humid weather, and crowded dormitory rooms containing 6-10 students. Furthermore, the isolation of MRSA from a school toilet seat suggests the possibility of indirect transmission from an infected perineum or buttocks (as shown in Figure 1B and C), and underscores the importance of covering these skin lesions appropriately and the need for regular cleaning of frequent-contact points in residential situations.

Based on these recognized risk factors, we educated all students about SSTIs and hygiene practices, installed alcohol-based handrub dispensers, and attempted to improve their life circumstances. Nurses and staff periodically remind students about improving hygiene practices. In the school clinic, although adequate cleansing of wounds is a primary therapy and systemic antibiotic administration is not always necessary when lesions are localized, MINO (available and effective medicine in the school clinic) is administered to treat SSTI as the first-line drug, when required. Furthermore, in the hospital, we perform cohorting for school inpatients to reduce the risk of MRSA transmission to other inpatients; thus far, no horizontal transmission between inpatients has occurred.

Nasal colonization of *S aureus*, especially MRSA, is considered a risk factor for subsequent infectious diseases.[12] In our investigation, some groups had very high carriage rates, which was regarded as a critical factor for the outbreak. Although intranasal mupirocin reportedly has been effective in some situations,[13] we did not administer topical mupirocin for infection control based on a previous,[14] and most MRSA carriers became MSSA carriers or non-*S aureus* carriers over the course of 1 year with combined infection controls throughout the school. This phenomenon of a natural decrease of MRSA carriers, as observed previously,[14] suggests that colonized strains of *S aureus* change more rapidly and dynamically than expected, and that a series of strengthened infection controls might have some impact on the ecological niche.

In Japan, previous studies have reported prevalence of several MRSA strains in communities, but most of these do not carry PVL genes.[7,8] The few PVL-positive MRSA isolates mostly belong to ST30 with SCC*mec* IV. In the United States, MRSA strains have been classified into several lineages according to PFGE banding patterns.[4] Among them, USA300 and USA500 strains belong to ST8,[4] and USA300 is beginning to spread across Japan.[5,6,15] Pulsed-field types of our PVL-positive ST8 strains differed from these strains, however. Considering that nearly all recently reported MRSA outbreaks in the United States have involved USA300,[2,3] our isolates might be distinct Japanese strains with equivalent virulence potential to the USA300 strains, although ACME was negative.

In this study, we identified the main dissemination of a PVL-positive SCC*mec* IVc clone in a boarding school by active surveillance and carriage examination. Nurses and staff in the school worked well together to strengthen infection control for SSTI prevention, leading to successful suppression of CA-MRSA dissemination. In the future, the spread of virulent CA-MRSA strains is highly possible even in Japan, in which case our study findings will surely contribute to their suppression.

We thank teachers and other staff members of the boarding school for their cooperation and are grateful to the managers for allowing us to publish this study.

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CASE REPORT

Epidural abscess caused by community-associated methicillin-resistant *Staphylococcus aureus* strain USA300 in Japan

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Abstract We report a case of epidural abscess caused by community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) strain USA300 in a previously healthy 25-year-old American woman who lived in Japan for more than 1 year. She started to complain of severe headache that continued for about 10 days after improvement of subcutaneous abscesses caused by MRSA. Computed tomography (CT) and magnetic resonance imaging (MRI) showed epidural abscess. As epidural abscess was not improved by treatment with vancomycin and ceftriaxone, craniotomy and drainage were performed, and the severe headache disappeared. Characteristics of the MRSA strain isolated from the abscess were identical to those of strain USA300; multilocus sequence typing sequence type 8, staphylococcal cassette chromosome *mec* type IVa, Panton–Valentine leukocidin positive, arginine catabolic mobile element positive, and pulsed-field gel electrophoresis type USA300. This may be the first report of epidural abscess caused by USA300 strain in Japan. Because CA-MRSA strains, including USA300, have begun to spread in Japan, epidural abscess should be taken into account in the diagnosis of previously healthy patients with persistent headache accompanied by skin lesions.

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Keywords Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) · USA300 · Panton–Valentine leukocidin (PVL) · Arginine catabolic mobile element (ACME) · Epidural abscess

Introduction

Although methicillin-resistant *Staphylococcus aureus* (MRSA) strains have been considered to be typical nosocomial pathogens, they have emerged as causes of infections in the community setting. These strains, which are known as community-associated MRSA (CA-MRSA) strains, are mostly isolated from patients with skin and soft-tissue infections [1], respiratory tract infections, and urinary tract infections. In some cases, CA-MRSA can cause severe and life-threatening infections, such as necrotizing fasciitis [2] and severe sepsis [3]. CA-MRSA strains emerged in the 1980s and began spreading globally in the late 1990s.

Recently developed molecular typing techniques have allowed us to differentiate MRSA strains among CA-MRSA strains or to differentiate CA-MRSA strains from health-care-associated MRSA (HA-MRSA) strains [4]. By determining chromosome types, e.g., via pulsed-field gel electrophoresis (PFGE), multilocus sequence typing (MLST), *spa* typing, typing based on the variety of tandem repeat region of protein A, and the types of staphylococcal cassette chromosome *mec* (SCC*mec*) elements, MRSA strains can be defined [5].

It was found that characteristic CA-MRSA strains were prevalent in each country. In the United States, where the spread of CA-MRSA strains has become a serious concern as a community pathogen, outbreaks are observed in groups prone to frequent contact, such as jailed prisoners,

members of the armed forces, and sports players [6–8]. Furthermore, it has also become the predominant isolate in some hospitals and health-care settings [9, 10]. In particular, two CA-MRSA strains, known as PFGE types USA300 and USA400, have been predominant in the USA [11]. Both strains are Panton–Valentine leukocidin (PVL) positive [12] and carry type IV SCC*mec*, whereas the former has spread widely throughout the USA, both in the community and in hospitals. USA300 isolates have since been recognized in many countries, including Denmark [13], Australia [14], and Japan [15].

In Japan, the characteristics of CA-MRSA strains are distinct from those in other countries. Most isolates are PVL negative, whereas only some MRSA strains belonging to ST30 are PVL positive. To date, only one case of USA300 infection [15] has been reported. Here, we report a case of epidural abscess caused by USA300 in Japan with the intention of warning Japanese clinicians of possible CA-MRSA spread.

Case report

The patient was a 25-year-old Caucasian woman who came to Japan from the USA more than 1 year earlier with her husband, who works for the US Navy. In early June 2008, she developed small subcutaneous abscesses on the abdomen and posterior side of the right thigh, without traumatic injury, from which MRSA strains were isolated at the American Navy Hospital Yokosuka. After improvement of the lesions by drainage, she started to complain of left-sided parietal headache persisting for about 10 days and visited the hospital emergency room (ER) on 26 June 2008. Plain head computed tomography (CT) was performed, but no intracranial lesions were noted, and she was prescribed Tegretol for neuralgic pain. However, her headache progressed in severity, with severe photophobia and clinical findings of papilledema, leading to emergent admission on 30 June. At that time, plain head CT revealed focal left parietal region soft-tissue swelling and left posterior extra-axial fluid collection without remarkable mass effect. Lumbar puncture was performed with a closing pressure of 34 cmH_2O. Initial cerebral spinal fluid (CSF) evaluation showed elevated CSF protein (87 mg/dl) with CSF glucose of 62 mg/dl. Cell count and culture of CSF were not performed. The patient demonstrated elevated systemic white blood cell (WBC) count (13,200/μl, neutrophils 89.8%), increased erythrocyte sedimentation rate (ESR 68 mm/h), and progressive neck stiffness. Magnetic resonance imaging (MRI) demonstrated epidural fluid collection with associated mass effect and reactive change. The causal agent was found to be MRSA by culture of blood and exudate from the left parietal region. The results of susceptibility testing by the disk diffusion method showed that the strain was susceptible to clindamycin (CLDM), gentamicin (GM), arbekacin (ABK), tetracycline (TC), trimethoprim/sulfamethoxazole, and vancomycin (VCM) and was resistant to oxacillin (OXA), penicillin, levofloxacin (LVFX), ciprofloxacin (CPFX), clarithromycin (CAM), and erythromycin (EM).

Antibiotic therapy with VCM and ceftriaxone was initiated, and she was transferred to our hospital (Japan Self-Defense Forces Hospital Yokosuka) on 2 July. Physical examination revealed the following: slight drowsiness but no disorientation, body temperature 37.0°C, heart rate 76 beats/min, blood pressure 126/81 mmHg, and meningeal signs of neck stiffness. Exudate discharge continued from the left parietal region. Small infiltrating skin lesions, partly crusted and partly purulent, were present on the abdomen and posterior side of the right thigh. Further MRI with gadolinium enhancement showed enhanced left posterior dura mater and epidural abscess (Fig. 1a, b). Echocardiogram revealed no valvular vegetation. Headache was controlled with morphine. Despite 1-week administration of antibiotics, abscess findings did not improve on MRI. We performed craniotomy and washed out the epidural abscess on 10 July. Collection of exudate was noted on the dura mater (Fig. 2), with no signs of infection or bone fracture and no continuity between epidural abscess and parietal soft-skin region. Epidural abscess was cultured, and MRSA, which had the same sensitivity to antibiotics as the previously isolated species, was again confirmed. After surgical treatment, her headache was fully alleviated and MRI showed no epidural abscess; WBC count normalized. She was transferred back to the former hospital on 18 July for sustained observation and was discharged with good clinical course a few days later.

Molecular characterization of two MRSA isolates from the epidural abscess and exudate discharge of the left parietal region was performed. MLST, *spa* typing, coagulase typing, and SCC*mec* typing were performed as described previously [16–18]. The presence of *PVL* genes and arginine catabolic mobile element (ACME) were confirmed by the presence of *lukS-PV* and *lukF-PV* and the *arcA* gene on polymerase chain reaction (PCR). PFGE was carried out as described previously [11] using the restriction enzyme *Sma*I and USA300-0114, kindly provided by Fred. C. Tenover, as a reference. A lambda ladder (Bio-Rad Laboratories, Tokyo, Japan) was used as the molecular size standard. The minimal-inhibitory concentrations (MICs) of isolated strains against 17 antimicrobial agents were determined by the agar dilution method, as recommended by the Clinical and Laboratory Standards Institute [19]. The antibiotics tested were as follows: OXA, cefazolin (CEZ), CAM, EM, TC, minocycline (MINO), LVFX, CPFX, imipenem (IPM), GM, trimethoprim, CLDM,

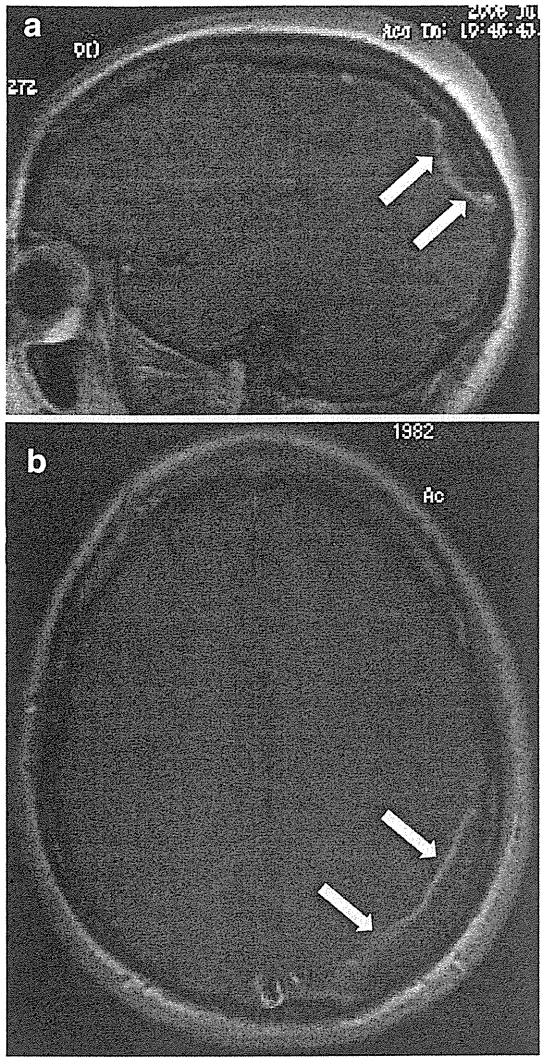

Fig. 1 T1-weighted magnetic resonance image (MRI) with gadolinium enhancement showing enhanced left posterior dura mater and epidural abscess. *Arrows* indicate epidural abscess (**a** sagittal view, **b** axial view)

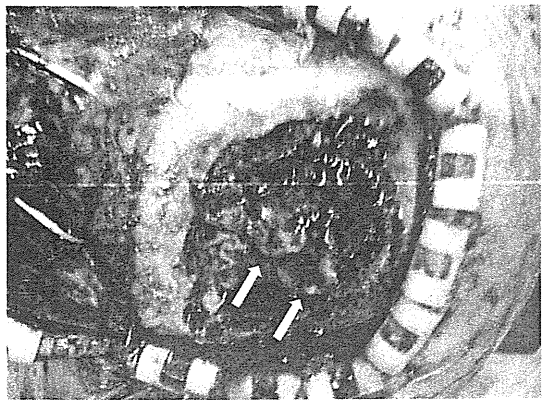

Fig. 2 Bone was removed and abscess was confirmed on dura mater (*arrows*)

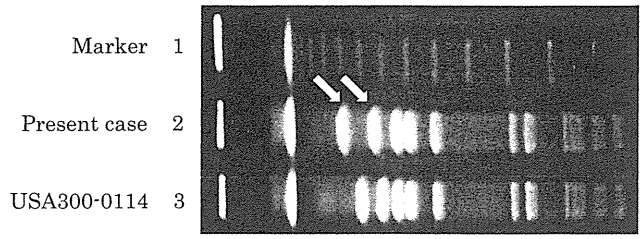

Fig. 3 Pulsed-field gel electrophoresis (PFGE) analysis of methicillin-resistant *Staphylococcus aureus* (MRSA) isolated from a 25-year-old American woman (*lane 2*), in comparison with USA300-0114 strain (*lane 3*). *Lane 2* presented the same banding patterns as *lane 3*, except for two bands (*arrows*)

VCM, teicoplanin (TEIC), linezolid (LZD), ABK, and mupirocin (MUP). Furthermore, PCR testing was performed to identify genes conferring beta-lactamase activity (*blaZ*), tetracycline resistance (*tetK*), macrolide resistance (*ermA*, *ermB*, *ermC* and *msrA*), and mupirocin resistance (*ileS*) [20–22].

The data showed that the two isolates had characteristics identical to the USA300 strain: ST8, *spa* type 8, coagulase type III, SCC*mec* IVa, ACME positive and PVL positive. Although *Sma*I-digested banding patterns on PFGE were not exactly identical to those of USA300-0114 (lanes 2 and 3 in Fig. 3, respectively), differences are seen only in two bands (arrows in Fig. 3). The results of susceptibility testing with the agar dilution method were the same as those of the disk diffusion test. The strains were resistant to OXA, CAM, EM, LVFX, and CPFX, with MIC values of 16, 64, 64, 4, and 8 μg/ml, and were susceptible to other tested antibiotics, with MIC values indicated in parenthesis: CEZ (8), TC (0.5), MINO (0.125), IPM (1), GM (0.5), trimethoprim (1), CLDM (0.25), VCM (1), TEIC (1), LZD (4), ABK (1), and MUP (0.25); *blaZ* and *msrA*, which are present on the plasmid in USA300-0114, were confirmed, and no other genes, *tet K*, *ermA, ermB, ermC*, or *ileS,* were detected.

Discussion

In this case, we isolated a PVL- and ACME-positive CA-MRSA strain that presented almost identical banding patterns as those of USA300-0114 on PFGE. USA300 pulsed-field type (PFT) strain includes several isolates presenting similar banding patterns [23]. USA300-0114 is usually used as a reference in PFGE to compare for similarities with suspected USA300. Our isolates presented the same banding patterns with one of several strains included in USA300 PFT [23]. Furthermore, the antimicrobial susceptibility characteristics and the resistance genes were identical to those of USA300-0114 isolates clarified in