CASE REPORT

Successful management of Panton-Valentine leukocidine-positive necrotising pneumonia and A/H1N1₂₀₀₉ influenza virus coinfection in adult

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SUMMARY

This paper presents a case of community-acquired necrotising pneumonia due to Panton-Valentine leukocidine-positive methicillin-susceptible *Staphylococcus aureus* and A/H1N1₂₀₀₉ influenza virus co-infection in a 26-year-old woman. Despite the presence of pejorative prognostic factors, the clinical course of the patient was favourable.

BACKGROUND

Staphylococcus aureus is responsible for 2% of community-acquired pneumonia.¹ *S. aureus* pneumonia is often characterised by rapidly progressing and extensive bilateral pneumonia, defining a necrotising pneumonia.²

Panton-Valentine leukocidine (PVL) is one of many toxins produced by *S. aureus*, which targets leucocytes. Necrotising pneumonia is associated with the production of PVL.³

The presence of PVL in *S. aureus* is associated with primary skin infections and necrotising pneumonia in young immunocompetent patients and is frequently associated to fatal outcome.

We report a community-acquired necrotising pneumonia due to PVL-positive methicillin-susceptible *S. aureus* and A/H1N1₂₀₀₉ influenza virus coinfection in a young adult woman with favourable outcome.

CASE PRESENTATION

In November 2012, a 26-year-old woman was admitted to our intensive care unit (ICU) for acute respiratory failure. She was free of any chronic disease. She made a 2-week journey to Mecca. On the eighth day of the journey, the patient suffered from cough, fever (39°C), fatigue and purulent sputum. Being a nurse, she autoprescribed amoxycillin-clavulanate, although this prescription needs a physician's order. Two days after her return to France, she was hospitalised in the ICU for severe dyspnoea associated with left thoracic pain.

INVESTIGATIONS

The nasal swab performed on admission of the patient was positive for the pandemic A/H1N1₂₀₀₉ influenza virus realised using the Xpert Flu Assay (Cepheid; table 1). The next day, a bronchoalveolar lavage (BAL) was performed for bacteriological, virological, mycological and parasitological analysis. The Seeplex RV16 PCR assay (Seegene) was positive for the A/H1N1 influenza virus to exclude viral coinfection. The bacteriological results of microscopic examination of the BAL revealed the presence of Gram-positive cocci with 10⁵ polymorphonuclear neutrophils/mL without epithelial cells. After 24 h of incubation, the quantitative culture yielded a monobacterial species *S. aureus* at

Table 1 Microbiological investigations

Sample	Tests	Results
Nasal swab	Xpert Flu Assay (RT-PCR)	A/H1N1 ₂₀₀₉ positive
BAL	Cytology	10 ⁵ PMNLs No epithelial cells
	Acid-fast bacilli direct examination	Negative
	Bacterial culture	<i>Staphylococcus aureus</i>
	MALDI TOF MS identification	<i>S. aureus</i>
	Antimicrobial susceptibility tests (VITEK)	Penicillin G-resistant tetracycline resistant
	<i>mecA</i> gene detection (PCR)	Negative
	<i>Mycobacterium tuberculosis</i> culture	Negative
	Panton-Valentine leukocidine detection (PCR)	Positive
BAL	Seeplex RV16 assay (PCR, RT-PCR)	A/H1N1 positive
	Respiratory virus screening (DFA)	Negative
	Virus culture	Negative
	Mers-CoV detection (RT-PCR)	Negative
	Blood cultures	Negative
	Giemsa and toluidine colourations	Negative
	Cultures on chromoagar and Sabouraud	Negative
	Aspergillus antigen detection	Negative
	<i>Pneumocystis jirovecii</i>	Negative
	<i>Aspergillus fumigatus/flavus</i> detections (PCR)	Negative

BAL, bronchoalveolar lavage; DFA, direct fluorescence assay; MALDI TOF MS, matrix-assisted laser desorption and ionisation time-of-flight mass spectrometry; PMNLs, polymorphonuclear leucocytes; RT-PCR, real-time PCR.

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10⁴ cfu/mL of BAL identified by matrix-assisted laser desorption and ionisation time-of-flight mass spectrometry (MALDI-TOF MS) using a thin smear of this strain on a MALDI-plate.

In vitro antimicrobial susceptibility tests of this strain were obtained using the VITEK 2 system (bioMérieux, Marcy l'Etoile, France). The strain was resistant only to penicillin G and tetracycline. The two tests detecting the methicillin-resistance were negative (cefoxitin screen and oxacillin: minimum inhibitory concentration ≤ 0.25 mg/L). The *mecA* gene was not detected by PCR on this strain using the primers described by Unal *et al.*⁴

The strain was associated with the sequence type (ST) 152 using the previously described method.⁵ As the state of the patient was worse and the thoracic therapeutic drug monitoring showed necrosis, the suspicion of a PVL was evoked: this methicillin-susceptible *S. aureus* strain was detected PVL positive by real-time PCR (RT-PCR) as described previously by Deurenberg *et al.*⁶

DIFFERENTIAL DIAGNOSIS

The BAL was tested for detection of adenovirus, influenza virus, parainfluenza virus, respiratory syncytial virus, metapneumovirus, herpes simplex virus, varicella-zona virus and cytomegalovirus using direct immunofluorescence assays (D³Ultra⁸ DFA Respiratory Virus Screening and Identification kit, Diagnostic Hybrids, USA) and was negative (table 1). The BAL was inoculated into monolayer human fibroblast MRC-5, Vero and BGM cells and viral cultures were negative. As the patient had returned from Mecca, the new human β -coronavirus (MERS-CoV) was suspected. The detection of the upE and ORF1b regions of the coronavirus genome by RT-PCR in BAL and nasal swab was negative.⁷

The microscopic examination after Giemsa and Ortho Toluidin Blue staining of BAL and the culture of BAL on chromogenic medium CHROMagar and Sabouraud medium with antibiotic did not reveal any mycological element. The *Aspergillus* antigen, a portion detection of the genome of *Pneumocystis jirovecii* and *Aspergillus fumigatus/flavus* were negative.⁸ The acid-fast bacilli were not shown after the direct examination. BAL to *Mycobacterium tuberculosis* was negative after 8 weeks of incubation.

Six blood culture sets (aerobic and anaerobic bottles, Bact/Alert, Biomerieux, Marcy l'Etoile, France) drawn on admission of the patient were negative.

TREATMENT

Oseltamivir was prescribed for 5 days. After detection of the PVL toxin, the initial empirical antimicrobial therapy was switched to oxacillin (during 1 month) and clindamycin (during 10 days) for antitoxin effect. The left lung presented a large destruction with necrosis, multiple abscesses and pleuritis. Thoracic surgery of partial lung resection and pleurostomy was performed on day 12.

OUTCOME AND FOLLOW-UP

After a difficult weaning from mechanical ventilation and two ventilator-acquired pneumonia, the patient was discharged from ICU on day 23. The total hospital length of stay was 60 days.

DISCUSSION

As PVL-positive *S. aureus* pneumonia is rare in the general adult population, especially in most Western European countries, this aetiology is often considered with delay by physicians. Our case shares many of the features of community-acquired PVL-positive *S. aureus* pneumonia described in previous studies. Indeed, this

form of pneumonia affects preferentially young immunocompetent healthy individuals. Haemoptysis, a common finding associated to acute respiratory distress syndrome, is frequent and previously described as a predictive factor of fatal outcome.⁹ Regarding biological data, leucopenia and thrombopenia were frequently observed at the initial stage of disease. Here, a white cell count at 1.95×10^9 /L was observed whereas previous study had demonstrated that a severe leucopenia is another predictive factor of fatal outcome with a mortality rate of 75% associated with white cell count $< 3000/\mu\text{L}$.¹⁰

In the case presented here, we have not found the origin of the PVL-positive *S. aureus* strain responsible for community-acquired pneumonia. We were not able to find a healthy carrier of the *S. aureus* strain in the environment of the patient. As the patient had not returned to work at the time of hospitalisation, the origin of the PVL-positive *S. aureus* strain seems community-acquired. Indeed, the carriage of the same PVL-positive *S. aureus* strain among the relatives of the patient with necrotising pneumonia has been described in the literature.⁸ Recently, the carriage of PVL-positive *S. aureus* strains has been described either in a population of adults and in a population of preschool children.^{11 12} The *S. aureus* strain was associated with the ST 152, infrequently found in Europe.⁵ The PVL-positive *S. aureus* colonisation of populations may play a key role in the epidemiology of community-associated infection by PVL-positive *S. aureus*.

In the case reported here, the A/H1N1₂₀₀₉ influenza virus was initially detected from nasal swab using a rapid PCR test and was confirmed the second time from BAL sample. During PVL-positive *S. aureus* community-acquired pneumonia, an influenza-like syndrome is often described in the days prior to the onset of necrotising pneumonia but the detection of influenza virus is rarely reported. The association of PVL-positive methicillin-resistant *S. aureus* and A and B influenza viruses has been previously reported.^{13 14} To our knowledge, this is the first report of a PVL-positive methicillin-susceptible *S. aureus* and A/H1N1₂₀₀₉ influenza virus coinfection in immunocompetent adult until the A/H1N1₂₀₀₉ influenza virus.

In the case presented, the detection of PVL was associated to favourable outcome. PVL-positive *S. aureus* necrotising pneumonia are often associated with a high death rate.^{15 16} The association of the PVL with virulence remains controversial. Indeed, several studies describe PVL as an independent indicator of virulence^{10 17} and other authors attribute the virulence of *S. aureus* to the isolates' entire genotype.^{18 19} All data suggest that the PVL contributes to the *S. aureus* pathogenesis but the importance of PVL in virulence must be elucidated.

Learning points

- ▶ If a healthy young immunocompetent adult presents with a necrotising pneumonia and with leucopenia and thrombopenia and A/H1N1₂₀₀₉ influenza virus infection Panton-Valentine leukocidine (PVL)-positive *Staphylococcus aureus* coinfection should be considered.
- ▶ A particular collaboration between physicians and microbiologists to quickly detect strains of PVL-positive *S. aureus* for the best treatment promotes favourable outcome for patients.
- ▶ Regarding the mortality rate associated with this disease, the treatment option (clindamycin, for antitoxin effect) chosen by the physicians was relevant.

Contributors KR-M, FW, CB and AG jointly wrote the report. CB was involved in the treatment and clinical management of the patient. KR-M, FW and AG were involved in the laboratory testing and interpretation of results from specimens. All co-authors provided comments and approved the final version of the report.

Competing interests None.

Patient consent Obtained.

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