Case series

A case series of necrotizing pneumonia due to community acquired MRSA

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Abstract

Community-acquired pneumonia (CAP) due to Methicillin Resistant Staphylococcus Aureus (MRSA) is uncommon. In this case series, wedescribe four young immune-competent healthy males presenting with severe respiratory distress progressing to necrotizing pneumonia. All required ventilation and recovered without sequelae. One patient developed myositis and the other three developed pleural effusions and pneumothoraxes; two of them needing intercostal tube (ICT) insertion and drainage.These cases highlight community acquired MRSA in developing countries where antibiotics are frequently used empirically with little laboratory guidance.

Key words: Community-acquired pneumonia; Methicillin Resistant Staphylococcus Aureus

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List of abbreviation
CA-MRSA: community acquired - methicillin resistant Staphylococcus aureus; ARDS: acute respiratory distress syndrome; ABG: arterial blood gas (analysis); IC tube: intercostal tube;MICU: medical intensive care unit; CXR: chest x ray; THA: Teaching Hospital, Anuradhapura; ESR: Erythrocyte Sedimentation Rate; CT: computerized tomography; BUN: blood urea nitrogen; CPK: creatine phosphokinase; CPAP: continuous positive airway pressure; BPM: Beats Per Minute; CAP: community acquired pneumonia; PVL: Panton-Valentine Leukocidin;

Introduction

We describe four young immune-competent males with community acquired necrotizing pneumonia due to MRSA which is infrequently seen. All of them presented within two months between April and May 2013 to Teaching Hospital Anuradhapura (THA).

First Patient

14 yr old healthy adolescent from Thalawa was admitted to surgical casualty April 2013 following a swelling ofthe right knee after a fall. A medical referral was done for shortness of breath.There was a preceding history of mild and intermittent fever for three days.It was accompanied by runny nose, arthralgia, myalgia and one episode of haemoptysis but no cough or wheezing. Shortness of breath was acute, developing within two to three hours. There was no external injury to the knee joint that was aspirated twice yielding scanty aspirate that was clear, acellular and sterile.

On examination, he was Ill, dyspnoeic, febrile butnot cyanosed, with GCS 15/15. His respiratory rate was 60 breaths per minute with intercostal recession. In the lower zone of right lung, percussion note was dull, vocal resonance was reduced and breath sounds were diminished. His pulse rate was 146 beats per minute (BPM) and blood pressure was 85/5O mmHg.

His blood count revealed aleukocytopaenia and thrombocytosis. Initial chest X-ray (CXR) revealed patchy opacities in the right lower zone,later progressing to cavities and pleural effusion. His ESR was 113 mm in the first hour while CRP was 22.5 mg/dl. His blood urea was 1.4mmol/L

His Blood culture was positive for MRSA on the second day. Two pockets of fluid in theright pleural cavity were aspirated yielding sterile blood stained thick fluid. Contrast enhanced computerized tomography of the chest confirmed the multifocal infection with pneumatocele formation and two discrete collections of fluid in right pleural space.

He was transferred to the medical intensive care unit for intubation and IPPV. Initially he was treated with Ceftriaxone, Levofloxacin and Oseltamivir and once the blood culture report was available medications were changed to Vancomycin and Clindamycin. As the fever persisted, Linazolidwere added. There was deferservence and patients' clinical condition improved leading to discontinuation of ventilation and extubation.

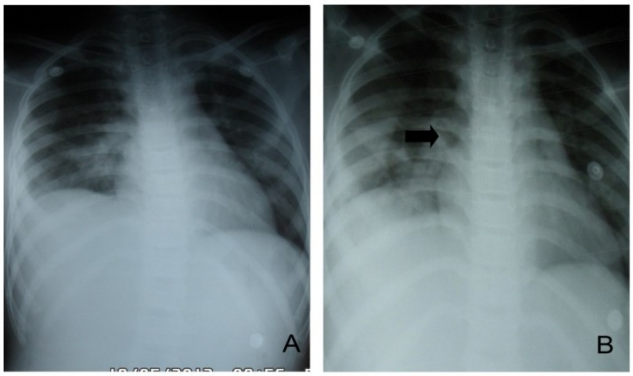

Figure 1 **Figure 1 (A)** X-Ray taken on admission showed bilateralpulmonary shadowing (Mainly on right side), **(B)** X – Ray taken on following day showed a formation of a cavity (arrow) on right side

Second Patient

Twenty six year old army officer from Nandikadal was admitted to General Hospital Vavuniya (GHV) with a three days history of fever, arthralgia, myalgia, runny nose, low platelet count and leucopenia on April 2013.At GHV his platelet count decreased to 10×10^9/L and haematocrit increased to 46% and he was managed as a probable Dengue infection. Subsequentlythe patient developed a cough and no defervesence after five days.He was given Meropenam & Clarythromycin. Bilateral coarse crepitations with absent breath sounds in the left middle and lower zones were heard on auscultation. Pneumothorax was diagnosed, Intercostal tube was inserted to the left pleural cavity and the patient was transferred to THA.

On admission he was severely dyspnoeic with a respiratory rate of 33 breaths per minute. He was conscious and rational with a GCS of 15/15. He was icteric, pale,and febrile with desquamation of skin on palms and soles. His pulse rate of 136BPM and his blood pressure was 80/50mmHg. Blood count revealed leukocytopenia. His CXR revealed patchy opacities with cavities in both lungs, and bilateral pnemothorax. Calrythromycin was stopped and levofloxacin was added. Dengue IgMantibodies were negative while IgG antibodies were positive and blood culture was positive for MRSA on the second day. His blood urea was 206mmol/L.

Oral Metronidazole and cefeperazone was added to Merpenum and Levofloxacin combination. An IC tube was inserted intothe right pleural cavity in addition to the one on the left. Once blood culture became positive, Vancomycin was administered. He was given IV vancomycin for 14 days. On discharge patient was afebrile and ESR was normal.

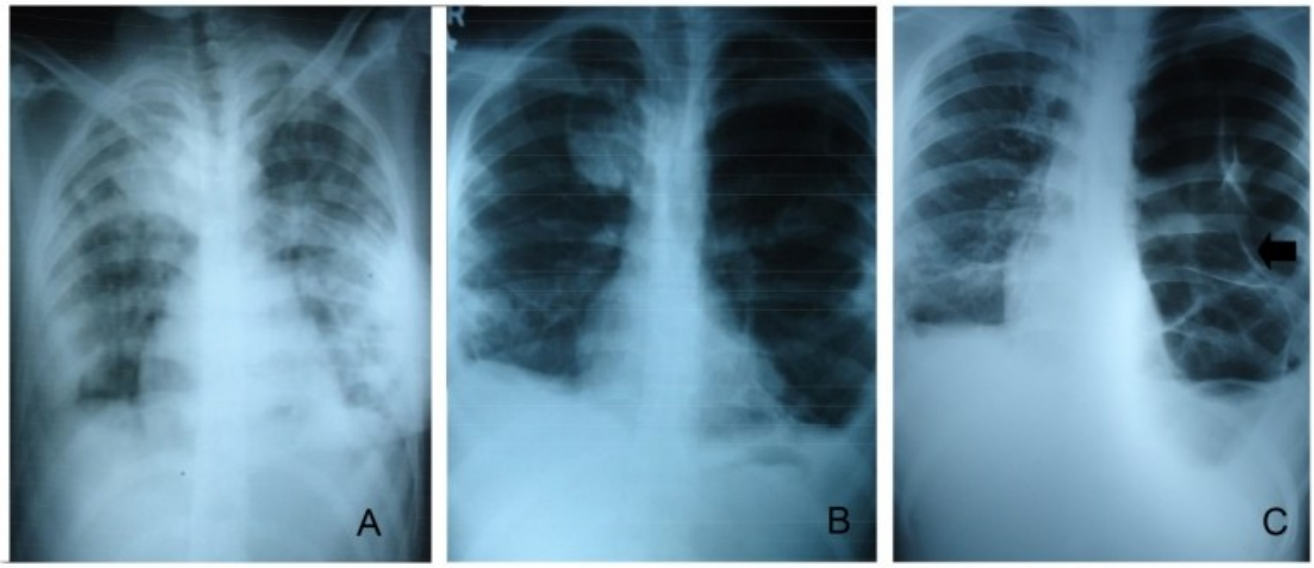

Figure 2 (**A) X - ray taken on admission showing multiple patchy shadows iin bilateral lung feilds, (B) X - ray taken on second day showing formation of a cavity in the right upper zone (arrow), (C) X - ray taken seven days after admission showing formation of multiple air fiilled cavities in left lung field. (arrow)**

Third patient

39 year old previously healthy male was admitted from Anuradhapura Town with shortness of breath and severe myalgia of both lower limbsfor one day on June 2013. He developed right shoulder pain a week ago and has taken treatment from a general practitioner. He also complained of passage of dark urine. There was no associated fever.

On examination he was ill looking and dyspnoeic with a respiratory rate of 36 breaths per minute but was conscious and rational. His pulse rate was 124 BPM and blood pressure was 80/50 mmHg. There were bilateral lung crepitations in lung bases. Lower limb muscle power was grade 3/5 proximally and distally on both sides with absentknee jerks but present ankle jerks bilaterally. Arterial blood gas on admission showed partially compensated respiratory alkalosis. CXR showed bilateral patchy opacities. His blood urea was 4.9 mmol/L.

Both his blood and sputum cultures were positive for MRSA respectively fourth and fifth day after admission. His CPK was 1314 but serum creatinine and blood urea were normal throughout.Initially he was ventilated with CPAP in the ward and subsequently with IPPV in the MICU. Initially he was administered Meropenum and Levofloxacin. After blood culture report was available, medications were changed to Clindamycin. Daily decolonization of MRSA was done.

Fourth Patient

55 year old male was admitted from Vijithapura with pain in the right neck radiating to the right upper limb for 10 days July 2013. On examination, he had a inverted supinator jerk in the right upper limb. After doing cervical X rays, a diagnosis of cervical spondylosis was made and the patient was transferred to Rheumatology ward. During his two weeks stay at Rheumatology ward he suddenly developed dyspnea and became restless. He was conscious and lucid. He was in respiratory distress with a respiratory rate of 55 breaths per minute and there were bilateral crepitataions on chest auscultation. His pulse rate was 110 beats per minute and blood pressure was 100/60 mmHg. His first CXR revealed a right mid zone cavity. His blood urea was 6 mmol/L.

He was put on to CPAP and Meropenum and Levofloxacin were administered. The following day he was transferred to MICU for ventilator support. Repeat CXR at the MICU showed a large cavity in the right mid zone and right sided pneumothorax. Suspecting MRSA pneumonia his medications were changed to Vancomycin and Clindamycin. An IC tube was inserted and subsequently blood cultures were positive for MRSA sixteen days after admission and two days after transfer from rehematology ward. Antibiotics were continued for 10 days and he improved gradually.

Discussion

All four patients in this case series were young immunocompetent males presenting with a short non specific symptoms. Nobody had high fever but developed respiratory distress acutely. The first two had a prodrome of influenza like illness, third shortness of breath and fourth patient hadpain in the shoulder and arm. Initially the second patient was suspected to have dengue like viral fever complicated by acute respiratory distress syndrome. All of them were sick enough to be admitted to the MICU and all required assisted ventilation. First second and fourth patient developed pneumothoraxes and effusions and first and fourth required ICT insertion and drainage. The first patient required bilateral ICT insertion. All had patchy consolidation with three of them having pneumatocoele, intrapulmonary abscesses, and pleuraleffusion suggesting necrotizing pneumonia. The term necrotizing is used to differentiate pulmonary necrosis with multiple small abscesses from single large abscess with or without cavitation. All of them responded

to linezolid, vancomycin or clindamycin without serious sequelae. All of them presented within four months from different geographical areas in the Anuradhapura & Mullathivu Districts.There was no necrotizing pneumonia patients admitted after that period (until November 2013). Fourth patient may have acquired the organism while in the rheumatology ward but his clinical findings were strikingly similar to other three patients. None of them had skin sepsis.

Until recently pneumonia caused by community acquired MRSA was considered an uncommon entitiyand occurred primarily in patients with influenza (1). Community acquired MRSA can cause skin and soft tissue infections, invasive disease such as purpurafulminans, osteomyelitis and necrotizing pneumonia (1,2,3). Panton-Valentine leukocidin (PVL), an extracellular toxin that destroys white blood cells is produced by some strains of *Staphylococcus aureus*and named after two scientists who first described this (4,7). Pneumonia caused by PVL secreting *S aureus* seems to be specific disease entity with a death rate of 75% causing necrotizing community acquired pneumonia (CAP) (1,6). PVL can be secreted by methicillin sensitive or resistant *S aureus* (4,5). PVL comprises of two subunits F and S binding and assembling on neutrophil membrane and causing pore formation (4). They are called synergohymenotropic toxins and recognition by phenotype or antibiogram is unreliable (1). Staphylococcal eneterotoxins and toxic shock syndrome toxins (TSST) can be co-secreted by PVL producing *S aureus*. Eneterotoxins and TSST are called superantigens because of their abilty to activate T cells causing cytokine storm (2).

CAP caused by MRSA affects younger and healthier patients (7). Early clinical diagnosis is difficult. Previously healthy young patient following a "flu-like" illness with rapid deterioration with respiratory distress and sepsis leading urgent admission and ventilation is a typical story. (7).

Classical clinical findings strongly suggestingthe diagnosis include haemoptysis, hypotension, “flu-like” illness myalgia, chills, fever of 39°C or above, tachycardia >140 beats/min, diarrhoea and vomiting (may be due to associated toxic shock) (7,3).

CXR findings include bilateral multilobular infiltrates on chest X-ray, usually accompanied by abcess, recurrent pneumothoraces, pneumatocele, pleural effusion and later cavitation(1,7,8). Laboratory investigations that are helpful in confirming the diagnosis include, Gram stain of sputum reveals gram-positive cocci in clusters, leukopenia, high CRP level, negative pneumococcal and legionella antigen (1). Elevated serum creatine phosphokinase suggests myositis.

Clinical management of necrotizing pneumonia due to MRSA should be aggressive with admission to high dependency unit(9).There are many differing opinions on therapy for PVL-associated pneumonia but intravenous flucloxacillin is not recommended (9). Although bactericidal, there are concerns that flucloxacillin may increase PVL toxin production(12).

Combinations of clindamycin with rifampicin,linezolid with rifampicin,vancomycin with rifampicin,and vancomycin with clindamycin have all been successful in treating, but may need intravenous therapy for a considerable long period of time (10, 12). Vancomycin should not be used alone because of poor penetration of lung tissue (1,11). Rifampicin has excellent tissue penetration, reaching intracellular staphylococci, and when used, itexhibits synergistic activity with other antibiotics, including linezolid (12). Summarising the best empirical therapy would be a combination of clindamycin, linezolid and rifampicin (12).

Adjunctive therapy with Intravenous Immunoglobulin in necrotising pneumonia should be considered in addition to intensive care support and antibiotics because of IVIG’s action in neutralizing exotoxins and superantigens, particularly enterotoxins A, B and C and TSST-1(7, 12, 13).

A young healthy immune-competent male with respiratory distress may be having PVL producing community acquired MRSA. A patient who appears to be having Dengue Shock Syndrome with ARDS may also be suffering from community acquired MRSA. The other differential diagnosis would be hantan virus infection with pulmonary syndrome and leptospirosis. The question that arises repeatedly is how long we have to rely on clinical suspicion with multiple implications of incorrect diagnosis making it imperative that advanced infectious disease diagnostics needs to be established (14).

This phenomena may be due to the growing problem of drug resistant bacteria beyond the confines of health care settings. High index of suspicion, early diagnosis and aggressive antimicrobial therapy with appropriate antibiotics is important since untreated community acquired MRSA has a high mortality rate.

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Competing Interests
None

References

1. Morgan MS. Diagnosis and treatment of Panton–Valentine leukocidin (PVL)-associated staphylococcal pneumonia *International Journal of Antimicrobial Agents* 2007; **30**: 289–296
2. Gillet Y, Issartel B, Vanhems P, et al. Association between Staphylococcus aureusstrains carrying gene for Panton-Valentine leukocidin and highly lethal necrotising pneumonia in young immunocompetent patients. *Lancet* 2002;**359**:753.
3. Kravitz GR, Dries DJ, Peterson ML, Schlievert PM. Purpurafulminans due to Staphylococcus aureus. *Clinical Infectious Diseases* 2005;**40**:941-7.
4. Kaneko J, Kamio Y. Bacterial two-component and hetero-heptameric pore-forming cytolytic toxins: structures, pore-forming mechanism, and organization of the genes. *Bioscience Biotechnology Biochemistry* 2004; **68**: 981–1003.
5. Suzanne F, Bradley MD. The role of toxins in the changing epidemiology and clinical presentation of staphylococcal pneumonia. *Medscape* 2005; **26**: 643-649.
6. Holmes A, Ganner M, McGuane S, et al. Staphylococcus aureus isolates carrying Panton-Valentine leucocidin genes in England and Wales: frequency,characterization, and association with clinical disease. *Journal of Clinical Microbiology* 2005;**43**:2384–90.
7. Morgan M, Staphylococcus aureus, Panton-Valentine leukocidin,andnecrotising pneumonia. *British Medical Journal* 2005;**331**:793–4
8. Hageman JC, Uyeki TM, Francis JS, et al. Severe community-acquired pneumonia due to Staphylococcus aureus. *Emergency Infectious Diseases* 2006; **12**: 894-9.
9. Centers for Disease Control Prevention. Severe methicillin-resistant Staphylococcus aureus community-acquired pneumonia associated with influenza. *Morbidity Mortality Weekly Report* 2007;56:325-9.
10. Maclayton DO, Hall RG.Medline Pharmacologic treatment options for nosocomial pneumonia involving methicillin-resistant Staphylococcus aureus.M*edscape* 2007; **41**: 234-44.
11. Georges H, Leroy O, Alfandari S, Guery B,et al.Pulmonary disposition of vancomycin in critically ill patients. European *Journal ofClinical Microbial Infectious Diseases* 1997; **16**:385-8.
12. HPA. Guidance on the diagnosis and management of PVL-associated Staphylococcus aureus infections (PVL-SA) in England. 2008. [cited 2013 October 21] Available from: www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1218699411960
13. Gauduchon V, Cozon G, Vandenesch F, et al. Neutralization of Staphylococcus aureus Panton Valentine leukocidin by intravenous immunoglobulin in vitro. *Journal of Infectious Diseases* 2004;**189**:346-53.
14. Dahanayaka NJ, Agampodi SB, Bandaranayaka AK, Priyankara S, Vinetz JM.Hantavirus infection mimicking leptospirosis: how long are we going to rely on clinical suspicion?.*J Infect DevCtries* 2014 ;**8**:1072-5.