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## CASE REPORT

# Community-Acquired Methicillin-Resistant Staphylococcus Aureus Pneumonia Complicated by Intracranial Diffuse Thrombotic Microangiopathy

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### SUMMARY

***Background:*** **Community-acquired methicillin-resistant Staphylococcus aureus (CA-MRSA) is a significant pathogen linked to severe infections like pneumonia, which can lead to complications such as thrombotic microangiopathy (TMA), characterized by microthrombi causing ischemia and organ dysfunction. Diagnosing these complications remains challenging, requiring timely identification and intervention.**
***Methods:*** **This case report presents a 24-year-old male with CA-MRSA pneumonia complicated by intracranial diffuse TMA, manifesting as high fever, wheezing, respiratory failure, and altered consciousness. Comprehensive laboratory and imaging studies confirmed the diagnosis. The patient recovered completely with antibiotic therapy, mechanical ventilation, and anticoagulation.**
***Conclusions:*** **This case highlights the severity of CA-MRSA pneumonia and its potential for intracranial microvascular complications, emphasizing the importance of brain MRI in septic patients with neurological impairment and the need for early intervention. To our knowledge, this represents the first reported case of CA-MRSA pneumonia-associated intracranial diffuse TMA, providing novel clinical insights for managing similar presentations.**
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### KEYWORDS

Community-acquired methicillin-resistant Staphylococcus aureus (CA-MRSA), thrombotic microangiopathy (TMA), sepsis, case report

### CASE PRESENTATION

The patient is a 24-year-old previously healthy young male admitted with a 3-day history of fever of unknown origin, reaching a peak temperature of 39°C, accompanied by productive cough with difficult expectoration, chills, fatigue, and poor appetite. Three days prior to admission, he developed these symptoms without identifiable triggers and subsequently presented to our hospital's emergency department for evaluation. Laboratory tests revealed WBC 4.29 x $10^9$/L, HGB 155 g/L, PLT 132 x $10^9$/L, neutrophils 3.21 x $10^9$/L, lymphocytes 0.61

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x $10^9$/L, with negative SARS-CoV-2 antigen and influenza A/B virus antigens. Presumed upper respiratory tract infection was diagnosed, and intravenous moxifloxacin 0.4 g was initiated. However, symptoms worsened with fever progression to 40°C, accompanied by marked wheezing, hypotension, and decreased peripheral oxygen saturation. Immediate endotracheal intubation with mechanical ventilation was performed, and the patient was admitted for further critical care management. Admission vital signs: Temperature 40°C, respiratory rate 45/minute, blood pressure 78/64 mmHg, $SpO_2$ 82%, with marked respiratory distress. Neurological exam: Altered mental status (GCS 2T: 1-T-1), pupils L:R = 2.5 mm: 2.5 mm, photoreactive (+), neck supple without rigidity. Respiratory exam: Bilateral coarse breath sounds with prominent dry and moist rales. Cardiovascular exam: Normal heart sounds with tachycardia, no pathological murmurs on auscultation. Abdominal exam: Soft, non-tender; tenderness and rebound tenderness unassessable due to noncompliance; liver/spleen not palpable below costal margins; no lower limb edema. Neurological assessment: Uncooperative for detailed exam; bilateral Babinski sign negative. Repeat blood tests: WBC 1.54 x $10^9$/L, neutrophils 1.05 x $10^9$/L, lymphocytes 0.38 x $10^9$/L (other parameters stable), interleukin-6 (IL-6) > 5,000 pg/mL (0 - 7), procalcitonin (PCT) > 100.0 ng/mL (0 - 0.046). DIC profile: PT 19.5 second, INR 1.65, PT% 39.5%, fibrinogen 5.21 g/L, D-dimer 7.43 µg DDU/mL. Arterial blood gas (mechanical ventilation, $FiO_2$ 100%): pH 7.442, $pCO_2$ 28.8 mmHg, $pO_2$ 49.2 mmHg, $HCO_3^-$ 19.2 mmol/L, BE -3.5 mmol/L, lactate 4.4 mmol/L, $PaO_2/FiO_2$ ratio 80.64. Biochemical profile: Total bilirubin (TBIL) 68.08 µmol/L (3 - 22), unconjugated bilirubin (BU) 56.53 µmol/L (0 - 19), conjugated bilirubin (BC) 11.55 µmol/L (0 - 5), NT-proBNP 654 pg/mL (20 - 125), creatinine (CREA) 109.32 µmol/L (58 - 110); other parameters unremarkable. Chest CT showed bilateral pulmonary high-density patchy opacities, nodules, and masses. Empirical broad-spectrum therapy (vancomycin 1 g q8hour + imipenem/cilastatin 1 g q6hour) was initiated. Metagenomic next-generation sequencing (mNGS) of bronchoalveolar lavage fluid detected Influenza A virus (1,268 reads), methicillin-resistant Staphylococcus aureus (MRSA, 1,555,041 reads), and mecA resistance gene. Airway mucosal pathology revealed multifocal acute fibrinous exudative necrosis with inflammation and lymphoid hyperplasia. Blood/sputum cultures identified methicillin-resistant Staphylococcus aureus (MRSA) resistant to penicillin, oxacillin, erythromycin, and clindamycin (positive at 13.9 hours), with weakly positive influenza A/B antibodies. Voriconazole was discontinued; vancomycin 1 g q8hour was maintained for antibacterial coverage. Imipenem-cilastatin was deescalated to piperacillin-tazobactam 4.5 g q8hour for combined anti-infective therapy, and baloxavir marboxil 40 mg was initiated for antiviral treatment. Supportive management included mechanical ventilation via oral endotracheal intubation, invasive hemodynamic monitoring with femoral artery PiCCO catheter, HA-380 hemoperfusion for inflammatory mediator clearance, immunomodulation with human immunoglobulin, hydrocortisone for anti-inflammatory therapy, continuous renal replacement therapy (CRRT) for hemodynamic stabilization, fluid resuscitation/volume expansion/vasopressors for shock correction, and sedation-analgesia to optimize ventilator synchrony. On day 7 of hospitalization, the patient developed acute oxygen desaturation and marked wheezing. Chest CT revealed right-sided pneumothorax with significant ipsilateral lung compression, coalescent bilateral pulmonary patchy opacities, worsened atelectasis, and left pleural effusion, prompting closed thoracic drainage. The vancomycin trough level was 9.82 µg/mL (therapeutic target for severe MRSA: 10 - 20 µg/mL), indicating subtherapeutic concentration, prompting a switch to linezolid 600 mg q12hour for anti-gram-positive coverage. Following these interventions, the patient demonstrated gradual improvement in symptoms, temperature, inflammatory markers, and imaging findings (Figure 1).

The patient remained unconscious. On hospital day 11, cranial MRI revealed diffuse punctate hypointense lesions on SWI sequences (Figure 2). Evaluations for differential diagnosis - including peripheral blood smear, tumor markers, ANA profile, anti-GBM antibodies, rheumatoid factor, thyroid function, ANCA, ADAMTS1, bone marrow aspiration (morphology/flow cytometry), and lumbar puncture (autoimmune encephalitis panel, CSF cytology/pathogen studies/biochemistry) - showed no abnormalities. DIC score: 5; SIC score: 4. Based on the above findings, intracranial infection, autoimmune encephalitis, systemic immune disorders, hematologic diseases, and malignancies were excluded. Combined with clinical and imaging features, the diagnosis was sepsis-associated thrombotic microangiopathy (TMA). Anticoagulation with low-molecular-weight heparin 4,100 U q12hour was initiated. The patient regained consciousness with stabilized condition, underwent extubation on hospital day 27, transferred to general ward on day 31, and was discharged asymptomatic on day 39. During 3-month follow-up, no recurrence was reported, with significant improvement in quality of life, restored functional capacity, and no residual deficits.

## DISCUSSION

The 2000 CDC criteria define CA-MRSA as community-onset infections without healthcare-associated risk factors: strains isolated in outpatient settings or within 48 hours of hospitalization; no prior MRSA infection/colonization; and no healthcare exposure (hospitalization, nursing home, shelter, daycare) or invasive procedures (dialysis, surgery, indwelling catheters/devices) within the past year. Predominantly affecting healthy children/adolescents, CA-MRSA exhibits rising incidence in China with high mortality rates, frequently sec-

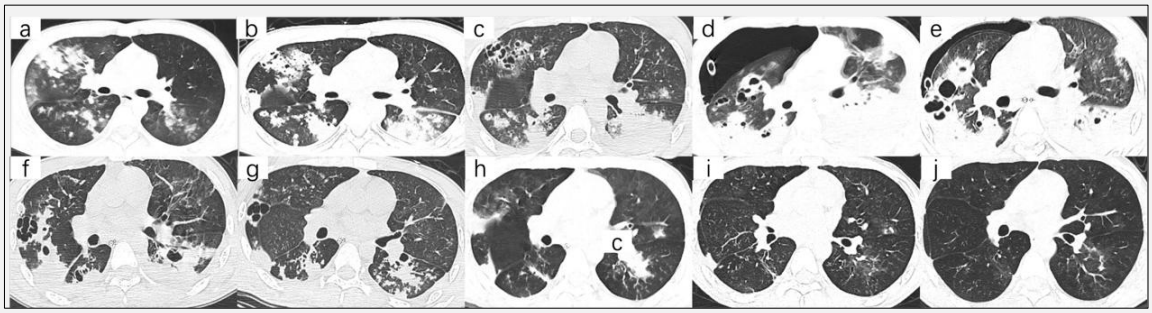


**Figure 1. Chest CT Scans: a Admission day 1, b Admission day 4, c Admission day 7, d Admission day 11, e Admission day 15, f Admission day 18, g Admission day 22, h Admission day 32, i Admission day 37, j Post-discharge day 30 demonstrated resolution of bilateral pulmonary consolidations, nodular opacities, and exudative shadows compared with prior imaging, with coalescence and reduction in size of cavitary lesions.**

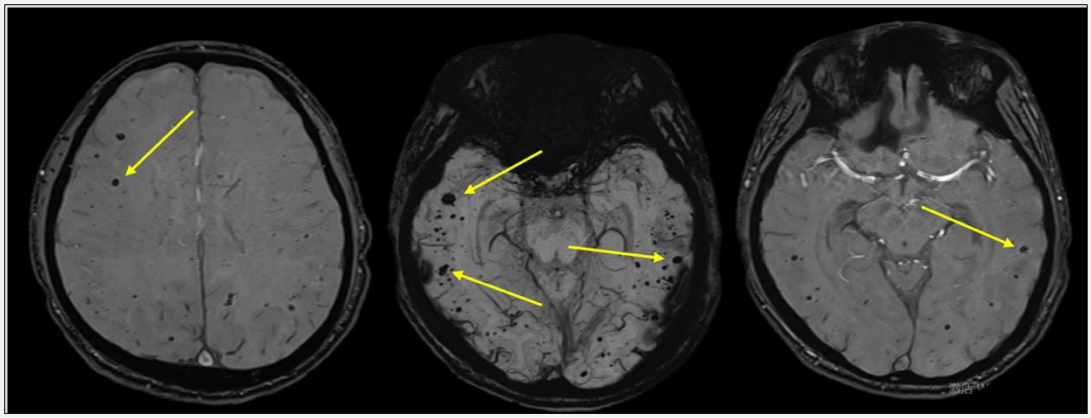

**Figure 2. MRI susceptibility-weighted imaging (SWI) sequence demonstrates diffuse punctate hypointense signals.**

ondary to influenza virus infections. Studies indicate that CA-MRSA exhibits lower antibiotic resistance but higher pathogenicity compared to HA-MRSA, primarily attributed to genetic distinctions and differential virulence factors, with PVL (Panton-Valentine leukocidin) serving as a signature cytotoxin of CA-MRSA [1,2]. Vancomycin remains the cornerstone therapy; however, linezolid is recommended when subtherapeutic vancomycin plasma concentrations occur. Linezolid demonstrates favorable lung tissue penetration and inhibits *Staphylococcus aureus* toxin production, making it a first-line alternative for cases with vancomycin MIC ≥ 1 μg/mL [3].

Thrombotic microangiopathy (TMA) is a pathological process characterized by platelet-rich microthrombi formation and endothelial injury in small vessels, which may involve multiple organs such as the brain and kidneys [4]. Brain MRI may demonstrate multiple small infarcts, microhemorrhages, or white matter lesions [5]. Etiologically, TMA can be classified into two major categories: primary (idiopathic) thrombotic microangiopathy and secondary thrombotic microangiopathy [5]. Primary thrombotic microangiopathies include thrombotic thrombocytopenic purpura (TTP) and typical hemolytic uremic syndrome (HUS). Secondary thrombotic microangiopathies may be triggered by malignant hy-

pertension, connective tissue diseases (e.g., systemic lupus erythematosus, antiphospholipid syndrome, systemic sclerosis), disseminated intravascular coagulation, malignancies, pregnancy, or infections, with 33% of cases being infection-induced (commonly Gram-negative bacilli or viral infections) and exhibiting non-specific clinical manifestations [6,7]. This patient was diagnosed with infection-associated TMA, though the pathogenesis remains unclear, potentially related to severe inflammatory response-induced vascular endothelial injury, marked platelet activation, aggregation, and consumption. Some scholars propose that TMA arises secondary to disseminated intravascular coagulation (DIC), while studies suggest that DIC and TMA may co-occur in sepsis with distinct pathogenic mechanisms. Approximately 35% of sepsis cases are complicated by DIC, whereas TMA is exceedingly rare in sepsis [7]. Diagnosing TMA during infection is highly challenging, and failure to promptly establish diagnosis, perform differential evaluation, and initiate appropriate therapy may lead to severe adverse outcomes. Yingxin Lin et al. reported cases of Salmonella septicemia complicated by disseminated intravascular coagulation (DIC) and thrombotic microangiopathy (TMA) [8]. However, no documented cases of methicillin-resistant Staphylococcus aureus (MRSA) infection associated with DIC and TMA were identified in literature searches [9]. This case represents the first reported instance, highlighting the importance of distinguishing between these conditions in clinical practice to avoid diagnostic oversight.

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**Ethical Approval:**
The study was approved by the Ethics Committee of Tianjin First Central Hospital. All procedures performed in studies were in accordance with the ethical standards. Informed consent was obtained.

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**Declaration of Interest:**
The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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