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An observational case study of necrotising pneumonia caused by Panton-Valentine toxin producing *Staphylococcus aureus*

According to data from the National Reference Centre (2008), 374 strains out of 2050 of *Staphylococcus aureus* were identified to be secreting the Panton and Valentine toxin (i.e. 18%). These were further divided into 57% of methicillin-resistant strains (MRSA) and 43% of methi-S strains. The median age of the patients was 28 years. In 69% of cases the infection site was skin and soft tissue; 13% in the lungs and 5% in bone and joints.

Staphylococcus can secrete numerous toxins: exfoliatins (responsible for cutaneous bullosa), enterotoxins (food poisoning), *staphylococcus* toxic shock syndrome toxin (TSST-1) and Panton-Valentine leukocidin (PVL). The secretion of this toxin is triggered when the strain is infected by a bacteriophage, which transmits PVL genes. The PVL toxin enhances the pathogenic power of *Staphylococcus aureus*. This pathogenicity is linked to the action of two sub-units, which operate in synergy on the cell membrane: S (LukS-PV) and F (LukF-PV). These sub-units create transmembrane pores by opening the calcium channels, which leads to cell lysis (polynuclear cells, monocytes and macrophages) and the release of inflammation mediators (cytokines etc.) worsening the overall clinical picture.

Clinical case: necrotising pneumonia

One Friday afternoon, a 38-year-old working military man of good health and no previous history of disease consults his GP for flu-like symptoms.

The clinical examination is normal; the patient is afebrile.

The full blood count results show slight leukopenia: 3840 / mm^3, platelets 240 000 / mm^3, the rest of the profile is normal.

The next day, he is urgently admitted to hospital for resuscitation for acute dyspnea. His vital signs were:

Respiration rate > 40 cycles/minute, SpO_2: 93 % (on mask at 15 l/min of O_2), heart rate: 130/min, temperature: 37.9 °C, blood pressure: 114/72 mm Hg. He suffers from bilateral lower thoracic pain and is asthenic.

Laboratory results:

- WBC = 1100/mm^3 i.e. 480 PNN/mm^3,
- Platelets = 120 000/mm^3,
- CRP = 314 mg/L, procalcitonin > 10 ng/ml (reference value < 2),
- Lactates = 2.7 mmol/l.

The chest x-ray confirmed non-systematised, bilateral pneumonia. The initial antibiotic treatment was a probabilistic approach: ceftriaxone + levofloxacin + amikacin.

Six hours after admission, the patient's condition severely deteriorates with the development of acute respiratory distress (ARDS), disseminated intravascular coagulation (DIC) and multiple organ failure, which requires intubation of the patient. At this point, the first protected distal sampling (PDS) was performed. The level of neutropenia worsens to 0.6 G/l. The thoracic scanner shows parenchymal necrotic lesions and bullosa lesions with bilateral pleural effusions.

Fourteen hours after admission, a lung infection of *Staphylococcus aureus* secreting Panton-Valentine leukocidin is suspected due to:

- a pure culture of *S. aureus* (> 10^8 UFC/ml) from the tracheal aspirations and blood culture
- or a haemorrhagic pneumonitis with ARDS
- leukoneutropenia

in a young patient, not immunocompromised who presented with flu-like symptoms.

The recommended treatment is clindamycin (Dalacin®) or linezolid (Zyvoxid®), antibiotics agents that inhibit the synthesis of toxins, combined with vancomycin and aminoside (treatment with bactericidal anti-staphylococcal antibiotics). IV immunoglobulins (Tegelin®1g/kg/day) block the toxin via the influx of anti PVL antibodies added when the patient presents with the severity criteria (haemoptysis, leukopenia < 3. 10^9/l).

The diagnosis of necrotising pneumonia caused by *Staphylococcus aureus* producing Panton and Valentine toxins was confirmed 48 hours later by the National Reference Centre for Staphylococci. The toxin was detected in the tracheal secretions using enzyme immunoassay testing, and the toxin gene was detected by multiplex PCR in colonies of isolated Staphylococci.

The influenza serology test was also positive.

The efficacy of antibiotic and immunoglobulin treatment was clinically verified in the patient and objectified mainly by a rise in the number of polynuclear neutrophils, which went from 112/mm^3 to over 1600/mm^3 in 24 hours.

Summary

Necrotising pneumonia caused by *Staphylococcus aureus* producing Panton and Valentine toxins is rare: less than 50 cases are notified in France each year. They are rapidly evolving lung diseases, with a mortality rate of nearly 70% and a clinical picture of shock and disseminated intravascular coagulation.

This diagnosis must be considered in a young, leukopenic patient with pre-existing flu syndrome which drastically worsens with lung disease with hemoptysic sputum (the influenza virus favours infection by *staphylococcus* in the bronchial epithelium).

Direct examination of respiratory samples showed Gram-positive cocci in clusters on a bed of red blood cells (the samples contained blood).

Treatment with bactericidal and anti-toxin anti-staphylococcus antibiotics: clindamycin, linezolid or rifampicin are effective, their anti-toxin effect persists if they are combined with vancomycin or a β-lactamin. Antibiotic treatment must be combined with polyvalent immunoglobulins when faced with severity criteria.

For more information:

- National Reference Centre of Staphlococci (Centre National de Référence des Staphylocoques). Centre de Biologie et de Pathologie Est – CBPE, Groupement Hospitalier Est 59 bd Pinel 69677 BRON Cedex, France. Telephone: +33 (0)4 72 12 96 25 fax: +33 (0)4 72 35 73 35.

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From a communication by Jacques-Yves Nizou at the 2011 SNBH conference.