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Staphylococcal Toxigenic Syndrome: Report of a Special Case and Review of Literature

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Case Report

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Abstract: Staphylococcus Aureus is responsible for two main clinical presentations in humans: suppurative infections and toxigenic syndromes. In this work, we report a case of a young patient with necrotizing pneumonia caused by staphylococcus aureus producer Leukocidin of Panton and Valentine which presents a special entity in staphylococcal toxigenic syndromes, owing to the fact that it affects healthy immunocompetent subjects, and that its escalation is extremely fast in time and in the diverse territories of the world.

Keywords: Staphylococcus Aureus, Toxigenic syndromes, Necrotizing pneumonia, Leukocidin of Panton and Valentine.

INTRODUCTION

Because of its virulence and its resistance to the usual antibiotics, Staphylococcus aureus still occupies today a great importance in human pathology [1]. Ubiquitous and saprophyte, this bacteria is involved in the occurrence of nosocomial infections, however, its isolation in a community setting is also common. The symptomatology is polymorphic, but dominated by two clinical situations: Mucocutaneous superficial suppurative infections which can be complicated by a blood-borne or a locoregional extension, and Staphylococcal toxemia or Staphylococcal toxigenic syndromes (STS) due to staphylococcal toxines, not to the direct bacterial action, and which regroup many entities: staphylococcal cutaneous syndromes, toxic shock syndrome, and toxigenic syndromes linked to Leukocidin of Panton and Valentine [2].

This last entity remains the most severe with a poor prognosis, such as our patient subject of this case report, who presented necrotizing pneumonia complicated by multi-organ failure, occurrence of septic shock, infectious lesional edema, and finally death of patient.

CASE REPORT

A 35-year-old athletic man, admitted to our hospital in a context of severe sepsis following a post traumatic septic arthritis of the left knee, with severe dyspnea, fever and hemoptysis. The emergency examination had found a dyspneic patient, and had objectified an edematous, inflammatory, hot left knee, seat of skin pustules evoking a septic arthritis. Anamnesis informed us that the patient had previously consulted for post-traumatic left knee pain; the examination concluded a benign knee injury. It informed us also about a notion of axillary furuncle treated one month before hospitalization.

Conventional chest radiography revealed bilateral interstitial alveolar infiltrates (Figure 1).

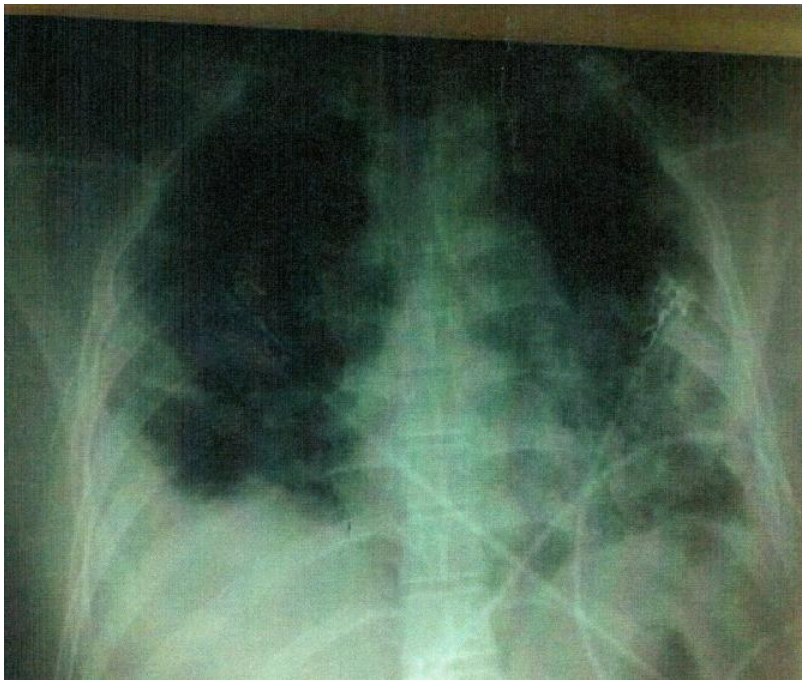


Fig-1: Chest radiography of our patient showing bilateral interstitial alveolar infiltrates

An echo-doppler was performed and objectified thrombophlebitis of the right popliteal vein. This assessment was completed by a thoracic angioscan that showed nodular infiltrates in both lung fields and discarded any signs of pulmonary embolism. Thoracic scan showed alveolar interstitial syndrome (Figure 2).

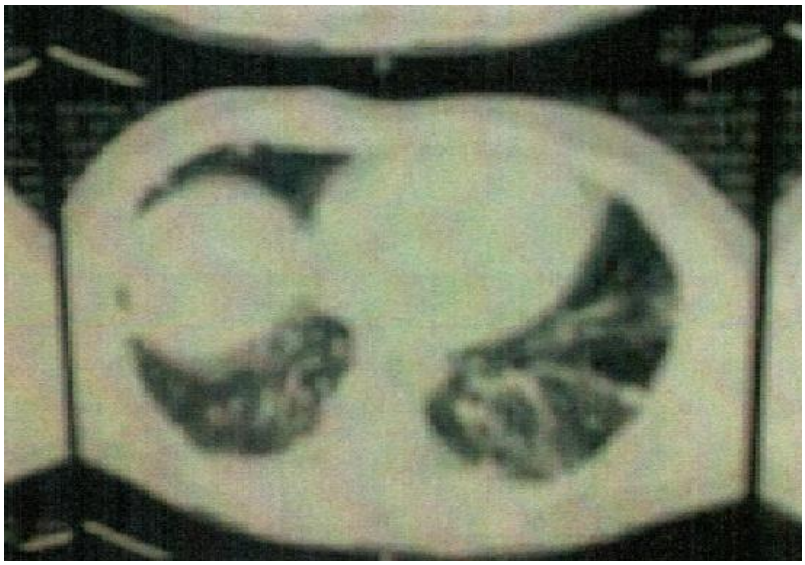


Fig-2: Thoracic scan of our patient showing alveolar interstitial syndrome

The left knee joint puncture brought out a turbid citrine-yellow fluid with 100,000 leukocytes/mm3 predominated by neutrophils, the direct examination after Gram staining showed Gram-positive Cocci in clusters.

The articular fluid was grown on two culture mediums

- Tripticase soy agar supplemented with 5% horse blood
- Enriched chocolate agar.

Enrichment on aerobic and anaerobic mediums was used, after 24 hours of incubation at 37 °, we had observed on these 2 agars, non-haemolytic, rounded, smooth and abundant colonies in pure culture. Catalase was positive. The Staphylococcus Aureus identification was made on Api Staph. The antibiotic sensitivity study of SA was established according to the method of diffusion in agar medium on Muller Hinton (MH), and interpreted according to the standards of the antibiogram committee of the French Microbiology Society (CA-SFM). It revealed that the strain is

sensitive to the following antibiotics: oxacillin, cefoxitin, gentamycin, tobramycin, érythromycin, pristinamycin, linézolid, levofloxacin, fosfomycin, rifampicin, cotrimoxazole, and chloramphenicol. It is resistant to penicilline G, fusidic acid kalamycin, and tetracycline.

Biologically, a protected distal sampling, and two blood cultures were positif to the same Staphylococcus aureus. The complete blood count has shown leukopenia (3000/mm3 8,4% of lymphocytes), and thrombopenia (22000/mm3), value of C Reactive Protein was 384 mg/l, and the liver function was disturbed (ASAT : 10463 ui/l, ALAT : 2848 ui/l).

The clinical situation rapidly deteriorated. The occurrence of an acute respiratory distress syndrome necessitated the use of artificial respiratory ventilation.

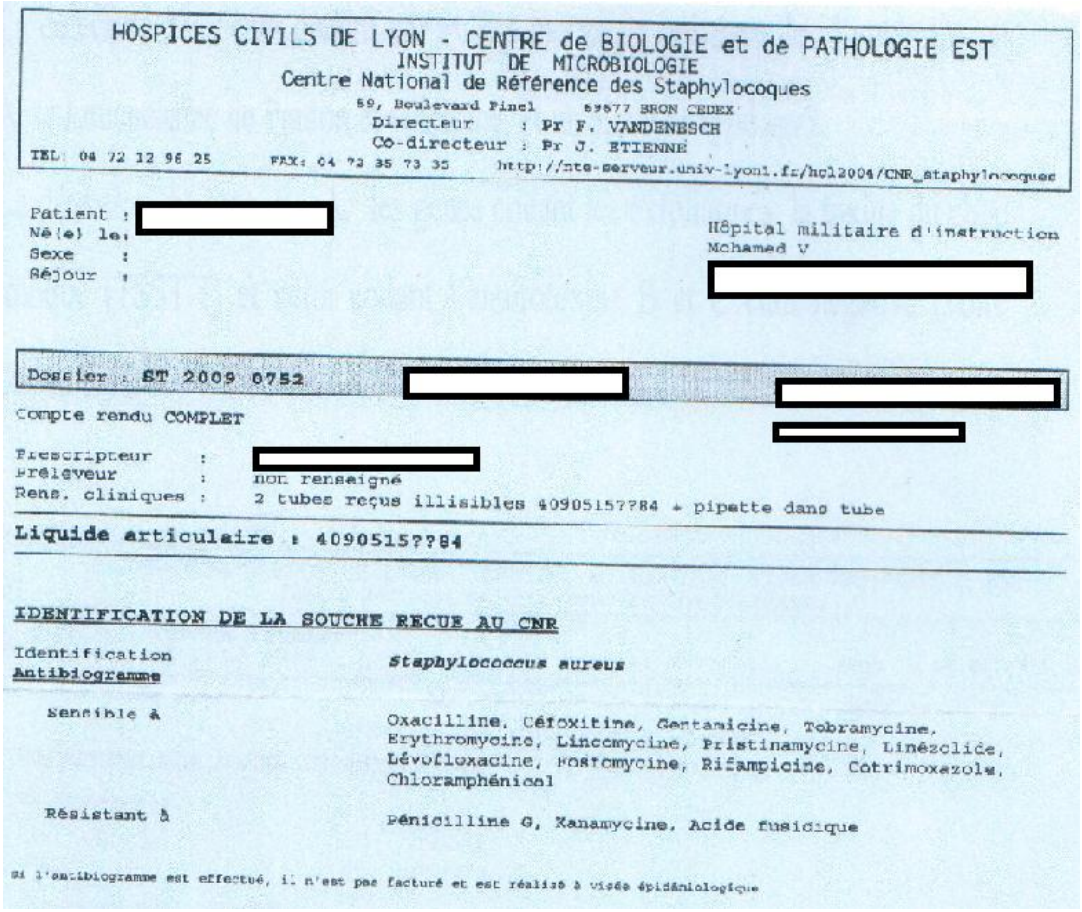
The patient was treated with Vancomycin 2g/d, Tienam, Aminoside, and Anticoagulants before bacteriological findings and antibiogram.

The evolution was marked by

+ Gradual worsening of hemodynamic and respiratory status.
+ Occurrence of staphylococcal septic shock and infectious lesional edema.
+ Multi-organ failure (disseminated intravascular coagulation, kidney failure)

The patient died after 72 hours in a context of refractory septic shock, while unfortunately the result of the search for staphylococcal toxins had not yet arrived.

In front of this symptomatology of severe pneumonia in young patient, with notion of furunculosis, with isolation of SA resistant to kanamycin and fusidic acid, a SA producer Leukocidin of Panton and Valentine, so the strain was sent at at the National Reference Center (CNR) of staphylococci in Lyon for further research of toxins. Results of these investigations showed that the strain was methicillin sensitive SA with same antibiogram as our (Figure 3).



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Patient : [redacted]
Né(e) le :
Sexe :
Séjour :

Hôpital militaire d'instruction
Mohamed V
[redacted]

Dossier : ST 2009 0752 [redacted]

Compte rendu COMPLET

Prescripteur : [redacted]
Prélèveur : non renseigné
Rens. cliniques : 2 tubes reçus illisibles 4090515?784 + pipette dans tube

Liquide articulaire : 4090515?784

IDENTIFICATION DE LA SOUCHE RECUE AU CNR

Identification : ***Staphylococcus aureus***

Antibiogramme

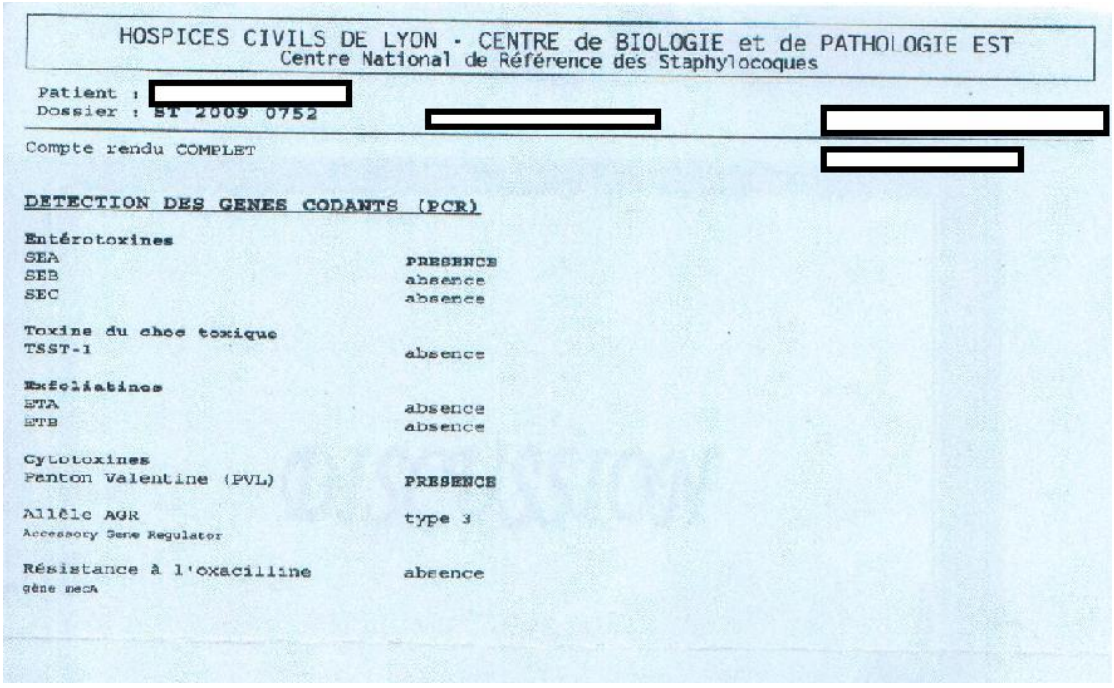
Sensible à : Oxacilline, Céfoxitine, Gentamicine, Tobramycine, Erythromycine, Lincomycine, Pristinamycine, Linézolide, Lévofloxacine, Fosfomycine, Rifampicine, Cotrimoxazole, Chloramphénicol

Résistant à : Pénicilline G, Kanamycine, Acide fusidique

Si l'antibiogramme est effectué, il n'est pas facturé et est réalisé à visée épidémiologique

Fig-3: Identification results and antibiotic sensitivity study of the strain isolated from the patient's articular fluid realized at the CNR of Staphylococci in Lyon

Protein-coding genes screening by Polymerase Chain reaction (PCR) has shown the presence of: Enterotoxin A, Leukocidin of Panton and Valentine, Allele type agr 3 (Figure 4). The detection of mecA gene, genes coding for exfoliatins, toxic shock syndrome toxin. (TSST-1) and enterotoxins B and C were negative (Figure 4).



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Centre National de Référence des Staphylocoques

Patient : [redacted]
Dossier : ST 2009 0752

Compte rendu COMPLET

DETECTION DES GENES CODANTS (PCR)

Entérotoxines	
SEA	PRESENCE
SEB	absence
SEC	absence
Toxine du choc toxique	
TSST-1	absence
Exfoliatines	
ETA	absence
ETB	absence
Cytotoxines	
Panton Valentine (PVL)	PRESENCE
Allèle AGR Accessory Gene Regulator	type 3
Résistance à l'oxacilline gène mecA	absence

Fig-4: Results of protein-coding genes screening by PCR realized at the CNR of Staphylococci in Lyon

DISCUSSION

Currently, the frequency of infections due to Staphylococcus Aureus (SA) producer of Leukocidin of Panton and Valentine (LPV) is not known. It occurs preferentially in adolescents and young adults as in our case (35-year-old) [3, 4].

A study realized by the team of the CNR of Staphylococci in Lyon allowed establishing clinical and para-clinical characteristics of infections due to SA producer of LPV. They are summarized in the following table (Table 1) and compared with our observation [5].

In our case, all the criteria are present except the flu syndrome preceding pneumonia, which appears to be frequent and would facilitate the colonization of the respiratory system by staphylococcus and would rather be related to a poor prognosis. In our patient, the pneumonia is accompanied by post traumatic septic arthritis of the left knee, with presence on the puncture fluid direct bacteriological examination, of a SA identical to that of the 2 blood cultures and protected distal sampling. Extra-pulmonary lesions are described in the literature, most often, it involves skin disorders (three cases of furuncle and one case of cellulite in the Lyon study) [6]. Boussaud *et al.* describe the case of a 25-year-old man hospitalized for pneumonia with SA producer of LPV with hemoptysis and infection of the pulp of a finger [7]. Osteoarticular involvement is much rarer. Lina et al. found 13 cases of osteomyelitis including 3 LPV + (23%) in the analysis of 171 strains of SA [8]. In our case the anamnesis informed us the notion of axillary furuncle treated one month before hospitalization.

Microbiologically, the SA strain of our patient was methicillin sensitive. Methicillin resistant strains have been reported [9,10]. In our case, the LPV was associated with an enterotoxin SEA: some authors suggest that this toxin would be responsible for the signs of shock and the cutaneous signs sometimes present (rash), because of their super-antigenic activity, activity which does not have the LPV [5,6].

In our observation, we may regret a possible delay in antibiotic treatment; osteo-articular involvement is probably present at the first consultation in traumatology, the lack of temperature measurement and the notion of anterior knee trauma led to diagnosis of mild knee trauma. Our treatment was started a few hours after the patient's admission. It did not prevent a fatal evolution, as reported in various publications [3, 5, 6, 7].

Clindamycin is especially recommended for streptococcal toxin shocks, but may have an interest in staphylococcal toxin shocks [4,11]. Studies on animal models and in vitro have shown the neutralizing capacity of intravenous immunoglobulin solutions against the pathogenic effects of LPV, these preparations contain antibodies neutralizing staphylococcal antitoxins [12,13].

Table-1: Clinical and para-clinical characteristics of Pneumonia due to SA producer of LPV (according to Gillet *et al.*) [5], comparison with data of our observation

	Lyon Study		Our observation
	Number	Percentage (%)	
Clinical signs			
Fever > 39 °C	13/16	81	yes
Signs of schock	15/16	94	yes
Respiratory distress	13/14	93	yes
Pulmonary haemorrage	8/16	50	Yes
Chest radigraphy			
Uni lobar condensation	4/15	27	no
Multi lobar condensation	10/15	67	yes
White lung	8/13	61	no
Bullous lesions	4/14	28	no
Pleural involvement	10/14	71	no
Necessity of assisted ventilation	12/16	75	yes
Biological signs			
Leukopenia	11/14	79	yes
Disturbed liver function	10/14	71	
Throbopenia	11/14	79	yes
Bacteriology			
Bronchopulmonary or pleural samples with SA	16/16	100	yes
Positive blood cultures	8/16	50	yes
Penicillin resistance	11/15	73	no
Mheticillin resistance	1/15	6	no
Clinical evolution			
Death	12/16	75	yes

In a recent work driven by Gillet *et al*. about 50 cases of LPV necrotizing pneumonia: hemoptysis, erythroderma and leukopenia were described as the main factors of poor prognosis. In our observation, the 3 factors of poor prognosis described by Gillet et al. were present. The action of the toxin itself, and the bacterial proliferation in situ, appears to be responsible for the massive necrotico-haemorrhagic alveolar lesions that cause hemoptysis.

Severe leukopenia, which persists for 4 days, is a direct consequence of the leuco-cytotoxic effect of LPV [14].

CONCLUSION

SA secretes many toxins, including some that are responsible for specific diseases well established: toxic-food infections, staphylococcal skin disorders, staphylococcal toxic shock syndrome and necrotizing pneumonia due to LPV. The advent of new molecular biology techniques allows rapid and low-cost LPV screening. In addition to the fact that it would bring a better clinical and epidemiological knowledge of these affections, this screening could be also improving the management of patients, therapeutically and preventively.

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