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Panton-Valentine Leukocidin–Secreting Staphylococcus aureus Pneumonia Complicating COVID-19

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1 **Running Title :** PVL-secreting *S. aureus* and SARS-CoV-2 coinfection

2 **Keywords :** COVID-19 ; necrotizing pneumonia; Panton-Valentine leukocidin; SARS-CoV-

3 2; *Staphylococcus aureus*

4 **Title:** Panton-Valentine leukocidin-secreting *Staphylococcus aureus* complicating SARS-

5 CoV-2 infection : a case report

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13 **Abstract – 42 words**

14 Necrotizing pneumonia induced by Panton-Valentine leukocidin (PVL) secreting
15 *Staphylococcus aureus* is a rare but life-threatening infection. It has been described following
16 influenza. We present a fatal case of this superinfection in a young adult infected by Severe
17 Acute Respiratory Syndrome Coronavirus 2.

18

19 **Text – 678 words**

20 Panton-Valentine leukocidin (PVL) is a cytotoxin produced by some strains of
21 *Staphylococcus aureus*. These strains are responsible for primary skin infections and
22 necrotizing pneumonia. This rare entity is mainly described in young immunocompetent
23 patients with an influenza-like prodrome and has a high lethality rate (1, 2). We report herein
24 a case of necrotizing pneumonia induced by PVL-secreting methicillin-susceptible *S. aureus*
25 in a patient infected by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2).

26 In March 2020, during SARS-CoV-2 outbreak in France, a man in his thirties without
27 comorbidities presented at the emergency department with fever, cough, and blood-streaked
28 sputum developing for 3 days. A diagnosis of pleuropneumonia was made and antimicrobial
29 therapy was initiated with cefotaxime plus metronidazole. *Streptococcus pneumoniae* and
30 *Legionella pneumophila* serotype 1 urinary antigens were negative; respiratory viruses
31 screening PCR was negative. The next day, further respiratory deterioration required his
32 transfer in Intensive Care Unit (ICU) for intubation, mechanical ventilation, and inotropic
33 support. Spiramycin was added to the previous probabilistic antibiotic. Chest CT pointed out a
34 parenchymal consolidation of the left upper lung, without ground-glass opacities commonly
35 described in Coronavirus Disease 2019 (COVID-19) (3). Four days after intubation, the
36 patient was not getting better. SARS-CoV-2 RT-PCR was performed on endotracheal
37 aspirate, using the method developed by the National Reference Centre for respiratory viruses

38 (Institut Pasteur, Paris), and was positive for the pandemic SARS-CoV-2 (4). Another chest
39 CT showed worsening of bilateral parenchymal damage with complete consolidation of the
40 left lung, cavitory lesions suggestive of multiple abscesses, and appearance of areas of
41 ground-glass opacities in the right lung (Figure 1). The chest radiograph also revealed a left
42 pleural effusion. The bacteriological analysis of pleural drainage revealed the presence of
43 Gram-positive cocci; the culture yielded a monomicrobial *S. aureus*, identified using MALDI-
44 TOF spectrometry mass (Bruker Daltonics, Wissembourg, France). The strain was resistant
45 only to penicillin G (VITEK 2 system, BioMérieux, Marcy l'Etoile, France). Because of this
46 necrotizing pneumonia associated with acute respiratory distress syndrome, a PVL-producing
47 strain was suspected. PVL production was confirmed using a specific PCR, as described
48 previously by Deurenberg et al. (5). Previous antimicrobial therapy was changed into
49 oxacillin plus clindamycin (for antitoxin effect) against methicillin-susceptible *S. aureus*, and
50 lopinavir/ritonavir (quickly stopped for suspected toxicity) plus azithromycin against SARS-
51 CoV-2. Three days later, given a lack of clinical improvement, antimicrobial therapy was
52 incremented for piperacillin-tazobactam plus linezolid (for antitoxin effect). At the
53 bronchoscopy, the left bronchial tree was obstructed by purulent secretions. Owing to
54 deterioration of respiratory, renal and liver functions, venovenous extracorporeal membrane
55 oxygenation (ECMO) and anticoagulation were initiated ten days after ICU admission. Two
56 days later, upper left lobectomy was performed, and antimicrobial therapy was incremented
57 with meropenem, gentamicin plus linezolid. Unfortunately, the patient finally died 17 days
58 after his admission to the hospital.

59 PVL-secreting *S. aureus* necrotizing pneumonia is frequently preceded by an
60 influenza-like infection (6), which may be a possible causative factor. Particularly, influenza
61 virus is known to impede phagocytic killing and damage the bronchial epithelium, thus
62 reducing secretin clearance and facilitating bacteria adhesion (2). It also induces an influx of

63 immune cells to lung tissues, including neutrophils; the rapid killing of these cells by PVL
64 and release of the inflammatory mediators may promote disease development by damaging
65 the epithelium (7, 8). The association of PVL-secreting *S. aureus* and influenza virus has been
66 previously reported in the literature (6, 9). We report a PVL-secreting *S. aureus*
67 superinfection in COVID-19. It points out that the new SARS-CoV-2 is, in the same way, a
68 facilitating factor for PVL-producing *S. aureus* necrotizing pneumonia.

69 In 2003, during SARS-CoV outbreak, an increase in *S. aureus* superinfection (mostly
70 methicillin-resistant *S. aureus* ventilator-acquired pneumonia) was described. Given common
71 points between SARS-CoV-2 and previous coronaviruses, Lupia et al. discussed this issue for
72 COVID-19, suggesting to consider anti-methicillin-resistant *S. aureus* coverage in order to
73 reduce the risk of superinfection (10).

74 In PVL-producing *S. aureus* superinfection, prescribing antibiotics that have an antitoxin
75 effect, such as clindamycin or linezolid, remains important (2). Thus, in previously healthy
76 young adults admitted in ICU for COVID-19 with *S. aureus* superinfection, a PVL-producing
77 strain should be evocated.

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