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LETTER

Epidemiology of post-influenza bacterial pneumonia due to Panton–Valentine leucocidin positive *Staphylococcus aureus* in intensive care units: a retrospective nationwide study

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Dear Editor,

During influenza, *Staphylococcus aureus* (SA) superinfection is one of the major causes of death [1]. Very little is known regarding SA producing Panton–Valentine leucocidin (SAPVL) post-influenza pneumonia and specifically its epidemiology [2–5].

The main goal of this study was to assess, in a retrospective French multicentre study, the in-intensive care unit (ICU) mortality and prevalence of SAPVL post-influenza pneumonia.

This retrospective observational multicentre French study was conducted in 25 ICUs. Adult patients were included if they were admitted to the ICU between January 2009 and December 2017 for influenza pneumonia with a proven superinfection with SAPVL. The complete methodology has been provided in the online supplemental material.

Among the 2053 patients identified with influenza pneumonia, 22 [1.1%, CI 95% (0.6–1.5)] presented an influenza superinfected by SAPVL. The included population was 44 years old [36–57].

At admission to ICU, diagnosis of influenza was systematically achieved in the first 24 h.

Methicillin-susceptible SA was found in 17 patients (77.3%), while methicillin-resistant SA (MRSA) was found in 5 patients (22.7%). Duration between the onset of symptoms and admission to hospital was 3 days [3–4]. All patients were transferred to ICU within 24 h following hospitalisation.

Eighteen patients (81.8%) had a diagnosis of acute respiratory distress syndrome with a median lowest PaO_2/FiO_2 of 100 [61–121] mmHg. Among the latter, 16 patients (73%) required a rescue extracorporeal membrane oxygenation (ECMO) support. Severity at admission and complications are described in Tables 1, S1 and S2. The prevalence of influenza superinfected by SAPVL was 1.1% with an associated all-cause in-ICU mortality of 54.5%, while the global in-ICU mortality of patients admitted for severe influenza without SAPVL was 20.5%.

Despite a high degree of failure at admission, no major prior comorbidities or risk factors was found for complicated influenza or MRSA infections.

The relatively low rate of prone positioning could be in part explained by the clinical presentation of the studied patients with high SOFA scores. Thus, the intensivist might have been reluctant to turn such severe patients to a prone position. Furthermore, 6/22 patients were included before the PROSEVA study which had been published in 2013 [6].

This study presents several limitations due to its retrospective design. The estimated prevalence is probably underestimated, due to the non-systematic screening of Panton–Valentine leucocidin production in all patients superinfected with SA. Over the ten past

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Table 1 Severity at admission and treatment performed

Characteristics	Overall			Survivor patients			Non-survivor patients			*p*
	n = 22	median [Q1–Q3]		*n* = 10	median [Q1–Q3]		*n* = 12	median [Q1–Q3]		
		n (%)			*n* (%)			*n* (%)		
Severity at admission										
SAPS 2		71	[52–83]		51.5	[31–72]		83	[60.5–90]	0.017
SOFA		12	[9–14]		9	[6–10]		14	[12–15.5]	0.017
Shock, *n* (%)		11	(50)		4	(40)		7	(58.3)	0.670
Diuresis for 24 h, (ml/24 h)	11	400	[0–1555]	4	1402.5	[825–1627.5]	7	300	[0–500]	
Respiratory failure										
ARDS, *n* (%)	20			9			11			
No, *n* (%)		2	(10)		1	(11.1)		1	(9.1)	0.421
Moderate, *n* (%)		2	(10)		2	(22.2)		0	(0)	
Severe, *n* (%)		16	(80)		6	(66.7)		10	(90.9)	
Lowest PaO2/FiO2	21	100	[61–121]	9	116	[100–150]	12	66	[50–96]	0.060
NO, *n* (%)		10	(45.5)	10	4	(40)	12	6	(50)	0.691
Prone position, *n* (%)		8	(36.4)	10	4	(40)	12	4	(33.3)	1
Duration of mechanical ventilation, (days)	21	8	[3–38]	9	43	[28–45]	12	4.5	[2–7.5]	0.007
Circulatory failure	22			10			12			
Norepinephrine, *n*, (%)		17			7	(70)		10	(83.3)	0.624
Epinephrine, *n* (%)		13			4	(40)		9	(75)	0.192
Dobutamine, *n* (%)		7			3	(30)		4	(33.3)	1
Duration of catecholamines infusion, (days)										
Norepinephrine	17	4	[1–8]	7	5	[1–16]	10	3.5	[1–6]	0.659
Epinephrine	13	2	[1–2]	4	3.5	[1–6.5]	9	2.0	[1–2]	
Dobutamine	7	3	[3–4]	3	3	[3–4]	4	4.5	[2.5–4]	
ECMO *n* = patients (%)		16	(73)							
VA ECMO, *n* = ECMO (%)		10	(62.5)	7	2	(28.6)	9	8	(88.9)	0.035
VV ECMO, *n* = ECMO (%)		10	(62.5)	7	6	(85.7)	9	4	(44.4)	0.145
Duration of ECMO, (days):										
VA	10	5.5	[3–10]	2	14.5	[3–26]	8	5.5	[3–8]	
VV	9	10	[4–28]	5	28	[6–29]	4	7	[3–13.5]	
Renal replacement therapy, *n* (%)	21	13	(61.9)	9	3	(33.3)	12	10	(83.3)	0.032

Categorical variables are presented as *n* (%) and non-parametric variables as median (interquartile range) or mean and *p* value for Fisher's exact test

Concerning ECMO, 16 patients had assistance with either VA or VV ECMO. Six patients had VA ECMO only, six had VV ECMO only and four patients benefited from both assistance VA and VV ECMO

SAPS 2 Simplified Acute Physiology Score, *SOFA* Sequential Organ Failure Assessment, *ARDS* acute respiratory distress syndrome, *NO* nitric oxide, *ECMO* extracorporeal membrane oxygenation, *VV* venovenous, *VA* venoarterial

years, development in respiratory critical care medicine has deeply transformed the prognosis of ARDS which was here the main complication. In the present study, due to the low sample size, the impact of these changes is most likely underestimated. Consequently, the difference in the reported mortality rates between influenza patients with and without SAPVL superinfection should be analyzed with caution. However, taken together, these limitations were also balanced by the multicentre design over a 9-year time period.

In summary, SAPVL post-influenza superinfection is a rare complication with an estimated prevalence rate of 1.1% and an associated in-ICU mortality rate of 54.5%. Thus, in patients admitted in ICU for influenza, the onset of a refractory shock with a profound leucopenia should be a "red flag" for suspecting a superinfection with SAPVL.

Electronic supplementary material

The online version of this article (https://doi.org/10.1007/s00134-019-05665-3) contains supplementary material, which is available to authorized users.

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Author contributions
AJ and EB participated equally in this work. ICU performed the statistical analysis and takes responsibility for the integrity of the data and the accuracy of the data analysis. AJ, AK, EB, EA, YB, ICU, CA, CP, MB and BL contributed substantially to the study design, data interpretation and the writing of the manuscript. AJ, EB, AK, CEL, CV, SH, JPQ, LZ, FS, PK, VP, SN, PJ, JM, MF, XV, AL, AM, NT, GS, CLM, EN, JL, AG, JNT, GP, RCJ, FV, CA, BH, ES, CP and BL contributed substantially to the study in including patients. ICU and EA contributed to statistical data.

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Conflicts of interest
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