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Health-care Associated KPC-BSI: The Time Has Come

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Dear Editor,

Klebsiella pneumoniae producing carbapenemases (KPC) has reached a worldwide diffusion and the associated mortality rate of infected patients is ranging from 45% to 56% [1]. Several risk factors for mortality were identified in patients with KPC bloodstream infections (KPC-BSI), such as the severity of the underlying disease or the delay in administration of appropriate therapy [2,3]. Usually KPC infections arise in patients with prolonged hospital stay which have been previously treated with antibiotics [3]. We report on patients with KPC-BSI diagnosed within five days after hospital admission [4].

The mortality was evaluated at 21 days after the first positive blood cultures and appropriate treatment has been considered as the administration for $\geq$48 hours of an antibiotic with *in vitro* activity [5].

Eighteen patients with HCA KPC-BSI were studied (Table 1). The majority of patients were males (11, 61%), with a mean age of 63 years-old (SD$\pm$14), a previous admission in the six months before the BSI onset (13; 72%) or underwent surgery during the hospital stay (13; 72%). Ten patients (56%) were in a medical ward at the time of diagnosis. The median days between hospital admission and KPC-BSI were 3$\pm$1 and the mean APACHE II score was 16 (range, 3-36). Five patients were colonized by KPC before KPC-BSI. The comorbidities more frequently reported were: malignancy (5; 36%), chronic renal failure (4; 29%), epatopathy (3; 17%) and cardiovascular diseases (3; 17%). After 2±1 days the empiric antibiotic treatment was changed and all patients were appropriately treated, mostly with combination therapy, according to the *in vitro* sensitivity. The overall mortality was 22% (4 patients). At univariate analysis the mortality was significantly associated with liver disease (p=0.031), chronic renal failure (p=0.047) and high APACHE II score (p=0.01). The survival was significantly associated with appropriate treatment administered for $\geq$ 48h (p=0.034).

Usually KPC-BSI infections are diagnosed after a median of 28-37 days by the hospital admission [6-8]. In this study we report for the first time 18 patients with KPC-BSI within five days after the hospital admission, which had a very low crude mortality rate [22%] compared with 45% in the above mentioned patients with nosocomial KPCBSI infections [6-8].

The pathogenesis of KPC-BSI infection seems to be consistent with a multistep process where comorbidities, host factors and prolonged antibiotic pressure contribute to the invasion of the bloodstream by KPC after the gastrointestinal tract is colonized. We could hypothesize that these factors are less active in the early days after admission, even if comorbidities such as renal failure and liver disease are significantly associated with mortality in our patients.

In conclusion, notwithstanding the low number and the heterogeneity of our patients, we report a new epidemiological finding, represented by HCA KPC-BSI. KPC should be considered as a potential pathogen of BSI early after hospital admission, underscoring the need for early screening of patients at risk to increase the likelyhood of empiric treatment.

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Table 1. Main clinical characteristics of patients with healthcare associated KPC-BSI.

	Non survivors [n=4]	Survivors [n=14]	P value
Demographic variables ***N [%]***			
Male, sex	2 [50]	35 [76]	NS
Age, years mean [±sd]	65 [±14]	62 [±13]	NS
Ward n[%]			NS
- Surgery	1 [25]	5[35]	
- Medicine	2 [50]	8 [57]	
- ICU	1 [25]	1 [7]	
Previous Hospitalization [6 months preceding]	1[25]	12 [86]	NS
Invasive procedures	3 [75]	13[92]	NS
Previous surgery	3 [75]	10 [71]	NS
Comorbidities			
- Hepatopathy	2 [50]	1 [7]	0.031
- Chronic renal failure	3 [75]	1 [7]	0.047
APACHE II score [mean± SD]	18 [±8]	15 [±7]	0.01
Post antibiogram therapy			
- Inappropriate therapy	0	0	0.034
- Appropriate therapy	4[100]	14 [100]	