

The changing microbiological and antimicrobial susceptibility profile of cerebrospinal fluid organism isolates in a teaching hospital, Tangerang, Indonesia

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Abstract

Background: Central nervous system (CNS) infections have become serious problems that contribute to morbidity and mortality in developing countries. In the recent years, antimicrobial resistance has arisen parallel with the changing trend of infectious pathogens, which resulted in the unavailability of an ideal antimicrobial agent. This study was designed to evaluate the central nervous system pathogens and their susceptibility profile using routine microbiological data.

Methods: The data of CSF culture and susceptibility testing were collected from January 2010 to August 2015. The majority of positive samples (68/9; 68.7%) had history of neurosurgical procedures. All CSF clinical samples were immediately inoculated onto Columbia blood agar base[®] (Difco[™]) with sheep blood agar (5%) and chocolate agar. CHROMagar (BBL-Difco[™]) and Sabouraud dextrose agar were also used for isolation and presumptive identification of yeast and filamentous fungi. Identification and antimicrobial susceptibility testing of all isolates were performed by an automated method from VITEX-2 Compact[®] (Biomérieux, France) in accordance with Clinical and Laboratory Standard Institute (CLSI) guideline

Results: The most common pathogens isolated were coagulase negative staphylococci (CoNS) 39/99 (39.4%), followed by *Acinetobacter baumannii* 10/99 (10.1%), *Pseudomonas aeruginosa* 7/99 (7.1%), *Sphingomonas paucimobilis* 5/99 (5.0%), and *Aeromonas salmonicida* 4/99 (4.0%). Almost of all Gram positive cocci were susceptible to

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tigecycline, linezolid, vancomycin, and trimethoprim/sulfamethoxazole. Most Gram negative bacilli (GNB) were multi-drug resistant with high susceptibility level to amikacin, tigecycline, and trimethoprim/sulfamethoxazole. The overall susceptibility testing to cephalosporins was low, ranging between 34.2% to 58.5%. The susceptibility to several antifungal remained high for *Candida spp.* and *Cryptococcus neoformans*.

Conclusion: The present study demonstrates the changing pathogens trend of CNS infections along with their antimicrobial susceptibility patterns in our hospital. There is a need to implement local guidelines for empirical antimicrobial therapy and surveillance system to control the usage of antimicrobial drugs.

Keyword: antimicrobial, susceptibility, neurosurgical procedures, CNS infections

Introduction

CNS infections are life-threatening and significant causes of morbidity and mortality, especially in developing countries [1,2]. Bacterial infections have been known as the most common cause of the CNS infections, meanwhile fungi and mycobacteria are also frequently reported [3]. The pattern of pathogens recovered from CSF culture varies from Gram-positive cocci to multidrug-resistant Gram-negative bacteria depending on geographic region, age, co-morbidities, type of neurosurgical procedures, and site of infection [1,4,5].

Neurosurgical site of infections after a neurosurgical procedure remains an important issue with overall infection rate of 0.4 % to 7.7% [3,6,7]. Studies have shown the main organisms that cause postneurosurgical infection were non-lactose fermenting gram-negative bacteria (GNB) followed by *A. baumannii*, *K.pneumoniae*, methicillin-resistant *Staphylococcus aureus* (MRSA), and *Candida species* [5,7,8].

The burden of health care associated infection in hospitals are frequently increased due to the excessive use of broad-spectrum antibiotics and because health professionals are caring less to safety precautions [8]. The development of many drug-resistant organisms, such as carbapenem-resistant and methicillin/oxacillin-resistant strains, and extended-spectrum beta-lactamase (ESBL) producing bacteria may reflect the changing trend of pathogens and their antimicrobial susceptibility pattern [9,10]. Therefore, microbiological surveillance is important to identify the common pathogens and their antimicrobial susceptibility patterns in order to select the rational empirical antimicrobial therapy based on regional and national data to reduce the emergence of resistant organisms [8,11,12].

Materials and methods

We conducted a retrospective, descriptive study using the routine microbiological data from Siloam General Hospital database. This health center is

a private teaching hospital affiliated to Faculty of Medicine, Pelita Harapan University, located in Tangerang, Indonesia. The data of CSF cultures and antimicrobial susceptibility results were collected from January 2010 through August 2015. Data were analyzed by using SPSS 21 version.

Identification and susceptibility testing of bacterial isolates

All CSF clinical samples immediately were inoculated onto Columbia blood agar base[®] (Difco[™]) with sheep blood agar 5% and chocolate agar. CHROMagar (BBL-Difco[™]) and Sabouraud dextrose agar were used for isolation and presumptive identification of yeast and filamentous fungi. All bacterial and fungal cultures were incubated at 37°C for 24-48hrs. Identification and antimicrobial susceptibility testing of all isolates was performed by an automated method from VITEX-2 Compact[®] (Biomérieux, France) in accordance with Clinical and Laboratory Standard Institute (CLSI) guideline [13]. *Escherichia coli* ATCC[®] 25922, *Pseudomonas aeruginosa* ATCC[®] 27853, *Staphylococcus aureus* ATCC[®] 29213, and *Streptococcus pneumoniae* ATCC[®] 49619 were used as control isolate for susceptibility testing. The susceptibility testing against first line TB drugs was accomplished using proportional method after cultured on Lowenstein-Jensen (LJ) medium [14].

Results

Out of the 659 CSF samples submitted, 99 (15%) revealed growth of microorganisms, of these 87 (87.9%) were bacterial, 8 (8.1%) grew yeast and the rest 4 samples (4%) grew *Mycobacterium tuberculosis*. The majority of positive samples 68 (68.7%) had history of neurosurgical procedures, such as cranial operation, brain biopsies, shunt or ventricle operation, burr hole, aspiration or drainage. Other profiles of CSF organisms are shown in **Table 1**.

Table 1. General characteristic of 99 CSF isolated organisms

General characteristic of 99 CSF isolated organisms	Total n (%)
Sex	
Male	62 (62.6)
Female	37 (37.4)
Age	
0 - < 1 year	10 (10.1)
> 1 - 14 year	27 (27.3)
> 14 - 65 year	56 (56.6)
> 65 year	6 (6.0)
History of post neurosurgical procedures	68 (68.7)

This study demonstrated that there is a trend towards an increased number of GNB isolates over the period (2010-2015) as demonstrated in **figure 1**. The highest number of GNB isolates was in 2013 with 11 isolates. Over the study period, CoNS accounted for most of the isolates (39.4%) as shown in Table 2. Among GNB isolates, *A. baumannii* was the most common (10.1%), followed by *P. aeruginosa* (7.1%) and *Sphingomonas paucimobilis* (5.1%). The number of *Cryptococcus neoformans* isolates were 4, and only one isolate of MRSA was recovered (**Table 2**).

Table 3 shows that about one-third of Gram positive cocci were susceptible to a group of beta-lactam antibiotics cephalosporins, while for GNB the rate of susceptibility was higher 16/27 (59.3%). All isolates of MRSA and CoNS (100%) and GNB (78.8%) were susceptible for tigecycline, respectively, and only 2.6% of CoNS isolates were resistant to vancomycin. The level of linezolid susceptibility among CoNS and other Gram positive cocci (MRSA, streptococci and enterococci) were 100%. Most GNB isolates (76.7%) were susceptible for meropenem. All *Candida spp.* and *Cryptococcus neoformans* isolates were found to be susceptible to tested antifungal drugs.

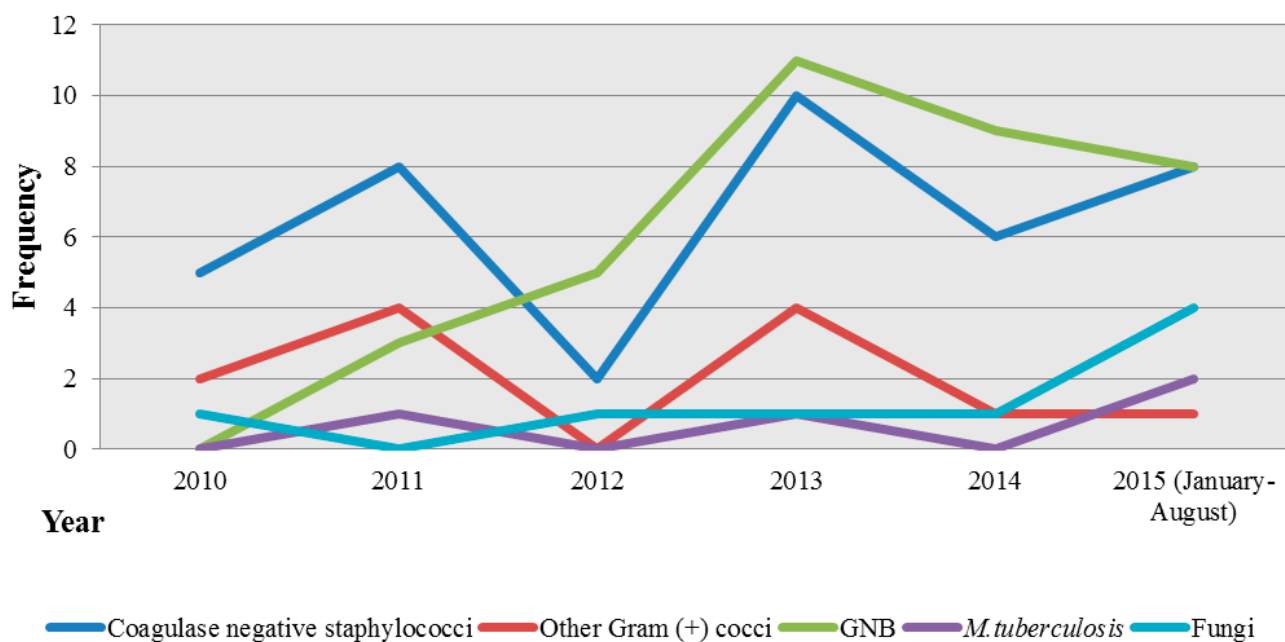


Figure 1. The changing trend of CSF isolates during 2010 – August 2015

Discussion

The best test to confirm CNS infection is the detection of pathogens in CSF culture [3,15]. This study included 68 (68.7%) positive CSF samples which had history of neurosurgical procedures. This result is much higher than several studies noted that the incidence of intracranial post-neurosurgical infection have been ranged between 0.4% to 7.7% [4,5,6,7]. The profile of CSF isolates in this study showed that certain bacteria species were the predominant cause of CNS infection and was similar to other studies [1,2,8,10]. Coagulase negative Staphylococci was responsible for 39.4 of CSF positive culture, which was similar to a recent Iranian study [16]. The high incidence of CoNS isolates in our study may be associated with the fact that majority of patients admitted to our hospital underwent neurosurgical procedures.

The number of GNB isolates has increased especially with *A. baumannii* as a major pathogen and it is similar to studies carried out in other countries [5,6,8]. This study showed that the *A. baumannii* isolates were mostly multi-drug resistant, and 55.6% of these were carbapenem-resistant. Recent studies from various countries also showed that rates of carbapenem-resistant *A. baumannii* (CRAB) varied from 55% to 88% and increased particularly in association with neurosurgical infection [5,17,18]. The high incidence of CRAB is a great concern in terms of nosocomial infection and it had been associated with serious therapeutic problem [5,17]. The inappropriate antibiotic usage in prophylaxis therapy, use of medical devices, length of hospitalization, and immunocompromised underlying diseases have contributed to increased morbidity and mortality due to *A. baumannii* infection [19]. Most CRAB infections led to death with mortality rate of 59.1% [17].

Table 2. Frequency of bacteria and yeast isolates from CSF cultures (2010-2015)

Type of isolate	Year						Total n (%) isolate
	2010 n(%)	2011 n(%)	2012 n(%)	2013 n(%)	2014 n(%)	2015 (January-August) n(%)	
CoNS ^a	5 (12.8)	8 (20.5)	2 (5.1)	10 (25.7)	6 (15.4)	8 (20.5)	39 (39.4)
MRSA ^b	-	1 (100.0)	-	-	-	-	1 (1.0)
<i>Streptococcus mitis</i>	1 (33.3)	1 (33.3)	-	1 (33.3)	-	-	3 (3.0)
<i>Streptococcus mutans</i>	-	-	-	-	-	1 (100.0)	1 (1.0)
<i>Propionibacterium acne</i>	1 (50.0)	1 (50.0)	-	-	-	-	2 (2.0)
<i>Enterococcus spp.</i>	-	1 (20.0)	-	3 (60.0)	1 (20.0)	-	5 (5.1)
<i>Aeromonas salmonocida</i>	-	1 (25.0)	-	2 (50.0)	-	1 (25.0)	4 (4.0)
<i>Pseudomonas spp.</i>	-	2 (28.6)	-	2 (28.6)	-	3 (42.8)	7 (7.1)
<i>Acinetobacter baumannii</i>	-	-	3 (30.0)	1 (10.0)	5 (50.0)	1 (10.0)	10 (10.1)
<i>Burkholderia cepacia</i>	-	-	2 (100.0)	-	-	-	2 (2.0)
<i>Citrobacter freundii</i>	-	-	-	1 (100.0)	-	-	1 (1.0)
<i>Escherichia coli</i>	-	-	-	2 (66.7)	1 (33.3)	-	3 (3.0)
<i>Sphingomonas spaucimobilis</i>	-	-	-	3 (60.0)	-	2 (40.0)	5 (5.1)
<i>Klebsiella pneumoniae</i>	-	-	-	-	3 (75.0)	1 (25.0)	4 (4.0)
<i>Mycobacterium tuberculosis</i>	-	1 (25.0)	-	1 (25.0)	-	2 (50.0)	4 (4.0)
<i>Candida spp.</i>	1 (25.0)	-	1 (25.0)	-	-	2 (50.0)	4 (4.0)
<i>Cryptococcus neoformans</i>	-	-	-	1 (25.0)	1 (25.0)	2 (50.0)	4 (4.0)

^aCoNS = Coagulase negative staphylococci

^bMRSA = methicillin-resistant *Staphylococcus aureus*

In our study, most Gram-positive cocci, especially CoNS were resistant to almost tested antibiotics and only susceptible to linezolid, vancomycin, tigecyclin and trimethoprim-sulfamethoxazole. This result is comparable with 100% susceptibility in previous study [10]. An earlier study in India has observed that the infection rate due to *Cryptococcus neoformans* was 2.93% to 3.13%, and it is lower than our finding (4%) [8]. A study conducted in Malawi had significantly higher frequency of *C. neoformans* (39.1%) and this high prevalence was likely related to prevalence of HIV infection in their patients and which is different in our study [9], where up to two-thirds of patients had neurosurgical procedures.

The limitation of this study is due to use of retrospective data, and lack of several variables such as patient's history and antibiotic treatment prior CSF sample collection which were not recorded in our database system. Therefore, this study can't distinguish between community-associated or hospital-associated CNS infection.

Conclusion

The present study demonstrates the changing pathogens trend of CNS infections along with their antimicrobial susceptibility pattern in an

Table 3. Antimicrobial susceptibility profile of CSF isolates

Antimicrobial	CoNS ^a	Other Gram positive Cocci ^b	GNB ^c	Yeast ^d	<i>M. tuberculosis</i>
	n/total (%)	n/total (%)	n/total (%)	n/total (%)	n/total (%)
Ampicillin	-	3/6 (50.0)	12/31 (38.7)	-	-
Amikacin	-	-	27/33 (81.8)	-	-
Aztreonam	-	-	10/28 (35.7)	-	-
Ceftazidime	11/35 (31.4)	1/3 (33.3)	20/34 (58.8)	-	-
Ceftriaxone	12/37 (32.4)	1/2 (50.0)	15/28 (53.6)	-	-
Cefotaxime	12/37 (32.4)	2/3 (66.7)	11/18 (61.1)	-	-
Cefepime	10/28 (35.7)	0/1 (0.0)	17/28 (60.7)	-	-
Linezolid	25/25 (100.0)	5/5 (100.0)	-	-	-
Meropenem	12/36 (33.3)	1/4 (25.0)	23/30 (76.7)	-	-
Trimethoprim/Sulfamethoxazole	22/36 (61.1)	1/1 (100.0)	15/26 (57.6)	-	-
Tigecycline	37/37 (100.0)	7/7 (100.0)	26/33 (78.8)	-	-
Vancomycin	37/38 (97.4)	8/8 (100.0)	-	-	-
Flucytosine	-	-	-	5/6 (83.3)	-
Fluconazole	-	-	-	8/8 (100.0)	-
Amphotericin-B	-	-	-	7/7 (100.0)	-
Voriconazole	-	-	-	6/6 (100.0)	-
Ethambutol	-	-	-	-	3/4 (75.0)
Isoniazid	-	-	-	-	4/4 (100.0)
Rifampicin	-	-	-	-	4/4 (100.0)
Streptomycin	-	-	-	-	3/4 (75.0)

^aCoNS = Coagulase negative Staphylococci

^bIncluding MRSA (1), *Streptococcus mitis* (3), *Streptococcus mutans* (1), *Propionibacterium acne* (2), and *Enterococcus spp.* (5)

^cGNB = Gram negative bacilli

^dIncluding *Candida albicans* (3), *Candida guilliermondii* (1), *Cryptococcus neoformans* (4)

Indonesian hospital. This finding highlights the need of local antibiotic surveillance system, guidelines to control the appropriate usage of antimicrobial regimens and selection of empirical antimicrobial therapy.

Acknowledgements

The authors express their gratitude to Siloam General Hospital in Tangerang, Indonesia who made this work realized.

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