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A Catheter-Related Bloodstream Infection Caused by Chryseobacterium Indologenes in a Hemodialysis Patient: A Case Report

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Abstract

Catheter Related Blood Stream Infection (CRBSI) is associated with significant morbidity and mortality in Hemodialysis patient, and it's a leading cause of hospitalization. Gram-negative organism is increasingly reported as a cause of CRBSI in hemodialysis patients. Recently, primary and catheter related bacteremia caused by Chryseobacterium indologenes is identified more frequently, but the reported bacteremia caused by this organism in Hemo Dialysis (HD) patients related to Central Vascular Catheter (CVC) is very rare. We present in this report a case of C. Indologenes bacteremia in HD patient with previous episode of culture negative line sepsis, treated with new line insertion after 2 days line free window, and 2 weeks of intravenous vancomycin and ceftazidime. His course was complicated by disseminated infection, few scattered hepatic and splenic abscesses identified on Computed Tomography (CT) Scan, resolved after long course of appropriate antibiotic therapy with Trimethoprim-Sulfamethoxazole (TMP-SMZ). Carful assessment of HD patients dialyzing though a CVC is indicated, with special attention towards Non-Fermenting Gram Negative Bacilli (NFGNB), and imaging is essential to investigate non-responders.

Introduction

Although CVC is not the gold standard access to provide and maintain effective dialysis in patients with End Stage Renal Disease (ESRD), due to increased risk of infection, thrombosis and other complications, it acts as an important way and the only option to deliver dialysis in certain conditions. A CRBSI in hemodialysis patient is associated with a significant morbidity and mortality, and it's a leading cause of hospitalization in HD patients. The incidence of CRBSIs reported in several large series ranged between 1.1-5.5 episodes/1000 catheter-days [1,5].

CRBSIs caused by gram-negative organisms are well documented in literature. Reporting infections caused by the NFGNB, which consists of various groups of aerobic non spore-forming bacilli, emerging as nosocomial pathogens in recent years [6]. It is really important to correctly identify these non- fermenters as they show a multidrug resistant pattern and can cause an invasive disease in certain conditions [7-14]. Of these NFGNB, *Pseudomonas* species and *Acinetobacter* species has a very high rate of isolation and has been studied extensively. Currently,

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several studies have been reported concerning NFGNB other than *P. aeruginosa* and *Acinetobacter* spp, one of them is Chryseobacterium indologenes, which is our focus in this report.

C. Indologenes can cause numerous infections in humans, particularly immune compromised individuals and patients with indwelling devices. Although bacteremia caused by C. Indologenes has been reported before, infection with this organism in hemodialysis patients was rarely reported [15-17]. In Saudi Arabia, 2 studies reporting C. indologenes, but none was in HD patients [6,18]. To our knowledge this is the first case reporting a C. indologenes bacteremia in hemodialysis patient dialyzing through a tunneled catheter in Saudi Arabia.

Case Report

A-74- year old Saudi male, who is known to have long standing diabetes mellitus, hypertension and end stage renal disease, on regular hemodialysis for 15 years, through arterio-venous fistula, which was occluded and he was maintained on HD through right internal jugular permanent catheter for the last 2 years, he is dialyzing in hemodialysis satellite center near home. Presented to the emergency room with history of fever 39°C, associated with chills and rigors during his session of hemodialysis. His symptoms started 2 weeks prior to his presentation to our hospital, and blood culture was sent from the dialysis center, which revealed a growth of chryseobacterium. Indologenes, sensitive to TMP-SMZ, intermediate sensitivity to ciprofloxacin and resistant to carbapenems. He was prescribed oral TMP-SMZ and oral ciprofloxacin for 2 weeks.

On his presentation to our hospital his BP was 130/66 mmHg, heart rate 85 bpm, temperature 37.2°C and no any clear focus of infection. Peripheral and central blood was sent for culture and he was started on meropenum and vancomycin empirically.

Three days on antibiotics, he spiked temperature 38.1°C, and his central blood culture grew C. indologenes, after consultation with the Infectious Disease (ID) specialist, his antibiotic changed to TMP-SMZ according to the sensitivity (Table 1). Five days later, he spiked temperature again 38.4°C, another blood sample was sent and a persistent growth of C. indologenes was reported from a peripheral blood and staphylococcus coagulase negative and streptococcus viridans reported from central blood culture. Vancomycin was added to TMP-SMZ, and he had no more fever, and was hemodynamically stable. Repeated blood culture was sent after seven days that was positive for C. indologenes from central and peripheral blood samples. He underwent permanent catheter exchange over a guide wire, considering he had a very difficult access.

He was sent home after permanent catheter exchange, and the plan based on ID team recommendations, to continue on antibiotic for a total of 2 weeks after culture negative, along with vancomycin lock and repeated blood culture prior to each HD session, to detect first negative sample. Prior to this presentation, 10 weeks earlier he was admitted to the hospital, with same presentation, and he was treated with ceftazidime and vancomycin, and a new PC insertion, after 2 days line free window, although his blood culture at that time was negative, but he had a persistent fever, without any other obvious source of infection.

A month later from his presentation, 10 days from discharge, he was admitted electively for bacteremia, MDR acinetobacter baumannii, at that time no growth of C. indologenes, this was sensitive to tigecycline, he was completely asymptomatic, and treated according to the sensitivity reported and had a Computed Tomography (CT) scan done to investigate for persistent bacteremia.

His CT scan revealed few scattered hypo-dense liver lesions the largest identified at segment seven measures 13.6 mm x 10 mm. Few splenic tiny hypo-dense lesions also identified, the largest seen in posterior lower aspect of the spleen measures 10.4 mm x 8 mm, which represents an abscess (Figure 1). After reviewing the CT scan finding with ID team, the plan was to add TMP-SMX as these abscesses are likely related to the previous infection with C. indologenes, he was prescribed TMP-SMX (800 mg/400mg) Intravenous post each session of HD, planned for 6 weeks, and to repeat another CT scan to follow on response to therapy.

Unfortunately 20 days later, he presented to our ED with malfunctioning permanent catheter, and underwent catheter exchange under a guide wire, then discharge home, during this admission a repeat CT scan showed same finding with regression in the lesions. ECHOcardiogram showed no evidence of infective endocarditis. 4 weeks later, he was electively admitted for liver biopsy under US guidance, where the US reported a resolution of all the lesions, likely responding to antibiotic use, he was treated initially with IV TMP-SMX (800 mg/400 mg) post each session of HD, oral TMP-SMX was added on non-dialysis days target dose of 10 mg/kg TMP (7.5 mg/kg adjusted body weight), after repeated CT scan. The only concern during his course of therapy was the associated nausea and vomiting, where he refused to take the antibiotics the last 2 days of his course. He felt fine otherwise, doing his HD session 3 times/week in the same center with no reported issues. Since then, he has been stable for more than 7 months following this episode of bacteremia.

Table 1: Blood culture/ sensitivity Central HD catheter.

Antibiotic	Susceptibility	
Amikacin	1	R
Cefepime	23	S
Ceftazidime	21	S
Ciprofloxacin	24	S
Gentamicin	1	R
Meropenem	13	R
Piperacillin/Tazobactam	26	S
Trimethoprim/Sulfa	22	S

Growth: Chryseobacterium indologenes.

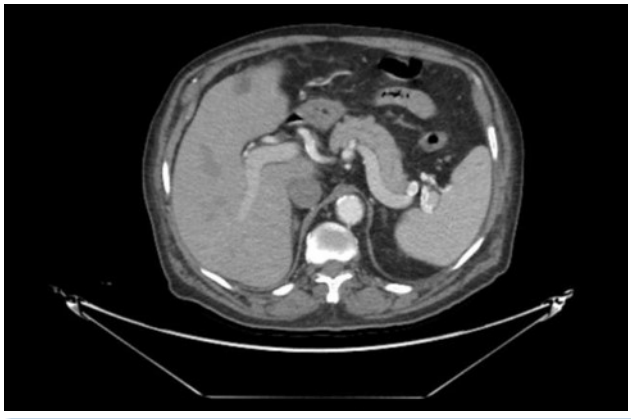

Figure 1: CT scan shows a scattered hepatic hypo-dense lesions.

Discussion

Vandamme et al. defined Chryseobacterium indologenes in 1994, it belongs to Chryseobacterium genus, previously known as Flavobacterium. The genus has 6 species, of these C. Elizabethkingia meningoseptica and C. Indologenes are commonly isolated from clinical specimens, while C. Elizabethkingia is the most virulent, C. Indologenes is the least virulent member of the genus (19), despite being widely spread in nature, plants, soil, food product and water, it is not a normal human micro flora and thus a rare cause of infection in humans [7, 20-23]. It is a yellow pigmented, non-motile, catalase positive, oxidase positive, indole positive, non-glucose-fermenting gram negative bacilli [7]. A variety of invasive infections has been reported with C.insologenes, such as primary bacteremia, catheter related bacteremia, cellulitis, wound sepsis, pyelonephritis, peritonitis, biliary tract infection, pleural effusion, ventilator associated pneumonia, meningitis, artificial shunt infections and others [7,11-14,17,29,30,33-35,46,47]. The most common infections caused by C. Indologenes are pneumonia and bacteremia [37,38]. The presence of protease activity plus the formation of biofilm on indwelling devices play a role in the virulence of invasive infection [39].

Majority of cases reported to have CRBSIs caused by C.indologenes were from Taiwan [24,25,43]. Only 10% of reported cases from outside Asia, mainly USA, India and Australia [13,26-28]. Few patients had community-acquired bacteremia [18,24,25]. C.indologenes is widely spread in nature, including chlorine- treated water, which makes water a good reservoir for this organism, and thus a nosocomial infection in majority of the cases [7,18,25,29-31].

Immune compromised status, underlying comorbid conditions, prolonged use of broad spectrum antibiotic, extreme age and the presence of invasive devices are all risk factors for the infection [24,25,32,33,35,46,47]. The presence of CKD as a risk factor of bacteremia caused by C.indologenes was equivocal [24,25].

Unfortunately, treatment is not well established, due to lack of high quality evidence. Treatment of bacteremia associated with CVC was possible without the removal of the catheter [7,25], or the use of inappropriate antibiotic but with the catheter removal, so removing the CVC was recommended when treating bacteremia caused by C.indologenes, as we are lacking well established therapeutic regimen and with the presence of wide range of antibiotic resistance [24].

The emergence of C.indologenes has been linked to use of colistin and tigecycline [25], which makes this organism resistant to several antibiotics including carbapenems. There is a documented resistance of Chryseobacterium species to several antibiotics including: aminoglycosides, tetracyclines, chloramphenicol, erythromycin, clindamycin, and teicoplanin [7], it can also produce several kinds of b- lactamase, so resistance to this class as well was reported [40], on the other hand, analysis of large number of isolates of C. indologenes collected worldwide revealed great sensitivity to TMP-SMZ [38,41], sensitivity to beta lactamase, fluoroquinolones (gatifloxacin and levofloxacin) and rifampin were reported from isolates outside Asia[13,26,27,38]. Unfortunately, no available evidence on management, except case reports.

Mortality related to bacteremia caused by C.indologenes is higher than mortality reported with pneumonia and UTI [42]. The reported rate was 17% [7,30], a higher rate was reported 28% from a recent study published 2018 [17]. This is could be related to the formation of biofilm on foreign material, protease and urease activity, as an important virulence factor [44], which might result in invasive infection [25,45].

Another possibility is the reported concurrent infection with other gram negative bacilli, candida and MRSA [24,25,42]. As well as the multidrug resistant nature of this organism.

Bacteremia caused by C.indologenes in hemodialysis patient was reported in a study from Brazil, where only 5 positive blood culture samples were positive for this organism out of 65 positive blood cultures reported from 37 hemodialysis patients through a non-tunneled CVC [15], and in a recently published case report in an African male with ESRD, dialyzing through a CVC for 10 months, with 2 previous episodes of CRBSI, but this episode of bacteremia documented while the patient still on cefepime for previous CRBSI with Acinetobacter baumannii [16].

In Saudi Arabia, isolating this organism from various samples was reported in a study done in Najran, Southern Region, there was 12 positive samples out of 125 samples of non-duplicating NFGNB nosocomial strains reported, none was from blood [6] , in another recent study conducted in Riyadh, C.indologenes was isolated in 3 children and one adult patient, no bacteremia reported in HD patient [18].

We report this case to draw attention for further investigating HD patients with CVC, when presented with recurrent episodes of line sepsis, even with culture negative, as NFGNB is identified more frequently, very difficult to treat and associated with morbidity and mortality, in our case no further assessment with a CT scan to evaluate the hepatic and splenic abscesses, as patient refused it, after the finding of the US.

Conclusion

In HD patients dialyzing through CVC, it is important to identify the pathogen causing bacteremia, to choose appropriate antibiotic and to apply effective diagnostic tests indicated. Comply with the Infection Prevention And Control (IPC) measures are very crucial in minimizing risk of infection, particularly in vulnerable, including HD patients. Although Infection with C. Indologenes is uncommon, there is increasing reported cases of bacteremia, particularly in HD patient. Treatment is difficult and mortality is high, considering multidrug resistance nature, protease and urease activity of the organism, the immune status of this subject, the concurrent infection with other gram negative bacilli and MRSA, along with other comorbidities, the formation of biofilm on the catheter and how precious the access is.

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