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Chryseobacterium indologenes Bacteremia: Clinical and Microbiological Characteristics of an Emerging Infection

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Abstract

Purpose: Since *Chryseobacterium indologenes* (*C. indologenes*) is a rare human pathogen, its clinical significance has not yet been fully established. *C. indologenes* contamination of medical devices involving fluids and of surgical implants has led to an increasing number of serious infectious reported in recent years, mainly in patients in extremes ages and an immunocompromised state. In this study, we describe the clinical and microbiological characteristics of seven adult patients with *C. indologenes* bacteremia treated in a tertiary medical center in Israel over a six-year period. **Methods**: Adult patients hospitalized in Rabin Medical Center, Israel, with a blood culture positive for *C. indologenes* during the period 2009-2014 were identified retrospectively and their medical records were reviewed. **Results**: Seven episodes of *C. indologenes* bacteremia in seven patients were identified during the study period. Five patients were females; the mean age was 76.8 years (41 - 92). Serious underlying conditions were present in all patients. All patients but one, presented after a recent invasive healthcare related intervention. Two patients required mechanical ventilation. Two patients died. All but one isolates were susceptible to ciprofloxacin. **Conclusions**: Despite our limited number of cases, to the best of our knowledge, our study serves as the largest cohort of adult patients with *C. indologenes* bacteremia reported in recent years.

Keywords

Bacteremia, *Chryseobacterium indologenes*, Invasive Intervention

*First and second author have equally contributed to the manuscript.

1. Introduction

Chryseobacterium indologenes is a non-fermentative, oxidase-catalase- and indole-positive, non-motile bacillus that belongs to the genius of *Chryseobacterium* (previously known as *Flavobacterium* CDC group IIb) [1]. It is widely found in nature, on soil, water and plants and only rarely causes human disease [2]. Since the organism can survive in chlorine treated water, it can colonize water supplies, thus creating potential reservoirs for infections in hospital settings [3]. Therefore, although not present in human microflora, contamination of medical devices involving fluids and of surgical implants has led to an increasing number of serious infectious reported in recent years. These include cases of pneumonia [4], indwelling device associated infections [5], peritonitis [6], ocular infections [7] and bacteremia [8]. Other reported infections included pyelonephritis, biliary tract infections, neurosurgical shunt infections and wound infections [9] [10]. Case series conducted mostly in Taiwan have demonstrated extremes of age and an immunocompromised state to be common risk factors [8]. The highly active proteases of *C. indologenes* as well as its biofilm production capacity are both responsible for its virulence [11]. *C. indologenes* is known to exhibit natural resistance to a wide variety of broad spectrum antibiotics, including aminoglycosides, tetracyclines, chloramphenicol, macolides, clindamycin and teicoplanin as well as to extended spectrum penicillins, first and second generation cephalosporins, aztreonam, ticarcillin-clavulanate and the carbapenems. Piperacillin-tazobactam, ceftazidime, minocycline, rifampicin, trimethoprim-sulfamethoxazole and quinolones usually remain effective [3].

Since *C. indologenes* is a rare human pathogen, its clinical significance has not yet been fully established. To the best of our knowledge, the latest case series published described six cases of *C. indologenes* infections, 2012-2015, all in pediatric patients [12].

We thus aimed in this study to describe the clinical and microbiological characteristics of seven adult patients with *C. indologenes* bacteremia in our institution over a six-year period (2009-2014).

2. Methods

The Rabin medical center is a 1000 bed, teaching, tertiary care facility located in central Israel. It serves a population of over 500,000 people and includes, among other services, advanced transplantation and oncology services.

Study population: All adult patients with a blood culture positive for *C. indologenes* in the study period (2009-2014) were identified retrospectively and their medical records were reviewed. There were no other inclusion or exclusion criteria.

An episode of clinical infection was defined by at least one blood culture positive for *C. indologenes* together with clinical sepsis. Recent surgery was defined by a procedure performed within the previous month. Empirical appropriate antibiotic therapy was defined as the use of at least one antibiotic to which the or-

ganism was susceptible prior its identification by the microbiological laboratory. Death was considered related to the bacteremia if the patient died within a week after its onset.

Blood culture samples were processed using BACTEC-FX (Becton Dickinson, USA). Positive cultures following Gram staining were subcultured on blood agar, chocolate agar and MacConkey agar plates.

The Brucker MALDI-TOF (Brucker, USA) system was used for *C. indologenes* identification. MIC values for *C. indologenes* isolates were determined by direct sensitivity using the disc diffusion method. The MICs for susceptibility were determined according to the CLSI standards.

The study was approved by Rabin Medical Center's Ethics Committee.

3. Results

3.1. Patients Characteristics

Seven episodes of *C. indologenes* bacteremia in seven patients were identified during the study period (2009-2014). The patients' clinical characteristics are presented in Table 1.

Female patients constructed the majority of our patient population (71%). The mean age was 76.8 years (41 - 92). Serious underlying conditions, such as chronic renal failure, diabetes and dementia were present in all patients. All patients but one, presented after a recent invasive healthcare related intervention: drainage of an intracranial epidural hematoma, complicated coronary artery

Table 1. Patient characteristics.

Patient no	Gender	Age	Comorbidities	Presentation	Invasive procedure	Mechanical ventilation	Proper empiric treatment	Outcome
1	M	86	Type II DM, AF, CVA	Epidural hematoma with sugrical drainage, pneumonia	Craniotomy	No	No	Recovery
2	F	92	Dementia, chronic care facility, AF, CRF	Sepsis	None	No	No	Died
3	M	79	AF, COPD, CRF, STEMI, CHF	Coronary angiography complicated with bleeding	Coronary angiography	No	Yes	Recovery
4	F	41	ESRD, DM	Infection of AV fistula	Removal of infected AV fistula, insersion of perma-cath	No	Yes	Recovery
5	F	68	Type II DM, recent renal transplantation	Renal abscess with drainage	Renal transplant	No	No	Recovery
6	F	88	AF	Hiatal hernia repair complicated with pneumonia	Hiatal hernia repair, tracheostomy	Yes	Yes	Recovery
7	F	84	Dementia, chronic care facility, AF, CRF	Abscess in amputation stump	Amputation	Yes	Yes	Died

Type II DM = type II diabetes mellitus; AF = Atrial Fibrillation; CVA = Cerebrovascular Accident; CRF = Chronic Renal Failure; COPD = Chronic Obstructive Pulmonary Disease; STEMI= ST Elevation Myocardial Infarction; ESRD = End Stage Renal Disease.

stents placement, arteriovenous shunt installment with a gortex graft, drainage of an abscess in a recently transplanted kidney, surgical correction of an incarcerated diaphragmatic hernia and the surgical debridement of an abscess complicating a limb amputation. Two patients required mechanical ventilation. Two patients died.

Four patients were treated empirically with appropriate antibiotics, of these, three patients survived. In all these cases, the agent given to which the isolate was susceptible was ciprofloxacin.

Among the three patients who were treated empirically with inappropriate antibiotics, only two survived.

3.2. Antimicrobial Resistance

The susceptibility and resistance results of all *C. indologenes* are presented in Table 2.

All isolated were susceptible to minocycline and to piperacillin-tazobactam.

Table 2. Culture resistance profile.

Antibiotic\Patient ID	1	2	3	4	5	6	7
Amikacin	I	R	R	R	R	R	I
Amoxicillin/Clavul Acid	R	R	I	R	R	R	R
Ampicillin	R	R	R	R	R	R	R
Ampicillin/sulbactam	R	R	R	R	R	R	R
Cefotaxime	I	R	R	R	R	I	I
Ceftazidime	S	S	S	S	R	S	S
Ceftriaxone	R	R	I	R	R	I	I
Cefuroxime	R	R	R	R	R	R	R
Cephalothin	R	R	R	R	R	R	R
Ciprofloxacin	S	S	S	S	R	S	S
Colistin	R	R	R	R	R	R	R
Ertapenem	R	R	R	R	R	R	R
Gentamicin	ND	R	R	R	R	R	S
Imipenem	R	R	R	R	R	R	I
Meropenem	R	R	R	R	R	R	R
Minocycline	S	S	S	S	S	S	S
Ofloxacin	S	S	S	S	R	S	S
Piperacillin	S	S	I	S	I	S	S
Sulfamethoxa/Trimeth	ND	ND	S	S	R	I	S
Tazocin	S	I	S	S	I	S	S
Ticarcillin/Clav Ac	R	R	R	R	R	R	I

R = Resistant; S = Susceptible; I = Intermediate; ND = no data.

All but one isolates were susceptible to quinolones, trimethoprim-sulfamethoxazole and ceftazidime.

All isolates were resistant to aminoglycosides, cephalosporins (apart from ceftazidime), penicillins (apart from piperacillin-tazobactam), colistin and the carbapenems.

4. Discussion

Chryseobacterium indologenes is a non fermentative Gram negative bacillus widely distributed in nature [1]. Although a rare human pathogen, serious infections caused by *C. indologenes* have been increasingly reported in recent years [5] [12] [13] [14]. Most of the reported infections occurred in immunocompromised patients or in patients with invasive devices during their hospital stay [15] [16] where it can persist on wet surfaces and in fluid containing apparatuses [17]. Most isolates reported are from clinical specimens other than blood [3], limited data is available on characteristics, treatment and outcome of patients with *C. indologenes* bacteremia.

We present a cohort of seven patients who had *C. indologenes* bacteremia over a period of six-year in a large tertiary medical center. As reported in previous publications, all patients had severe underlying conditions, such as diabetes, end stage renal disease, pneumonia necessitating mechanical ventilation, heart failure and intracranial bleeding. All patients were, to a different extent, immunocompromised: either due to age related immunosenescence, diabetes or immunosuppressant medications. All but one of the patients had undergone a recent invasive procedure in a hospital: Drainage of an epidural hematoma, a coronary percutaneous intervention with complications, the formation of an arteriovenous fistula, drainage of a transplanted kidney abscess, the correction of a diaphragmatic hernia and debridement of an abscess complicating a surgical amputation wound. The mean age of our patients was 76 years, but four of them were above the age of 80 years, which is older than in previous reports [8] [18] [19]. In contrast to previous reports, females were predominant in our study [8] [18]. Also in contrast to previous reports, most of our patients had not received previous, prolonged courses of antibiotics [8]. We therefore suggest that *C. indologenes* is a pathogen that might cause bacteremia in elderly patients with multiple co-morbidities who have undergone various hospital procedures, most probably as a result of a breach in infection control practices.

C. indologenes is inherently resistant to many antimicrobial agents [3], with a nearly uniform resistance to extended spectrum penicillins, cephalosporins (other than ceftazidime, cefepime), aztreonam, ticarcillin-clavulanate, the carbapenems, macrolides, aminoglycosydes and macrolides and chloramphenicol has been reported. *C. indologenes* remains susceptible, in most reports, to minocycline, ceftazidime, piperacillin-tazobactam, rifampin, the quinolones and trimethoprim-sulfamethoxazole [20]. In our study, the resistance and susceptibility patterns, as determined by the disc diffusion method, were consistent with

prior reports. In all four cases where empirical antibiotic treatment was deemed appropriate, ciprofloxacin was the administered agent. One isolate demonstrated was pan-resistant, fully susceptible only to minocycline. It had infected a 68-year-old renal transplant patient who recovered after her kidney abscess was successfully drained despite not having received appropriate empirical treatment. The resistance patterns we observed remained stable during the study period.

One of the four patients who received appropriate empirical antibiotic treatment died, as compared to one of the three patients who did not receive such treatment. Both these patients were elderly, had dementia and resided in chronic care facilities. The attributable mortality of *C. indologenes* as suggested in previous literature is around 17% [2] [18]. Although the calculated mortality in our study (two out of seven patients, 28%) was higher than previously reported, the two patients who died were both elderly, with advanced dementia and residing in chronic care facilities, for which appropriate treatment did not confer a survival benefit, just as inappropriate treatment was not associated with a higher mortality rate. Therefore, our results are in agreement with the literature published thus far, according to which *C. indologenes* bacteremia is not necessarily associated with an unfavorable outcome. We believe patients' outcome is mainly driven by host factors rather than bacterial virulence factors.

Despite our limited number of cases, to the best of our knowledge, our study serves as the largest cohort of adult patients with *C. indologenes* bacteremia reported in recent years. Risk factors repeatedly reported for *C. indologenes* bacteremia include advanced age, immunosuppression, and previous invasive procedures. Although the optimal antibiotic choice remains to be determined, quinolones as well as trimethoprim-sulfamethoxazole seem to provide appropriate antimicrobial coverage. Further surveillance programs are necessary to fully elucidate the clinical importance of this rare pathogen and to inform recommended antibiotic therapies.

Conflicts of Interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

Ethical Approval

This study was approved by the ethics committee in Belinson Hospital, Rabin Medical Center, PetachTikva, Israel, and had therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

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