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Original Article

Clinical and Microbiological Characteristics of *Chryseobacterium indologenes* Bacteremia

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BACKGROUND/PURPOSE: Reports detailing bacteremia caused by *Chryseobacterium indologenes* remain limited, with most cases reported in Taiwan. The clinical significance of *C. indologenes* has not been fully established. This retrospective study investigated the clinical features and antimicrobial susceptibility of *C. indologenes* bacteremia.

METHODS: Patients with *C. indologenes* bacteremia were identified at a medical center/teaching hospital in northern Taiwan between January 1, 2004 and January 31, 2008. Clinical features and the antimicrobial susceptibilities of these patients were analyzed.

RESULTS: Sixteen isolates of *C. indologenes* from 16 episodes in 16 patients were identified, with all patients having underlying diseases. Two patients (12.5%) had polymicrobial bacteremia. The portal of bacteremia was not determined in most cases. Other clinical syndromes included catheter-related bacteremia, urinary tract infection and peritonitis. The majority of patients had undergone invasive procedures. Other associated conditions included immunosuppression, neutropenia and prolonged use of antibiotics. Only three patients were treated with appropriate antibiotics according to minimum inhibitory concentrations. The susceptibilities of isolates to trimethoprim-sulfamethoxazole (75.0%), levofloxacin (62.5%), piperacillin-tazobactam (50.0%), ciprofloxacin (43.75%) and cefepime (12.5%) were variable and the bacteremia-related mortality rate was 6.25%.

CONCLUSION: *C. indologenes* isolates are resistant to multiple antibiotics, with newer fluoroquinolones and trimethoprim-sulfamethoxazole possibly representing the most appropriate antimicrobial agents to treat infections caused by this pathogen. However, the pathogenicity and factors of virulence for

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C. indologenes remain unclear, with our study revealing favorable outcomes of *C. indologenes* bacteremia. Epidemiological surveillance of this organism in Taiwan and extensive worldwide surveillance programs are required.

KEYWORDS: antibacterial agents, bacteremia, *Chryseobacterium indologenes*

Introduction

Chryseobacterium species are a group of non-motile, catalase-positive, oxidase-positive, indole-positive and non-glucose-fermenting Gram-negative bacilli. The genus *Chryseobacterium* includes six species that were previously designated as members of the genus *Flavobacterium*.[1] *C. gleum* and *C. indologenes*, formerly known as *Flavobacterium* CDC group IIb, have been clearly differentiated by DNA–DNA homology and eight phenotypic characteristics.[2] *C. meningosepticum* and *C. indologenes* are two species commonly isolated from clinical specimens with *C. meningosepticum* the most pathogenic member of the genus. However, the clinical significance of *C. indologenes* has not been fully established because this bacterium is not frequently recovered from clinical specimens. *C. indologenes* is a rare pathogen in humans and is not normally present in the human microflora although it is widely distributed in nature.[3] To the best of our knowledge, there are only 42 reported cases of *C. indologenes* bacteremia in the literature, with most cases reported in Taiwan.[3–12]

In this study, we analyzed 16 patients with *C. indologenes* bacteremia in our institute over a 4-year period. We highlighted the clinical features of *C. indologenes* bacteremia as well as the antimicrobial susceptibility pattern of this pathogen.

Methods

Patient identification

Patients with *C. indologenes* bacteremia were identified retrospectively from blood culture reports, from the clinical microbiology laboratory at Taipei Veterans General Hospital (TVGH) between January 1, 2004 and January 31, 2008. The TVGH is a medical center and teaching hospital with a capacity of 2,900 beds in northern Taiwan. All medical records of patients whose blood cultures positive for *C. indologenes* were reviewed retrospectively. Patients younger than 18 years of age were excluded. There was no apparent outbreak of *C. indologenes* infection during the time of our study.

Definitions

An episode of significant bacteremia was defined as one or more blood cultures positive for *C. indologenes* together with clinical sepsis. Bacteremia without clinical sepsis was considered contamination and was excluded. Nosocomial bacteremia was defined as bacteremia occurring ≥ 48 hours after admission, or bacteremia for which the patient had been hospitalized at any time within the previous month. Central venous catheter (CVC)-related bacteremia was recorded when *C. indologenes* was isolated simultaneously from blood and either the tip of the catheter or purulent discharge from the CVC site, or there was a positive blood culture for *C. indologenes* with the presence of inflammation at the CVC site without another identifiable source of infection. Prolonged antibiotic use defined as administration of intravenous antibiotics for more than 14 days within a 30-day period prior to the diagnosis of bacteremia. Immunosuppressive therapy was defined as the use of cytotoxic agents or corticosteroids (> 30 mg prednisolone daily or equivalent for ≥ 1 week). Neutropenia defined as an absolute neutrophil count less than 500/μL. Recent surgery defined as a surgical procedure performed within 1 month prior to the onset of *C. indologenes* bacteremia. Appropriate antibiotic therapy defined as the use of at least one intravenous antibiotic to which the microorganism was susceptible according to minimum inhibitory concentration (MIC) testing within 72 hours of the diagnosis of bacteremia. Death was considered to have been related to bacteremia if the patient died ≤ 14 days after the onset of bacteremia and if no other cause of death was identified.

Microbiology

Blood culture samples were processed using the BACTEC NR-660 instrument (Becton Dickinson, Sparks, MD, USA). All positive cultures were examined following Gram staining and were subcultured on blood agar plates and eosin-methylene blue agar plates for further identification. All isolates were oxidase-positive Gram-negative rods that did not ferment glucose. The ID32 GN system (bioMérieux, Marcy l'Etoile, France) was used for identifying *C. indologenes*. All blood culture isolates were stored at –70°C and these frozen stocks were subcultured twice before further confirmation. The VITEK 2 system (bioMérieux) with a VITEK 2 GN card was used to confirm bacterial identification according to the manufacturer's instructions.

The MIC values for bacteremic isolates of *C. indologenes* were performed using the VITEK 2 system with an AST GN-09 card following the manufacturer's instructions. The breakpoints of MICs for susceptibility were determined by applying the Clinical and Laboratory Standards Institute (CLSI) standards for susceptibility for *Pseudomonas aeruginosa* and non-*Enterobacteriaceae*.[13]

Results

Bacterial isolates

Sixteen isolates of *C. indologenes* were initially identified by the ID32 GN system during the study period. The VITEK 2 system with a VITEK 2 GN card was used to confirm the identity of bacteria. All 16 microorganisms were identified as *C. indologenes*.

Clinical characteristics

Sixteen significant episodes of *C. indologenes* bacteremia in 16 patients were identified during the study period. The clinical characteristics of the 16 patients with *C. indologenes* bacteremia are summarized in Tables 1 and 2. Male patients predominated (75%), and the mean age of affected patients was 66 years (range, 44–86 years), with seven patients older than 80 years.

Underlying diseases were present in all patients and all bacteremic episodes were nosocomial. Two patients (12.5%) had polymicrobial bacteremia and *C. indologenes* was also isolated simultaneously from other sites in two patients. Of the 16 patients, 13 patients had associated conditions, including central venous catheterization ($n=7$), indwelling urinary catheter ($n=7$), immunosuppression ($n=5$), prolonged antibiotics use ($n=5$), ventilator use ($n=3$), neutropenia ($n=3$), recent surgery ($n=2$), intensive care unit admission ($n=2$), total parenteral nutrition ($n=1$), percutaneous nephrostomy ($n=1$) and jejunostomy ($n=1$). The most common clinical manifestation was primary bacteremia. In addition to the 12 patients with primary bacteremia, two patients had catheter-related bacteremia and one patient had urinary tract infection and peritonitis.

Three patients (18.8%) were treated with antibiotics appropriate to the MIC test results; their condition improved within 5 days of the initiation of treatment. Of the 13 patients not treated with appropriate antibiotics, 10 patients improved within 7 days of the initiation of antibiotics. The CVC was removed from the two patients not treated with appropriate antibiotics for catheter-related bacteremia. Two patients died within 14 days after the onset of bacteremia. One patient (patient 13) died of acute myocardial infarction on the second day of admission; therefore, the clinical response to antibiotics could not be determined. Only one patient (6.3%) not treated with appropriate antibiotics fulfilled the definition of bacteremia-related mortality. Bacteremia occurred on the 58th day of hospitalization and he received antibiotics for a prolonged period before the onset of bacteremia. Sepsis progressed despite treatment with cefepime and he died on the 12th day after bacteremia onset.

Antimicrobial susceptibility

The results of susceptibility testing with antimicrobial agents are shown in Table 3. Our isolates were susceptible to trimethoprim-sulfamethoxazole (75.0%), levofloxacin (62.5%), ciprofloxacin (43.8%), piperacillin-tazobactam (50.0%) and cefepime (12.5%), but at various levels. All isolates were resistant to other β-lactam antibiotics and aminoglycosides.

Discussion

C. indologenes is widely distributed in nature but is a rare human pathogen. It has been isolated from clinical specimens but rarely from blood[3] and has been shown to cause a variety of invasive infections, such as primary bacteremia, catheter-related bacteremia, wound sepsis, cellulitis,

Table 1. Demographic and clinical characteristics of 16 patients with bacteremia caused by *Chryseobacterium indologenes*

Case	Age (yr)/sex	Underlying conditions	Other associated conditions	Clinical syndrome	Date of isolation (day after admission)	Department[b]	Other bacteria isolated[c]	Other sites of *C. indologenes* isolation
1	81/M	DM, HTN	Ventilator, prolonged ABX use, UIC	Primary bacteremia	20040316 (Day 89)	Chest	*P. aeruginosa*, *Enterobacter cloacae*	–
2	46/M	Burkitt's lymphoma	CVC, immunosuppression neutropenia	Primary bacteremia	20040401 (Day 1)	Oncology	–	–
3	83/M	DM, HTN, Dementia in bed ridden status	CVC, UIC, prolonged ABX use, recent surgery	Catheter-related bacteremia	20041022 (Day 30)	Urology	–	CVC tip
4	77/M	Old CVA in bedridden status	CVC, TPN, UIC, jejunostomy, prolonged ABX use	Primary bacteremia	20041220 (Day 58)	Infectious disease	–	–
5	66/F	DM, HTN, CKD, Urothelial cell carcinoma of right kidney	CVC, left PCN, immunosuppression, neutropenia	Primary bacteremia	20050106 (Day 4)	Oncology	–	–
6	83/M	Prostate cancer, HTN, CKD	UIC, prolonged ABX use	Urinary tract infection	20050413 (Day 131)	Allergy-Immunology-Rheumatology	–	Urine
7	66/M	Motor neuron disease, COPD, HTN, DM	Ventilator, UIC, recent surgery, ICU admission, prolonged ABX use	Primary bacteremia	20050930 (Day 9)	ICU	–	–
8	44/M	Neuroendocrine tumor of liver, CKD	CVC, immunosuppression	Peritonitis	20050926 (Day 13)	Oncology	*E. coli*	–
9	56/F	Breast cancer	CVC, immunosuppression	Catheter-related bacteremia[a]	20051011 (Day 14)	Oncology	–	–
10	54/F	Right knee MFH, HTN	CVC, immunosuppression, neutropenia	Primary bacteremia	20051217 (Day 18)	Oncology	–	–
11	81/M	CHF, CVA, DM, CKD	–	Primary bacteremia	20060222 (Day 13)	Cardiology	–	–
12	86/M	CHF, DM, HTN	–	Primary bacteremia	20070930 (Day 5)	Nephrology	–	–
13	72/F	CHF, lymphoma	ICU admission	Primary bacteremia	20071017 (Day 17)	ICU	–	–
14	84/M	Compression fracture of L spine in bed ridden status	UIC	Primary bacteremia	20071218 (Day 15)	General Rehabilitation	–	–
15	78/M	CHF, CKD, COPD, DM	CVC, ventilator, UIC, prolonged ABX use	Primary bacteremia	20080131 (Day 89)	Respiratory Intensive Care Unit	–	–
16	80/M	CHF, DM, CKD, HTN	–	Primary bacteremia	20080122 (Day 8)	Nephrology	–	–

[a]Case 9 presented with inflammation at the insertion site of CVC without another identifiable source of infection; [b]Department in which bacteremia occurred; [c]other bacteria isolated (polymicrobial bacteremia). M=male; F=female; DM=diabetes mellitus; HTN=hypertension; ABX=antibiotics; CVC=central venous catheter; TPN=total parenteral nutrition; CVA=cerebrovascular accident; PCN=percutaneous nephrostomy; CKD=chronic kidney disease (the CKD listed above only includes those at a stage greater than 3); ICU=intensive care unit; COPD=chronic obstructive pulmonary disease; CHF=congestive heart failure; MFH=malignant fibrous histiocytoma; UIC=urinary indwelling catheter; *P. aeruginosa*=*Pseudomonas aeruginosa*; *E. coli*=*Escherichia coli*.

Table 2. Treatment and outcomes of 16 patients with bacteremia caused by *Chryseobacterium indologenes*[a]

Case	Antibiotic treatment	Appropriate antibiotic use	Clinical response	Outcome	Day of mortality[b]
1	Ciprofloxacin	Yes	Improved	Died of other causes	Day 58
2	Piperacillin-tazobactam plus amikacin	No	Improved	Survival	–
3	Oral cefadroxil associated removal of CVC	No	Improved	Survival	–
4	Cefepime	No	Failure	Bacteremia-related mortality	Day 12
5	Piperacillin-tazobactam	No	Improved	Survival	–
6	Ciprofloxacin	No	Failure	Died of other causes	Day 28
7	Amoxicillin-clavulanate plus isepamicin	No	Improved	Survival	–
8	Cefepime + fosfomycin	Yes	Improved	Died of other causes	Day 21
9	Ceftazidime associated removal of CVC	No	Improved	Died of other causes	Day 52
10	Ceftazidime + isepamicin	No	Improved	Survival	–
11	Amoxicillin-clavulanate	No	Improved	Survival	–
12	Amoxicillin-clavulanate	No	Improved	Survival	–
13	Ceftriaxone	No	Indeterminate	Died of other causes	Day 2
14	Cefuroxime	No	Improved	Survival	–
15	Ciprofloxacin	Yes	Improved	Survival	–
16	Ceftazidime	No	Improved	Survival	–

[a]Infections were nosocomial in all patients. Patient 2 was discharged from oncology department 1 week earlier; Patient 13 was transferred from a local medical department where she had been hospitalized for 17 days prior to admission to our hospital. Bacteremia occurred in different wards of the oncology department. Patients 1 and 6 died of ventilator-associated pneumonia. Patients 8 and 9 were in the terminal stages of underlying malignancy and subsequently died. Patient 13 died of acute myocardial infarction; [b]day of mortality after onset of bacteremia. CVC = central venous catheter.

Table 3. Antimicrobial spectrum of selected antimicrobial agents against *Chryseobacterium indologenes*

Antimicrobial agent	MIC range (μg/mL)	MIC_{50} (μg/mL)	MIC_{90} (μg/mL)	Susceptibility breakpoint (μg/mL)	No of isolates susceptible[a]
Ciprofloxacin	1 to ≥ 4	2	≥ 4	≤ 1	7 (43.75)
Levofloxacin	1 to ≥ 8	1	≥ 8	≤ 2	10 (62.5)
Piperacillin	64 to ≥ 128	≥ 128	≥ 128	≤ 16	0 (0)
Piperacillin-tazobactam	≤ 4 to ≥ 128	16	≥ 128	≤ 16	8 (50.0)
TMP-SMZ	≤ 1/19 to ≥ 16/304	2/38	≥ 16/304	≤ 2/38	12 (75.0)
Cefepime	4 to ≥ 64	≥ 64	≥ 64	≤ 8	2 (12.5)
Ceftazidime	16 to ≥ 64	≥ 64	≥ 64	≤ 8	0 (0)
Ceftriaxone	≥ 64	≥ 64	≥ 64	≤ 8	0 (0)
Aztreonam	≥ 64	≥ 64	≥ 64	≤ 8	0 (0)
Imipenem	≥ 16	≥ 16	≥ 16	≤ 4	0 (0)
Meropenem	≥ 16	≥ 16	≥ 16	≤ 4	0 (0)
Amikacin	32 to ≥ 64	≥ 64	≥ 64	≤ 16	0 (0)
Gentamicin	8 to ≥ 16	≥ 16	≥ 16	≤ 4	0 (0)
Tobramycin	≥ 16	≥ 16	≥ 16	≤ 4	0 (0)

[a]Data presented as *n* (%).TMP-SMZ = trimethoprim-sulfamethoxazole; MIC = minimal inhibitory concentration; MIC_{50} = MIC for 50% of isolates; MIC_{90} = MIC for 90% of isolates.

pyonephrosis, peritonitis, biliary tract infection and ventilator-associated pneumonia.[3–12] In the hospital environment, it is frequently recovered from wet surfaces and water systems by virtue of its ability to contaminate and persist in fluid-containing apparatuses.[12]

It is interesting to note that infections caused by *C. indologenes* have been reported mainly from patients in Taiwan.[3–5,8] However, studies aimed at epidemiological surveillance of this organism in various hospitals in Taiwan are lacking, and further molecular typing of these isolates may help us elucidate the linkage of nosocomial infection.

In the literature, most cases of *C. indologenes* bacteremia were detected in hospitalized patients with a severe underlying disease, such as malignancies or diabetes mellitus, or indwelling devices.[3–12] In the present report, the majority of underlying diseases were malignancy, diabetes mellitus, hypertension, congestive heart failure and chronic kidney disease greater than stage 3. The mean age of our patients was 66 years, which is older than in a previous report (50.5 years).[5] Male were predominant in our study, and this finding is compatible with previous reports.[3–12] Twelve of the 16 patients had undergone various invasive procedures, such as central venous catheterization, urinary catheterization, respiratory assistance or recent surgery. It was uncertain as to whether these procedures were responsible for bacteremia, and it may suggest that a breakdown of infection control techniques was a likely cause of infection. As a result, we suggest that *C. indologenes* should be included in the list of pathogens that cause bacteremia in immunocompromised hosts, patients with multiple comorbidities, patients who have undergone various invasive procedures and patients who received antibiotics over a prolonged period during hospitalization.

In the present study, bacteremia were nosocomially acquired and most bacteremia (11/16) developed at least 10 days after admission. This finding was consistent with the literature that most cases of *C. indologenes* bacteremia were due to nosocomial infection.[3–12] Hsueh et al found nosocomial pneumonia and catheter-related bacteremia accounted for most cases.[3–5] In this series, primary bacteremia was the most common clinical syndrome, accounting for 75.0% (12/16) of cases. Although the portal of bacteremia was not clearly defined in most patients, it may be the result of insufficient microbiological study and the retrospective characteristic of this study. Most bacteremia developed when the CVC was kept in place and catheter-related bacteremia may be underestimated in our study. The production of biofilm on foreign materials and protease activity may play an important role in the virulence of invasive infections due to *C. indologenes*.[13]

The choice of an effective drug for the empirical treatment of infections due to *C. indologenes* is sometimes difficult due to the limited data in the literature. In addition, the results of susceptibility testing vary when different methods are used. However, *in vitro* susceptibilities determined by the disk diffusion method showed poor correlation compared with the broth microdilution method, which is the preferred methodology.[15–17] The MIC breakpoints for these organisms have not been established by the CLSI.[14] Nearly uniform resistance to extended-spectrum penicillins, first- and second-generation cephalosporins, ceftriaxone, aztreonam, ticarcillin-clavulanate, imipenem, meropenem, chloramphenicol, erythromycin and aminoglycosides has been reported. Piperacillin-tazobactam, piperacillin, cefoperazone, ceftazidime, cefepime, cefpirome, minocycline, rifampicin and trimethoprim-sulfamethoxazole, however, are usually effective.[5,15–17] According to the results obtained from the SENTRY Antimicrobial Surveillance Program, the newer fluoroquinolones (garenoxacin, gatifloxacin and levofloxacin) may represent the most appropriate antimicrobial agents to treat *C. indologenes* infections. *C. indologenes* is usually resistant to imipenem due to constitutive production of metallo-β-lactamase.[17]

In this study, *C. indologenes* isolates showed various susceptibilities to trimethoprim-sulfamethoxazole, levofloxacin, ciprofloxacin, piperacillin-tazobactam and cefepime. All of the isolates were resistant to other β-lactam antibiotics and aminoglycosides, which was in accordance with previous reports.[3–12,17] However, contrary to previous reports,[3–12,17] all our isolates were resistant to ceftazidime and piperacillin. Cefepime exhibited poor activity (12.5% susceptible) against these pathogens, which was significantly lower. Among the β-lactams, the most active agent overall was piperacillin-tazobactam (50% susceptible), which showed a much lower susceptibility rate. Our analysis showed that trimethoprim-sulfamethoxazole (75% susceptible) was the most potent agent against the overall collection of *C. indologenes*. Fluoroquinolones also showed lower activity (ciprofloxacin 43.8% susceptible,

levofloxacin 62.5% susceptible) than in the SENTRY Antimicrobial Surveillance Program (ciprofloxacin 85% susceptible, levofloxacin 100.0% susceptible). However, only one report on the treatment of *C. indologenes* infection with newer fluoroquinolones was identified in the literature; this case was treated with levofloxacin successfully.[6] Further research is required to define the role of newer fluoroquinolones in the treatment of *C. indologenes* infections.

Our study revealed an increased rate of resistance in *C. indologenes* to previously potent antibiotics. We have two explanations for this phenomenon. First, the age of patients in our series was older than in previous reports.[3–5,17] Marchaim et al described an increase in the incidence and resistance of Gram-negative organisms causing bacteremia, concomitant with older patients.[18] Second, our analysis covered the years from 2004 to 2008. The isolates in the SENTRY Antimicrobial Surveillance Program were collected from 1997 to 2001.[18] The isolates of Dr Hsueh's report were from 1992 to 1995.[3–5] A 13-year study in a hospital demonstrated that significant changes in antimicrobial use might have affected antimicrobial resistance in certain Gram-negative bacteria from the hospital.[19] Hence we speculate that the resistant pattern of *C. indologenes* may evolve over time and vary according to different trends of antibiotic usage.

In the present study, our patients received antibiotics on the basis of the results of the routinely used disk diffusion test, and the appropriate use of antibiotics was judged according to MIC testing. Although most of our patients did not receive appropriate antibiotics according to MIC testing, they recovered from *C. indologenes* bacteremia and only one patient died. This patient had been subject to prolonged antibiotic usage hospitalization before the onset of bacteremia. Multiple indwelling devices were kept in place in this patient, possibly implying that the production of a biofilm on foreign materials contributed to invasive disease and poor outcome. In other literature, the mortality attributable to *C. indologenes*-related infections was around 14–17%.[3–5] In one study, only one-third of the patients infected with *C. indologenes* received appropriate antibiotics according to MIC testing.[5] Although our data showed a lower rate (18.8%) of appropriate antibiotic usage according to MIC testing, our data implied a favorable outcome of *C. indologenes* bacteremia. Additionally, our study revealed that the outcome of *C. indologenes* bacteremia was not principally influenced by the antibiotic itself. Underlying immune defenses and other associated clinical conditions may determine the prognosis of *C. indologenes* bacteremia. The possibility exists that these are cases of pseudobacteremia due to contamination by *C. indologenes* during the management of blood cultures. However, this possibility is difficult to verify, especially in patients with severely debilitating diseases.[5]

Hsueh et al indicated that indwelling-device-related infections caused by *C. indologenes* did not always require removal of devices. In his report, six of seven patients were successfully treated with appropriate antibiotics when the devices were kept in place.[3] Two patients in our study with catheter-related bacteremia were successfully treated without appropriate antibiotics against *C. indologenes* when the catheter was removed. Due to the wide range of antibiotic resistance and difficulty in determining optimal therapeutic regimens, we suggest that indwelling devices should be removed as soon as possible if indwelling device-related *C. indologenes* infection is suspected.

In conclusion, despite the limited case numbers in this study, it serves as the largest analysis of clinical and microbiological data on *C. indologenes* bacteremia over the last 10 years. The pathogenicity and factors for virulence of *C. indologenes* remain unclear, yet our data implied a favorable outcome of bacteremia. The source of bacteremia has not yet been clearly identified. The risk factors for *C. indologenes* bacteremia included invasive procedures, immunosuppression, neutropenia and prolonged use of antibiotics. The unique resistance of this organism to multiple antibiotics makes it difficult to determine the optimal therapeutic option. Newer fluoroquinolones and trimethoprim-sulfamethoxazole may represent the most appropriate antimicrobial agents to treat infections caused by this pathogen. Further studies aimed at epidemiological surveillance of this organism in Taiwan are essential to clarify the linkage to nosocomial infections. Furthermore, extensive worldwide surveillance programs are vital to the formulation of appropriate antimicrobial therapies and understanding the clinical context in which this rare pathogen is isolated.[18]

References

1. Vandamme P, Bernardet JF, Segers P, Kersters K, Holmes B. New perspectives in the classification of the flavobacteria: description

of *Chryseobacterium gen. nov*., *Bergeyella gen. nov*., and *Empedobacter nom. rev*. *Int. J. Syst. Bacteriol* 1994;44:827–31.

2. Yabuuchi E, Hashimoto Y, Ezaki T, Ido Y, Takeuchi N. Genotypic and phenotypic differentiation of *Flavobacterium indologenes* Yabuuchi et al 1983 from *Flavobacterium gleum* Holmes et al 1984. *Microbiol Immunol* 1990;34:73–6.
3. Hsueh PR, Hsiue TR, Wu JJ, Teng LJ, Ho SW, Hsieh WC, et al. *Flavobacterium indologenes* bacteremia: clinical and microbiological characteristics. *Clin Infect Dis* 1996;23:550–5.
4. Hsueh PR, Teng LJ, Ho SW, Hsieh WC, Luh KT. Clinical and microbiological characteristics of *Flavobacterium indologenes* infections associated with indwelling devices. *J Clin Microbiol* 1996;34: 1908–13.
5. Hsueh PR, Teng LJ, Yang PC, Ho SW, Hsieh WC, Luh KT. Increasing incidence of nosocomial *Chryseobacterium indologenes* infections in Taiwan. *Eur J Clin Microbiol Infect Dis* 1997;16: 568–74.
6. Green BT, Nolan PE. Cellulitis and bacteraemia due to *Chryseobacterium indologenes*. *J Infect* 2001;42:219–20.
7. Nulens E, Bussels B, Bols A, Gordts B, Van Landuyt HW. Recurrent bacteremia by *Chryseobacterium indologenes* in an oncology patient with a totally implanted intravascular device. *Clin Microbiol Infect* 2001;7:391–3.
8. Lin JT, Wang WS, Yen CC, Liu JH, Chiou TJ, Yang MH, et al. *Chryseobacterium indologenes* bacteremia in a bone marrow transplant recipient with chronic graft-versus-host disease. *Scand J Infect Dis* 2003;35:882–3.
9. Cascio A, Stassi G, Costa GB, Crisafulli G, Rulli I, Ruggeri C, et al. *Chryseobacterium indologenes* bacteraemia in a diabetic child. *J Med Microbiol* 2005;54:677–80.
10. Christakis GB, Perlorentzou SP, Chalkiopoulou I, Athanasiou A, Legakis NJ. *Chryseobacterium indologenes* non-catheter-related bacteremia in a patient with a solid tumor. *J Clin Microbiol* 2005; 43:2021–3.
11. Akay M, Gunduz E, Gulbas Z. Catheter-related bacteremia due to *Chryseobacterium indologenes* in a bone marrow transplant recipient. *Bone Marrow Transplant* 2006;37:435–6.
12. Bayraktar MR, Aktas E, Ersoy Y, Cicek A, Durmaz R. Postoperative *Chryseobacterium indologenes* bloodstream infection caused by contamination of distillate water. *Infect Control Hosp Epidemiol* 2007;28:368–9.
13. Pan HJ, Teng LJ, Chen YC, Hsueh PR, Yang PC, Ho SW, et al. High protease activity of *Chryseobacterium indologenes* isolates associated with invasive infection. *J Microbiol Immunol Infect* 2000;33:223–6.
14. Clinical and Laboratory Standards Institute (CLSI). *Performance standards for antimicrobial susceptibility testing. 17th informational supplement*. CLSI document M100-S17. Wayne, PA: Clinical and Laboratory Standards Institute, 2007.
15. Chang JC, Hsueh PR, Wu JJ, Ho SW, Hsieh WC, Luh KT. Antimicrobial susceptibility of *flavobacteria* as determined by agar dilution and disk diffusion methods. *Antimicrob Agents Chemother* 1997;41:1301–6.
16. Fraser SL, Jorgensen JH. Reappraisal of the antimicrobial susceptibilities of *Chryseobacterium* and *Flavobacterium* species and methods for reliable susceptibility testing. *Antimicrob Agents Chemother* 1997;41:2738–41.
17. Kirby JT, Sader HS, Walsh TR, Jones RN. Antimicrobial susceptibility and epidemiology of a worldwide collection of *Chryseobacterium* spp.: report from the SENTRY Antimicrobial Surveillance Program (1997–2001). *J Clin Microbiol* 2004;42:445–8.
18. Marchaim D, Zaidenstein R, Lazarovitch T, Karpuch Y, Ziv T, Weinberger M. Epidemiology of bacteremia episodes in a single center: increase in Gram-negative isolates, antibiotics resistance, and patient age. *Eur J Clin Microbiol Infect Dis* 2008;27:1045–51.
19. Hsueh PR, Chen WH, Luh KT. Relationships between antimicrobial use and antimicrobial resistance in Gram-negative bacteria causing nosocomial infections from 1991–2003 at a university hospital in Taiwan. *Int J Antimicrob Agents* 2005;26:463–72.