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Original Article

Chromobacterium violaceum infection: A clinical review of an important but neglected infection

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Abstract

Background: Increasing reported cases with *Chrombacterium violaceum* infection has been noticed in recent decades. It is noteworthy for its difficult-to-treat entity characterized by a high frequency of sepsis, easily distantant metastasis, multidrug-resistance, and frequent relapse, and high mortality rate.
Methods: The English-language literature was reviewed from 1952 through December 2009 by an electronic view via the PubMed and Medline databases and manual searches.
Results: One hundred and six patients with *Chrombacterium violaceum* infection from the literature were studied. The four leading clinical manifestations reviewed in the published literature, in the order of frequency, were fever (100%), sepsis (82%), skin lesions (67.9%), and abdominal pain (31.1%). Localized abscess was found in 52 patients (49%) and liver was the mostly common involved organ. Fifty-six patients (53%) were dead. Almost all of the penicillin, ampicillin, and first and second-generation cephalosporins exhibited totally resistant to *Chrombacterium violaceum*. The most important risk factors in mortality in 61 patients with *Chrombacterium violaceum* bacteremia were at a young age ($p = 0.0789$), presence of localized abscess ($p = 0.030$), shorter clinical course ($p < 0.001$), and inappropriate antimicrobial treatment ($p < 0.001$). Seven patients (6.6%) experienced of relapse or reinfection, with a median interval of 135 days (range, 4 to 1095 days).
Conclusions: A high index of suspicion for *Chromobacterium violaceum* infection is required along with prompt diagnosis, optimal antimicrobial therapy, and adequate therapeutic duration for a successful therapy.

Keywords: abscess; *Chromobacterium violaceum* infection; difficult-to-treat; metastasis; multidrug-resistant; relapse

1. Introduction

Chromobacterium violaceum is a gram-negative, facultative anaerobe, motile, oxidase-positive bacillus.[1] It is widely distributed in natural aquatic environments and is sensitive to temperature.[1–3] Usually it can produce an antioxidant pigment called violacein associated with remarkable purple color.[1] It grows easily on nutrient agar (blood agar and MacConkey agar media with incubation at 30 °C to 45 °C), producing distinctive smooth low convex colonies with a dark violet metallic sheen in the typical pigmented strain.[1] Infection due to *C. violaceum* is rare, so most clinicians are not familiar with it. However, human infection, while rare, does occur. In this review, most of the patients with this infection were healthy and young. Rapid progress to sepsis with metastatic abscess (liver, lung, or spleen) was the striking feature in *C. violaceum* infection.[1,4,5] Also, it is noteworthy to emphasize the multidrug-resistant characteristic of *C. violaceum* and the possibility of relapse. In addition, this microorganism may not be confined to a narrow geographic range (between latitudes 35°N and 35°S) as previously considered because of the effect of global climate change.[1–3] This study reviews and analyzes the patients with *C. violaceum* infection from the reported literature. The primary objective was to emphasize the characteristics of the difficult-to-treat in *C. violaceum* infection.

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2. Methods

2.1. Study design and patients

A English-language literature search from 1952 through 2009 was reviewed via the PubMed, Medline databases, and manual searches. Foreign-language cases were included only if the data provided were sufficient for evaluation.[6–10] One case with *C. violaceum* infection that occurred in Taiwan in September 2009 was enrolled in this study.[11] Eleven cases cited by Johnson and colleagues[12] in 1971 and eighteen cases cited by Anah and others[13] in 2008 were excluded because no relevant data could be evaluated. Because of the published nature of this review, patients with *C. violaceum* infection may be underestimated. The published journals were reviewed and clinical information, if available, including demographics, incubation period, predisposing factor, comorbidity, clinical presentation, laboratory and microbiologic data, antimicrobial therapy, outcome, complication, and clinical course, were obtained for analysis.

2.2. Definition

The referred year was defined as the time when patients were infected; however, if the author did not mention the time when patient was infected, the year referred to the time when the journal was published. Sepsis was considered if patients fulfilled the sepsis definition.[14] Patients were considered to have skin lesions if they had any of the following manifestations: papular rashes, ulcer, nodular lesion, skin abscess, vesicles, pustules, or lymphadenitis. Incubation period was defined as definite exposure to the predisposing factors to disease onset. Clinical course was defined as the interval from the onset of symptoms to death or discharge from hospital. A patient was considered to have exposure history if he/she had been exposed to water or soil before the illness. Antimicrobial susceptibility tests were obtained from the reviewed journals, if available. *C. violaceum* with an intermediate result during a susceptibility test was classified as resistant. Antimicrobial therapy was considered appropriate if the treatment regimen included at least one antimicrobial agent active against *C. violaceum in vitro*. However, it was considered inappropriate if the drugs did not have *in vitro* activity against the isolated strain or if the patient did not receive antimicrobial therapy. Healthcare-associated infection was defined as infection that occurred more than 48 hours after hospital admission. Isolation of *C. violaceum* with the same susceptibilities obtained from different clinical specimens in the same patient is defined as one isolate. The year 1990 was used as a reference year because of generally available of new antibacterial agents, including ciprofloxacin (U.S. Food and Drug Administration [FDA] approval in 1987) and imipenem/cilastatin (FDA approval in 1985).

2.3. Statistical analysis

Two-sample *t*-tests were used to compare the differences in continuous variables. Categorical data were compared using Fisher's exact test to resolve the concern of small sample sizes and sparse data. All statistical tests were analyzed with SPSS Statistics 17.0 software (SPSS Inc., Chicago, IL, USA). A p value of <0.05 was considered statistically significant.

3. Results

3.1. Demographic data of the patients

We studied 106 patients who presented with *C. violaceum* infection between 1952 and 2009.[1,4–10,12,13,15–36] More than one-half of the patients (65%) were infected after 1990 (Fig. 1). Reported infections were far more common in the northern hemisphere than in the southern hemisphere. Forty-four (42%) of the 106 patients were reported in the region of Americas, 43 (41%) in the East Western Pacific [including 10 in Australia, three in Vietnam, seven in Taiwan, one in Japan, three in Korea, six in China (including Hong Kong), seven in Malaysia, three in Singapore, one in Papua New Guinean, one in Cambodia, and one in Laos], 16 in South East Asia (including 10 in India, two in Sri Lanka, and four in Thailand), and three in Africa (Fig. 2).

3.2. Clinical characteristics and laboratory data of patients

The baseline demographic and medical characteristics of the 106 cases are listed in Table 1. Eighty percent of the infections occurred in males. Most of the infected patients were young, with a median age of 19.1 years old, ranging from 0 (newborn) to 80 years old, 46 (42%) of whom were ≤10 years old. All of the 106 patients were febrile. Incubation period from the available 46 patients revealed a median duration of 3 days (range, 1–90 days). Of the 106 patients, 33 (31.1%) had experienced abdominal pain, emergency surgery was undertaken in six (18.2%) during the clinical course, and localized abscess was found in four.[7,8,31] Seventy-two (68%) of the 106 patients had skin lesions during the clinical course, 87 (82%) had sepsis at presentation, and 61 (58%) had *C. violaceum* as

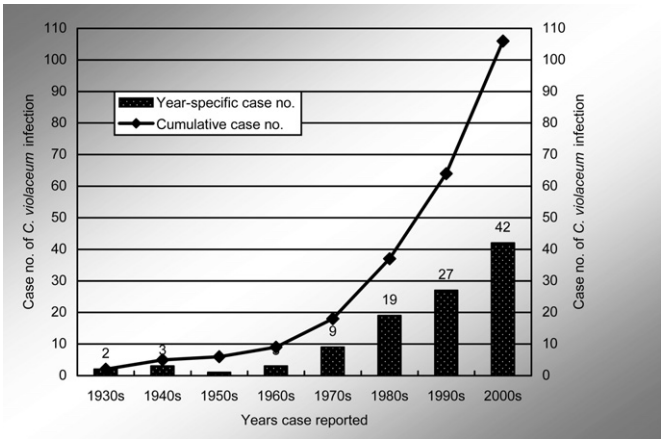

Fig. 1. Cases of *C. violaceum* infection reported in the world. Number above each bar indicates the number of published cases with infection by each decade.

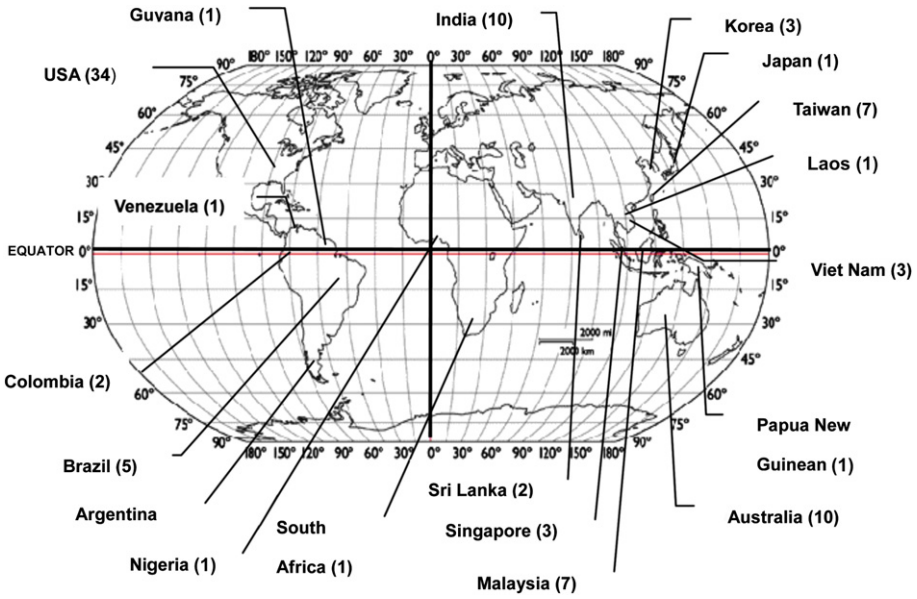

Fig. 2. International distribution of patients with *C. violaceum* infection, indicating that *C. violaceum* infection occurs around the world. However, most of the cases usually occur in tropical and subtropical regions.

the single causative agent in blood culture. Of the 75 patients with an available hemogram, 46 (61%) had marked leukocytosis with a median white blood cell (WBC) count of 20.9×10^9 cells/L (range, $12–61.9 \times 10^9$ cells/L); 12 (16%) had marked leukopenia with a median WBC of 1.9×10^9 cells/L (range, $0.09–3.3 \times 10^9$ cells/L); and 13 (17%) of the 106 patients had band form with a ratio of >10% in peripheral WBC count. Sixteen (15%) of the 106 patients had comorbidities: nine had chronic granulomatous disease (CGD), two had glucose-6-phosphatase deficiency, three had diabetes, one had leukemia, and one had uremia. Localized abscesses were found in 52 patients (49%). Among these patients, only the liver was involved in 37 (35%); only the lung in 25 (24%); only the spleen in 14 (13%); the liver plus the lung in 11 (10.4%); and the liver plus the lung and spleen in 10 (9.4%). No specific factor could be used to predict whether there was a metastatic abscess or not in early *C. violaceum* infection. Nonpigmented strains were found in 12 patients (11%).

Patients who had died had a shorter clinical course, with a median duration of 7 days (range, 1–97 days), while the survivors had a longer clinical course and a median duration of 18.5 days (range, 1–153 days). Fifty-three (50%) of the 106 patients received appropriate antimicrobial treatment. A comparison of patients with *C. violaceum* infection with and without bacteremia appears in Table 2. The group of patients without bacteremia tended to be younger ($p = 0.007$), had a presence of sepsis ($p < 0.001$), and a lower-case fatality rate ($p = 0.003$).

3.3. Potential predisposing factors associated with C. violaceum infection

Of the 106 patients, 60 (57%) had potential factors predisposing them to invasive *C. violaceum* infection. These included trauma, exposure to water or soil, or both (Table 3). Fourteen (23%) of the 60 patients with predisposing factors had both histories of trauma and exposure. Of these patients, 35 (58%) had history of specific exposure. Most of the young patients had distinct predisposing factors, such as wading in water, playing in muddy water, swimming, or falling in water, and these patients tended to have a higher mortality rate. Of them, five patients fell or played in muddy water; all five were children with a median age of 2 years (range, 1.3–6 years), and they all subsequently died. Nearly all of the patients had community-acquired infection; however, two patients may have had a healthcare-associated infection. One patient, a man aged 64 years, had persistent sepsis after cervical surgery.[32] *C. violaceum* was cultured from his blood and femoral line tip. He succumbed to uncontrolled sepsis 3 months after cervical laminoplasty. Another patient, a 16-year-old female, had received chemotherapy for acute leukemia,[34] then developed pneumonia with septic shock during hospitalization. Cultures from her blood and Hickman catheter yielded nonpigmented *C. violaceum*.

3.4. Microbiological data and antimicrobial susceptibilities

Most of the isolated strains were pigmented; however, there were 12 (11%) isolated nonpigmented strains. Comorbidity ($p = 0.017$) and localized abscess ($p = 0.029$) were less common in patients with nonpigmented strain infection. Disease severity in these two groups showed no statistically significant difference: sepsis ($p = 0.222$), bacteremia ($p = 1.0$), and death ($p = 0.063$). Seventy-two isolated cases of *C. violaceum* from various clinical specimens of 69 patients were studied for antimicrobial susceptibility tests (Table 4). Piperacillin/tazobactam, aminoglycosides, chloramphenicol, tetracycline, trimethoprim-sulfamethoxazole, carbapenem, and fluoroquinolones exhibited

Table 1
Baseline demographic and medical characteristics of published *C. violaceum* infection

Variable	Patients ($n = 106$), no. (%)
Age (yr), mean ± SD, median (range)	20.1 ± 19.1, 14.5 (<1–80)
Male sex[a]	84/105(80)
Incubation period, median days (range)[b]	3 (1–90)
Presence of skin lesion during clinical course	72/106 (67.9)
Presence of predisposing factor (any)	60/106 (56.6)
Presence of abdominal pain during clinical course	33/106 (31.1)
Sepsis at presentation	87/106 (82)
Bacteremia	61/106 (57.5)
White blood cell count, 10^9 cells/L	
<12, no. (%) of patients, median (range)	46/75 (61.3), 20.9 (12–61.9)
4-12, no. (%) of patients, median (range)	17/75 (22.7), 9.07 (5.4–11.7)
>4, no. (%) of patients, median (range)	12/75 (16), 1.9 (0.09–3.3)
Band form >10%, no. (%) of patients, median (range, %)	13/75 (17.3), 29 (10–62)
Comorbidity (any)	16/106 (15.1)
Chronic granulomatous disease	9/106 (8.5)
Glucose-6-phosphatase deficiency	2/106 (1.9)
Others[c]	5/106 (4.7)
Localized abscess (any)	54/106 (50.9)
Liver	41/106 (38.7)
Lung	28/106 (26.4)
Spleen	13/106 (12.3)
Liver + lung	11/106 (10.4)
Liver + lung + spleen	10/106 (9.4)
Other location[d]	9
Year-specific case numbers	
<1990	37/106 (34.9)
>1990	69/106 (65.1)
Appropriate antibiotic treatment	53/106 (50)
Relapse, no. (%), median days of relapse (range)	7/106 (6.6), 135 (4–1095)
No. of patients with non-pigmented strain	13/106 (12.3)
Mortality	56 (53)
Clinical course, median days (range)[e]	
Survivor	18.5 (1–153)
Death	7 (1–97)

[a] One neonate was excluded.
[b] Information on incubation period was available for 46 patients.
[c] Other comorbidities included three patients with diabetes, one with uremia, and one with leukemia.
[d] Other locations of abscess included brain (three), breast (one), kidney (one), intraabdomen (one), nasopharyngeal space (one), pericardium (one), and psoas muscle (one).
[e] Information on clinical course was available for 95 patients.

relatively acceptable activities to *C. violaceum*. Of them, fluoroquinolones exhibited the greatest susceptibility rate. Polymyxin B or colistin did not have a reliable susceptibility rate given the limited data.

3.5. Outcome and antimicrobial therapy

Fifty-six patients (53%) died of *C. violaceum* infection. Of the 106 studied patients, 53 (50%) received appropriate antimicrobial treatment. The most important risk factors in mortality for the 61 patients with *C. violaceum* bacteremia were young age ($p = 0.0789$), presence of localized abscess ($p = 0.030$), shorter clinical course ($p < .001$), and inappropriate antimicrobial treatment ($p < 0.001$; Table 5). Forty-four (94%) of the 47 survivors received appropriate antimicrobial treatment. Among them, 34 (77%) received combination therapy. Before 1990, chlorampenicol was the most common antimicrobial agent for this infection; however, after 1990, ciprofloxacin and carbapenem became the predominant antimicrobial agents.

Table 2
Comparison of patients with *C. violaceum* infection with and without bacteremia

Characteristics	Patients with bacteremia ($n = 61$)	Patients without bacteremia ($n = 45$)	p
Age (yr), mean ± SD (range)	24.1 ± 22.1 (<1–53)	14.8 ± 12.4 (<1–80)	0.007
Male sex	47/60 (78.3)	37/45 (82.2)	0.806
Comorbidity (any)	7/61 (11.5)	8/45 (17.8)	0.406
Predisposing factor (any)	34/61 (55.7)	26/45 (57.8)	0.846
Skin lesion (any)	46/61 (75.4)	27/45 (60.0)	0.137
Sepsis	60/61 (98.4)	26/45 (57.8)	<0.001
Localized abscess (any)	32/61 (52.5)	19/45 (42.2)	0.330
Year-specific case numbers			
<1990	20/61 (32.8)	17/45 (37.8)	0.543
>1990	41/61 (67.2)	27/45 (60.0)	
Appropriate antimicrobial therapy	28/54 (51.9)	28/42 (66.7)	0.145
Death	40/61 (65.6)	16/45 (35.5)	0.003

Data are no. (%) patients, unless otherwise indicated.

3.6. Relapse

Seven patients (6.6%) experienced relapse or reinfection, with a median interval of 135 days (range, 4–1095 days). Of the seven patients, four had two episodes of *C. violaceum* infection: one was infected a second time 13 months after completion of appropriate antimicrobial treatment, and one died of a recurrent infection 2 weeks after adequate treatment[17,18]; two patients who received inappropriate antimicrobial treatment had two episodes of infection, separated by 1 week and 2 weeks, respectively.[23,26] One patient had an infection relapse because of the inadequate duration of treatment.[4] Two patients experienced reinfection in two different episodes: one had two episodes of infection, separated by 3 years after exposure to the same source,[24] while another was infected a second time 2 years after the first episode.[22]

4. Discussion

C. violaceum is widely distributed in natural aquatic environments and is sensitive to temperature; therefore, it has a predilection to the tropical and subtropical areas.[1,2] It is worth noting that the effects of global warming may increase, and the geographic distribution of this microorganism may change in the future. Several patients with *C. violaceum*

Table 3
Predisposing factors in patients with *C. violaceum* infection ($n = 60$)

Variable	Patients no.(%)	Age, median yr (range)	Appropriate antimicrobial Therapy, no. (%)	No. of deaths	Mortality (%)
Trauma	9 (15)	24 (0.8–54)	6(67)	4	44
Exposure to water/soil	35(58)	—		19	54
Near-drowning	5 (8)	39 (18–53)	3(60)	2	40
Swimming	12 (20)	10.5 (3–40)	8(67)	4	33
Wading in water	4 (7)	8.5 (6–24)	1(25)	2	50
Fall or play in muddy water	5 (8)	2 (1.3–6)	1(20)	5	100
Others	9 (15)	15 (4–44)	3(33)	6	67
Trauma and exposure to water/soil	14 (23)	31.5 (9–80)	5(39)[a]	8	57

Data are no. (%) of patients, unless otherwise indicated.
[a] The data for antimicrobial theapy were available for 13 patients.

infection went beyond the microorganism's previous territory (confined between latitudes of 35°N and 35°S).[1–3,26] At the same time, reported cases of *C. violaceum* infection in the literature surfaced in recent decades. Of the 106 patients, 69 (65%) were infected after 1990, which indicated that the number of infections have substantially increased in recent decades.

Human infection was first described in 1927.[16] Less than 140 human cases (106 cases enrolled, but 29 cases were excluded in this study) have been reported in the world. In 1988, Miller and colleagues[37] conducted a study that compared virulent and avirulent strains of *C. violaceum*, in which virulent strains had elevated levels of superoxide dismutase and catalase that may protect the microorganism from

Table 4
Antimicrobial susceptibilities in 72 isolates of *C. violaceum*

Antimicrobial agent	No. tested	No. (%) of susceptible isolates
Penicillin	9	0
Ampicillin	39	1 (3)
Amoxicillin/clavulanate	9	0
Ampicillin/sulbactam	9	1 (11)
Carbenicillin	12	5 (42)
Ticarcillin	5	1 (20)
Piperacillin	15	10 (67)
Mezlocillin	3	1 (33)
Ticarcillin/clavulanate	9	5 (56)
Piperacillin/tazobactam	11	9 (82)
Cephalothin (or cephalexin/cefazolin)	39	0
Cefuroxime	16	0
Cefamandole	6	0
Ceftizoxime	7	0
Cefoxitin	9	1 (11)
Cefotaxime	21	6 (29)
Ceftriaxone	19	2 (11)
Ceftazidime	33	11 (33)
Cefepime	13	10 (77)
Aztreonam	12	9 (75)
Moxolactam	3	2 (67)
Carbapenem[a]	34	31 (91)
Gentamicin	63	55 (87)
Netilmicin	11	11 (100)
Amikacin	35	27 (77)
Tobramycin	15	10 (67)
Kanamycin	5	4 (80)
Isepamicin	3	1 (33)
Ciprofloxacin	36	34 (94)
Levofloxacin	5	5 (100)
Ofloxacin	4	4 (100)
Pefloxacin	2	2 (100)
Chloramphenicol	42	41 (98)
Tetracycline	26	24 (92)
Trimethoprim/sulfamethoxazole	48	45 (94)
Polymyxin B (or colistin)	7	1 (14)

[a] Includes imipenem/cilastatin or meropenem.

Table 5
Demographic data, clinical characteristics, laboratory data, and treatment associated with mortality in 61 patients with *C. violaceum* bacteremia

Variable	No. of deaths/No. of cases	Mortality (%)	*p*
Sex[a]			
Men	32/47	68	0.349
Women	7/13	54	
Age, y			
<6	13/20	65	0.0789
7–20	12/15	80	
21–65	15/23	65	
>65	0/3	0	
Predisposing factor			
Yes	23/33	70	0.462
No	17/28	61	
Skin lesion			
Yes	27/45	60	0.124
No	13/16	81	
Abdominal pain			
Yes	15/23	65	0.964
No	25/38	66	
Comorbidity			
Yes	14/19	74	0.561
No	26/42	62	
Localized abscess (any)			
Yes	26/33	79	0.030
No	14/28	50	
Course, duration (d)[b]			
<5	18/18	100	<0.001
6–20	14/16	88	
>20	7/24	29	
Appropriate antimicrobial treatment			
Yes	5/24	21	<0.001
No	29/30	97	

Values are reported as no./no. (%), unless otherwise indicated.
[a] Excluded one case of 8-day neonate.[4]
[b] Information on patient's courses was available for 58 patients.

phagocytic attack in humans, possibly leading to its extreme virulence. Thus, it is possible that the place where patients developed the infection may depend on the exact strain that they contracted.

The distribution of the reported patients was quite different, with 42% in the Americas and 39% in the East Western Pacific. Approximately 42% of the patients were younger than 10 years. Patients without a predisposing factor were nearly all children (≤6 years of age [$p = 0.061$]). The scenario of "the more outdoor activities, the more chance to be exposed to water or soil and traumatic injury" may explain this phenomenon.

Of the 106 patients, 56 died, with an overall mortality rate of 53%. Most of the patients had a short incubation time. The most common symptoms of *C. violaceum* infections were fever, pain over the infected site associated with various skin lesions, abdominal pain, and rapid progression to sepsis. Thirty-three (31.1%) patients experienced abdominal pain, emergency surgery was performed in six (18.2%), and localized visceral abscess was found in four patients. Seventy-two (68%) patients had skin lesions with various manifestations, in which pustules may have developed in the early period or presented as a late manifestation preceding or accompanying sepsis. Deposition of septic embolism in the small vessel was the probable pathogenesis. Laboratory data were nonspecific in *C. violaceum* infection; however, an abnormal hemogram with leukocytosis, leukopenia, or left shift may occur (Table 1). Patients who died had a shorter clinical course compared with the survivors. Seven patients (6.6%) experienced relapse.

It is possible that occult microabscess or hidden septic focus may persist in a patient's internal organs despite adequate treatment. Therefore, it is necessary to treat patients with *C. violaceum* infection for an extended period and maintain close follow-up procedures. On the other hand, healthcare-associated infection was considered in two cases in this review.[32,34] One study for neonatal sepsis conducted by Anah and others in 2008 had demonstrated isolation of *C. violaceum* from 10 inborn neonates (6.3%).[14] These data indicate that this microorganism might have existed in hospital settings, and this warrants attention.

Rapid progression to life-threatening sepsis associated with metastatic abscess in *C. violaceum* infection is the most striking feature. Eighty-seven (82%) patients presented with sepsis in the early manifestation of the infection (Table 1). Localized abscess in visceral organs was found in nearly one-half of the patients (52/106). It is worth noting that the metastatic abscess could be the early clinical presentation of the *C. violaceum* infection. The liver (35%) was the organ that was most commonly involved. However, multiple visceral abscesses may be present. Nonpigmented strains of *C. violaceum* were found in 12 patients. Disease severity in these two groups has not been shown to be statistically significant, indicating that the pathogenicity of nonpigmented strains seems to have similar virulence to that of pigmented strains. This is consistent with the reported literature.[37,38] Patients with chronic granulomatous disease (CGD) have been considered to be vulnerable to *C. violaceum* infection[39]; however, there were only nine cases (8.5%) of proven CGD in this survey. Sixty (57%) patients had potential factors that predisposed them to invasive *C. violaceum* infection. Mosret importantly, specific exposure, including near drowning, swimming, wading in water, and falling or playing in muddy water were risk for developing *C. violaceum* infection. It is also worth noting that the clinical symptoms of *C. violaceum* infection may not occur immediately after specific exposure to water or soil; instead, they may occur 60 days after exposure. The clinical spectrum of *C. violaceum* infection is protean, including urinary tract infection, pneumonia, gastrointestinal infection, localized cutaneous lesions, localized or metastatic abscesses, osteomyelitis, meningitis, peritonitis, brain abscess, endocarditis, hemophagocytic syndrome, respiratory distress syndrome, and fulminant sepsis. Diagnosing *C. violaceum* infection is currently based on a culture of clinical specimens followed by subsequent biochemical identification. There is no available examination for a serological test. In 2006, Scholz and colleagues[40] developed a method for detecting *C. violaceum* by multiplex polymerase chain reaction, but it has not been widely accepted to date.

Although antimicrobial susceptibility data on *C. violaceum* remain very limited because this pathogen is rarely isolated from clinical specimens, results of susceptibility testing vary in different clinical settings. The Clinical and Laboratory Standards Institute has not yet established a zone diameter for resistance and susceptibility associated with minimum inhibitory concentration (MIC) breakpoints. *C. violaceum* is found to be extremely resistant to penicillins and cephalosporins (Table 4). Increased beta-lactamase activity in *C. violacerum* was reported in one study by Farrar in 1976.[41] In 1988 Aldridge and others[5] conducted another study to compare the *in vitro* activity of ciprofloxacin and other antimicrobial agents against clinical strains of *C. violaceum*. The effective agents of *C. violaceum*, including ticarcillin, carbenicillin, and cefoxitin, which were reported in 1976, no longer have acceptable susceptibility rates.[5] Before 1990, the usual treatment for *C. violaceum* infection was chloramphenicol, trimethoprim-sulfamethoxazole, tetracycline, or aminoglycosides. However, several new potent antimicrobials that were introduced after 1990, which include fluoroquinolone and carbapenem, have demonstrated good activity against this microorganism. According to study by Aldridge,[5] ciprofloxacin was the most active drug to combat *C. violaceum*.

Among the patients who survived, 44 (93.6%) received appropriate antimicrobial treatment. Among these patients, 34 (77.3%) had received combination therapy with a regimen of chloramphenicol, beta-lactams, trimethoprim-sulfamethoxazole, or fluoroquinolones along with one of the aminoglycosides. As shown in Table 4, most of the beta-lactams do not exhibit good activity with respect to *C. violaceum*. An extensive treatment period of parenteral antimicrobials for 2–4 weeks for *C. violaceum* infection, followed by maintenance therapy with an oral agent, such as trimethoprim-sulfamethoxazole, tetracycline, or fluoroquinolone, for 2–3 months to prevent relapse is recommended.[4,15,21,30] Only 50% of the patients received appropriate antimicrobial treatment (Table 1), and appropriate antimicrobial treatment was the significant risk factor for mortality in patients with *C. violaceum* bacteremia ($p < 0.001$;

Table 5). Therefore, it is important for physicians to be aware of *C. violaceum* infection and its appropriate antimicrobial treatment regimen.

In conclusion, *C. violaceum* infection may become an emergent infection after further global climate change. It represents a difficult-to-treat entity, so special attention is required. A prompt diagnosis, optimal antimicrobial therapy, and adequate therapeutic duration for *C. violaceum* infection are the keys for successful therapy.

References

1. Ponte R, Jenkins SG. Fatal *Chromobacterium violaceum* infections associataed with exposure to stagnant water. *Pediatr Infect Dis J* 1992;**11**: 583−6.
2. Koburger JA, May SO. Isolation of *Chromobacterium* spp. From foods, soil, and water. *Appl Environ Microbiol* 1982;**44**:1463−5.
3. Byamukama D, Farnleither AH, Kansiime F, Manafi M, Burtsher M, Mach RL. Contrasting occurrence of *Chromobacterium violaceum* in tropical drinking water springs of Uganda. *J Water Heath* 2005;**3**: 229−38.
4. Sirinavin S, Techasaensiri C, Benjaponpitak S, Pornkul R, Vorachit M. Invasive *Chromobacterium violaceum* infection in children: case report and review. *Pediatr Infect Dis* 2005;**24**:559−61.
5. Aldridge KE, Valaninis GT, Saners CV. Comparison of the in vitro activity of ciprofloxacin and 24 other antimicrobial agents against clinical strains of Chromobacterium violaceum. *Diagn Microbiol Infect Dis* 1988;**10**: 31−9.
6. Martinez R, Velludo MASL, Santos VRD, Dinamarco PV. *Chromobacterium violaceum* infectin in Brazil: a case report. *Rev Inst Med Trop S Paulo* 2000;**42**:111−3.
7. Watine J, Courtade A, Pham E, Lievrouw C, Dubourdieu B, Guerin B, et al. *Chromobacterium violaceum* peritonitis: case report and literature review. *Ann Biol Clin (Paris)* 2006;**64**:327−30.
8. Guevara A, Salomon M, Oliveros M, Guevara E, Guevara M, Medina Z. Sepsis caused by pigmented and non pigmented *Chromobacterium violaceum* [in Spanish]. *Rev Chilena Infectol* 2007;**24**:402−6.
9. Julio Alexander DP, Jorge G, Laura Andrea RV. Sepsis by *Chromobacterium violaceum*: first case report from Colombia. *Braz J Infect Dis* 2007;**11**:441−2.
10. Martinez P, Mattar S. Fatal septicemia caused by *Chromobacterium violaceum* in a child from Colombia. *Rev Inst Med Trop S Paulo* 2007;**49**:391−3.
11. Yang CH. Non-pigmented *Chromobacterium violaceum* bacteremic cellulitis after fish bite. *J Microbiol Immunol Infect* 2011;**44**:401−5.
12. Johnson WM, DiSaivo AF, Sieuer RR. Fatal *Chromobacterium violaceum* septicemia. *Am J Clin Path* 1971;**56**:400−6.
13. Anah MU, Udo JJ, Ochigbo SO, Abia-Bassey LN. Neonatal septicemia in Calabar, Nigeria. *Trop Doct* 2008;**38**:126−8.
14. American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference Committee. definitions for sepsis and organ failure and guidelines for use of innovative therapies in sepsis. *Crit Care Med* 1992;**20**:864−74.
15. Patterson RH, Banister GB, Knight V. Case reports: Chromobacterial infection in man. *Arch Int Med* 1952;**90**:79−86.
16. Sneath PHA, Whelan JPF, Singh RB, Edwards D. Fatal infection by Chromobacterium violaceum. *Lancet* 1953;**2**:276−7.
17. Victorica B, Baer H, Ayoub EM. Successful treatment of systemic *Chromobacterium violaceum* infection. *JAMA* 1974;**230**:578−80.
18. Tucker RE, Winter WG, Wilson HD. Osteomyelitis associated with *Chromobacterium violaceum* sepsis. *J Bone Joint Surg Am* 1979;**61**:949−51.
19. Annapurna F, Reddy SV, Kumari PL. Fatal infection by *Chromobacterium violaceum*: clinical and bacteriology study. *Indian J Med Sci* 1979;**33**: 8−10.
20. Lee TS, Wright BD. Fulminating chromobacterial septicemia presenting as respiratory distress syndrome. *Thorax* 1981;**36**:557−9.
21. Petrillo VF, Severo V, Santos MM, Edelweiss EL. Recurrent infection with *Chromobacterium violaceum*: first case report from South America. *J Infect* 1984;**9**:167−9.
22. Chattopadhyay A, Kumar V, Bhat N, Rao P. *Chromobacterium violaceum* infection: rare but frequently fatal disease. *J Pediatr Surg* 2002;**37**: 108−10.
23. Bilton BD, Johnson LW. Recurrent nonfatal *Chromobacterium violaceum* infection in a nonimmunocompromised patient. *Infect Med* 2000;**17**:686−9.
24. Suarez AE, Wenokur B, Johnson JM. Nonfatal chromobacterial sepsis. *South Med J* 1986;**79**:1146−8.
25. Kaufman SC, Schugurensky A. First case report from Argenina of fatal septicemia caused by *Chromobacterium violaceum*. *J Clin Microbiol* 1986;**23**:956−8.
26. Hiraoka N, Yoshioka K, Inoue KI, Kawahito Y, Kasamatsu Y. *Chromobacterium violaceum* sepsis accompanied by bacteria-associated hemophagocytic syndrome in a Japanese man. *Arch Intern Med* 1999;**159**: 1623−4.
27. Atapattu DN, Jayawickrama DP, Thevanesam V. An unusal bacterium causing a brain abscess. *Emerg Infect Dis* 2001;**7**:1−2.
28. Dromigny JA, Fall AL, Diouf S, Perrier-Gros-Claude JD. *Chromobacterium violaceum*: a case of diarrhea in Senegal. *Pediatr Infect Dis J* 2002; **21**:573−4.
29. Hodge RA. Non-chromogenic *Chromobacterium violaceum* in a urinary tract infection. *Clinic Microb Newsl* 2002;**24**:15.
30. Jitmuang A. Human *Chromobacterium violaceum* infection in Southeast Asia: case reports and literature review. *South Asian J Trop Med Public Health* 2008;**39**:452−60.
31. de Siqueira IC, Dias J, Ruf H, Ramos EAG, Maciel EAP, Rolim A, et al. *Chromobacterium violaceum* in siblings, Brazil. *Emerg Infect Dis* 2005; **11**:1443−5.
32. Teoh AYB, Hui M, Ngo KY, Wong J, Lee KF, Lai PBS. Fatal septicemia from *Chromobacterium violaceum*: case reports and review of the literarure. *Hong Kong Med J* 2006;**12**:228−31.
33. Manjunath M. Fatal septicemia due to Chromobacterium violaceum. *West Indian Med J* 2007;**56**:380−1.
34. Bosch FJ, Badenhorst L, Le Roux JA, Louw JV. Successful treatment of *Chromobacterium violaceum* sepsis in South Africa. *J Med Microbiol* 2008;**57**:1293−5.
35. Baker S, Campbell JI, Stabler R, Nguyen HVM, To DS, Nguyen DV, et al. Fatal wound infection caused by *Chromobacterium violaceum* in Ho Chi Minh City, Vietnam. *J Clin Microbiol* 2008;**46**:3853−5.
36. Lim IWM, Stride PJ, Horvath RL, Hamilton-Craig CR, Chau PP. *Chromobacterium violaceum* endocarditis and hepatic abscesses treated successfully with meropenem and ciprofloxacin. *Med J Aust* 2009;**190**:386−7.
37. Miller DP, Blevins WT, Steele DB, Stowers MD. A comparative study of virulent and avirulent strains of Chromobacterium violaceum. *Can J Microbiol* 1988;**34**:249−55.
38. Sivendra R, Lo HS, Lim KT. Identification of *Chromobacterium violaceum*: pigmented and non-pigmented strains. *J Gen Microbiol* 1975;**90**: 21−31.
39. Winkelstein JA, Marino MC, Johnston RB, Boyle J, Curnutte J, Gallin JI, et al. Chronic granulomatous disease: report on a National Registry of 368 patients. *Medicine* 2000;**79**:155−69.
40. Scholz HC, Witte A, Tomaso H, Dahouk SA, Neubauer H. Detection of *Chromobacterium violaceum* by multiplex PCR targeting the *prgI, spa*O, *inv*G, and *sip*B genes. *Syst Appl Microbiol* 2006;**29**:45−8.
41. Farrar WE, O'Dell NM. β-lactamase activity in Chromobacterium violaceum. *J Infect Dis* 1976;**134**:290−3.