

Impending *Chromobacterium violaceum* Sepsis, Successfully Treated by Conventional Antibiotics

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Abstract

Chromobacterium violaceum infection in human is rare. Most of the patients died because of unrecognized rapid clinical deterioration. We reported a 13-year-old boy presented with fever, chills and inguinal lymphadenitis after having exposed his thigh ulcer to water. Impending clinical sepsis with unstable vital signs despite cloxacillin and amikacin administration was evident 48 hours later. He was improving with rapid defervescence during the next 24 hours after trimethoprim/sulfamethoxazole, gentamicin and chloramphenicol therapy. Clinical similarity between *Chromobacterium violaceum* and *Burkholderia pseudomallei* infections : discussed. (*J Infect Dis Antimicrob Agents* 1996;13:67-70.)

A uniformly fatal human infection caused by *Chromobacterium violaceum*, a facultative anaerobic gram-negative bacteria, was firstly reported from Malaysia in 1927 (1). Since then only 52 cases have been documented in English literatures, none of whom was from Thailand. We are now reporting a nonfatal chromobacteriosis in a Bangkok resident who acquired the infection after water exposure at Cha-am, Phetchaburi.

CASE REPORT

A previously healthy 13-year-old Thai boy presented with eleven days history of small subcutaneous nodule over right thigh. After an exposure to both fresh and sea water during a short vacation at Cha-am, Phetchaburi, 180 km. South of Bangkok, 8 days before admission, the nodule was broken as a 1-2 cm ulcer with purulent discharge. Three days later he developed very high fever, chills and painful swollen lymph node at right groin. This had been treated at a private clinic with 3 days

of cloxacillin and then co-amoxyclov plus two injections of lincomycin without any improvement. He lost 3 kg of body weight and was unable to walk during the illness. His past medical history was significant only for minor cerebral concussion 10 years ago.

Physical examination revealed a young boy in moderate distress, splinting his right thigh in abduction, well conscious, not icteric, and not anemic. His body weight was 37 kg, blood pressure 120/80 mmHg, temperature 39°C, respiratory rate 25/minute, and pulse rate 100/minute. Physical examination was nonrevealing with negative HEENT, lung, cardiovascular, abdominal and neurologic examination except an ulcer of 2 cm diameter with necrotic tissue and minimal purulent discharge at lower part of his right thigh. There was also a 5 cm diameter, firm, tender right inguinal mass detected.

Laboratory studies included hemoglobin 13.1 g/dl, hematocrit 40 vol %, white blood cell count of 12,500/

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mm³, polymorphonuclear cells 69 percent lymphocytes 19 percent, monocytes 10 percent, eosinophils 2 percent and platelet counts of 348,000 mm³, ESR was 5 mm/hr, BUN 5 mg/dl, and creatinine 0.8 mg/dl. Urinalysis was normal. Pus from ulcer and inguinal mass needle aspiration revealed numerous polymorphonuclear leukocytes without organism seen from gram stain. His chest and right hip radiographs were normal.

Cloxacillin 6 g/day intravenously was given immediately as staphylococcal sepsis from primary skin infection was the most likely diagnosis. But without gram-positive cocci from gram stain of pus and also a history of water exposure, amikacin 500 mg/day intravenously was added to cover for possible gram-negative bacteria. Forty-eight hours later, he was restless, developed tachycardia and hypotension of 90/60 mmHg with persistently high fever, increasing leukocytosis of 15,800/mm³, polymorphonuclear cells 85 percent, and ESR 43 mm/hour. Pus from ulcer and lymph node then grew the same bacteria, identified as *Chromobacterium violaceum* which produced violet pigment (violacein) shown as violet colony on blood agar and MacConkey agar. Blood cultures were subsequently reported as sterile. Intravenous cotrimoxazole of 320 mg of trimethoprim/day, gentamicin 180 mg/day and chloramphenicol 3 g/day were started. He became afebrile and had more stable vital signs within the next 12 hours. The treatment was continued for another 48 hours when these three antibiotics were switched to oral cotrimoxazole of 320 mg of trimethoprim/day plus doxycycline 100 mg/day due to difficult venous access. He continued to improve and could be discharged after 9 days of admission. The treatment were given for 3 weeks as an out-patient with complete curing of an ulcer and inguinal mass. He has been without recurrence of infection during 18 months of follow-up. Immunologic studies on 5 and 6 months after his illness revealed normal immunoglobulin levels (IgG 19.7 g/l, IgA 2.31 g/l, IgM 2.0 g/l) but abnormally low phagocytosis by 2 NBT tests (5 and 13% vs 40 and 50 percent of stimulated level on patient and control respectively) (Table 1).

DISCUSSION

Chromobacterium violaceum, a violet pigment (violacein)-producing, facultative anaerobic, non-spore-forming, catalase and oxidase - positive, gram - negative bacilli was firstly found as a soil and water saprophyte in 1881 by Bergonzini (2). Pathogenic potential was

Table 1. NBT test results.

Study period after illness	Percentage of cell positive			
	Patient		Normal control	
	Nonstimulated	Stimulated	Nonstimulated	Stimulated
5 months	6	5	2	40
6 months	10	13	10	50

reported by Wooley in 1904 as fatal septicemia in water buffalo in the Phillipines (3). First reported case of human chromobacteriosis occurred in a chinese Malayan who developed fatal septicemia due to liver abscesses in 1927 (1). Since then there have been only 52 cases reported during the last 68 years (1,4-34). Twenty-five cases were from United States and 16 of them were from Florida. Eighteen cases were from Southeast Asia, most of which from Malaysia (13 Malaysia, 3 Vietnam, 2 Singapore). The other nine cases were from other countries in both sutropical and tropical areas (1 France, 1 Brazil, 1 Nigeria, 1 Argentina, 3 Australia, 1 India, 1 west Africa). Despite being in the same demographic area as Malaysia and apizootic disease in gibbon has been reported in Thailand since 1970 by Johnsen, no human chromobacteriosis was officially documented (35). Their paucity may be due to physician unawareness of the clinical entity and its growth on the culture media was recognized as a usual contaminant with low pathogenic potential.

Disease affected nearly all age group ranging from fatal meningitis in newborn from India to 53-year-old man in Florida with fatal septicemia, pneumonia and liver abscess after drowning (15,24). Male was 4 times more frequently affected than female (33:8). More than 50 percent of cases had a history of water exposure (19/34), indicating an environmentally-acquired nature of chromobacteriosis. Incubation period of reported cases ranged from 3 days to 1 year after a history of exposure to contaminated soil and/or water (33). The organism gained access to the body *via* skin abrasions or cuts while wading or swimming, and aspiration of large volume of water. Fatal septicemia and liver abscess after 3 days of abdominal cramp, vomiting and diarrhea in 19-year-old American soldier in Vietnam also suggested gastrointestinal route possibly after ingestion of contaminated food or water (11). Severe necrotizing conjunctivitis with fatal sepsis 3 days after falling into muddy water raised the possible mucous membrane contact as another route of acquisition (27).

Clinical signs of cutaneous infection on our reported case began few days after water exposure. Chromobacteriosis affected virtually every organ namely skin, subcutaneous tissue, lymph node and rarely gastrointestinal tract serving as primary focuses. Initial skin lesions ranged from pustules, pyogenic ulcer, eschar-like, gangrenous ulcer, and uniquely dark or purple micro-nodule (14,22). If unrecognized, rapid hematogenous spreading to the liver, lung, spleen, bone, joint, meninges, brain, and urinary tract may occur. Fatal septicemia was the most common terminal event of human chromobacteriosis (Table 2). Multiple pyogenic abscesses were consistently found in various internal organs at autopsy (10).

The overall disease mortality was 70 percent (30/43) and even higher of 82 percent (23/28) among septicemic cases. Chromobacterium isolates were uniformly susceptible to chloramphenicol and aminoglycosides especially gentamicin (20,21). This was corresponding with the observation that the reported survivors from the infection had been treated with either one or both of the above antibiotics (27). Among aminoglycosides, gentamicin was more active than amikacin and tobramycin. The organism was also susceptible to tetracycline, trimethoprim/sulfamethoxazole, mezlocillin, piperacillin, imipenem, quinolones especially ciprofloxacin (36). It was uniformly resistant to penicillin, cephalosporin/cephamycin (except cefotetan), rifampicin, vancomycin, and betalactam-betalactamase inhibitors.

Our reported case responded rapidly to triple conventional antibiotic therapy which was started on the verge of clinical sepsis. It also contained both chloramphenicol and gentamicin. Our isolate was susceptible to chloramphenicol, gentamicin, tetracycline, trimethoprim/sulfamethoxazole, and ceftriaxone.

Duration of treatment has been uncertain but at least 4 weeks was recommended (33). Rapid fatal recurrences within 2 weeks have been reported after 3 and 4 weeks of therapy (14,33). Our case report also confirmed the above recommendation, at least for nonbacteremic sepsis.

At least 6 patients with an inherited disorder, chronic granulomatous disease, who pruned to infection with catalase - positive bacteria, have been reported to have infection from chromobacterium. Without previous history of infections, our patient had abnormal NBT tests after chromobacteriosis was subsided. This may suggest variant of chronic granulomatous disease which was more subtle with clinically unrecognized leukocyte

Table 2. Site of infection in 48 reported cases of chromobacteriosis.

Site	Number
1. Septicemia	28
2. Skin & subcutaneous	22
3. Liver abscess	18
4. Pneumonia & Lung abscess	15
5. Lymphadenitis	7
6. Splenic abscess	3
7. Osteomyelitis, arthritis	2, 2
8. Meningitis, brain abscess	2, 1
9. Diarrhea, urinary tract infection	2, 2
Total	104

defect.

Several clinical similarities between chromobacteriosis and melioidosis have been mentioned (18). They were both endemic in tropical area plus subtropical area for chromobacteriosis. Both bacteria were found in soil and stagnant fresh water. They enter human body via skin abrasion and mucous membrane, causing multiple abscesses in various internal organs. Both diseases carried very high septicemic mortality. They were treated with the same antibiotics such as chloramphenicol, tetracycline, trimethoprim/sulfamethoxazole, and aminoglycosides. Ideal duration of treatment were both unknown. Minimum duration were recommended differently (Table 3).

Chromobacteriosis should be recognized in a patient who suffered from multiple cutaneous abscesses and septicemia due to gram-negative bacilli after water exposure in endemic area. Early initiation of appropriate antibiotics therapy would then be a key step of successful outcome.

Table 3. Clinical similarities between chromobacteriosis and melioidosis.

	Chromobacteriosis	Melioidosis
Endemic area	Subtropical/tropical	Tropical
Source	Water/soil	Water/soil
Route of infection	Skin/mucous membrane	Skin/mucous membrane, respiratory
Common site of infection	Skin, Lung, Liver	Skin, Lung, Liver
Septicemic mortality	82%	85-95%
Antibiotic treatment	Chloramphenicol, Gentamicin, TMP/SMZ, Tetracycline	Chloramphenicol, Kanamycin, TMP/SMZ, Tetracycline
Duration of treatment	Unknown (>4 weeks)	Unknown (3-6 months)

TMP/SMZ = Trimethoprim/sulfamethoxazole

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