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NOTES

Septic Arthritis Involving *Capnocytophaga ochracea*

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Septic arthritis of the knee developed in a 21-month-old child. The causative organism, isolated from two separate arthrocenteses, was identified as *Capnocytophaga ochracea* morphologically and by biochemical reactions. Previous human infections (bacteremias) have occurred in granulocytopenic hosts with concomitant oral pathology including periodontitis and gingivitis. No abnormalities of oral hygiene were present in this patient, and granulocyte numbers were normal or elevated. Eradication of the infection was accomplished with 8 weeks of antibiotic therapy combined with surgical drainage. Septic arthritis expands the spectrum of infections reported to be caused by *Capnocytophaga* spp.

Bacterial arthritis in children is most often caused by *Hemophilus influenzae* or *Staphylococcus aureus*, although other organisms have been causative. The diagnosis may occasionally be inferred from positive blood culture isolates; however, direct aspiration of affected joints is more specific. Antimicrobial therapy is optimally determined from susceptibility tests performed on the isolated organism.

An infant female presented with an acute monoarticular arthritis of the knee. Separately performed arthrocenteses yielded an unusual gram-negative pleomorphic bacillus identified as *Capnocytophaga ochracea*. Previous literature reports did not demonstrate septic arthritis as being caused by this organism.

This report details the management course of septic arthritis due to *C. ochracea*.

Case report. A 21-month-old female developed an acute monoarticular arthritis of the left knee. Approximately 6 weeks before presentation she experienced the onset of an asymptomatic swelling of the left calf and popliteal fossa. Roentgenograms of the knee revealed soft tissue swelling without evidence of bony involvement. The clinical impression was that of a hematoma secondary to trauma. Over the following few weeks the calf edema subsided, but a boggy swelling of the knee (felt to be synovitis) was noted. Throughout this period there was no pain or limitation of motion or weight bearing of the leg, and the child was free of fever. On the day of admission to Wilford Hall Medical Center she awakened from sleep with a complaint of pain in the left knee and would not bear weight on the leg. An oral temperature of 103°F (39.4°C) was documented by the parents. The left knee was larger than previously noted, with local warmth. At no time before admission were antibiotics administered.

Historically, the child's mother had an autoimmune inflammatory arthritis syndrome. At this time she was in remission and on no medications.

There was no previous significant medical history for the child, and she was breast feeding.

Physical examination disclosed a well-nourished female with a temperature of 101.4°F (38.5°C), a pulse of 188, and blood pressure of 85/40. The left knee circumference was 23.5 cm; the right knee was 21.5 cm. The knee was edematous without erythema and with decreased extensor motion. The remainder of the exam was noncontributory.

A complete blood count showed a leukocyte count of 19,500/mm^3 with 53% polymorphonuclear leukocytes, 2% bands, 32% lymphocytes, and 13% monocytes. The platelet count was 521,000. An erythrocyte sedimentation rate (Westergren) was 25. Roentgenograms of the knee again showed soft tissue swelling without bony abnormalities. A technetium-99 radionuclide scan revealed hyperemia of the knee without evidence of osteomyelitis. An arthrocentesis yielded purulent fluid. The cell count was 25000/mm^3 with 95% polymorphonuclear leukocytes. The synovial fluid glucose was 37 mg% with a protein of 2.5 g%. A Gram stain was negative for organisms. A Bactogen (Wampole Laboratories, Div. Carter-Wallace, Inc., Cranberry, N.J.) test was negative on knee fluid.

Treatment of the child was begun presumptively with parenteral cefamandole and penicillin due to the possibility of *H. influenzae* arthritis. She became afebrile within 24 h. Clinical improvement was noted as well, but the knee edema persisted at the prehospitalization size. An arthrotomy was performed on day 4 due to persistent effusion. About 8 ml of purulent fluid was obtained; the cartilage did not exhibit any destructive changes. Tissue specimens for histopathological analysis were lost.

The initial arthrocentesis fluid was received in the laboratory in aerobic and anaerobic Bactec bottles. A second arthrocentesis fluid taken on the same day was received in the laboratory and was inoculated aerobically to Trypticase soy agar (BBL Microbiology Systems, Cockeysville, Md.) with 5% sheep blood, enriched chocolate agar, MacConkey agar, and cooked meat broth. The specimen was also inoculated to Centers for Disease Control (CDC) anaerobic blood agar, anaerobic phenylethyl alcohol agar, kanamycin-vancomycin blood agar, bacteroides bile esculin agar, and cooked meat broth with thioglycolate and incubated anaerobically.

An organism was initially isolated in the anaerobic Bactec bottle containing material from the first arthrocentesis. Subsequently, the same organism was isolated from the anaerobic culture of material from the second arthrocentesis. A Gram stain of anaerobic broth on day 4 revealed a gram-negative, pleomorphic, fusiform bacillus. An anaerobic subculture on day 10 grew a pure culture of an organism with identical staining characteristics.

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No growth occurred in the aerobic Bactec bottle or on MacConkey agar. The anaerobic Bactec bottle was subcultured to CDC anaerobic blood agar, anaerobic phenylethyl alcohol agar, kanamycin-vancomycin blood agar, and bacteroides bile esculin agar and aerobically to Trypticase soy agar with 5% sheep blood, enriched chocolate agar, and MacConkey agar. After 96 h, pinpoint-sized colonies were observed growing anaerobically on CDC blood agar and phenylethyl alcohol agar. A slight, golden, partial hemolysis occurred on CDC anaerobic blood and phenylethyl alcohol agars. (After several subcultures, alpha-hemolysis was produced on an enriched chocolate formulation prepared in-house.) With continued incubation two different colony types were apparent. These were identified separately and yielded identical reactions. One colony type was circular, smooth, and slightly convex. The second colony type was flat with an irregularly spreading edge and appeared to pit the agar. Some adherence of the colonies was noted and light yellow pigmentation was observed.

As originally isolated, this organism was strictly anaerobic, but after subculture could be grown in a CO_2-enriched atmosphere. The second arthrocentesis and all anaerobic subcultures were incubated at 35°C in a Forma Scientific glove box under 5% H_2–10% CO_2–85% N_2 for periods ranging from 2 to 10 days. Later subcultures were incubated from 48 to 72 h under increased CO_2

TABLE 1. Biochemical reactions of *C. ochracea* recovered from two isolates from synovial fluid

Substrate	API A	Minitek	Tubed media
Oxidase	−	−	−
Catalase	−	−	−
Triple sugar iron			
Slant acid			+
Butt acid			+
Esculin hydrolysis	+	+	+
Nitrate	−	−	−
Gas from NO_3	−	−	−
Indole	−	−	−
Dextrose	+	+	+
Arabinose	−	−	−
Glycerol	−	−	−
Lactose	+	+	+
Maltose	+	+	+
Mannitol	−	−	−
Rhamnose	−	−	−
Salicin	−	−	−
Sucrose		+	+
Trehalose	+	+	
Xylose	−	−	−
Cellobiose	−	−	−
Mannose	−	−	−
Raffinose	−	−	−
Sorbitol	−	−	−
Saccharose	+		
Urease	−	−	−
Gelatin hydrolysis	−		−
o-Nitrophenyl-β-D-galactopyranoside			+
Arginine dihydrolase			−
Lysine decarboxylase			−
Ornithine decarboxylase			−
Motility agar		Slow	+
Melozoite	−	−	−
Lecithinase	−	−	−
Lipase	−	−	−

The initial isolate was inoculated anaerobically to API A (Analytab Products, Plainview, N.Y.) and to Minitek systems. Characteristics are shown in Table 1. Later subcultures from isolates grown in a CO_2-enriched environment were inoculated to Corning Uni-N/F-Tek (Flow Laboratories, McLean, Va.) and to API E systems incubated aerobically. No biochemical changes had occurred after 72 h of incubation at 35°C.

The isolate from the second arthrocentesis was identified with API A and Minitek systems incubated anaerobically. In addition, it was inoculated to standard tubed media with infusion sugars according to the Elizabeth O. King protocol (18). Calf serum was added to the inoculum to enhance growth. Biochemical reactions are shown in Table 1.

With the (anaerobic) API A system supplemented with calf serum, the organism had positive reactions to glucose, lactose, saccharose, maltose, trehelose, and *o*-nitrophenyl-β-D-galactopyranoside. Negative reactions were noted to oxidase, catalase, indole, gelatin, and carboxylase. Nitrate was also negative. Esculin hydrolysis was positive.

On oxidation-fermentation glucose (open and closed), the organism was fermentative by both the Corning (Flow Laboratories) Uni-N/F-Tek and API methods. (Motility was delayed and slow to be observed and was similarly observed on motility medium.)

This bacterium was identified as *C. ochracea*.

One colony of *S. aureus* was recovered from a single plate (Trypticase soy agar with 5% sheep blood) after several subcultures. The *S. aureus* colony was not located on the streaked area of the plate and was not recovered from cooked meat broth or from either Bactec bottle; therefore, it was considered to be a plate contaminant and not significant to the child's illness. Although its significance was doubted, the antibiotic regimen chosen covered both organisms.

Antimicrobial susceptibility tests were performed by an anaerobic broth disk elution susceptibility test (method of Wilkins and Thiel [19]). The organism was sensitive to cefamandole, cephalothin, cefoxitin, and metronidazole but was resistant to penicillin.

After 8 days of parenteral cefamandole the child was switched to oral cefaclor. A peak serum minimal inhibitory dilution and minimal bactericidal dilution was 1:16. Penicillin had been discontinued after 3 days of therapy. Cefaclor was continued for a total of 6 weeks. After discussion with S. Finegold (the organism was thought to be a *Fusobacterium* species), metronidazole was given for an additional 2 weeks (total therapy, 8 weeks).

Repeated roentgenograms were negative for osteomyelitis.

Boggy synovitis persisted for 6 months before resolution. An intensive range-of-motion exercise program resulted in total return of function of the knee. At last examination, 12 months after discharge, the sole residual was a slightly longer leg on the left (2 cm), probably due to reactive bony growth of the epiphysis on the left.

Capnocytophaga is a recently defined genus of bacterial organisms capable of unique gliding motility (14). As the genus name implies, the organisms are capnophilic and will grow favorably in a CO_2 or anaerobic environment. When initially isolated, however, they may exhibit anaerobic growth characteristics only.

The ecological niche of this group of organisms appears to be the gingival crevice and oral cavity (10, 11). *Capnocytophaga* spp. have been implicated in gingivitis and juvenile periodontosis (10, 13). Investigations of juvenile periodontosis have demonstrated that these organisms elaborate potent

toxins, one of which inhibits chemotaxis of granulocytes (2, 13). Other elaborated products have been identified, but their significance remains undetermined (5, 6, 15, 16).

Identification of the organisms depends on microscopic morphology and biochemical reactions. The organism is a pleomorphic, fusiform, gram-negative bacillus. As stated above, it grows anaerobically or in a CO_2 environment. Biochemical reactions differ among the three species (14, 20). Interspecies variations may also be seen.

Cultural isolates have been obtained from the throat, blood, finger, vagina, submaxillary gland, gingiva in periodontitis, spinal fluid, and from a neck infection (11). Clinically encountered systemic infections have been infrequently reported. Thirteen patients (seven adults and six children, [<16 years old]) with bacteremia, one with concomitant pneumonia, have been reported (1, 4, 7–9, 12, 13). Four had acute myelogenous leukemia, three had acute lymphocytic leukemia, two had multiple myeloma, and one each had Hodgkin's disease, poorly differentiated lymphocytic lymphoma, myeloid metaplasia, and metastatic adenocarcinoma of the colon. Of note was that almost all patients were granulocytopenic or were being treated with chemotherapy at the time of infection. In addition, only one patient did not have oral pathology defined as gingivitis, oral ulcerations, or periodontitis.

Blood cultures exhibited delayed growth macroscopically. Several isolates became positive at 5 to 7 days, usually in the anaerobic bottle. Macroscopic growth did not occur in one case, and the organism was recovered from a blind subculture on day 7. The synovial fluid culture (anaerobic Bactec bottle) in the present case became positive on day 4, but the interpretation of true macroscopic growth was questioned.

Most of these patients survived their sepsis due to *Capnocytophaga* spp. Only one death could be directly attributed to the infection. That patient had not been treated with any antibiotic regimen.

Numerous empiric antibiotics have been used in the therapy of the febrile patient with neutropenia and sepsis due to *capnocytophaga* spp. Two recently completed studies have shown susceptibility of most strains to penicillin, ampicillin, carbenicillin, clindamycin, erythromycin, tetracycline, chloramphenicol, and metronidazole (3, 17). Cefoxitin was the best cephalosporin tested, with variable results obtained with other cephalosporin antibiotics

In contrast to all previously described patients, this child was not granulocytopenic, nor were oral ulcerations or oral pathology noted. Presumably a transient bacteremia had occurred, possibly related to brushing of the teeth with secondary infection of the knee joint. Chronicity of the synovitis-arthritis may have been partially related to the relative avirulence of the organism and possibly local dysfunction of neutrophils.

Treatment with cefamandole and cefaclor for 6 weeks and metronidazole for 2 weeks eradicated the infection. Adequate serum killing power was documented while the patient was being treated with the oral cephalosporin antibiotic.

This report documents the occurrence of septic arthritis involving *capnocytophaga* sp. in a non-granulocytopenic patient with normal oral hygiene and extends the recognized pathogenic spectrum of infection by these organisms.

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