Capnocytophaga Bacteremia in Neutropenic Patients: Report of Two Cases

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Recently, several cases of blood-borne infections by *Capnocytophaga* species have been reported in immuno-compromised patients [1-5]. Although these microorganisms are an infrequent cause of bacteremia in neutropenic patients, we have recently observed two such infections, which occurred in our department within a short time period.

The first patient was a 63-year-old male with acute nonlympho-blastic leukemia, diagnosed in October 1991, who entered complete remission after appropriate induction chemotherapy. The patient's condition was complicated by invasive pulmonary aspergillosis (IPA) successfully treated with itraconazole. His leukemia relapsed in February 1993, and salvage chemotherapy was delivered, using a protocol which includes intermediate-dose cytarabine, intermediate-dose methotrexate, vindesine, mitoxantrone and cyclophosphamide [6]. This treatment was further complicated by severe oral mucositis (grade IV according to the WHO classification), diarrhea (grade II) and severe vomiting (grade III). During the period of severe neutropenia (absolute neutrophil count $< 0.5 \times 10^9/l$), which lasted 21 days, three blood cultures drawn from a peripheral vein ($n = 1$) and a central venous catheter ($n = 2$) during an initial febrile episode were positive for *Escherichia coli* and *Capnocytophaga* sp. Empirical antibiotic treatment with meropenem was instituted, with rapid clinical improvement and no further positive blood cultures. Fever later reappeared due to reactivation of the IPA, which again resolved with oral itraconazole and recovery of the neutrophil count.

In vitro susceptibility testing showed that *Capnocytophaga* was sensitive to penicillin, cephalosporins, imipenem, meropenem, fluoro-quinolones, chloramphenicol and tetracyclines whereas it was resistant to aminoglycosides, vancomycin and trimethoprim-sulfamethoxazole. The second patient was a 61-year-old female who suffered from advanced-stage low-grade non-Hodgkin's lymphoma since 1980, and had received outpatient treatment with combination chemotherapy and involved-field

radiotherapy. She was admitted to our hospital in February 1993 because of generalized bone pain secondary to bone marrow infiltration by diffuse large-cell lymphoma. With the diagnosis of transformation of her previous low-grade lymphoma, treatment with a salvage combination chemotherapy protocol which includes ifosfamide, cytarabine, etoposide and prednisone [7] was delivered. During the period of severe neutropenia she developed a fever, and two blood cultures yielded *Capnocytophaga* sp., with the same in vitro susceptibility profile as the previous case. Empirical antibiotic treatment with ceftazidime and amikacin was instituted; the fever disappeared within 24 h and successive blood cultures were sterile. Although the patient did not develop mucositis, she showed signs of extensive periodontal disease.

Capnocytophaga spp. are fusiform, gram-negative, cap-nophilic and facultatively anaerobic rods that are usually found in the normal oral flora [2] and are involved as pathogens in periodontal disease [8]. Species identification by conventional methods is difficult and is not routinely performed in the clinical microbiology laboratory, as in our two cases [3, 9].

These bacteria have recently been reported as opportunistic pathogens causing bacteremia in immunocompromised hosts, especially in neutropenic patients with concomitant oral pathology following chemotherapy and/or radiotherapy [1,3,4]. As usually occurs in this setting, antibiotic prophylaxis can potentially inhibit the sensitive gastrointestinal flora and promote the growth of resistant microbial species [2]. This mechanism was probably of little importance in our patients since both had received nor-floxacin (400 mg q 12 h) for intestinal decontamination, and both isolates were susceptible to this agent. The presence of severe neutropenia, the severe gastrointestinal

mucositis present in the first patient and the periodontal disease observed in the second case were probably the mechanisms involved in the development of these blood-borne infections. We do not have an adequate explanation for the almost simultaneous occurrence of these two bacteremias, but interpatient transmission through the medical or nursing staff or environmental factors seems highly unlikely.

Although infrequently, *Capnocytophaga* infections can also affect nonimmunocompromised and nonneutropenic hosts (bacteremias, lung infections, sinusitis, osteomyelitis, abdominal infections, etc.), usually as part of polymicrobial infections [4,5]. Most strains of *Capnocytophaga* are susceptible to penicillin, cephalosporins, imipenem, fluoroquinolones, chloramphenicol and tetracyclines and

are resistant to aminoglycosides, vancomycin and cotrimoxazole [2, 4], although β -lactamase-producing strains are not infrequent [10]. Both of our isolates were susceptible to β -lactam antibiotics, with a favorable clinical and microbiological outcome after empirical treatment with meropenem and ceftazidime and no signs of organ infection.

We conclude that *Capnocytophaga* must be added to the long list of opportunistic gram-negative bacteria found in patients submitted to intensive chemotherapy and/or radiotherapy, especially when mucosal lesions are present. Most empirical antibiotic treatments used in this setting, however, include agents effective against these relatively rare infections (i.e., imipenem, meropenem, ceftazidime), and their outcome is usually good.

References

Baquero F, Fernandez J, Dronda F, Erice A, Perez de Oteiza J, Reguera JA, Reig M: Capnophilic and anaerobic bacteremia in neutropenic patients: An oral source. *Rev Infect Dis* 1990;12:152-160.

Bilgrami S, Bergstrom SK, Peterson DE, Hill DR, Dainiak N, Quinn JJ, Ascensao JJ: Capnocytophaga bacteremia in a patient with Hodgkin's disease following bone marrow transplantation: Case report and review. *Clin Infect Dis* 1992;14:1045-1049. Forlenza SW: Capnocytophaga: An opportunistic pathogen. *Clin Microb Newsletter* 1985; 7:3:17-19. Ramos JM, Pacho E, Bernacer M, Fernández-Roblas R, Soto C, Soriano F: Bacteriemia por Capnocytophaga en pacientes comprometidos. *Enf Infect Microbiol Clin* 1993;11:46-48. Parenti DM, Snyderman DR: Capnocytophaga species: Infections in nonimmunocompromised and immunocompromised hosts. *J Infect Dis* 1985;151:140-147. Martino R, Brunei S, Sureda A, Altés A, Mateu R, Domingo-Albós A: Treatment of refractory and relapsed adult acute leukemia using a uniform chemotherapy protocol. *Leuk Lymph* 1993;11:393-398. Mateu R, Martinez C, Sureda A, Brunei S, Nondedéu J, Lopez R, Martino R, Altés A, Domingo-Albós A: Resultado de un protocolo poliquimioterápico de rescate (IAPVP-16) en linfomas no Hodgkin resistentes (abstract No 401); in Abstracts of the 25th Congress of the Spanish Society of Hematology and Hemotherapy, Pamplona. *Sangre* 1993;38(suppl 4): 117.

Newman MG, Socransky SS, Savitt ED, Propas DA, Crawford A: Studies of microbiology of periodontitis. *Periodontology* 1976;47:373-379. Pickett MS, Hollis DG, Bottone EJ: Miscellaneous gram-negative bacteria; in Balows A, Hansler WS, Herrmann KL, Isenberg HD, Shadomy HS (eds): *Manual of Clinical Microbiology*, ed 5. Washington, American Society of Microbiology, 1991, pp 410-428.

10 Roscoe DL, Zemcov SJV, Thornber D, Wise R, Clarke AM: Antimicrobial susceptibilities and β -lactamase characterization of capnocytophaga species. *Antimicrob Agents Chemother* 1992;36:2197-2200.