Brain Abscess Associated with Multidrug-Resistant \textit{Capnocytophaga ochracea} Infection

Hua-Kung Wang,\textsuperscript{1,*} Yee-Chun Chen,\textsuperscript{2} Lee-Jene Teng,\textsuperscript{3} Chien-Ching Hung,\textsuperscript{2} Mei-Lin Chen,\textsuperscript{2} Shin-Hei Du,\textsuperscript{4} Hui-Ju Pan,\textsuperscript{4} Po-Ren Hsueh,\textsuperscript{4} and Shan-Chwen Chang\textsuperscript{2}

Division of Infectious Diseases, Department of Medicine, En Chu Kong Hospital, Taipei County,\textsuperscript{1} and Division of Infectious Diseases, Department of Medicine, National Taiwan University Hospital,\textsuperscript{2} Department of Clinical Laboratory Sciences and Medical Biotechnology, National Taiwan University College of Medicine,\textsuperscript{3} and Department of Laboratory Medicine, National Taiwan University Hospital,\textsuperscript{4} Taipei, Taiwan

Received 1 September 2006/Returned for modification 20 September 2006/Accepted 15 November 2006

Brain abscesses are occasionally associated with a dental source of infection. An unusual case of frontal lobe abscess in a nonimmunocompromised child infected with multidrug-resistant \textit{Capnocytophaga ochracea} is described and confirms the pathogenic potential of this organism to cause human disease in the central nervous system.

CASE REPORT

A 7-year, 11-month-old boy was admitted on 12 December 2005 with a 6-month history of intermittent fever, headache, and vomiting. The only significant medical history was extraction of several teeth between ages 3 and 7 years, the most recent extraction having been in May 2005. He had no pets and was a well-developed child.

Upon admission he appeared severely ill, with a temperature of 38.0°C. The left mandibular cheek was erythematous and swollen. He complained of toothache in his left mandibular jaw. His examination was not significant for meningeal signs and was without positive Brudzinski and Kernig signs. The initial laboratory findings included a C-reactive protein of 2.11, a white blood cell (WBC) count of 9,800/mm\textsuperscript{3} (with 70.6% neutrophils and 21.2% lymphocytes), and a platelet count of 613,000/mm\textsuperscript{3}. Lumbar puncture revealed cerebrospinal fluid (CSF) with WBC (12/mm\textsuperscript{3}; 100% lymphocytes), glucose at 65 mg/dl, and protein at 67.1 mg/dl. A CSF Gram stain revealed no bacteria. Analysis of magnetic resonance imaging (MRI) data on the date of admission showed a large, regular, thick-walled, ring-enhanced lesion (about 5.6 cm by 4.7 cm by 3.8 cm) with severe perifocal edema in the left deep frontal lobe (Fig. 1), severe intracranial pressure, and a slight anterior midline shift to the right.

Craniotomy was performed on the second day, and more than 50 ml of purulent pus was aspirated from the left frontal lobe. Gram-negative bacilli were isolated from aerobic and anaerobic cultures of the pus after 3 days of incubation. After subculture on blood agar plates incubated in a CO\textsubscript{2} atmosphere, the bacteria were motile by gliding and grew into yellowish orange colonies. The organisms were identified as \textit{Capnocytophaga} species, with a similarity of 99\%, by the bioM\textregistered erieux VITEK anaerobe identification system. Empirical antimicrobial therapy (ceftriaxone [CRO], 1 g every 12 h; penicillin G [PEN G], 1.5 million units every 4 h; metronidazole, 250 mg every 8 h) was initiated, but on day 6 after surgery the patient developed fever and generalized seizure. An antimicrobial susceptibility test showed resistance to PEN, CRO, vancomycin (VAN), gentamicin (GEN), and cefpirome and susceptibility to imipenem (IPM)-cilastin, ciprofloxacin (CIP), and clindamycin (CLI) (Table 1). Treatment was shifted to intravenous IPM-cilastin (250 mg every 6 h for 4 weeks), CIP (200 mg every 12 h for 2 weeks), and metronidazole (250 mg every 8 h for 4 weeks). To detect possible local disease, abdominal examination, cardiac echogram, and otorhinolaryngologic examination were performed, all of which yielded normal results. However, a dental examination revealed caries in the left second primary molar, which may have been the focus of infection.

The isolate was subsequently identified by 16S rRNA gene amplification and sequencing. PCR was performed with the

\* Corresponding author. Mailing address: Division of Infectious Diseases, Department of Medicine, En Chu Kong Hospital, No. 399 Fuhsing Rd., San-Shia Town, Taipei Hsien 237, Taiwan. Phone: 886-2-2672-3456, ext. 6472. Fax: 886-2-8671-1998. E-mail: clae@ms10.hinet.net.

\textsuperscript{7} Published ahead of print on 29 November 2006.

FIG. 1. Gadolinium-enhanced T\textsubscript{1}-weighted magnetic resonance image obtained before aspiration, revealing a ring-enhanced lesion with significant perilesional edema in the left frontal lobe region.
and encephalomalacia was noted with no neurological

2006. At his most recent follow-up (3 months), brain MRI

on 12 January 2006 revealed left frontal abscess shrinkage to

C. ochracea.

were consistent with species identification of the isolate as

nose, no starch hydrolysis, and no oxidase/catalase activity)

chemical testing (acid production from galactose and raffi-

accession no. U41354) (98% identity). The results of bio-

est match was obtained with

technology Information with the BLAST N algorithm. Theclos-

the GenBank database of the National Center for Biotech-

step [72°C, 7 min]) was carried out in a DNA thermal cycler

extension [72°C, 1 min] followed by a single final extension

denaturation [94°C, 1 min], annealing [55°C, 1 min], and

/H9262

amplification reaction mixtures contained 50 μl of 10 mM

Tris-HCl (pH 8.3), 50 mM KCl, 1.5 mM MgCl₂, 0.001% gelatin, 1 U of Taq polymerase (Perkin-Elmer, Norwalk, CT), 200 μM (each) deoxyribonucleoside triphosphates (dATP, dGTP, and dTTP [Perkin-Elmer]), 50 pmol (each) of the primers, and 2 μl of the DNA sample. PCR (30 cycles of denaturation [94°C, 1 min], annealing [55°C, 1 min], and extension [72°C, 1 min] followed by a single final extension step [72°C, 7 min]) was carried out in a DNA thermal cycler (MJ Research Inc., Watertown, MA). The partial sequence (640 nucleotides) was compared to published sequences in the GenBank database of the National Center for Biotechnology Information with the BLAST N algorithm. The closest match was obtained with Capnocytophaga ochracea (GenBank accession no. U41354) (98% identity). The results of biochemical testing (acid production from galactose and raffinose, no starch hydrolysis, and no oxidase/catalase activity) were consistent with species identification of the isolate as C. ochracea.

The patient's clinical condition improved and brain MRI on 12 January 2006 revealed left frontal abscesses shrinkage to 2.3 cm. He was discharged in good condition on 26 January 2006. At his most recent follow-up (3 months), brain MRI revealed left frontal abscesses shrinkage to less than 1.0 cm, and encephalomalacia was noted with no neurological sequela.

Capnocytophaga species are gram-negative gliding bacteria that require CO₂ for both microaerobic and anaerobic growth and produce yellow colonies on solid media (7). By DNA hybridization and 16S rRNA gene sequencing, five species with clinical significance in humans have been identified: C. ochracea, C. sputigena, C. gingivalis, C. haemolytica, and C. granulosa (4). They may play a role in the pathogenesis of juvenile periodontitis (6, 10) and cause disease (e.g., empyema, lung abscess, and conjunctivitis, etc.) in both immunocompromised and nonimmunocompromised hosts (14). C. canimorsus (an oral commensal of dogs and cats) can also be a pathogen in humans. Capnocytophaga species have been isolated from immunocompromised patients with endocarditis, meningitis, endophthalmitis, and septicemia (3, 7, 8, 11, 12, 13, 15, 17). A Medline search of the literature found only four cases of Capnocytophaga sp. brain abscess (5, 16, 18). The association of frontal brain abscess with upper teeth infections may be due to the connection of the apical venous drainage with the cavernous sinuses, which could allow a septic embolus to enter via reverse flow during yawning and mastication (9).

Most Capnocytophaga strains are susceptible to PEN, ampicillin (AMP), CLI, CLORamphenicol, tetracycline (TET), metronidazole, and erythromycin (ERY). In recent years, PEN- and amoxicillin (AMX)-resistant strains that produce β-lactamase have been isolated. Our strain was found to be highly resistant to cephalosporins, including cefuroxime, ceftazidime, CRO, cefepime, and cefixime (MIC > 256 μg/ml). Susceptibility to AMP, ticarcillin, or piperacillin (PIP) was not tested. If Capnocytophaga species are resistant to AMP or PIP but sensitive to AMP-sulbactam, AMX-clavulanic acid, or PIP-tazobactam, they may be β-lactamase producers (1, 7). Our isolate was very susceptible to CLI and olfoxacin and moderately susceptible to TET, azithromycin, and, to a lesser degree, to quinupristin-dalfopristin, VAN, teicoplanin, and GEN. The child had had intermittent fever with toothache for 6 months, and his treatment with oral antibiotics may have caused the emergence of multidrug-resistant bacteria. Narrow-spectrum cephalosporins are the most commonly used antimicrobials in local clinics in Taiwan. Our strain was found to be highly resistant to cephalosporins. IPM-cilastin, CIP, and metronidazole treatment was selected because (i) Capnocytophaga ochracea had good susceptibility to CIP; (ii) the poor oral condition of the patient was due to anaerobes; (iii) IPM-cilastin is a very effective way to treat brain abscesses, either alone or in combination with neurosurgical drainage of pus (2); and (iv) IPM penetrates well the blood-CSF barrier.

In conclusion, a previously unreported antibiotic regimen can be used to successfully treat brain abscesses due to multidrug-resistant Capnocytophaga, and gene sequencing can be used for rapid identification of the species of Capnocytophaga, which is especially important in the treatment of central nervous system infection. The evidence suggests that dental caries are the focus of infection.

REFERENCES


