**Fusobacterium nucleatum** Multiple Brain Abscesses in an HIV-infected Patient

Supitcha Ongkittikul, M.D., Pornpan Koomanachai, M.D.
Division of Infectious Diseases and Tropical Medicine, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand.

ABSTRACT

This is a report of multiple brain abscesses caused by *Fusobacterium nucleatum* in a 60-year-old human immunodeficiency virus-infected man without any history of dental infection or manipulation. Abscesses material revealed no organisms detected by Gram stain, acid fast stain and modified acid fast stain. Aerobic and anaerobic cultures were negative. The amplification and sequencing of 16S rRNA gene revealed *F. nucleatum* from the specimen. The patient’s symptoms improved after the therapy, surgical drainage and intravenously ceftriaxone and metronidazole. (*J Infect Dis Antimicrob Agents* 2014;31:187-91.)

INTRODUCTION

Brain abscess is caused by direct inoculum or hematogenous spread of organism(s). A single brain abscess usually resulted from a contiguous focus of sinusitis, chronic otitis media or dental caries, while hematogenous spread from bacteremia typically causes multiple lesions. The multiple brain abscesses are commonly caused by polymicrobial pathogens.1 However, this present report was a case report of multiple brain abscesses caused by monomicrobial, *Fusobacterium nucleatum*, in an HIV-infected patient, which was resolved with surgical intervention and antibiotic therapy.

CASE REPORT

A 60-year-old Thai male with the diagnosis of diabetes, hypertension and hypercholesterolemia for several years and received regular treatment, was referred from another hospital. He presented with a history of progressive headache for 2 months then developed alteration of consciousness and intermittent low-grade fever for 1 month. The first physician performed the investigation and found that the patient had HIV infection with CD4+ T-cell 236 cells/mm³ (15%). His complete blood cell count revealed hemoglobin of 11.2 g/dL, leukocyte count of 9,300/mm³ (72% neutrophils and 19% lymphocytes), platelet count of 316,000/mm³. Computed tomography (CT) of the head was performed and showed three rings with contrast enhancement lesions and perilesional edema at left temporal lobes and bilateral parieto-occipital area (Figure 1). Other investigations including serum venereal disease research laboratory (VDRL) test, serum *Toxoplasma* IgG, serum cryptococcal antigen and chest X-ray were normal. A diagnosis of multiple brain abscesses was made. Ceftriaxone and metronidazole intravenously were prescribed.
for 2 days then switched to ertapenem, vancomycin and clindamycin for 2 weeks and changed to meropenem for a week. Unfortunately, the reason for all of the antibiotic regimens were not provided. Subsequently, the patient did not improve and then he was referred to our hospital, Siriraj Hospital, Bangkok, Thailand.

The patient was febrile and semicoma. A repeated cranial CT was performed and demonstrated an increase of three uniform thin rim enhancing hypodense lesions (Figure 2). The surgical therapy was performed for the definite diagnosis and adjunctive treatment (approximately 40 mL turbid yellow fluid was drained out). The numerous leukocytes without microorganisms were shown on Gram stain, AFB and modified AFB stain. No bacterial growth from both aerobic and anaerobic cultures was observed. Pus culture for fungus and mycobacteria were all negative. The sequences of the PCR product showed highest homologies to the 16S rRNA gene of *Fusobacterium nucleatum*. According to the PCR results, de-escalation of antimicrobial therapy to intravenously ceftriaxone and metronidazole were prescribed. Later on, the patient was prescribed treatment for HIV with tenofovir, lamivudine and efavirenz.

Three weeks after the drainage, the follow-up CT of the head demonstrated a new linear enhancement along wall of right lateral ventricle and increase in size of lesion at left occipital region (Figure 3). Therefore, the surgical aspiration of the left occipital abscess was performed again and continued the same antimicrobial regimen. The patient was gradually improved and afebrile. However, the recovery of neurological defect was very slow. The total intravenously antimicrobial therapy was 3 months.
Fusobacterium nucleatum multiple brain abscesses in an HIV-infected patient: Ongkittikul S & Koomanachai P.

**DISCUSSION**

*Fusobacterium nucleatum* is an anaerobic bacteria of upper respiratory tract flora. The existence of anaerobes caused brain abscesses mainly from the contagious site of existing infection, such as dental infection, sinusitis or chronic otitis media. However, hematogenous spread of an anaerobic organism from a distant focus can occasionally lead to bacteremia that seeds the cerebral cortex and results in multiple abscesses as well.\(^1\,^2\) Several studies have shown 50% of the patients with brain abscess caused by anaerobe were usually polymicrobial infection.\(^3\,^4\) The most frequently isolated anaerobes were *Fusobacterium* spp., followed by *Prevotella* spp., *Bacteroides* spp. and *Actinomyces* spp.\(^4\) Among the *Fusobacterium*...
genera that have been reported, *F. nucleatum* was the most common cause of brain abscess.\(^3\) There was a report of 122 patients with culture positive bacterial brain abscesses, that 6% of monomicrobial infection was *Fusobacterium* spp.\(^5\)

*Fusobacterium nucleatum* is obligate anaerobic gram-negative bacilli that associated with periodontitis in both immunocompetent and immunocompromised patients.\(^1,6,7\) HIV-infected patients with *F. nucleatum* infection, especially brain abscess, was rarely reported. This organism was more reported as bacteremia and liver abscess in HIV infection.\(^8,9\) From literatures reviewed, there was no report of brain abscesses caused by *F. nucleatum* in HIV-infected patients. Identification of the causative organism is necessary to permit the administration of appropriate antimicrobial therapy, especially in a patient with any previous antibiotics therapy. Twenty-four to 40% of intracerebral abscesses produced negative culture results, due to patients receiving antibacterial therapy.\(^10\) Accordingly, the anaerobes are difficult to be isolated and cultured from infected specimens, gene amplification and sequencing tests assist in the diagnosis of culture-negative brain abscesses.

The management of brain abscesses has required a combination of surgical and parenteral antimicrobial therapy with the antimicrobial therapy duration of at least four to eight weeks. The follow-up assessment of clinical response and imaging studies should be performed. In some cases, even longer antimicrobial treatment is necessary.

*Fusobacterium* spp. is commonly sensitive to the anti-anaerobic antibacterial agents including penicillin G, piperacillin, amoxicillin/clavulanate, cefoxitin, cephalor, tetracycline, clindamycin, metronidazole, and chloramphenicol\(^1,5,11\) However, there were few studies that reported beta-lactamase production by *Fusobacterium* spp. A study from Kuwait, demonstrated 14.6% of *Fusobacterium* spp. isolates were resistant to penicillin and 2.6% were resistant to clindamycin.\(^12\) The presented patient was successfully treated with combination of ceftriaxone, metronidazole and surgical drainage.

In conclusion, anaerobic bacteria including *F. nucleatum* infection should be considered in the differential diagnosis of brain abscesses even though there is no previous history of dental manipulation or dental infection. Successful management requires a combination of antimicrobial and adequate drainage. Despite the therapy when appropriate antimicrobial agent is administered, the failure and complication of treatment mostly occurs without the surgical drainage. Bacterial 16S rRNA gene PCR and sequencing test may aid in the detection of fastidious and anaerobic pathogens, leading to appropriate antibiotic therapy.

References


