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BRIEF COMMUNICATION

# *Aggregatibacter aphrophilus* brain abscess secondary to primary tooth extraction: Case report and literature review

**Sofia Maraki [a,*], Ioannis S. Papadakis [a], Efkleidis Chronakis [b], Dimitrios Panagopoulos [b], Antonis Vakis [b]**

[a] *Department of Clinical Microbiology, Parasitology, Zoonoses and Geographical Medicine, University Hospital of Heraklion, Heraklion, Crete, Greece*
[b] *Department of Neurosurgery, University Hospital of Heraklion, Heraklion, Crete, Greece*

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We report on a rare case of *Aggregatibacter aphrophilus* brain abscess of odontogenic origin in a 6-year-old previously healthy boy, who had close contact with a pet dog. The poodle was the most likely source of the infecting organism, which subsequently colonized the patient's oral cavity. The abscess was surgically removed and he recovered completely after prolonged antibiotic treatment with meropenem. We also review the relevant medical literature on *A. aphrophilus* pediatric brain abscesses.


## Introduction

*Aggregatibacter aphrophilus* (formerly *Haemophilus aphrophilus* and *Haemophilus paraphrophilus*) is a Gram-negative, nonmotile, capnophilic, fermentative, oxidase- and catalase-negative, and X and V independent on primary isolation coccobacillus that is part of the normal oropharyngeal flora.[1,2] It has been isolated from dental plaque, interdental material, and gingival pockets.[1,2] This microorganism was first described by Khairat[3] in 1940, when it was recovered from a patient with endocarditis. Other infections due to *A. aphrophilus* such as brain abscess, empyema, meningitis, sinusitis, otitis media, bacteremia, pneumonia, osteomyelitis, peritonitis, and wound infections have also been described.[4]

We report a case of brain abscess due to *A. aphrophilus*, discuss the potential sources of infection, and review the English medical literature on pediatric cases of brain abscesses due to this rare pathogen.

## Case report

A 6-year-old boy was brought by his parents to the Emergency Department of the University Hospital of Heraklion due to symptoms of worsening drowsiness and repeated

* Corresponding author. Department of Clinical Microbiology, Parasitology, Zoonoses and Geographical Medicine, University Hospital of Heraklion, 71 110 Heraklion, Crete, Greece.
*E-mail address:* sofiamaraki@yahoo.gr (S. Maraki).


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episodes of vomiting. His past medical history was unremarkable except for a recent extraction of a central upper incisor, approximately 2 weeks prior to the onset of his symptoms. The boy was changing his primary teeth, and although he had no signs of periodontitis, he had poor dental hygiene. The parents also reported that he had frequent and close contact with the family's pet dog.

On admission the boy was afebrile, with a heart rate of 110 beats/minute, blood pressure 110/85 mmHg, and oxygen saturation 97%. He was pale, with supple neck, dry mucous membranes, and had a slightly decreased level of consciousness (Glasgow coma scale 12). The remaining of the physical examination was normal. Laboratory investigations showed leukocytes 10.9 $\times$ $10^9$/L with 9.4 $\times$ $10^9$/L neutrophils and 0.1 $\times$ $10^9$/L bands, hemoglobin 131 g/L, glucose 7.4 mM (normal range, 3.8–6.3 mM), blood urea nitrogen 8.9 mM (normal range, 8–16.4 mM), creatinine 52 μM (normal range, 50–110 μM), sodium 140 mM (normal range, 135–145 mM), potassium 4.2 mM (normal range, 3.5–5.0 mM), fibrinogen 14.5 μM (normal range, 5.1–11.8 μM), and C-reactive protein 3.3 mg/L (normal range, 0.8–8 mg/L). Hormonal examinations, tumor markers, virology tests, and a chest radiograph were normal. A computed tomography scan of the head after administration of intravenous contrast revealed a sizable ring-enhancing lesion in the left frontal lobe, along with surrounding brain edema that caused a slight midline shift.

A magnetic resonance imaging scan of the head confirmed the computed tomography findings (Fig. 1). The boy was immediately subjected to a frontoparietal (pterional) craniotomy, which revealed a sizable abscess containing purulent and bloody material that was appropriately drained. Then, the lesion was totally removed with its capsule. Empiric antibiotic therapy was initiated pending culture results with intravenous metronidazole (10 mg/kg every 8 hours), and high-dose meropenem (40 mg/kg every 8 hours), while dexamethasone (0.5 mg/kg/day) was added as an adjunct therapy.

Cultures of the purulent material revealed an oxidase negative, catalase negative, and X and V factor independent Gram-negative coccobacillus. The isolate was identified with the use of the Vitek 2 automated system and by individual biochemical tests as *A. aphrophilus*. Using E-test, the isolate was found to be susceptible to ampicillin, amoxicillin plus clavulanic acid, cefuroxime, ceftriaxone, cefotaxime, imipenem, meropenem, clarithromycin, azithromycin, ciprofloxacin, levofloxacin, cotrimoxazole, tetracycline, and chloramphenicol. Metronidazole was discontinued and intravenous high-dose meropenem was administered as monotherapy for a total of 8 weeks. The patient underwent thorough screening for other possible sources of infection, such as congenital heart diseases, but none was found. The boy's symptoms resolved and he was discharged home in good clinical condition. A magnetic resonance imaging scan of the head conducted just prior to discharge showed remarkable improvement (Fig. 2).

**Figure 1.** Coronal T2 flair magnetic resonance imaging showing the abscess in the left frontal lobe.

## Discussion

Brain abscess is an uncommon pathologic entity in children. Overall, about 25% of brain abscesses in some series occur in children, mostly in the age group 4–7 years.[5] The microorganisms can reach the brain by several different mechanisms. The most common is spread from a contiguous focus of infection, most often the middle ear, mastoid cells, or paranasal sinuses.[5] Other mechanisms include

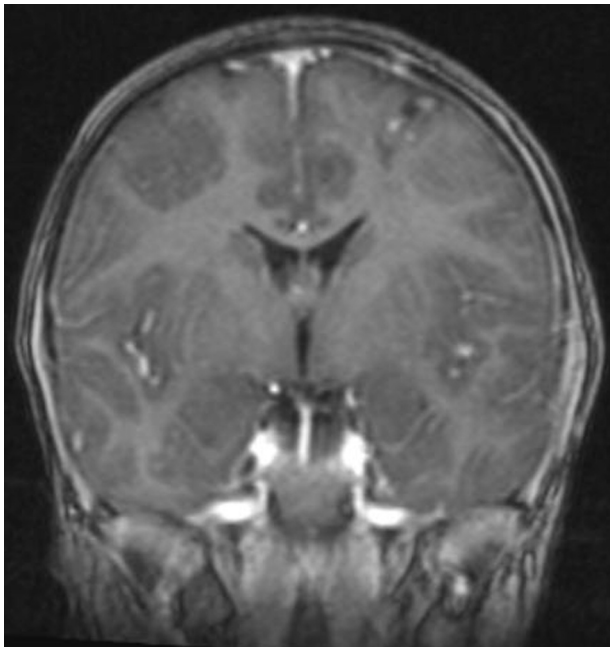

**Figure 2.** Coronal T1 flair image 3 months after the abscess removal.

**Table 1** Clinical characteristics of *Aggregatibacter aphrophilus* brain abscesses in pediatrics

| Year | Reference | Age/ gender | Underling illness or predisposing factors | Therapy | Outcome |
|---|---|---|---|---|---|
| 1964 | Isom et al[12] | 11 F | Sinusitis | Surgical + antibiotics (oxacillin, sulfadiazine, chloramphenicol, streptomycin, tetracycline) | Recovery |
| 1966 | Page and King[24] | 8 F | None | Penicillin G, chloramphenicol | Death |
| 1966 | Page and King[24] | 7 M | Congenital heart disease | Surgical | Death |
| 1966 | Page and King[24] | 14 M | None | Surgical + antibiotics (unspecified) | Recovery |
| 1966 | Page and King[24] | 3 M | None | Surgical + penicillin G | Recovery |
| 1972 | Yamashita et al[14] | 11 F | Meningitis, otitis | Surgical + antibiotics (Ampicillin, streptomycin, sulfadimidine) | Recovery |
| 1973 | Fischbein et al[16] | 4 F | Congenital heart disease | Surgical + antibiotics (penicillin, chloramphenicol) | Recovery |
| 1973 | Fischbein et al[16] | 6 F | Congenital heart disease | Surgical + antibiotics (penicillin, chloramphenicol) | Recovery |
| 1973 | Fischbein et al[16] | 5 F | Congenital heart disease | Surgical + antibiotics (penicillin, ampicillin) | Recovery |
| 1978 | Bieger et al[9] | 8 F | Recurrent otitis media | Surgical + antibiotics (penicillin, ampicillin, streptomycin, tetracycline) | Recovery |
| 1978 | Bieger et al[9] | 16 M | Congenital heart disease, pulmonary hypertension | Surgical + antibiotics (chloramphenicol, gentamicin, cephalothin) | Death |
| 2005 | Bayraktar et al[23] | 6 M | None | Surgical + antibiotics (unspecified) | Recovery |
| 2008 | Wolf and Curtis[7] | 12 M | Application of dental braces | Surgical + antibiotics (flucloxacillin, cefotaxime, metronidazole) | Recovery |
| 2008 | Hoefele et al[22] | 3 M | Otitis media | Surgical + antibiotics (3rd generation cephalosporins, metronidazole) | Recovery |
| 2012 | Present case | 6 M | Tooth extraction | Surgical + antibiotics (meropenem) | Recovery |

F = female; M = male.

hematogenous dissemination to the brain from a distant focus of infection, and trauma secondary to an open cranial fracture with dural breach, or as a result of neurosurgery or a foreign body injury. The most common distant sources of brain abscesses are infective endocarditis, osteomyelitis, bacteremia, and pulmonary, pelvic, skin, or dental infections.[5] Criteria used to implicate a dental source of infection for a brain abscess include finding no other source of infection, oral microorganisms isolated from the brain abscess, and clinical signs of dental infection, tooth extractions, and application of braces.[6,7]

The most commonly isolated microorganisms in cases of pediatric brain abscesses are viridans streptococci, anaerobic streptococci, and occasionally *Haemophilus* species. Milnes et al[8] found that *A. aphrophilus* is a component of the commensal oral microbiota of preschool children. In the case of our patient, who had no evidence of any other associated conditions the mouth was the most likely source of infection. We assume that the brain abscess in our patient was due to bacteremia and hematogenous spread following a dental extraction that took place 2 weeks earlier. Bieger et al[9] reviewed 90 cases of *A. aphrophilus* infections and a dental source was implicated in eight patients. Huang et al[10] reviewed 28 cases of invasive *A. aphrophilus* infections. Overall, in 11 (39%) of them recent dental procedures or dental infections were identified. Possible transmission from dog to man has been suggested on several occasions, because this Gram-negative coccobacillus has been found to be part of the normal canine oral flora.[11] Isom et al[12] and Abla et al[13] reported two cases of *A. aphrophilus* brain abscesses in patients who had close contact with a dog. *A. aphrophilus* was isolated from the dogs' saliva, whereas in the cases reported by Yamashita et al[14] and Kao et al[15] cultures did not yield such an organism. In 1973 Fischbein et al[16] reported three pediatric cases of *A. aphrophilus* brain abscesses associated with congenital heart disease; in two (67%) of them close contact with a dog was reported, although no animal cultures were performed. Our patient likewise had lengthy and direct contact with the family poodle. Although cultures from the dog's oral cavity were not performed, we speculate that the patient's poodle was the most likely source of the infecting organism, which subsequently colonized the oral cavity of our patient.

Cyanotic congenital heart disease (CCHD) is an important predisposing factor for brain abscess formation in children, and accounts for 6—50% of cases in published series.[17] The highest incidence of this complication appears to be among children with cardiac defects, such as tetralogy of Fallot or transposition of the great vessels; however, any condition resulting in a significant right-to-left shunt appears to increase the risk. Decreased oxygen saturation and increased blood viscosity may cause focal areas of brain ischemia that serve as nidi of infection.[18] In a pediatric series of cerebral abscesses in patients with CCHD, *A. aphrophilus* was identified as the second most frequent infecting organism.[16]

Clinical isolates of *A. aphrophilus* have been demonstrated to be susceptible to penicillin, ampicillin, and cephalosporins. However, a clinical failure with cefotaxime has been reported in a case of a β-lactamase negative strain.[19] Ciprofloxacin and the newer fluoroquinolones have potent activity against *A. aphrophilus*, and can be used as alternatives for penicillin allergic individuals, and for those infected with strains resistant to cephalosporins. The present strain was susceptible to all antibiotics tested according to the guidelines of the Clinical and Laboratory Standards Institute.[20] We elected to use high-dose meropenem due to the track record of this antibiotic that has excellent central nervous system penetration in the treatment of brain abscesses.[21]

If the condition is promptly diagnosed and appropriately treated, brain abscess mortality is low in patients with no predisposing conditions. By contrast, it is high (30–40%) in those with CCHD.[6] A review of the English language medical literature since 1964 showed only 14 previously reported pediatric cases of brain abscess due to *A. aphrophilus* (Table 1).[7,9,12,14,16,22–24] Eight (53%) of the 15 patients (including the present case) were males. Associated conditions were congenital heart disease in five cases, otitis media in three, dental procedures in two, and sinusitis in one case. No obvious source of infection was identified in the remaining four patients. Treatment consisted of surgical drainage combined with antimicrobial therapy in 13 (87%) cases. The overall mortality rate was 20%. One of the patients who died had underlying congenital heart disease, pulmonary hypertension and multiple brain abscesses, whereas the others were treated with surgery or antibiotics alone.[9,24]

In conclusion, *A. aphrophilus* should be considered in the differential diagnosis of brain abscesses in children. Dental procedures, close contact with dogs, and CCHD are predisposing conditions. Prompt surgical drainage and prolonged antibiotic treatment are necessary to achieve a favorable clinical outcome.

## Conflicts of interest

All contributing authors declare no conflicts of interest.

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