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Single Case – General Neurology

### First Case of Intracranial Mycotic Aneurysm Caused by *Prevotella intermedia* Associated with Chronic Sinusitis in a Korean Adult

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#### Keywords

Prevotella intermedia · Mycotic aneurysm · Anaerobes · Sinusitis · 16S rRNA

#### Abstract

Intracranial infection caused by anaerobic bacteria is rare, and it is difficult to identify absolute anaerobes in the clinical laboratory, especially when the bacterial load is low. Here, we report the first case of intracranial mycotic aneurysm caused by *Prevotella intermedia* associated with chronic sinusitis and successful identification of the bacteria by 16S rRNA sequencing from bacterial growth in broth only.

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#### Introduction

A mycotic aneurysm is an abnormal focal arterial dilatation [1, 2], and an intracranial mycotic aneurysm (IMA) is a mycotic aneurysm within the cerebral arteries, caused predominantly by bacterial infections [3]. IMA is associated with significant morbidity and mortality because of spontaneous rupture [4]. The majority of IMAs are caused by viridans group streptococci and *Staphylococcus aureus* [2, 3]; there are a few reports of IMA caused by anaerobes, which are rare pathogens, after dental treatment [5]. This report describes a previously

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healthy adult who had an IMA caused by anaerobic *Prevotella* species, which was identified by 16S rRNA sequencing.

#### **Case Report**

A 47-year-old woman presented with a headache, vomiting, and fever for 3 days. She was previously healthy and had no drug history or recent dental treatment. On admission, she had left ocular pain, a temperature of 37.2°C, and neck stiffness. Cerebrospinal fluid (CSF) examination revealed a protein level of 145 mg/dL (reference range 15–45 mg/dL) and glucose level of 88 mg/dL (reference range 74–109 mg/dL). The white blood cell (WBC) count in CSF was 300/mm<sup>3</sup>, with 80% polymorphonuclear cells (PMNs). The WBC count in blood was 9,630/µL, with 84.9% PMNs. The C-reactive protein level was 11.1 mg/dL. Computed tomography and magnetic resonance imaging (MRI) of the brain revealed diffuse leptomeningeal enhancement and chronic maxillary sinusitis. No abnormality was detected on brain magnetic resonance angiography (MRA), and there was no evidence of endocarditis. Gram stain and bacterial culture of CSF and blood were performed. CSF was inoculated on a mixture of chocolate agar, 5% sheep blood agar, Brucella blood agar, and enriched thioglycolate broth. No microorganisms were seen with Gram staining after 3 days of incubation or in blood cultures after 5 days.

The following empirical antibiotics targeting bacterial meningitis were administered from the first hospital day: intravenous ceftriaxone (2 g every 12 h) and vancomycin (20 mg/kg every 12 h). The patient's headache did not subside, and her fever reached 38.0°C. A second CSF examination on hospital day 6 showed worsening CSF leukocytosis, with a WBC count of 1,060/mm<sup>3</sup> (92% PMNs). On hospital day 10, she complained of sudden left ocular pain and subsequent horizontal diplopia, which implied left abducens nerve palsy. A third CSF examination, brain MRI, and computed tomography angiography were performed. A 1.1-cm aneurysm was found in the posterior communicating artery, which was not detected by MRA at admission (Fig. 1). A subarachnoid hemorrhage in the posterior fossa was found, suggesting aneurysm rupture. She was transferred to another hospital for angiographic intervention using coil embolization. Metronidazole (500 mg every 8 h) was added to the initial empirical antibiotic treatment.

The third CSF culture revealed no growth after 3 days, but after 10 days, red bacterial growth of gram-negative rods was observed in thioglycolate broth (Fig. 2). 16S rRNA gene sequencing in the isolate was performed using PCR according to a published method [6], and the results identified the isolate as *Prevotella intermedia*, revealing 99.05% identity (1,352/1,365 bp) with *P. intermedia* ATCC 25611T (GenBank accession number CP019301). The patient was diagnosed with IMA caused by *P. intermedia*. She improved rapidly after angiographic intervention and metronidazole treatment. She was given intravenous metronidazole for 2 weeks and discharged on hospital day 34. She signed a written informed consent to publish her case, including images.

#### **Discussion/Conclusion**

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*P. intermedia* is a gram-negative, obligate anaerobic rod that is commonly involved in periodontitis [7]. It produces a pigment that results in black colonies on solid agar. Although there have been reports of anaerobic bacterial meningitis and brain abscesses caused by *P*. 122

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intermedia, it is mostly involved in mixed infections and has not been reported to cause IMA [8, 9]. Because we did not initially consider bacterial meningitis due to anaerobic bacterial infection, the appropriate antibiotic treatment was delayed, causing IMA rupture.

The patient had no evidence of endocarditis or history of dental treatment, which are the typical predisposing conditions for anaerobic bacterial meningitis. Instead, she had maxillary sinusitis; therefore, her IMA and meningitis were thought to be related to the maxillary sinusitis, considering that *P. intermedia* is a common cause of chronic sinusitis [10, 11]. Clinicians need to consider the possibility of anaerobic infection in bacterial meningitis with comorbid sinusitis.

Commercial kits for bacterial identification require pure colonies grown on solid agar for broth microdilution and agar dilution, which are reference methods for testing anaerobes [12]. When grown only in liquid medium, the bacteria should be subcultured on solid medium to obtain pure single colonies. Obligate anaerobes including Prevotella species do not tolerate oxygen exposure [13]; therefore, culturing them on solid medium requires strict conditions, and obtaining single colonies is difficult. In this case, red growth was detected only in thioglycolate broth. Pigment production varies from tan to black, depending on the species [7]. The red growth in thioglycolate broth was the first in our laboratory in 20 years. It made identification difficult, and we could not use a commercial kit because we failed to obtain colonies from solid medium. 16S rRNA gene sequencing successfully identified the pathogen as P. intermedia. 16S rRNA gene sequencing is a better and more rapid method for identifying anaerobic bacteria compared with conventional identification methods [14], as in this case.

Anaerobic pathogens in adult meningitis are very rare and, thus, are often overlooked and undertreated [8]. In the current Korean guidelines for the treatment of adult meningitis, standard empirical treatment includes third-generation cephalosporin and vancomycin for immunocompetent patients, which does not cover anaerobic meningitis [15]. Without molecular identification, the appropriate treatment may be delayed, leaving the patient in a more critical condition.

To our knowledge, this is the first case of IMA caused by *P. intermedia*. The possibility of anaerobic infection should be considered when standard empirical treatment is ineffective for bacterial meningitis. Prompt identification of the pathogen using molecular methods would be helpful.

#### **Statement of Ethics**

The patient signed a written informed consent to publish her case, including images. The Institutional Review Board (IRB) of Inje University Ilsan Paik Hospital has determined that our project does not meet the "Common Rule" definition of human subjects' research and does not require IRB review. The IRB number is 2019-10-013.

#### **Disclosure Statement**

The authors have no conflicts of interest to declare.

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### **Author Contributions**

All authors contributed to the study conception and design. Study preparation and data collection and analysis were performed by H.R.P., J.C., C.R.C., and S.K. The first draft of the manuscript was written by J.C. and T.H.U., and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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**Fig. 1.** Brain magnetic resonance imaging and computed tomography angiography findings on hospital day 10. **a** T1-enhanced magnetic resonance image showed a filling defect and perilesional enhancement suggesting cavernous thrombosis and thrombophlebitis in the cavernous sinus. **b** Gradient echo image revealed a subarachnoid hemorrhage in the posterior fossa. **c** A 1.1-cm posterior communicating artery aneurysm was observed on computed tomography angiography.



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Fig. 2. Red bacterial growth in thioglycolate broth after incubation for 10 days.

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