

Dental Infections and Risk for Brain Abscess: A Literature Review

Greggory D Boatright II¹, Michell A Llerena¹, David J Gorelov¹, M Tahseen Alkaelani¹, Joel R Goeckeritz², and Brandon Lucke- Wold^{3*}

¹College of Medicine, Florida State University, Tallahassee, FL 32304, USA

²College of Medicine, University of Florida, Gainesville, FL 32611, USA

³Department of Neurosurgery, University of Florida, Gainesville, FL 32601, USA

***Corresponding Author:** Brandon Lucke-Wold, Department of Neurosurgery, University of Florida, Gainesville, FL 32601, USA.

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Abstract

Dental work is commonly accepted as a low-risk procedure but has been associated with serious brain abscesses. Bacteria from the oral cavity can spread to the brain and cause life-threatening infections. In this literature review, the focus was placed on the relevant causative bacteria, surgical procedures, and correlated medical conditions revolving around brain abscesses following dental work. This paper is written from a neurological surgery perspective, using information collected from several case studies, case reviews, and other related published manuscripts. Several risk factors have been identified to predispose oral cavity bacterial infection to cause brain abscess: dental work done in the upper molars; right-to-left shunts in the heart; and poor dental hygiene. If the bacterium of the abscess is correctly identified, there is a greater effectiveness of treatment, but prolonging antibiotic and/or surgical treatment increases morbidity.

Keywords: brain abscess; dental; infection; oral flora; immunocompromised; needle aspiration; surgical excision; antibiotics; congenital heart defects.

Introduction

Numerous bacterial strains populate the natural flora of the oral cavity, with certain strains capable of spreading to the brain following odontological procedures [1]. Specifically, it was discovered that dental plaque can contain about 350 different possible bacterium types [2]. Odontological bacterial infection spreading to cause a brain abscess is a very unlikely outcome of dental work, yet the sheer number of dental procedures done every year elicits a clear indication that understanding the etiology of this unique occurrence is worth consideration. Incidence of brain abscess in developed countries is 0.3-0.9 per 100,000 habitants with mortality between 17% and 37% [3]. Although the treatment of brain abscesses has well established treatment protocols, the understanding behind what factors predispose patients to odontogenic infections to become brain abscesses is lacking [4]. This literature review covers current published work

regarding brain abscess causing bacteria arising from the oral cavity. The breadth of this manuscript focuses on the causative organisms, surgical evacuations, predisposing factors, and subsequent medical management of bacterial brain abscesses.

Methods

Pre-defined search terms were used to search PubMed from inception to 17 September 2022. 193 results showed with "Brain abscess oral," then 64 results showed with "Brain abscess dental infection." The search terms included ("Brain abscess"[Mesh]) AND "Dental infection". Included in the study were all original, peer-reviewed studies that reported on the development of brain abscess due to dental infection. All published manuscripts before 2003 were excluded from our review, allowing focus on modern treatment. Abstracts and studies not easily translated into the English language were excluded from the study. This included a title and abstract screening, followed by a full-text review and subsequent data extraction step,

narrowing the pool of studies to 43. All articles used had free full article access, allowing simple reference material for subsequent reader reference analysis.

Data extraction was done via Microsoft Excel®, and included information on study design, causative organism, predisposing factors, proposed treatment approach, surgical evacuation, and subsequent medical management. Then the articles were cited in order of use in the most logical pattern of literature review progression.

Microbial Infection, Identification, and Proposed treatment

Odontogenic infections, procedures, and trauma have been linked with the development of brain abscesses in unique instances [5,6]. Infection of the upper molars and surrounding gingiva has been correlated to a high risk of developing brain abscess - see Figure 1 [7]. The natural oral flora is the most common cause of subsequent brain infections, specifically *Streptococcus* species and mixed anaerobes (such as *Anaerococcus prevotii*) [3,4]. *Streptococcus intermedius* causes approximately 50-80% of bacterial brain abscesses; along with placing immunocompromised patients at higher risk for thalamic abscesses [8–10]. *Streptococcus viridans* have been demonstrated to cause brain abscess in patients with infected pulp [11]. One descriptive and comparative metagenomic study showed how there was a 65.5% overlap between microorganism species of empyemas and brain abscesses, with *Streptococcus intermedius*, *Fusobacterium nucleatum* and *Aggregatibacter aphrophilus* being the most common pathogens [12]. Additionally, an

immunocompromised status is a predisposing factor for developing brain-related infections [8,11,13].

Odontogenic brain abscesses from oral origin have been reported in neonatal and pediatric cases. In addition to those above, common pathogens affecting neonates include bacteria from the *Proteus*, *Citrobacter*, and *Enterobacter* genres. In children with compromised immune systems the most common agents predisposing brain abscess development are from the *Nocardia spp.*, *Mycoplasma tuberculosis*, *Eikenella corrodens*, and certain fungi species [11,14]. In addition, *Streptococcus viridans* and *Prevotella spp.* have been associated with the development of brain abscesses in neonatal and pediatric patients with pre-existing or congenital cardiovascular defects such as patent foramen ovale (PFO) [15].

Other organisms associated with periodontal disease, dental caries, and poor oral condition that can lead to brain abscess in adults include *Bacteroides*, *Actinomyces meyeri*, *Porphyromonas gingivalis*, *Pseudomonas aeruginosa*, *Fusobacterium*, *Aggregatibacter actinomycetemcomitans*, *Prevotella spp.*, and *Mycoplasma salivarium* - see Table 1 [3,11,15–21]. Some case studies have described unsuspecting diseases such as group-A streptococcal pharyngitis leading to brain abscess that could be prevented by diagnoses and therapy of *Streptococcus pyogenes* infection [22]. These bacteria highlight the wide spectrum of microorganisms that can play a role in the advent of a brain abscess.

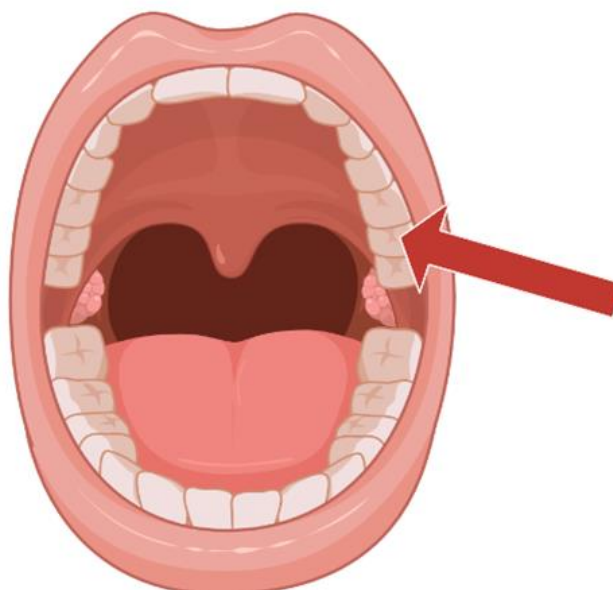


Fig 1: Shown above is a visual depiction of the upper molar area of the mouth, where dental work is most highly correlated with odontogenic bacterial brain abscesses [7].

Table 1: Summary of brain abscess causing organisms and cited papers

	Findings	Source
Streptococcus spp. & mixed anaerobes like <i>Anaerococcus prevotii</i>	Normal flora and common cause of brain abscess	Sasmanto et al. 2022 [3,4]
<i>Streptococcus intermedius</i>	Most common brain abscess forming bacteria	Basyuni et al. 2015 [8-10]
<i>Streptococcus viridans</i>	Correlated with infected pulps leading to brain abscess	AlHarmi et al. 2018 [11]
<i>Staphylococcus aureus</i>	Most common cause of post-surgical brain abscesses	
<i>Streptococcus viridans</i>	Associated with brain abscesses in neonatal patients with congenital cardiovascular defects	Akimoto et al. 2018 [15]
<i>P. revotella</i>		
<i>Eikenella corrodens</i>	Predisposing agents to brain abscesses in immunocompromised pediatric patients	Valdes-de la Torre et al. 2017 [11,14]
<i>Mycobacterium tuberculosis</i>		
<i>Nocardia</i>		
<i>Actinomyces meyeri</i>	Other organisms documented to cause brain abscess in adults	Kichenbrand et al. 2020; Funakoshi et al. 2020 [3,11,15-20]
<i>Aggregatibacter actinomycetemcomitans</i>		
<i>Fusobacterium</i>		
<i>Mycomplasma salivarium</i>		
<i>Peptostreptococcus</i>		
<i>Porphyromonas gingivalis</i>		
<i>Pseudomonas aeruginosa</i>		
<i>Streptococcus pyogenes</i>		

Brain abscess can be challenging to diagnose on clinical symptoms alone as its presentation could be due to other etiologies. Common presentations include headaches, fever, altered mental status, decreased consciousness, seizures, cerebellar involvement, as well as the constellation of abdominal pain, nausea, vomiting, and diarrhea [6,16,23]. The characteristic triad of headache, fever, and focalization only occurs in 20-30% of cases [14].

Computed Tomography (CT) is the preferred scanning method, although sometimes Magnetic Resonance Imaging (MRI) is used to give more detailed images [11]. Although treatment can be started without the isolation of the specific pathogen causing the brain abscess, having an identified microbial pathogen can help identify the best treatment for the patient [7]. Gram staining, culture, and histopathology are the preferred methods for accurately identifying the pathogen [8,9,11,16,23,24]. In addition, the use of matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) technology has led to the rapid identification of microorganisms. MALDI-TOF tech uses computerized scans analyzed through computer algorithms to rapidly identify bacteria [23].

Additionally, bacterial brain abscesses from oral cavity bacteria can occur following intracranial surgical procedures. In cases of trauma related to procedures or surgeries to the brain, *Staphylococcus aureus* is the most common pathogen amongst post-surgical brain abscesses. The second most likely bacteria for post-surgical abscesses are *Streptococci* spp. and *Enterobacteriaceae* spp. genres of

bacteria [11]. The risk of surgical procedures within the skull includes the possibility of introducing other pathogens, which may respond to different antibiotic treatments and require alternative subsequent management. Thus, the neurosurgical drainage approach is only added to the antibiotic treatment when there is sufficient size of tumor to use more than antibiotics, due to the risk the procedure itself can present [12,25].

Surgical Evacuation, Alternative Treatments, and Subsequent Management

Once identified on CT or MRI treatment of brain abscesses follow a well-established methodology as seen in Figure 2 [25]. Though ordering of steps may vary on a case-by-case basis, major considerations include when antibiotic treatment is given, medication choice accounting for patient allergies, and the number of neurosurgeries (drainage) needed for the patient [25].

For brain abscesses greater than 1 cm in size, treatment first consists of draining the abscess, either by needle aspiration or surgical excision, and then administering broad-spectrum antimicrobial therapy [1,26]. However, effective treatment of brain abscesses relies on identifying the underlying bacteria causing the abscess [4,19]. Correct identification the bacteria allows for the use of the most effective antibiotic, thereby minimizing drug resistance. Brain abscesses smaller than 1 cm in size, are treated using antibiotics without the need for surgical resection [27-28].

Abscess drainage being part of the neurosurgical

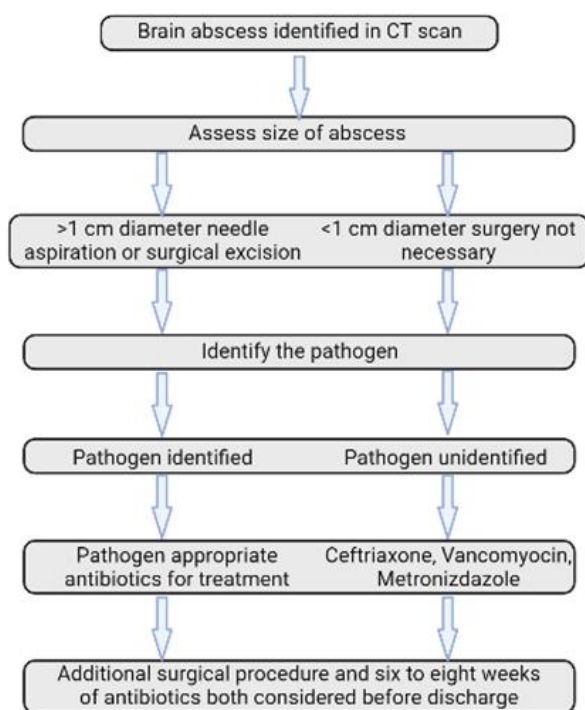


Fig 2: This is a flowchart of the Surgical Evacuation section of this literature review. Shown are the steps of brain abscess treatment following the discovery of the Brain abscess (via CT scan). First the abscess size is taken into consideration, then the pathogen is attempted to be identified, then antibiotics and possible additional surgeries are considered.

treatment has demonstrated benefits on its own [11,28]. Surgical excision and neurosurgical aspiration of the brain abscess is helpful as it can prevent the infection from spreading to nearby tissue and help identify the type of bacteria causing the abscess [4,29].

Furthermore, the earlier the causative agent is identified, the more effective the treatment will be in reducing mortality rates and improving the overall prognosis [30]. Stereotactic-guided aspiration is the most common procedure for draining a singular abscess larger than 1cm in diameter and is performed by drilling a burr hole for fluid drainage of the brain abscess. Whereas, total surgical resection by craniotomy is a procedure reserved for larger, multi-lobulated abscesses with severe intracranial hypertension [19].

Upon consistent inspection of the abscess site, any indications of bacterial growth or site inflammation is treated with antibiotics post-surgery [18,25]. If the underlying cause cannot be identified, brain abscesses should be treated empirically with Ceftriaxone 2 g twice daily, Vancomycin 1 g three times daily, and Metronidazole 500 mg four times daily [1,31]. Alternative broad-spectrum IV antibiotics include Ampicillin with Sulbactam or oral Amoxicillin with Clavulanate [8,13,16,28]. Treatment may also

include Amphotericin B to cover possible fungal pathogens, rifampin for resistant microbes, metronidazole as an additional antibiotic, and corticotherapy to reduce inflammation [24]. Multiple surgical treatments may be required if upon repeat MRI inspection the abscess is shown attempting to reform or if more abscesses arise [32].

Antimicrobial therapy is determined post-surgery, after the abscess and tissue specimens extracted are analyzed by a microbiology department and antibiotic susceptibility tests are carried out [4,30]. Once the antibiotic therapy is started, imaging studies (i.e. MRI or CT specific) focusing on changes in the size of the lesion, edema and mass effect should be performed weekly to evaluate the effectiveness of the antimicrobial therapy [14,19]. Using appropriate antibiotic therapy, the abscess should decrease in size within 1-4 weeks however the radiological resolution could take up to 16 weeks. Until abscess and overall infection has fully resolved multiple rounds of antibiotics and surgeries may be required, potentially retaining the patient for months of hospital stay. Typically, antibiotics are given for six to eight weeks following correct bacterial identification of the brain abscess [33]. Additional nosocomial diseases are prevented via personal protective equipment and possible visitation restrictions, especially with immunocompromised patients [4,8,11,22,34].

Discussion

Brain abscesses typically occur in the frontotemporal, frontal-parietal, parietal, and cerebellar-occipital lobe areas of the brain - see Figure 3 [35]. This is most likely attributed to the middle meningeal artery transportation of the bacteria to the brain being the most likely route of bacterial flow, with posterior communicating artery being the less likely alternate route of travel. Along with the frontal and temporal lobes being physically closer to the nasopharynx and oral cavity.

Brain abscess due to dental infections may be predisposed in certain patients with preexisting conditions such as right-to-left shunts that can be seen in a PFO, thoracic venous anomalies, Ebstein's anomaly, and venous atrial septal defects [12,34,36-37]. Dental procedures, such as dental scaling, done to these vulnerable patients can increase the risk of a brain abscess due to veno-arterial seeding.

Odontogenic brain abscesses may include extra intermediate steps as the bacteria spreads from the oral cavity, such as sinusitis. Bacterial and fungal sinusitis can lead to orbital, intracranial, and osseous

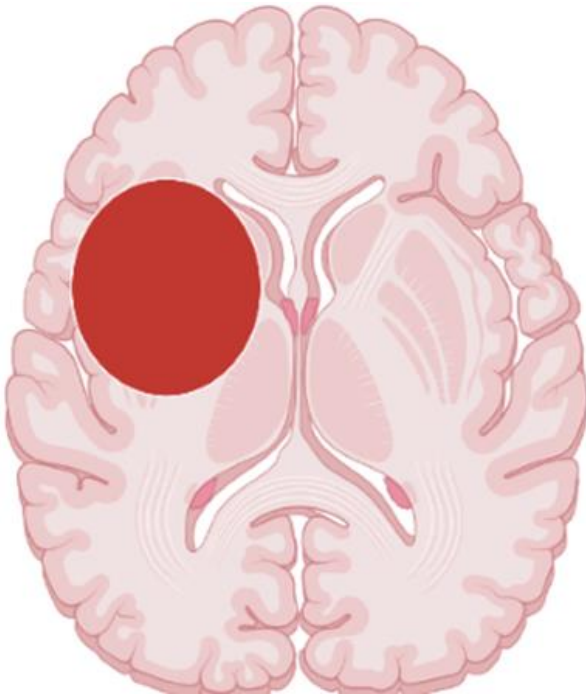


Fig 3: Shows the most common area for a frontotemporal brain abscess to occur [35]. The red circle on the coronal view of this brain image denotes where the frontal, parietal, and temporal lobes intersect as a common place abscess form.

extra-sinus complications with odontogenic sinusitis being the most prevalent cause of operative extra-sinus infectious complications [38]. Patients at risk for extra-sinus spread have bony wall defects and may increase the likelihood of brain abscess. Odontomas that obstruct sinus drainage can lead to a potential brain abscess [39]. More can be understood about this possible oral cavity infection to brain abscess through sinusitis in alternative studies such as in Douglas et al, 2022.

Dental work primarily focuses on dental extractions and dealing with teeth root infections, but there are additional odontogenic problems that can cause bacterial brain abscesses [20]. Oral carcinoma, as an example, can contribute to brain abscess in certain circumstances. One retrospective study showed how carbon-ion radiotherapy for major salivary gland carcinoma had an associated late toxicity that led to a rare case of a grade 3 brain abscess [40].

Possible pre-clinical prevention includes maintaining excellent oral hygiene, screening for congenital heart defects leading to right-to-left shunting, prompt treatment of dental infections, and treatment of sinusitis. Dentists have an integral role in the proper diagnosis of oral cavity infections that could spread to the brain. These diagnoses can often be made with radiographic films in dental offices, which allows early prevention and treatment of brain abscesses [5]. During regular dental cleanings and regular X-ray scans at dental offices, keen awareness of oral

infections can prevent their spread. Antibiotic prophylaxis may be considered for patients that have several periodontal treatments, and extraction of teeth to prevent inflammation may be needed as seen in one unsuspecting healthy individual that presented with a brain abscess [41].

Patients that present with a brain abscess with an unknown source should obtain a transthoracic echocardiography in order to rule out a congenital heart defect of a right-to-left shunt cause, even with elderly patients [34]. An atypical, proposed treatment for brain abscesses is hyperbaric oxygen therapy due to its helpful physiological effects and better outcomes [42]. Hyperbaric oxygen therapy should only be considered after first-line treatment is exhausted and the patient is determined to be in stable condition [42].

Early diagnosis and appropriate treatment of brain abscesses is one area that needs improvement, since delaying treatment negatively affects patient outcome [43]. Brain abscesses due to odontogenic origin typically show nonspecific symptoms, therefore these types of cases are usually delayed in diagnosis and management [2]. One study reported a change in patient mortality from 40% to 10% when the brain abscess is identified and treated in a timely manner [33]. Misdiagnosis is a concern that can delay treatment. Patients with dental infections should be treated promptly and aggressively to prevent the potential risk of complications such as a brain abscess. Patients should be counseled on keeping good oral hygiene, recognizing symptoms, and having good communication between physicians and dental specialists. Future care for the patients in recovery from a brain abscess is individualized by a case-by-case basis with options including various antibiotic therapy duration, antiepileptics, surgery to fix congenital heart defects, and dental treatment. Advancements in imaging and the advancement of novel antibiotics are helping reduce poor complications and mortality from brain abscesses; from a 40-60% mortality rate in the pre-CT era to a 0-10% mortality rate currently [43].

Conclusion

Several bacteria were identified as sources of brain abscesses over a variety of cases. The treatment protocols of surgery and medication usage are largely dependent on the specific bacteria cultured out of the abscess, using MRIs to check how the bacteria react to treatment. Congenital heart defects (like PFO), immunocompromised condition, and dental work in the upper molars were associated with brain abscess formation. Correctly identifying the bacteria of the

brain abscess is correlated with a more effective antibiotic and/or surgical treatment. Though an uncommon complication, odontogenic bacteria spread following dental work to form brain abscesses, is a real and well published relationship. The communication of dental and medical professionals assists in early detection of this possible outcome of dental work, possibly lowering brain abscess occurrence.

Obtaining cause-and-effect relationships between brain abscesses and odontogenic bacteria is the major limiting factor in this study. Even in murine models, the rare occurrence of brain abscesses would make cause-and-effect relationships difficult to prove. Limitations of X-rays in dental offices limit the detection of brain abscesses without CT or MRI examination, restricting early detection of brain abscesses. Possible protocol implementation of giving head CT scans for hospital patients with odontogenic infections may be warranted for brain abscess detection. More reporting of odontogenic-origin brain abscesses is warranted for future possible systematic reviews and meta-analysis studies.

Conflict of interest

The author declares no conflict of interest.

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