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Review

Intracranial bacterial infections of oral origin

Alan A. Moazzam [a,*], Sowmya M. Rajagopal [b], Parish P. Sedghizadeh [b], Gabriel Zada [c], Mina Habibian [b]

[a] Department of General Internal Medicine, Keck Hospital of University of Southern California, 1500 San Pablo Street, Los Angeles, CA 90033, USA
[b] Ostrow School of Dentistry of University of Southern California, Los Angeles, CA, USA
[c] Department of Neurosurgery, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA

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ABSTRACT

Brain abscesses are rare but potentially deadly complications of odontogenic infections. This phenomenon has been described mainly in the form of case reports, as large-scale studies are difficult to perform. We compiled a total of 60 previously published cases of such a complication to investigate the predisposing factors, microbiology, and clinical outcomes of intracranial abscesses of odontogenic origin. A systematic review of the literature using the PubMed database was performed. Men accounted for 82.1% of cases, and the mean age was 42.1 years. Caries with periapical involvement and periodontitis were the two most common intra-oral sources, and wisdom tooth extraction was the most common preceding dental procedure. In 56.4% of cases, there were obvious signs of dental disease prior to development of intracranial infection. Commonly implicated microorganisms included *Streptococcus viridans* (especially the anginosus group), *Actinomyces, Peptostreptococcus, Prevotella, Fusobacterium, Aggregatibacter actinomycetemcomitans* and *Eikenella corrodens*. There was an 8.3% mortality rate. Intracranial abscesses can form anywhere within the brain, and appear unrelated to the side of dental involvement. This suggests that hematogenous spread is the most likely route of dissemination.

1. Introduction

Brain abscesses are life-threatening infections that require immediate neurosurgical attention. The incidence is between one and eight per 100,000 patients per year in the USA [8]. Brain abscesses most frequently occur due to bacterial dissemination from a primary lesion at a distant site. They can also occur from direct contiguous invasion from an adjacent site of infection.

The oral cavity harbors a diverse and abundant microflora. As part of the Human Microbiome Project, culture-independent molecular approaches have identified more than 1200 different types of microbes in the human mouth [7]; 350 different bacterial strains have been isolated in marginal periodontitis and 150 in endodontic infections [5]. Bacteria can disseminate from these locations due to a variety of dental conditions such as gingivitis and periodontitis, and also from procedures such as tooth extractions, endodontic treatments, and oral surgery. Even simple tooth brushing has been shown to induce transient bacteremia in 38.5% of cases [8]. Currently, the Council of Dental Therapeutics of the American Dental Association has recommended against routine antibiotic prophylaxis for dental procedures specifically to prevent brain abscesses given the relative low incidence of this complication and the potential for development of resistant strains [8].

Due to the rarity of this occurrence, to our knowledge no studies have specifically investigated this phenomenon in a comprehensive manner. The literature primarily consists of individual case reports. We systematically reviewed the literature to identify and analyze all cases representing central nervous system (CNS) infections of oral origin. Our goal was to provide a synthesis of available knowledge on the natural history, pathogenesis, microbiology, interventions and outcomes of this potentially fatal pathology.

2. Materials and methods

Our review followed recommendations as outlined in the AMSTAR guidelines for systematic reviews [17]. We used an *a priori* research design that would allow us to better understand this clinical problem and provide insight into PICO-related questions (Patient problem or population, Intervention, Comparison and Outcome) in the context of brain abscesses of oral origin. A protocol specifying all aspects of the review method was developed before commencing the review. This protocol included ascertainment criteria for considering studies for this review, search methods for identification of studies, data collection and analysis.

* Corresponding author. Tel.: +1 858 342 0874.
E-mail address: alan.moazzam@usc.edu (A.A. Moazzam).

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The protocol was planned to minimize the effect of author bias on the review and the potential to alter or misinterpret data presented on study findings. We critically appraised the selected works and synthesized the data according to a predetermined and explicit methodology. This included quality assessment of reviewed papers, determination of levels of evidence, and evaluation of outcome measures but no statistical analyses given the nature of the available data and literature which we describe shortly.

The PubMed electronic database was searched for all English-language case reports of CNS abscesses that were the result of primary oral infections. A broad search strategy was employed using any combination of the Medical Search Heading keywords from the following two groups: Group 1 = "brain abscess," "intracranial abscess," "CNS infection", "meningitis" and "cavernous sinus thrombosis" and Group 2 = "odontogenic source," "dental treatment," "tooth extraction", "periodontitis", and "oral infection." Search results were screened by title and abstract to select for reports of intracranial abscesses arising from oral-related pathology. In addition, references from screened case reports were reviewed to identify additional cases for inclusion. Articles that met the following criteria were included in our data: (1) cases involving a confirmed intracranial infection; (2) cases describing a presumed dental origin of the infection; (3) a well-described clinical course, including symptoms at presentation and diagnostic work-up; and (4) manuscripts published after 1980.

Included articles were subsequently read and data were extracted into an electronic database for analysis. When available, these data included information pertaining to patient demographics, prior medical history, preceding dental procedure or pathology, location of both intra-oral and intracranial infection, time course of symptoms to presentation, results from bloodstream, intra-oral, and intracranial cultures, treatments provided or performed, and clinical outcomes. Authors M.H. and S.M.R. independently reviewed these cases for extraction of all relevant dental and neurosurgical data.

As part of our assessment to determine whether dental pathology had spread to CNS locations via direct venous or hematogenous dissemination, we counted the number of times the side of dental involvement was concordant with the side of intracranial pathology. Ipsilateral dental and intracranial pathology would imply direct venous drainage, whereas discordant laterality could imply hematogenous spread. Bilateral dental pathology/procedures were considered concordant with intracranial pathology of either side (tongue piercing procedures were treated as midline, therefore "bilateral", procedures), while unilateral dental pathology/procedures were considered concordant only with intracranial pathology on the same side. Midline intracranial lesions were considered concordant with dental pathology/procedures from either side. Some cases recorded abscesses that spanned across multiple areas within the brain, such as "fronto-parietal"; these cases were counted as both frontal and parietal involvement.

3. Results

3.1. Patient demographics

Figure 1 shows the search strategy and results. Twenty-two manuscripts were excluded from the analysis (Supp. Table 1). One manuscript did not report evidence of obvious intracranial infection, one reported numerous alternative sources of bacterial infection, and one did not report any obvious intra-oral pathology [16]. Twelve manuscripts were published before 1980 and were therefore excluded. Seven additional manuscripts were excluded because they reported intra-oral bacterial dissemination to spinal structures; we could not discern whether this represented infection of bony column structures or true trans-dural bacterial translocation, and therefore these manuscripts were excluded.

A total of 55 manuscripts were identified that met our criteria (Supp. Table 2). From these manuscripts, 60 individual patients were identified and were included in data analysis. No cohort studies or prospective studies were found, and thus all included works represented a relatively low level of evidence. The distribution of publication dates are presented in Figure 2. Of the cases that reported patient sex, males and females accounted for 82.1% (46/56) and 17.8% (10/56) of patients, respectively. The mean patient age was 42.1 years, with a range of 3 to 70 years. Medical co-morbidities were poorly reported; most manuscripts did not mention chronic underlying medical conditions, and of those that did, the descriptions were not well-elaborated. No cases reported active immunocompromised conditions; however two cases did report diabetes mellitus, three reported active alcohol abuse, and two reported active polysubstance abuse. Five patients had anatomic cardiac anomalies (three patent foramen ovale, and two unspecified congenital cardiac anomalies), and three patients had hereditary hemorrhagic telangiectasia.

3.2. Precipitating dental pathology or procedures

Preceding dental procedures were reported in 41.7% (25/60) of patients and underlying intra-oral pathology was noted in 86.7% (52/60) of patients. In patients without underlying intra-oral pathology, the brain abscess was assumed to be the result of the preceding dental procedure. Many patients had more than one dental pathology. The frequencies of each intra-oral procedure and pathology are presented in Table 1. The majority of procedures were related to molar teeth. Tooth extraction accounted for 60.0% (15/25) of precipitating dental procedures. Dental symptoms or procedures preceded the onset of neurologic symptoms in 40.0% (24/60) of patients. The average time between the performance of a dental procedure and the onset of neurologic symptoms was 17.6 days.

3.3. Microbiology

In 13 patients, cultures were obtained from various dental locations, such as the extraction socket, the periodontal pocket, dental plaque, or purulent fluid from intra-oral abscesses. Of these, only eight publications reported micro-organisms that matched those grown from intracranial cultures. Fifty-five cases reported intracranial culture results; two were negative, 49.1% (27/55) were monomicrobial and 47.3% (26/55) were poly-microbial. The frequencies of grown pathogens are presented in Table 2.

3.4. Route of CNS dissemination

The locations of reported intracranial involvement are presented in Table 3. As stated in the Methods section, we investigated the route of spread of intra-oral infections into the brain by analyzing the laterality of intra-oral and intracranial infections and whether they were concordant (implying direct venous dissemination) or discordant (implying systemic hematogenous dissemination). Seventy percent (42/60) of cases reported intracranial pathology to be on the same side as underlying intra-oral pathology. Many cases reported generalized intra-oral conditions (for example, gingivitis or periodontitis) and were therefore considered to have "bilateral" intra-oral pathology. Even if these cases are excluded (that is, only taking into account cases reporting clearly defined unilateral intra-oral pathology), again 70.0% (14/20) reported concordant laterality of intra-oral and intracranial pathology. When only taking into account cases with intracranial locations most specifically associated with direct venous drainage