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CASE REPORT

Case of a cerebral abscess caused by *Porphyromonas gingivalis* in a subject with periodontitis

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SUMMARY

We report the case of a 65-year-old man presenting with generalised seizures after developing a right frontal brain abscess. Stereotactic aspiration and subsequent matrix assisted laser desorption/ionisation time-of-flight analyzer (MALDI-TOF) spectrometry revealed *Porphyromonas gingivalis* as the only causative anaerobe microorganism. Secondary incision and drainage was required due to neurological deterioration with increased dimensions of the abscess, intracranial pressure and formation of a subdural occipitoparietal empyema. Oral imaging was positive for apical periodontitis of multiple elements; therefore, the remaining dentition was removed. Targeted antibiotic treatment included intravenous ceftriaxone and ornidazole. The patient was discharged to our revalidation unit 59 days after admission to make a full recovery. To the best of our knowledge, this is the sixth reported case of *P. gingivalis* causing an intracranial abscess and the third case of a true intracerebral parenchymal abscess caused by this bacterium.

BACKGROUND

Brain abscesses of odontogenic origin are rarely seen and account for only a small fraction of all reported cerebral abscesses. The incidence of cerebral abscesses ranges from 0.4 to 0.9 cases per 100 000 people and is more frequent in immunocompromised patients. Oral pathogens cause 3–10% of abscesses,[1] while other causative pathogens are non-oral bacteria, mycobacteria, fungi or parasites. The underlying pathogenic mechanisms are poorly understood. Contiguous spread of a pathogen is the most frequent route of infection. Haematogenous or lymphatic dissemination is seen in a limited number of cases.[2] The initial presentation, symptoms and results from clinical and radiological investigations vary widely and are non-specific for the causative pathogen.[3–4] Morbidity and mortality have improved in recent years due to better imaging techniques and therapeutic options. Mortality ranges from 0 to 24% for odontogenic brain abscesses.[5] *Porphyromonas gingivalis*, a gram-negative oral pathogen, has rarely been reported in subjects with cerebral abscess formation, but has been widely associated with periodontitis. Its pathogenesis is still being investigated, but includes a wide variety of immunological escape mechanisms.

We searched databases (Medline, Scopus, Web of Science, EMBASE, Cochrane library) and manually searched reference lists for relevant articles and related cases. Well-accepted reviews served as the foundation for this article. Additional original articles were selected by reading the abstract and obtaining the full text when needed. Search terms included: brain abscess, cerebral abscess, *P. gingivalis*, odontogenic, periodontitis, parodontitis, tooth infection and oral pathogen. Five articles were selected that discussed intracranial abscess formation by *P. gingivalis*.

CASE PRESENTATION

We report the case of a 65-year-old man with a medical history of prostate carcinoma, for which he underwent radical prostatectomy with adjuvant radiotherapy. The patient also had type 2 diabetes, hypertension, hypercholesterolaemia and epilepsy of unknown origin during his childhood. Home medications included acetylsalicylic acid, olmesartan medoxomil, rosuvastatin, lixisenatide, metformin and gliclazide. The patient was previously treated with valproate, which was reduced and then stopped 6 months earlier as the patient was seizure free for over 20 years. Previous imaging reports never mentioned intracranial anomalies. Detailed findings and events are illustrated in the patient's timeline (figure 1).

In August 2016, he was admitted after a generalised epileptic seizure at home. The patient's wife reported that he was increasingly confused in the preceding days. The clinical neurological examination was normal with a Glasgow Coma scale (GCS) of 15/15. Blood tests were unremarkable except for a slightly increased C reactive protein (CRP) of 5.9 mg/L (reference <5.0 mg/L). An EEG was normal. A CT scan of the skull was performed showing a hypodense, contrast-enhanced lesion surrounded by oedema in the right frontal lobe (figure 2, video 1). No midline shift or ventricular anomalies were noted. An initial oncologic screening was advised with imaging of the chest and abdomen due to the medical history, but did not show primary malignancies or recurrence. After neurosurgical counsel, MRI with diffusion-weighted imaging (DWI) was added to the diagnostic workup and a brain abscess with pachymeningitis was diagnosed (figure 3, video 2). In light of these findings, a transthoracic ultrasound was negative for cardiac vegetations or signs of infection. Initial treatment consisted of systemic valproate (1.5 g/day), levetiracetam (1 g/day), vancomycin (2 g/day), ornidazole (1 g/day) and ceftriaxone (2 g/day). Stereotactic drainage was performed and

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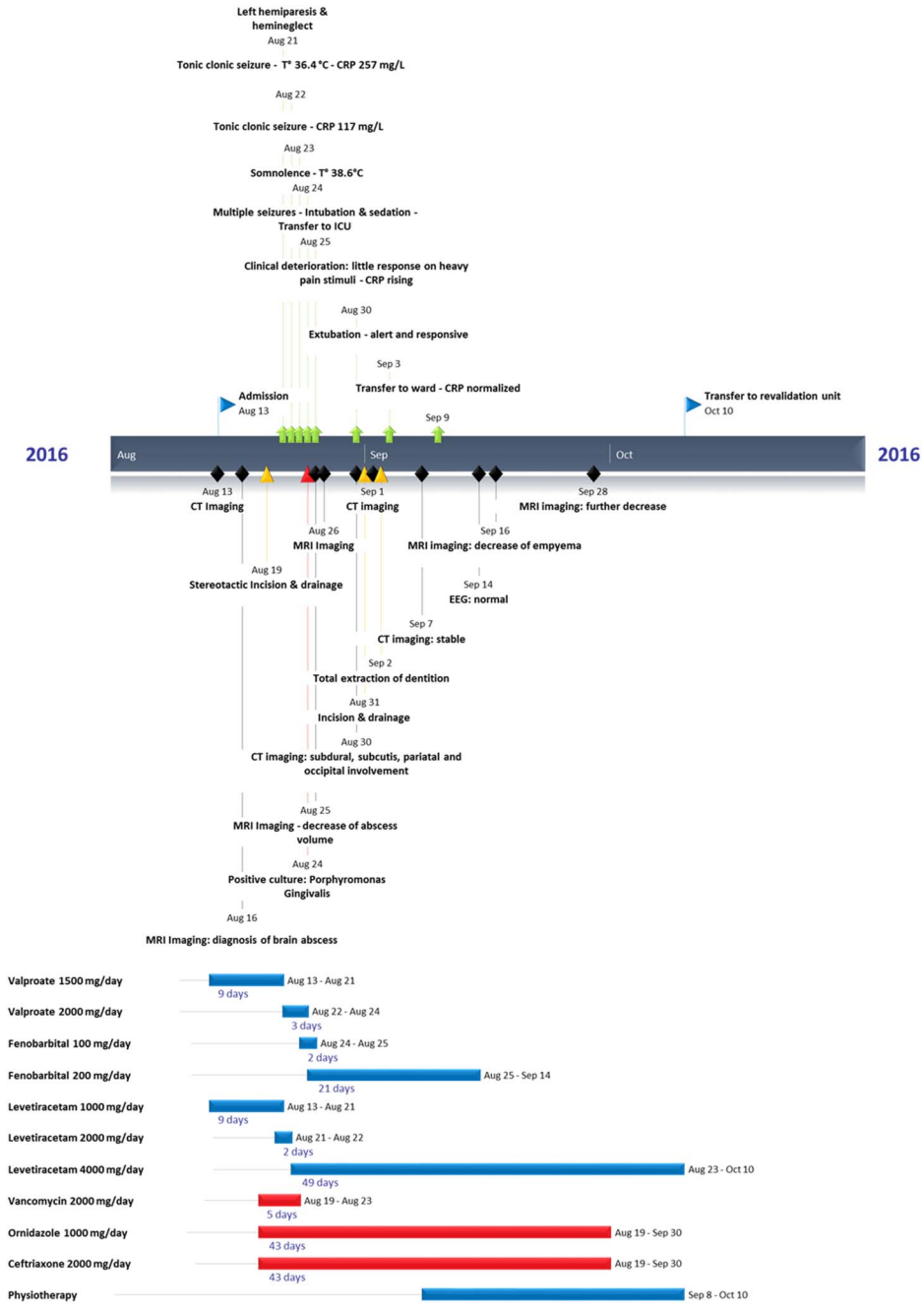


Figure 1 Timeline of patient showing important clinical events, imaging and intervention dates, and antibiotic and antiepileptic treatments. T°, temperature; CRP, C reactive protein.

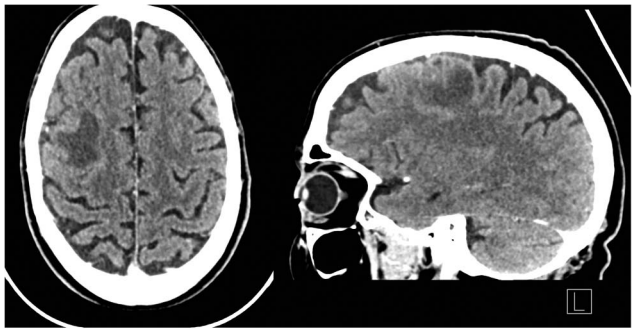
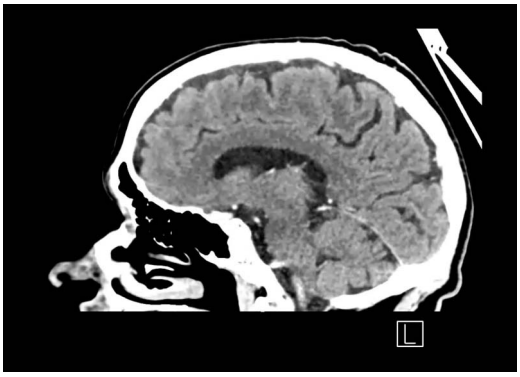


Figure 2 Initial contrast-enhanced CT imaging at the day of admission showing a hypodense nodular lesion in the right frontal lobe with peripheral ring-like contrast uptake as well as perilesional oedema. The conclusion was possible malignancy, preferably metastasis.



Video 1 Initial contrast-enhanced CT imaging at the day of admission showing a hypodense nodular lesion in the right frontal lobe with peripheral ring-like contrast uptake as well as perilesional oedema. The conclusion was possible malignancy, preferably metastasis.

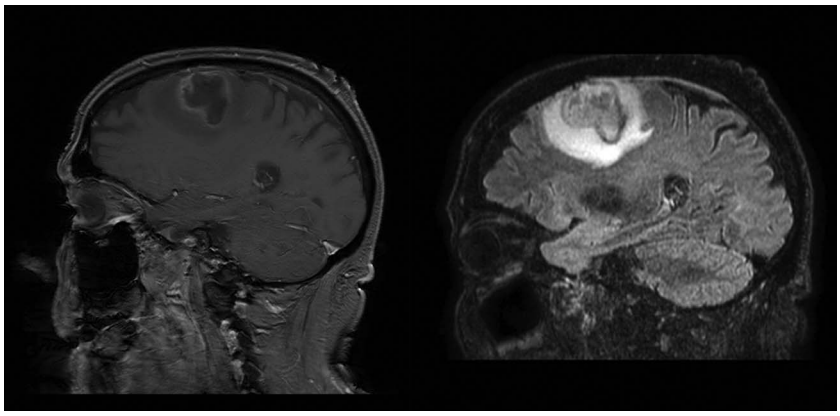
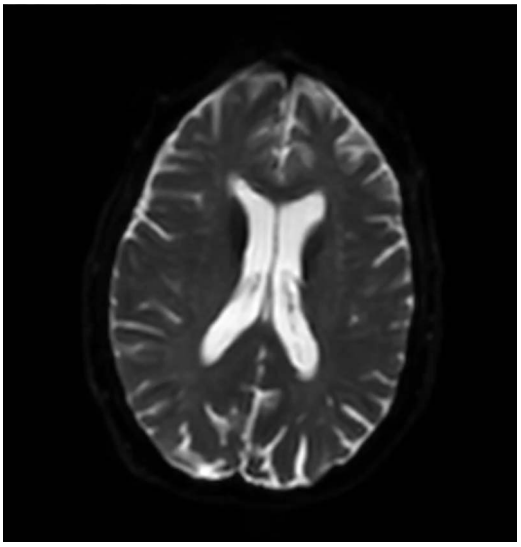


Figure 3 MRI with T1 (left) and diffusion-weighted imaging (right) showing central diffusion restriction suggestive of a cerebral abscess. The dural layer is thickened, indicating pachymeningitis.



Video 2 MRI with diffusion-weighted imaging showing central diffusion restriction, suggestive of a cerebral abscess. The dural layer is thickened, indicating pachymeningitis.

MALDI-TOF spectrometry of the pus (Bruker Daltonik Maldi Biotyper) revealed *P. gingivalis* as the sole causative bacterium (score 2.231, high-confidence identification). Intraoral inspection showed partial dentition complicated with parodontitis. On previous CT imaging, apical periodontitis was seen around the elements 16, 23 and 34 (figure 4), and the sinus cavities appeared normal. The antibiotic regimen was reduced to intravenous ornidazole (1 g/day) and ceftriaxone (2 g/day).

Nineteen days after initial drainage, left hemiparesis and left hemineglect developed as well as an increase in epileptic seizures with one tonic–clonic seizure. The patient further deteriorated with need for intubation and intravenous sedation. Imaging showed the intracerebral abscess was extending to the subdural space and subcutis, forming a subdural empyema and spreading to the occipital–parietal regions; therefore, incision and drainage (figure 5) was necessary. Owing to clinical instability, total extraction of the remaining dentition was performed in a separate procedure. Antibiotic treatment included intravenous ceftriaxone (2 g/day) and ornidazole (1 g/day), which were continued for a total of 43 days until clinical, biochemical and radiological improvement. The patient was discharged from the neurosurgical ward after 59 days with almost complete resolution of the neurological deficit. He was referred for inhospital physiotherapy to regain full motor function.

DISCUSSION

To the best of our knowledge, this is the sixth reported case of intracranial abscess formation by *P. gingivalis* and the third case of a true intracerebral parenchymal abscess.[6–10] An overview of reported cases is given in table 1. It is well known that the oral cavity hosts a wide variety of microbiological organisms. Studies identified up to 350 different bacterial strains in marginal periodontitis and up to 150 strains in endodontic infection.[5] Some of these oral commensals cause opportunistic infections, for example, streptococcal endocarditis after dental procedures has been the rationale for endocarditis prophylaxis in high-risk cardiac patients. Iatrogenic or covert bacteremia arising from the oral cavity rarely causes clinical pathology requiring intervention. It is extremely rare for *P. gingivalis* to cause an intracranial abscess and it has only been reported five times in current literature (table 1). This highly adapted non-motile gram-negative oral anaerobe is strongly associated with periodontitis and can be cultured in 85.7% of patients diagnosed with periodontitis compared with 23.1% of healthy subjects.[11] Being an opportunistic pathogen, it has high virulence as indicated by biofilm formation, dipeptidyl peptidase intravenous activity, strong

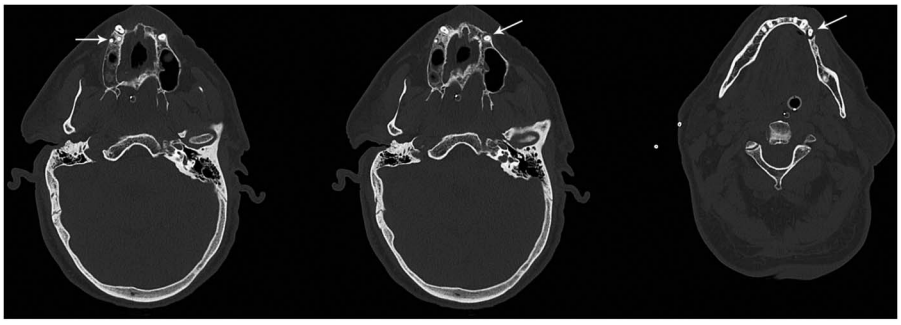


Figure 4 Periodontal apical radiolucent areas of elements 16 (left), 23 (middle) and 34 (right).

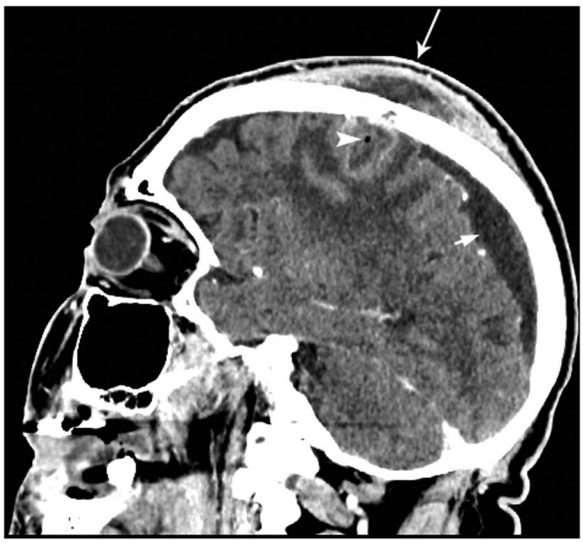


Figure 5 CT imaging 12 days after initial abscess drainage. Subcutaneous collection (arrow) with gas locules (arrowhead), new manifestation of the subdural occipitoparietal empyema (small arrow) and increased cerebral oedema.

induction of proinflammatory cytokine secretion and the invasion potential of epithelial cells to escape immune response activation.[12] Other reported extraoral infections, other than intracranial, caused by *P. gingivalis* include otitis media, appendicitis, gas gangrene, thoracic empyema and lung abscess formation.[13]

An analysis of the cases (table 1) indicated most subjects present over the age of 50; however, one case of subdural empyema was reported in a 34-year-old man. In all previous case reports, no underlying immunodeficiency was reported. Our patient suffered from type 2 diabetes mellitus, an autoimmune inflammatory condition known to disrupt the blood–brain barrier leading to leakage of small arterioles, possibly facilitating haematogenous dissemination.[14] Presenting symptoms were non-specific for the causative organism and depended on the location and elevated intracranial pressure. Suspicion should be raised when an oral or dental pathology is present. Comorbidities must be taken into account. A full blood count with inflammatory markers, electrolytes, kidney and liver function tests, blood glucose levels and blood cultures are advised. Cranial contrast-enhanced CT imaging is the preferred initial radiologic investigation followed by MRI with DWI. This case demonstrates the additional benefit of MRI-DWI in

Table 1 Reported cases of intracranial abscesses caused by *Porphyromonas gingivalis*

Reference	Sex	Age (years)	Predisposing factors	Pathogen	Oral pathology	Presenting symptoms	Localisation	Treatment	Outcome
[8]	F	64	Eisenmenger's syndrome, ventricular septal defect	*Lactobacillus catenaformis* *P. gingivalis* *Fusobacterium nucleatum*	Periodontitis 15	Seizures	Right temporal lobe	Initial AB: Ceftriaxone, metronidazole, vancomycin Switched AB (D2): sulbactam/ampicillin Surgical: drainage (D2), craniotomy (D26)	Discharge after 27 days, referred to other hospital
[6]	F	57	?	*P. gingivalis* detected in CSF	Single tooth infection, not further specified	Fever Headache Gait disturbance	Site not specified. Additional ventriculitis	Initial AB: fosfomycin, panipenem, cephalothin (intraspinal) Switched AB (D10): piperacillin, cefozopran, cephalothin (ventricular injection) Surgical: tooth extraction	Discharge after 21 days. Full recovery
[10]	M	67	None reported	*P. gingivalis*	None reported	Throbbing right-sided headache	Right cavernous sinus Infraorbital cavity Sphenoid sinus	Initial AB: carbapenem Switched AB (D15): ampicillin, sulbactam Surgical: drainage, endoscopic sphenoidotomy	Full recovery
[7]	M	54	None reported	*P. gingivalis*	Periodontitis	Right-sided homonymous hemianopsia Right hemiparesis	Left parieto-occipital lobe	Initial AB: vancomycin, 3rd generation cephalosporin, metronidazole Switched AB (D10): ampicillin, sulbactam Switched AB (D14): amoxicillin, clavulanate Surgical (D0): craniotomy	Full recovery
[9]	M	34	None reported	*P. gingivalis*	Sinusitis (bilateral frontal, ethmoid, and left maxillary)	Fever Headache Photophobia Left hemiparesis Repeated vomiting	Right frontal subdural empyema	Initial AB: ceftriaxone, metronidazole Surgical: frontoparietal craniectomy (D2), ethmoidectomy (D2), bilateral anterior ethmoidectomy (D2), bilateral frontal sinectomy (D2), second drainage (D15)	Full recovery

AB, antibiotic treatment; CSF, cerebrospinal fluid; D, day; F, female; M, male.

differentiating benign abscesses from primary or metastatic malignancies; moreover, MRI-DWI can screen for ventriculitis. If present, hydrocephalus can develop with the need for ventricular drainage. After a diagnosis is made, possible sites of origin should be further clinically or radiologically investigated. Transthoracic ultrasound to visualise possible endocarditis or valvulitis with bacterial vegetations and oral inspection is of paramount importance to treat underlying infective sources.

Treatment should always include neurosurgical expertise to assess the feasibility of diagnostic and therapeutic stereotactic aspiration. Empiric antibiotic treatment should begin as soon as a brain abscess is suspected. Usually a third-generation broad spectrum antibiotic such as cephalosporin, metronidazole and vancomycin is administered intravenously until positive culture growth or identification through mass spectrometry directs the antibiotic treatment. In most previously reported cases, this approach was followed (4/5). Treatment duration varies but is usually 4–6 weeks. The need for additional interventions should be based on clinical, laboratory and radiological findings. Drainage was performed in all reported cases. Tooth extraction was only reported in one previous case. The mortality and morbidity rates after intracranial *P. gingivalis* abscess formation are hopeful. All patients (6/6) made a full recovery; however, reported mortality rates vary from 0 to 24% in cerebral abscesses due to odontogenic infection.[5] Small sample size does not allow to draw statistically significant conclusions however, we caution not to minimize the possible pathological severity of this organism.

Learning points

- *Porphyromonas gingivalis* is a rare but potentially life-threatening anaerobe that can cause intracerebral abscesses.
- CT imaging cannot always diagnose a cerebral abscess; thus, MRI with diffusion-weighted imaging should be added to the diagnostic workup.
- Quick initiation of broad-spectrum antibiotics, preferably after taking cultures, is paramount.
- Neurosurgical intervention and timing depends on clinical, laboratory and radiological findings but can be useful diagnostically to elucidate the causative pathogen.
- The source of infection should be investigated and treated accordingly.

Contributors FVdC was responsible for the study concept and design. FVdC carried out the literature search. KG and HM were responsible for initial proof reading. KG, HM and CP critically reviewed the manuscript for important intellectual content. CP was the study supervisor. All authors read and approved the final version of the manuscript.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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