A Case of Brain Abscess Caused by Actinomyces Cardiffensis and Parvimonas Micra

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Brain abscesses occur in 0.3−1.3 per 100,000 worldwide each year with 0.4−0.9 in Japan alone. Most of the causes are direct infection from a nearby infectious lesion and are rarely caused by an odontogenic infection. Here, we reported a case of brain abscess suspected to be associated with odontogenic infection.
The patient was a 55-year-old woman. Blurred eyes and pain in the left eye noted, for which she consulted an ophthalmologist, but her eyes were normal. She was conscious and was able to converse clearly, but she could not read the letters and had difficulty in writing at the time of admission. A brain abscess was diagnosed based on the head magnetic resonance imaging (MRI) and clinical course, and a small craniotomy abscess drainage was performed. *A. cardiffensis* and *P. micra* were detected in the abscess, suggesting the involvement of periodontal disease bacteria. After the surgery, antimicrobial treatment was performed for about 2 months. At the same time, perioperative treatment was performed. On the 70th day after the surgery, tooth extraction, which was considered as the source of infection, was performed. The patient was discharged 74 days after surgery. A good turning point was obtained without relapse of symptoms.

Key words: brain abscess, odontogenic infection, Periodontitis, *Actinomyces cardiffensis*, *Parvimonas micra*

INTRODUCTION

Intracranial abscesses include brain, subdural, and epidural abscesses as the most frequent brain abscesses. The frequency of brain abscess is estimated to be 0.3−1.3 peoples in the world per 100,000 a year, and 0.4−0.9 in Japan [1−3]. The mortality rate of brain abscess is still as high as 8 to 32%, even though the treatment results have improved due to improvements in anaerobic culture technology, new antibiotics, and advances in diagnostic imaging technology [4−6]. Most of the causes are direct infection from a close-infectious lesion, and odontogenic infections are rarely caused by about 2% of cases of brain abscess. Here, we reported a case of a brain abscess suspected to involve the periodontal pathogens *Actinomyces cardiffensis* and *Parvimonas micra*.

CASE PRESENTATION

A 55-year-old woman visited our Department of Ophthalmology due to blurred vision and pain in the back of her left eye. On February 13, 201X, she became aware of blurred vision after waking up. The symptoms improved within 2−3 hours, but pain in the left eyeball persisted. In February 20, the patient reported that her TV screen appeared blurry and the pain in the left eye improved after taking NSAIDs and visited our hospital. She had no medical history or family history. Despite no notable diseases in her eyes, an intracranial lesion was suspected, and she was admitted to the Department of Neurology on the same day for detailed medical treatment.

Physical findings on admission included the Japan Coma Scale: 1, and Glasgow Coma Scale: eye opening response, 4; best verbal response, 5; and best motor response, 6. However, she could not read the letters and had difficulty in writing. No other neurological findings were observed. Body temperature was 36.2℃, blood pressure 128/84 mmHg, and pulse 78/min. No cervical lymph node was palpable, no noise was heard in the cardiopulmonary system, abnormalities in the abdomen and lower leg edema was not observed. She showed no inflammatory response. Her white blood cell count was 5700/μL, neutrophil was 57.6%, erythrocyte sedimentation value was 11 mm/h, C-reactive protein level was 0.052 mg/dL, blood tumor marker carcinoembryonic antigen (CEA) was 2.7 ng/dL (0−5 ng/dL), carbohydrate antigen 19−9 (CA 19−9) was 8.2 U/mL (0−37 U/mL). Magnetic resonance imaging (MRI) of the head showed a falsely enhanced structure of gadolinium about 1.5 cm in the left occipital lobe, which was surrounded by a low density area. Gliomas, metastatic brain tumors, and brain abscesses were listed as differential diagnoses (Fig. 1A).

From the day of hospitalization, infusion of glyceol was started to improve cerebral edema. Since a metastatic tumor was suspected, the presence or absence of systemic lesions was searched. Abdominal ultrasound showed no abnormalities in the liver, gall, pancreas, spleen, or kidneys. No clear lymphadenopathy was

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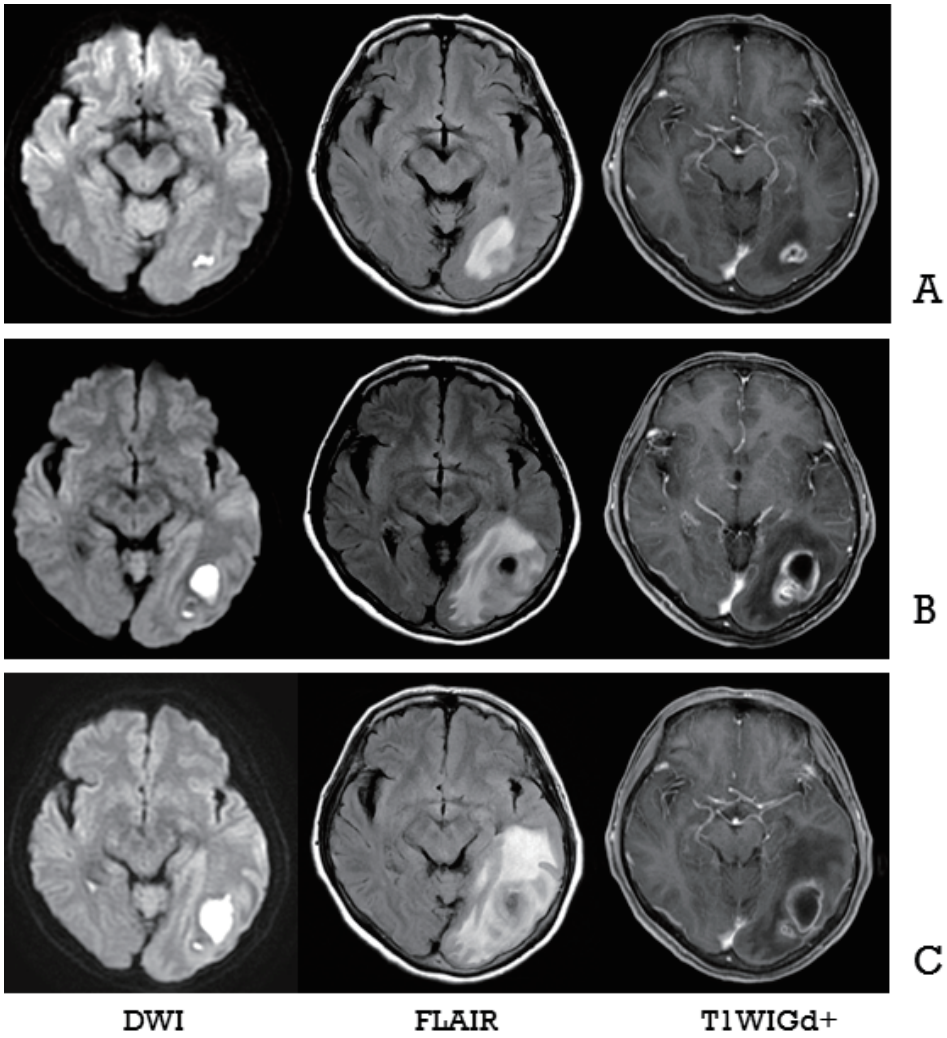

Fig. 1 MRI (Axial) of the head shows temporal changes in lesions in the left occipital lobe. A) Hospitalization date B) 8th day C) 17th day (before drainage). High signal with DWI in the left occipital lobe, ring enhancement effect with Gd-T1WI.The high signal is widening in FLAIR images reminiscent of edema.

observed around the abdominal aorta, and no abnormality was observed in upper gastrointestinal endoscopy. On fluorodeoxyglucose (FDG) accumulation on positron emission tomography-CT (PET-CT), a ring-shaped highly accumulated image (SUVmax: 6.31) was observed subcutaneously in the left occipital cortex. In addition, no abnormal accumulation image was observed in the whole body. Therefore, metastatic brain tumors and central nervous system lymphomas were negative.

Articulation disorder occurred on the 8th day of hospitalization. Head MRI showed exacerbation of cerebral edema and an increase in ring-shaped enhancement effect on Gd-enhanced T1-weighted images (T1WI) (Fig. 1B). Since brain abscess formation was suspected, intravenous administration of vancomycin (VCM) 2.0 g/day and meropenem (MEPM) 6.0 g/day was started. Cerebrospinal fluid was examined on the same day. It was colorless and transparent, cell number 148 (nut 5%, Ly 82%, mono 12%), protein 98 mg/dL (8–58), and sugar 54 mg/dL (50–75). Cerebrospinal fluid cytology was class II. As a result of echocardiography, left ventricular wall movement was maintained and no vegetation was observed in the atrioventricular valve or meniscus valve.

On the 10th day of hospitalization, she was referred to our Department of Oral Surgery for identification of the source of infection. Occasionally, she complained of repeated swelling and pain in the gingiva of the lower right molars. Although there was no tooth pain at the time of examination, the periodontal pocket of the lower right first molar was 10 mm, which was quite deep. Orthopantomography, there were X-ray transparent lesions around the roots of the upper right second premolar, the upper right first molar, and the lower right second molar, and the findings of chronic apical periodontitis were observed (Fig. 2).

On the 16th day of hospitalization, body temperature increased to 38.2˚C, and headache and vomiting were observed. On the 17th day of hospitalization, the lesion of the left occipital lobe was detected by MRI (FLAIR) with low signal in the central region and spread to the range of high signal suspected of edema around the center, and a midline shift was observed. An abscess formation was suspected, which may have caused ventricular puncture. A subdural abscess drainage operation was performed under general anesthesia by our Department of Neurosurgery. The

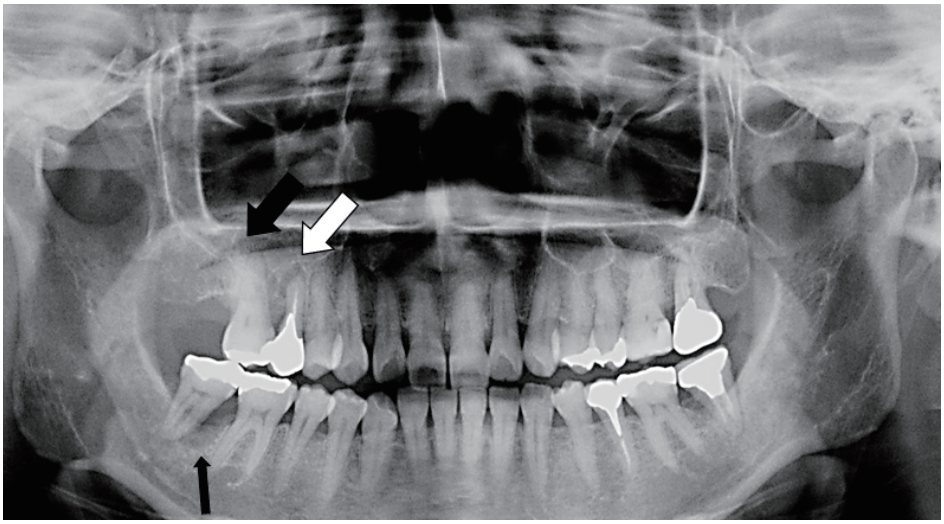

Fig. 2 Orthopantomography. There were X-ray transparent lesions around the roots of the upper right second premolar (white arrow), the upper right first molar (black thick arrow), and the lower right second molar (black thin arrow), and the findings of chronic apical periodontitis were observed.

internal solution had a yellow viscous property, the amount of aspirated fluid was 4 mL, and Cytology was negative for malignant cells. Gram stain of the fluid revealed, leukocyte 1+, Gram-positive cocci (GPC) 2+, and Gram-negative rod (GNR) were few. As a result of bacterial identification, actinomyces spp. and anaerobic gram-negative rods were detected. For both bacteria, Minimal Inhibitory Concentration (MIC) was ampicillin(ABPC) ≤ 0.25, penicillin G(PCG) ≤ 0.25, piperacillin(PIPC) ≤ 8, cefozopran(CZOP) ≤ 4, latamoxef(LMOX) ≤ 4, cefmetazole(CMZ) ≤ 4, imipenem(IPM) ≤ 1, minocycline(MINO) ≤ 1, clindamycin(CLDM) ≤ 0.5 and chloramphenicol(CP) ≤ 4. They were sensitive to all the antimicrobials tested. The bacteria were also examined at Division of Anaerobe Research, Life Science Research Center, Gifu University for further investigation, and were identified as Actinomyces cardiffensis (Fig. 3A, B) and Parvimonas micra (Fig. 3C, D).

On postoperative day 7 (24th day of hospitalization), disappearance of the abscess was confirmed by head MRI, and there was a tendency toward improvement in ventricular inflammation and cerebral edema (Fig. 4).

VCM continued to be used until the 8th day and MEPEM was the 22th day after surgery, but they were discontinued due to the onset of drug eruption. Instead, ABPC 12 g/day was administered by infusion and Metoronidazole (MNZ) 1 g/day was taken orally. A cerebrospinal fluid test confirmed a decrease in cell number, so we decided to end the antibiotics. ABPC was terminated the 74th day and MNZ was the 110th day after surgery (Fig. 4). After the operation, antibiotics were continuously administered. However, although the drug was forced to stop and change due to the onset of drug eruption, the clinical symptoms gradually improved (Fig. 4). At 70th day after surgery, the upper right second molar, the upper right first molar, and the lower right first molar were extracted, which were suspected to be the causative teeth. The progress of the wound was good. She was discharged on the 74th after surgery(91th day of hospitalization). At the time of discharge, she had no headache, left eye pain, digestive symptoms, dysarthria, or dyslexia.

DISCUSSION

The frequency of brain abscess is reported to be 0.3–1.3 peoples in the world per 100,000 annually, and 0.4–0.9 in Japan [1–3]. Sixty percent of the infection routes of brain abscess are (1) secondary infection after head trauma or brain surgery and (2) direct infiltration from nearby infection sites such as otitis media and sinusitis, while 25% are due to (1) remote infection, (2) bloodstream infections such as infectious endocarditis, and (3) pulmonary arteriovenous fistula [7]. It has been reported that 2% originate from a dental infection. *Streptococcus*, *Staphylococcus*, *Proteus* spp., *Klebsiella pneumoniae*, and *Escherichia coli* are the causative bacteria of the abscess, accounting for about 60% of cases [7]. The infection route and representative causative bacteria are the following: *Streptococcus*, *Haemophilus* in ear; *Enterobacteriaceae* and *Streptococcus* in lung; *Streptococcus* and *Fusobacterium* in urinary tract; *Pseudomonas*, *Enterobacter* in perforating head injury; and *Staphylococcus*, *Enterobacter endocarditis*, *Viridansst reptococci*, and *S. aureus*. The shunt heart disease is *Streptoococcus* [8]. From the oral cavity, there are *streptococcus viridans* (particularly *S. anginosus* group), *Actinomyces*, *Peptostreptococcus*, *Prevotella*, *Fusobacterium*, *Eikenella corrodens*, *Aggregatibacter actinomycetecomitans*.

Although anaerobes have been identified in many cases since 1981, it has been reported that causative bacteria cannot be demonstrated in approximately 30% of anaerobic abscesses [9]. Therefore, it is important to keep anaerobic infection in mind when starting antimicrobial treatment before the identification of the causative organism. In this case, the inflammation could be identified from the pus collected by craniotomy drainage. The final pathogens were *Actinomyces cardiffensis* and *Parvimonas micra*.

The genus *Actinomyces* is a Gram-positive anaerobic bacillus that is resident in the human oral cavity, phar-

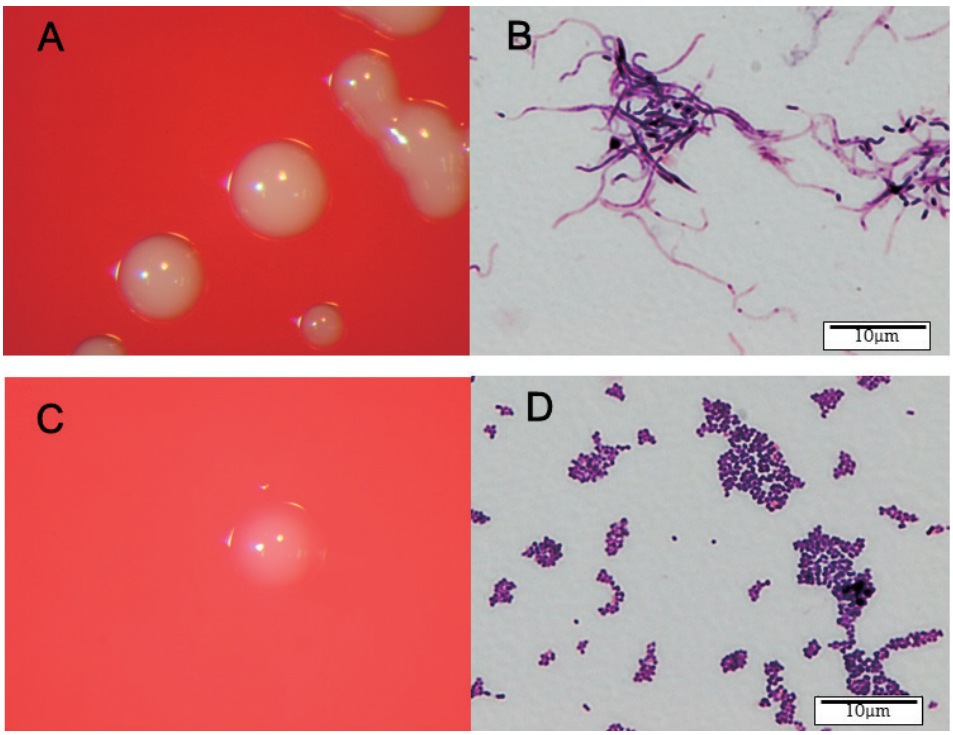

Fig. 3 (A) Actinomyces cardiffensis and (C) Parvimonas micra colonies culturedand on TSA II 5% Sheep Blood Agar M for 2 days. (B) Actinomyces cardiffensis and (D) Parvimonas micra Gram - stain of the pus Drainage from the brain abscess shows Gram - positive rod.

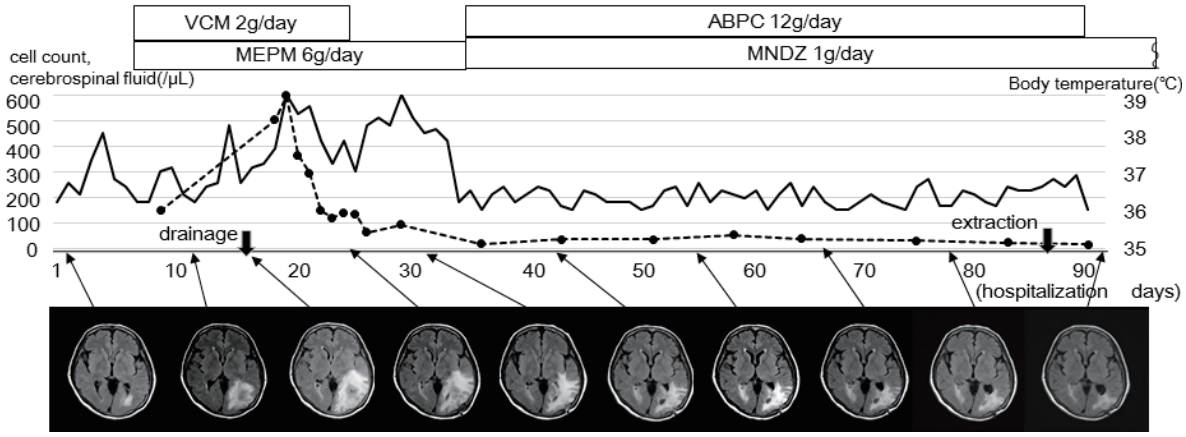

Fig. 4 Clinical course during hospitalization.
Head MRI (FLAIR) taken regularly shows that the lesion in the left occipital lobe continues to shrink after drainage. The number of cells in the cerebrospinal fluid peaked on the 4th day of drainage and tended to decrease thereafter.
VCM: vancomycin, MEPM: meropenem, ABPC: ampicillin, MNZ: metronidazole

ynx, and digestive tract, and *Actinomyces cardiffensis* is a species newly isolated in 2002 [9]. A characteristic of this bacterium is that it progresses from the damaged site of the mucous membrane to the submucosa while forming a fistula. Rarely, hematogenous dissemination occurs. It may follow a subacute/chronic course and may not be accompanied by inflammatory changes such as fever. The cause of this bacterial infection is poor oral hygiene. In addition, it is reported that the risk of infection is increased by catheter infection such as infusion, transplantation treatment, radiotherapy, chemotherapy and other immunodeficiency conditions, and intrauterine contraceptives. It has been reported that actinomycete infection in the central nervous system is as low as 2–3%. On the other hand, *Parvimonas micra* (Study *Micromonas Micro*, *Peptostreptococcus micros*) is a Gram-positive anaerobic coccus group that constitutes the bacterial flora of the oral cavity and digestive tract. As a pathogenic bacterium for inflammation, chronic otitis media, and pulmonary pyogenic disease, the involvement of this bacterium in deep infections is known. Often isolated from bloodstream infections.

Alan *et al.* have reported a review of 60 cases of intracranial abscesses with odontogenic source [10]. It has been pointed out that oral diseases with the highest

risk of intracranial infection among them are caries or periodontal disease accompanied by periapical lesions of the molars.

In addition, Sato *et al.* showed that FDG-PET imaging in a patient with a brain abscess whose infection source was unknown, and that FDG accumulated in the chronic gingival lesion, which was useful for identifying the infection source [11].

In this case, there were three molars suspected to be the causative teeth, all of which were in bad condition with apical lesions and teeth with bone resorption up to the apex due to periodontal disease. There was no direct continuity between the lesion in the oral cavity and the abscess, and it was considered that a brain abscess was formed due to hematogenous spread.

Imaging features of abscesses are characterized by mild hyperintensity of the capsule at T1WI of the head MR, hypointensity of the parenchyma, hypointensity of the capsule at T2, and hyperintensity of the parenchyma. Usually, it is characterized by a markedly high signal and is accompanied by ring enhancement with a contrast agent [12, 13]. This is because the internal solution of an abscess is generally highly viscous and limits the diffusion of water molecules. However, it should be noted that some high-density brain tumors, such as metastatic brain tumors and gliomas, may show high signals. It has been reported that it is possible to distinguish between brain abscess and brain tumor using diffusion-weighted imaging (DWI) due to advances in MRI imaging [14, 15].

In the case of glioblastoma multiforme with necrosis, it is similar to a brain abscess in that it has a ring-shaped enhancement effect, but it is distinguished from the low-intensity region in the diffusion-weighted image, whereas it is distinguished from the high-intensity region in the abscess. It is considered important. This is because the inside of the brain tumor is mainly necrotic tissue, and the poor diffusion of protons in the inflammatory cells is maintained, whereas the inside of the brain abscess is pus, and due to the high consistency and cell density, it is thought that this is due to limited movement.

In this case, the first MR scan showed a marked ring-shaped enhancement effect on the contrast-enhanced T1WI, and a part showing high signal intensity was observed on DWI. In MR images taken after the change in clinical symptoms, MRI findings of brain abscess were confirmed by increased ring-shaped enhancement effect on contrast-enhanced T1WI, markedly high signal on DWI, and increased cerebral edema. Was similar to. In order to distinguish between tumors and abscesses, it is important to carry out MR imaging for clinical observations as well as clinical findings in order to make a careful and prompt diagnosis, in addition to imaging findings.

Treatment of brain abscesses requires both medical and surgical treatment. Administration of antibacterial drugs before drainage reduces culture sensitivity, but antibacterial drug administration should not be delayed while waiting for drainage. Antibiotics should be administered immediately after suspicion of a brain abscess, but antibiotics may be administered after aspiration of the abscess only if the surgical procedure can be completed within a few hours. Although, it is possible to start with empirical treatment based on a primary infection site that seems to be the cause of a brain abscess, it is important to collect a sample before the start of treatment as much as possible. Due to the large number of streptococci involved, PCG or 3rd generation cephem is used in combination with, and MNZ added to cover anaerobes including Bacteroides and Prevotella. If S. aureus is suspected, VCM is added until a culture result is obtained. If the causative organism is unknown, cefotaxime (2 g every 6 hours) or ceftriaxone (2 g every 12 hours) +MNZ (500 mg every 6–8 hours) or VCM (15 mg/kg every 8–12 hours) with target trough value 15–20 is administered.

Although there are no specific clinical symptoms of brain abscess, headache, fever, nausea, vomiting, neurological deficit, consciousness disorder, and convulsions are common. Only 20% have all three classic symptoms of fever, headache, and focal symptoms, and blood tests often do not show leukocytosis or elevated CRP, so general blood tests may not be useful for diagnosis [1, 16, 17]. In this case as well, there was no fever or headache at first, mild lesions were observed, and blood tests showed normal values, indicating the same tendency as observed in previous reports.

With regard to prognosis, the mortality rate of affected persons is as high as approximately 25%, and even in cured cases, 30% to 55% have neurological sequelae, such as convulsions, persistent neurologic deficits, and behavioral changes. There is a report that the mortality rate of patients with poor consciousness and immunodeficiency before the start of treatment is high, but in a clinical study of 20 patients with brain abscess by Kosuge *et al.*, age, sex, medical history, and abscess diameter, there is no relation between the antibiotic administration period, consciousness on admission, and prognosis [19]. However, cerebral abscesses that have complicated by ventriculitis have a poor prognosis. In this case, clinical aggression was suspected and intracranial rupture was sensed based on the imaging findings, and urgent surgical abscess drainage resulted in improvement. Intracranial abscesses may have a poor prognosis due to late diagnosis, so it was considered important to observe the changes in clinical symptoms and examine the images over time.

CONCLUSION

Here, we reported a case of brain abscess suspected of involvement of Actinomyces cardiffensis and Parvimonas micra that are the causative bacteria of periodontal disease.

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