Brain Abscess in the Contralateral Frontal Lobe Associated with Frontal Sinusitis that Spread from Odontogenic Maxillary Sinusitis

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We encountered a case involving a brain abscess in the right frontal lobe of a 12-year-old girl who was diagnosed with a chief complaint of headache and nausea. Left maxillary sinusitis, a dental infection related to dental caries and apical periodontitis, was observed in the left maxillary first molar in addition to left frontal sinusitis also being present. In addition to administering antibacterial agents, extraction of the left maxillary first molar and drainage of the paranasal sinuses and brain abscess were performed. Follow-up over the course of 1 year and 5 months indicated that the patient had progressed without any sequelae; therefore, the prognosis was good. In this case, although bone destruction was observed in the posterior wall of the frontal sinus, which could be a route for bacteria to enter the skull, we considered the possibility of direct invasion from the same site to be low because the brain abscess occurred on the opposite side. We believe that a route for hematogenous invasion from apical periodontitis, in addition to sinusitis, is also possible. Regardless of the route, the outset was an infection in the dental field; therefore, this case reaffirmed the importance of dental cavity treatment in childhood.

Key words: Dental infections, maxillary sinusitis, frontal sinusitis, sinusitis, brain abscess

INTRODUCTION

The frequency of brain abscesses has been declining over the past few decades, with a 2015 report indicating that it was a relatively rare condition, with an incidence of 3.3 per 1 million people. Thus, it is a significant disease because proper diagnosis and treatment have a large impact on its prognosis thereof [1]. Although brain abscesses associated with congenital heart disease with right-left shunts are well known in childhood, it is also known to be caused by infections in the otorhinolaryngology field, such as sinusitis and otitis media, as well as infections in the dental and oral surgery fields, such as dental caries and apical periodontitis, trauma, and surgery, just as in adulthood. The rate of brain abscesses caused by infections in the field of dentistry and oral surgery is less than 5%, which is considered relatively rare. However, recent studies indicate that the rate is 13.6% or 57%, depending on the report, suggesting that this is more common than previously thought [2, 3]. There are two main routes by which bacteria invade the skull: one in which tissues near the brain, such as the sinuses, become inflamed, causing bone destruction and direct penetration into the skull, and another in which the hematogenous route of invasion is via veins from sinusitis or infection in the dental area, even without bone destruction. We herein present a case of a child with dental caries in the left maxillary first molar, apical periodontitis, left maxillary sinusitis, left frontal sinusitis, and a brain abscess in the right frontal lobe on the opposite side.

CASE

The patient was a 12-year-old girl who had visited a dentist several years previously for dental caries. However, the details of the treatment were unknown and because her pain subsided spontaneously she did not continue the treatment. Additionally, the patient often experienced nasal congestion and nasal discharge. Eight days prior to her admission, she started experiencing frontal headaches, nausea, and vomiting, which prompted her to visit a local physician on the same day. She was taking prescribed analgesics and antiemetics and was being monitored at home. However, her symptoms did not improve, with persistent headache and vomiting after meals. She did not experience fever or cheek pain. However, because her headache worsened on the night of admission, she was transferred to our hospital's emergency department. The patient had no

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Table 1 blood tests on admission

< complete blood count >			< venus blood gas analysis >			< biochemical test >					
WBC	12500	/μL	pH	7.527		TP	7.8	g/dL	Na	136	mEq/L
RBC	4.63	10^6/μL	PCO_2	31.9	mmHg	Alb	4.1	g/dL	K	3.5	mEq/L
Hb	12.8	g/dL	BE	4.2	mmol/L	CK	26	U/L	Cl	99	mEq/L
Ht	37.2	%	HCO_3^-	26.3	mmol/L	AST	15	U/L	Ca	9.5	mg/dL
Plt	52	10^4/μL	Lac	1.1	mmol/L	ALT	23	U/L	CRP	0.156	mg/dL
						LDH	116	U/L			
						Cr	0.46	mg/dL			
						BUN	11	mg/dL			
						UA	4.1	mg/dL			
						Glu	114	mg/dL			

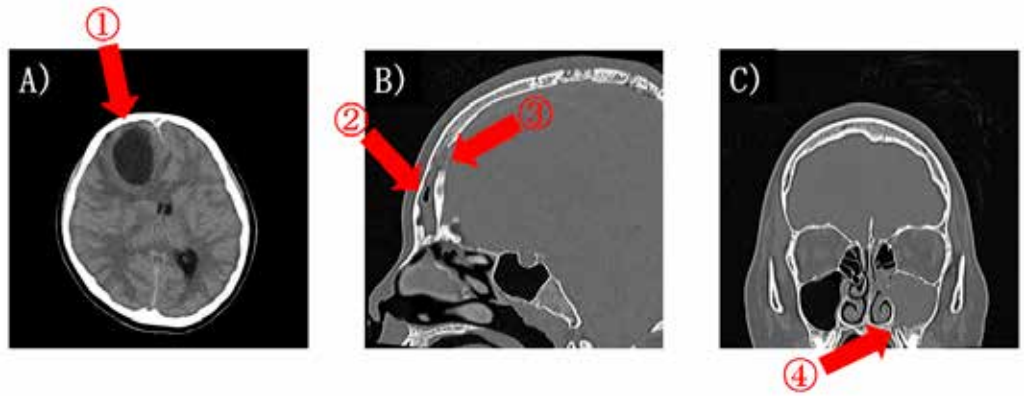

Fig. 1 Plain head CT examination upon admission
A) Horizontal section: A cyst-like lesion measuring 48 × 26 mm was found in the right frontal lobe (Arrow ①).
B) Sagittal view: Mucosal thickening is observed from the left maxillary sinus to the frontal sinus (Arrow ②). Bone destruction is seen on the dorsal side of the left frontal sinus (Arrow ③).
C) Coronal section: At the root apex of the left upper first molar, a low resorption area is observed that partially penetrates the maxillary bone and reaches into the maxillary sinus (Arrow ④).

notable medical or family history. She was born via caesarean section at 37 weeks and 0 days of gestation. The patient's developmental history was unremarkable and she had received all required vaccinations.

A physical examination on admission revealed the following: height, 165 cm; weight, 56.4 kg; consciousness, clear; body temperature, 36.7°C; respiratory rate, 18 breaths/min; pulse rate, 61 beats/min; blood pressure, 120/71 mmHg; and SpO_2, 97% (room air). There was no tenderness or pounding pain in the forehead or cheek. Swelling was not observed in the cervical lymph nodes. Stiff neck was not observed. The patient had no heart murmurs. No breathing sound abnormalities were observed. Her abdomen was flat and soft with no hepatosplenomegaly. No obvious rash, subcutaneous bleeding, or abrasion was observed on the skin. A neurological examination revealed no Kernig sign a pupil diameter of 3 mm/3 mm, light reflex +/+ with no difference between the left and right sides, or obvious paralysis of the extremities. There was no enhancement or attenuation of the deep tendon reflexes and no left/right differences were observed.

Although the blood tests (Table 1) revealed an increase in peripheral blood leukocytes, there was no increase in CRP levels. Plain computed tomography (CT) of her head (Fig. 1) revealed a cystic lesion measuring 48 × 26 mm in the right frontal lobe. Mucosal thickening and fluid accumulation were observed in the left maxillary sinus, part of the left ethmoid sinus, and left frontal sinus, and bone destruction was observed in the posterior wall of the left frontal sinus. Furthermore, a low-resorption area was observed at the root apex of the left upper first molar, which partially penetrated the maxilla and reached the left maxillary sinus. A contrast-enhanced MRI scan of her head (Fig. 2) revealed a mass in the right frontal lobe, with a margin indicating a capsule-like structure with low signal intensity on T2WI and high signal intensity on T1WI. Contrast-enhanced imaging revealed ring-shaped deep staining around the tumor edges. Edema was observed in the surrounding brain parenchyma, and the tumor had shifted to the midline. Echocardiography revealed no structural abnormalities, a normal cardiac function, and no warts.

Based on the imaging findings, the lesion in the right frontal lobe was diagnosed as a brain abscess.

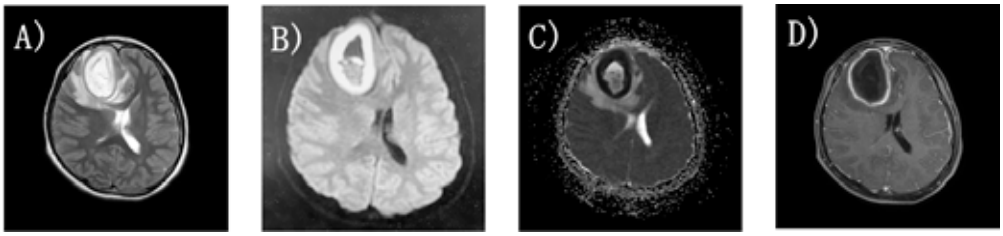

Fig. 2 Contrast head MRI examination at admission
A) T2WI: There is a capsule-like structure with a low-signal area at the edge of the tumor and edema in the brain parenchyma around the tumor.
B) DWI: A capsule-like structure with a high-signal area was observed at the edge of the tumor.
C) dADC: A low-signal area is observed at the edge of the tumor.
D) T1WGd: Ring-shaped deep staining was observed at the edge of the tumor.

Fig. 3 Abscess collected from tooth root, maxillary sinus, and brain
A) Abscess taken from the root of a tooth
B) Abscess taken from inside the maxillary sinus
C) Abscess drained from the brain

She had persistent symptoms consistent with sinusitis, including nasal congestion and discharge. The left maxillary sinusitis was considered to be a dental infection that spread from dental caries in the left maxillary first molar and apical periodontitis. Furthermore, mucosal thickening and pus accumulation continued in parts of the left ethmoid sinus and left frontal sinus, while bone destruction of the posterior wall of the left frontal sinus occurred as a result of inflammation. Although the site of occurrence was on the opposite side, a relationship with the development of a brain abscess was suspected. We admitted the patient to our hospital for treatment, and intravenous ceftriaxone (4 g/day) and metronidazole (1500 mg/day) were initiated immediately. In addition to the administration of antibacterials, on the fourth day of hospitalization, the left upper first molar was extracted, endoscopic sinus surgery was performed to open the left maxillary sinus, part of the left ethmoid sinus, and left frontal sinus, and a burr drainage procedure was performed for the abscess in the right frontal lobe. Pus cultures collected from the root of the tooth, maxillary sinus, and brain during surgery (Fig. 3) revealed *Streptococcus* sp. and obligate anaerobic non-spore-forming Gram-positive bacilli from all sites. Although specific identification of the bacteria was not possible, these bacteria showed the same pattern of susceptibility to antimicrobial agents even though they were collected from different sites. On the 17th day of hospitalization, based on the susceptibility of the detected bacteria, the antibacterial agent was changed to intravenous ampicillin (4 g/day) and metronidazole (1500 mg/day. Both sets of blood culture results obtained on admission were negative. Symptoms such as headaches improved and she did not experience any convulsions. Contrast-enhanced magnetic resonance imaging (MRI) of the head confirmed that the abscess cavity and surrounding edematous changes had shrunk over time. On the 30th day of hospitalization, the patient was discharged from the hospital after switching to oral antibacterials, which were discontinued after seven weeks. No convulsions or other neurological symptoms were observed after that time point, and an MRI scan of the head at 1 year and 5 months after the onset of symptoms confirmed that the abscess cavity and surrounding edematous changes had shrunk. No new abscess cavities were observed (Fig. 4).

DISCUSSION

Symptoms such as fever, headache, nausea/vomiting, and impaired consciousness vary depending on the location and size of the brain abscess, along with the presence or absence of edema in the surrounding brain tissue [4]. Furthermore, all of these symptoms are seen in other diseases and cannot be said to be specific to a brain abscess. The frequency of accompanying fever is reported to be 30–70% [4], and it should be noted that there are cases, such as this case, that are not accompanied by fever. In this case, although the main symptoms were headache, nausea, and vomiting, they were thought to be caused by brain edema with midline deviation around the brain abscess.

The route of infection can be broadly divided into two routes: one route in which the bacteria directly

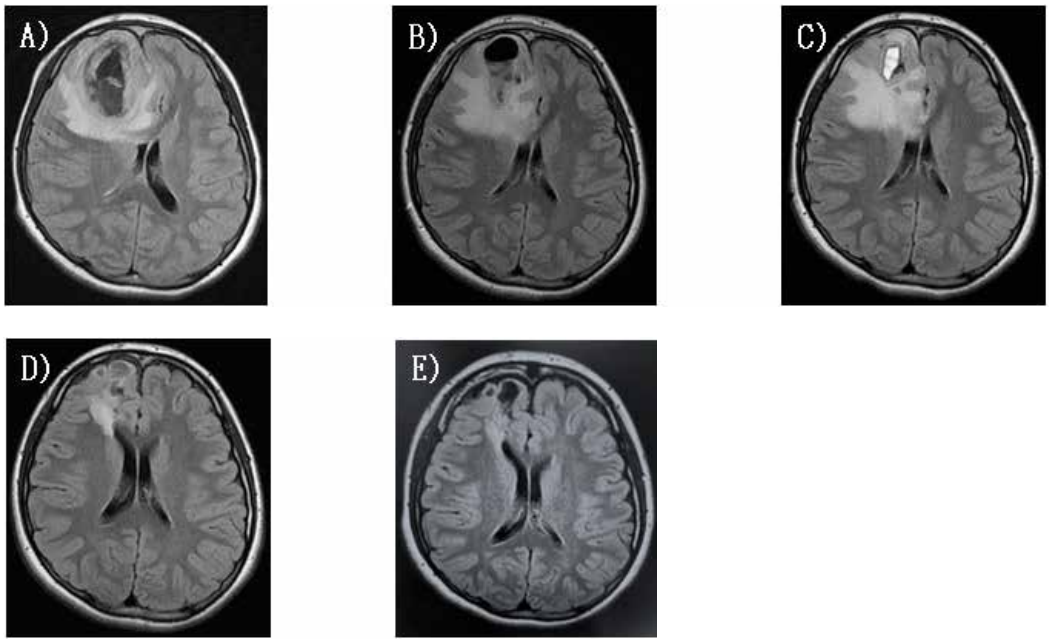

Fig. 4 Changes of the brain abscess over time on head MRI (FLAIR images)
A) Day of admission
B) 10th hospital day
C) 25th hospital day
D) 55th hospital day
E) 1 year and 5 months after the onset

invade the skull from the infection of tissues near the brain and another route in which the bacteria invade through the bloodstream. Regarding the former route, frontal sinusitis is known to spread in most cases [5, 6]. The frontal sinus is a cavity formed between the inner and outer plates of the skull that is separated from the intracranial cavity by a thin posterior wall. Therefore, bacteria can enter the skull from the frontal sinus when frontal sinusitis causes bone destruction in the posterior wall. Furthermore, because the frontal sinus mucosa is in contact with the bone marrow of the skull, osteomyelitis is likely to occur with the veins in the frontal sinus mucosa communicating with the interlaminar and dural veins. It has been reported that these veins are prone to regurgitation due to low perfusion pressure and lack of venous valves, making them easy routes for intracranial invasion [7, 8]. Intracranial infections secondary to frontal sinusitis include meningitis, epidural abscess, subdural abscess, and brain abscess [6, 9]. In our case, frontal sinusitis also caused bone destruction in the posterior wall of the frontal sinus, suggesting that the bacteria may have entered the skull from the same site. However, frontal sinusitis was found on the left side, while an intracranial brain abscess was found in the right frontal lobe, making it difficult to believe that this was due to direct spread. Rather, it was thought that the disease may have entered the skull through the intramucosal veins. In this case, there was also a focus of infection accompanied by mucosal thickening in part of the ethmoid sinus, suggesting that there was also a route for bacteria to enter the skull intravenously from this area. To the best of our knowledge, most reports of brain abscess with complications of sinusitis, such as frontal sinusitis and ethmoid sinusitis, occurred on the same side, with only a few reports on cases occurring on the contralateral side [10, 11]. Although it was difficult to identify the invasion route of the bacteria in this case, it is possible that the bacteria may reach the contralateral side when entering the skull hematogenously from the infection focus of sinusitis, which we found interesting. On the other hand, it is also known that dental infections that are not accompanied by sinusitis can cause brain abscesses [12, 13]. There are two routes of invasion: one that spreads directly, similar to sinusitis, and the other that invades intracranially intravenously. In this case, the brain abscess occurred on the opposite side of the apical periodontitis; therefore, a hematogenous route was assumed. It is believed that the incidence of brain abscesses caused by infection in the dental area is rare (approximately 5%). However, recent reports suggest that it may be more common than previously thought, at 13.6% and 57% in some cases [2, 3]. Although it is unclear whether frontal sinusitis or apical periodontitis was the source of infection that invaded the bloodstream, it was thought that the pathogenic bacteria of apical periodontitis spread, regardless of the route. Multiple bacteria were detected in the brain abscess cavity, frontal sinus cavity, and pus in the roots of the dental caries, indicating that they were the same bacteria. In this case, maxillary sinusitis is thought to be the so-called odontogenic maxillary sinusitis, caused by dental caries that was left untreated. The earliest focus of infection in the pathogenesis of this case was apical periodontitis, demonstrating the importance of dental caries treatment in children.

In addition to the administration of sufficient antibacterial agents, drainage using otolaryngological and neurosurgical approaches is essential for the treatment of brain abscesses, which we believe was successful in this case. Although there is no consensus on treatment, it has a poor prognosis; therefore, complete treatment

with intravenous antibacterials is currently recommended until the abscess disappears. While some people recommend intravenous administration of antibacterials for at least 6 weeks [14], specific criteria for discontinuation are not clearly specified. That said, there are also retrospective observational studies on brain abscesses in which patients who were administered intravenous antibacterials for 1 to 2 weeks before switching to oral administration found no worsening of neurological prognosis or mortality, compared to patients treated with oral antibacterials alone [15]. In this study, surgical intervention was performed in the majority of cases, with antibacterial agents having a high rate of penetration into tissues selected for use. The antibacterial treatment was discontinued in this case, confirming that 4 weeks of intravenous administration was followed by 7 weeks of oral administration, the clinical symptoms remained stable, the head MRI indicated that the abscess cavity of the brain abscess tended to shrink over time, and no new brain abscesses appeared. Subsequently, at 1 year and 5 months after the onset of the disease, the patient is progressing well without any local neurological symptoms or seizures. When switching from oral antibacterials for the treatment of brain abscesses, it is desirable to select antibacterials that require surgical intervention and have high tissue penetration. However, no consensus has been reached regarding the method and duration of antibacterial treatment with the concomitant use of otorhinolaryngological sinus drainage or neurosurgical drainage of brain abscesses, which is an issue to be discussed.

CONCLUSION

We experienced a brain abscess that occurred in the opposite right frontal lobe, in a case in which left maxillary sinusitis developed as a dental infection due to dental caries in the left first molar, and apical periodontitis, which spread to the left frontal sinusitis. While it is well known that brain abscesses are associated with sinusitis, especially frontal sinusitis, there are few reports of the disease occurring on the opposite side, which is interesting when considering the route of infection. Additionally, apical periodontitis is thought to be the earliest stage of the disease; therefore, this case illustrates the importance of appropriate dental caries treatment and regular dental checkups. Although there is still room for debate regarding switching to oral antibacterials in the treatment of brain abscesses, this may lead to early social reintegration of patients and an improvement in their quality of life.

We provided an explanation to the patient's guardian regarding the case report in this paper and obtained written consent. In accordance with our hospital's regulations, this case did not require review by an ethics committee.

There are no conflicts of interest to disclose as defined by the Japan Pediatric Society.

AUTHOR ROLE

Takeru Obara conceived and wrote the paper as the first author and gave the final approval of the manuscript for publication.

Kota Hirai, Mami Ichinose, Takashi Sakama, Masahiko Kato, and Hiroyuki Mochizuki were involved in the conception and design of the paper along with data acquisition. They were involved in critical proofreading of important intellectual content and gave their final approval.

Yasuhiro Nakanishi, as an oral surgeon; Daisuke Maki, as an otorhinolaryngologist/head and neck surgeon; and Masaaki Imai, as a neurosurgeon, provided insight into the pathology, provided advice on writing the paper, and gave final approval of the manuscript for publication.

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