CASE REPORT

A brain populated with space-occupying lesions: identifying the culprit

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Accepted 28 March 2018

SUMMARY

This is a case of an 8-year-old girl who was previously healthy and presented with unresponsiveness on a background of fever that resolved within 2 days of onset. History was significant for recurrent dental abscesses requiring drainage. Imaging revealed what was unexpected: a brain overloaded with multiple space-occupying lesions and diffuse oedema. The patient was started on mannitol and dexamethasone in addition to antimicrobials. Her condition improved dramatically within few days. Multiple aspiration procedures were performed later and she recovered fully with minor deficits.

BACKGROUND

The incidence of brain abscess in patients younger than 15 years of age is 15%–30%. Multiple brain abscesses account for 5%–50% of all brain abscesses; often seen in immunocompromised patients and resulting from haematogenous spread. Headache, fever, seizures and focal neurological deficits are common presenting symptoms. There is no definite rule for the treatment as it should be tailored according to individual cases. It includes antibiotic therapy and surgical management. If not promptly treated, brain abscess can lead to permanent neurological sequelae and death.

The aim of this report is to present a case of an immunocompetent child who presented with multiple brain abscesses attributable to odontogenic infection. Additionally, in this patient, the employment of mannitol, dexamethasone and full antimicrobial coverage have led to a dramatic improvement in a short period of time. By writing this case, we provide further evidence on the effectiveness of corticosteroid use in brain abscess which is considered controversial. Also, we want to stress on the importance of early diagnosis and intervention in the successful management of brain abscess.

CASE PRESENTATION

This is about an 8-year-old girl who was in her usual state of health until 1 week prior to presentation when she developed fever which subsided after 2 days. However, during the subsequent days, her parents noticed that she had excessive sleepiness associated with decreased activity. Few days later, her parents found her to be unresponsive, and she was brought to the emergency department in our institute. Her parents reported a history of

repeated vomiting. There was no history of neck pain, photophobia, convulsions, cyanosis, respiratory or abdominal symptoms. Neither a history of recent trauma, surgical procedure, contact with sick person, travelling abroad, similar previous episode nor of congenital heart disease (CHD) could be elicited. History was significant for on and off headache over the last couple of months and repeated dental abscesses requiring drainage. Developmentally, the child had excellent school performance with no recent changes or complaints. Besides, there is a family history of meningitis/encephalitis that affected the mother and cousin from paternal side when young which resolved completely.

On examination, the patient was febrile but otherwise vitally stable. She was found to be markedly unresponsive with a Glasgow Coma Scale (GCS) of 5–6 out of 15 and had no response to deep painful stimuli. Neurological examination revealed mildly constricted pupils (2 mm in size) with a bilaterally equal sluggish reaction to light, reduced power on the left side, hyporeflexia and upward plantar reflex bilaterally (positive Babinski sign). Her neck was supple. She was also found to be incontinent. The rest of the physical examination was unremarkable.

INVESTIGATIONS

Initial investigations revealed the presence of leucocytosis (15.54×10^9 cells/L) with neutrophilia (86.5%), microcytic hypochromic anaemia (107 g/L), elevated erythrocyte sedimentation rate (120 mm/hour), elevated C reactive protein (153.27 mg/L), normal coagulation profile, electrolytes, renal and liver functions. Serum serological tests, including immunoglobulins, toxoplasmosis, other, rubella, cytomegalovirus, and herpes infections (TORCH) screening, HIV, hepatitis B, hepatitis C, syphilis, antinuclear antibody and anti-double-stranded DNA were within normal. Other investigations including urine creatinine and vanillylmandelic acid were within the normal range. Blood cultures were repeated multiple times during hospital course, and all were negative. Urine and endotracheal aspirate cultures were negative as well.

An urgent CT scan of the brain was done and showed multiple space-occupying lesions with perilesional oedema in both cerebral hemispheres with the majority at the corticomedullary junction causing uncal herniation and descending

To cite: AlHarmi RA, Henari DF, Jadah RHS, et al. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2018-224286

Figure 1 Axial section of CT brain without contrast showing multiple supratentorial intra-axial isodense lesions with perilesional oedema.

transtentorial herniation on the right side. Mild mass effect on the right lateral ventricle and diffuse cerebral oedema can be noted as well. MRI correlation was required which showed multiple round masses involving all lobes bilaterally, sparing the structures of posterior cranial fossa, surrounded by vasogenic oedema. On administration of contrast, thin capsular enhancement of the masses is seen. In addition, fluid and retained mucus is seen in the left maxillary and ethmoidal sinuses. Findings are demonstrated in figures 1–8.

Further imaging modalities were recruited to trace the origins of the lesions seen on brain imaging. An abdominal ultrasound, chest radiograph, carotid Doppler, echocardiography and bone scan were all negative for a primary source. Electroencephalography (EEG) was done to rule out subclinical seizures, and the

Figure 2 Postcontrast section of CT brain showing minimal peripheral ring enhancement.

Figure 3 T1-weighted MRI showing intra-axial lesions which appear isointense at the centre while having a hypointense peripheral ring.

study was abnormal with generalised slowing, indicating encephalopathy of various aetiologies.

DIFFERENTIAL DIAGNOSIS

Due to the clinical dilemma over the sudden deterioration in the patient's condition and with the aid of imaging, a provisional differential diagnosis of multiple brain abscesses (pyogenic,

Figure 4 Axial T2-weighted MRI showing the lesions which are predominantly hyperintense.

Figure 5 An example of one of the lesions showing a very thin, smooth, complete low and high-signal intensity peripheral rim; known as the dual rim sign.

toxoplasmosis or tuberculomas) and brain neoplasms (primary or metastatic) was suggested.

TREATMENT

The patient was admitted to the intensive care unit, intubated and connected to cardiac monitor and ventilator on continuous

Figure 6 T1 MRI postcontrast demonstrating peripheral rim enhancement of the lesions.

Figure 7 Diffusion-weighted MRI confirming the presence of restricted diffusion.

mandatory ventilation mode. Due to the presence of diffuse oedema as seen on brain imaging, she was started on mannitol and dexamethasone. Considering the critical state of the patient and the severity of infection, she was initially started on broad spectrum antibiotics; meropenem and vancomycin according to the guidelines. Later on, when no significant improvement was noted in addition to persistence of fever, rifampin was added to provide coverage for resistant organisms. Liposomal amphotericin B was added lastly to cover fungal organisms. Neurosurgery consultation was sought for brain biopsy. About 4 days following admission, a craniectomy was performed along with excisional biopsy and abscess drainage which was productive of yellow-green pus. The sample was sent for culture and histopathology review. Culture results are shown in [table 1](#).

Figure 8 Apparent diffusion coefficient map image confirming the presence of restricted diffusion.

Table 1 Summary of microbiological tests performed on brain biopsy sample

Pus swab:	► Leucocytosis ► Negative microscopy and culture
Brain tissue:	► Few white cell counts ► Negative microscopy and culture
Mycology:	► Negative culture after 4 weeks of incubation
Pus for AFB:	► Negative AFB stain ► Negative MTB detection by PCR ► Negative culture after 3 weeks of incubation

AFB, acid fast bacilli; MTB, *Mycobacterium tuberculosis*.

Histopathology report was as follows:

- Macroscopic examination: multiple fragments of greyish tissues measuring altogether 1×0.7 cm and weighing 0.4 g.
- Microscopic examination: multiple pieces of brain tissue showing mild oedema, gliosis, mild perivascular lymphocytic inflammatory cell infiltrate and tiny fragments of necrotic tissue present. Furthermore, no granulomas, infectious pathogens or features suggestive of malignancy can be seen. Appearance is suggestive of an inflammatory origin.

Otolaryngology consultation was sought and after reviewing images, no evidence of mastoid or ear pathology which can cause intracranial extension was seen. Sinuses were declared clear as well. Also, oral and maxillofacial team was invited to review the patient. On examination, she had fair oral hygiene, dental caries and no gingival swelling.

Her general condition improved dramatically, and she was extubated on day 8 of admission and on this she was transferred to the general paediatric ward for 21 more days. During the period spent in the ward, she had several spikes of fever which responded to paracetamol and cooling measures and she was continued on antibiotics and limb physiotherapy. Brain CT and MRI were repeated on several occasions and have shown resolution of oedema but persistence of lesions.

OUTCOME AND FOLLOW-UP

The general condition of the patient improved noticeably. On discharge, she was fully conscious and oriented, with a GCS of 15 out of 15. She only had mild left-sided weakness, mainly involving the upper limbs and could walk with support. She was discharged on levetiracetam. Since she required further specialised care and management, she was transferred to a specialised neurosurgical centre abroad where she underwent multiple aspiration procedures and had a dramatic improvement.

DISCUSSION

Brain abscess is a localised infection within the brain parenchyma that starts with inflammation and evolves into encapsulated pus collection.¹ The incidence of brain abscess in patients younger than 15 years of age is 15%–30%.² Abscesses can arise either by direct or haematogenous spread. Direct spread accounts for 25%–50% of the cases. Sources for direct spread include paranasal sinuses, otogenic and odontogenic infections. In the largest case series published to date on brain abscess involving 973 patients, otorhinogenic infections accounted for 38.5% of the cases compared with 0.9% attributed to odontogenic infections. Oral cavity organisms spread through haematological, lymphatic and direct routes to the brain. Bacteraemic or haematogenous spread is associated with distant infections such as pulmonary, cardiac, abdominal, pelvic and skin infections. It often results in multiple abscesses.^{3–6} Common predisposing factors in children

include CHD, congenital lesions of the head and neck, immunosuppression, neurosurgical procedures and penetrating skull injury and fractures.¹ The cause is unknown in up to 40% of the cases.⁴ In our case, the source of infection is most likely odontogenic, spreading directly to the brain. Distant spread is less likely since a remote focus of infection was not present and blood cultures failed to grow any organism on several occasions.

Brain abscess is caused by a wide spectrum of organisms. Factors such as the site of the primary infection, age and immunity play an important role. In immunocompetent individuals, the abscess is more likely to be bacterial while in immunocompromised individuals, a variety of pathogens have been implicated including fungi and parasites.³ In neonates, *Proteus*, *Citrobacter* and *Enterobacter* species are commonly isolated. *Nocardia*, fungi and *M. tuberculosis* are usually seen in immunocompromised children. Furthermore, in children with CHD, *Streptococcus viridans* is a common pathogen.¹ Following trauma or neurosurgical procedures, *Staphylococcus aureus* is usually responsible, in addition to *Streptococci* and *Enterobacteriaceae*.^{1,3} Abscesses secondary to odontogenic, otogenic and sinus infections often involve *Streptococci* (aerobic and anaerobic), *Enterobacteriaceae* and *S. aureus*, among others.¹ Most commonly isolated organisms in abscesses secondary to odontogenic infections are *S. viridians*, *Bacteroides* and *Aggregatibacter actinomycetemcomitans*.⁶

Multiple abscesses account for 5%–50% of all brain abscesses. These are often seen in immunocompromised patients and are the result of haematogenous spread as mentioned earlier. *Streptococci* and *Staphylococci* are common causative organisms. Fungal infections, if present, mostly result in multiple brain abscesses.^{2,3} In contrast to literature, our patient is immunocompetent and had no remote focus of sepsis.

Headache is the most common presenting symptom, occurring in 72%–92.8% of the cases.^{3,4} Fever (54.5%–60%), seizures (21%–25.3%) and various focal neurological deficits are common symptoms as well. In neonates, irritability, bulging fontanelles and increase in head circumference may be the presenting complaints and thus high index of suspicion is necessary.^{1,4} Clinical manifestations depend on the location of the abscess as well. The locations are as follows (ordered from the most to the least common site): frontal, temporal, frontal-parietal, parietal, cerebellar and occipital.³

While CT is preferred in emergent settings, MRI is the modality of choice in diagnosing brain abscess.³ In infants with open fontanelles, ultrasound of the head is often useful. Lumbar puncture is contraindicated when signs of increased intracranial pressure are present.⁷ Specimens obtained by means of aspiration or surgery should be sent for Gram's stain, special stains and cultures. Serum and cerebrospinal fluid (CSF) sample serology can be of aid in diagnosis. However, definitive diagnosis is made by histopathological examination of brain biopsy. Identification of the causative organism can be achieved as well.³

Differential diagnoses include bacterial or pyogenic, fungal, nocardial and tuberculous abscesses, primary and metastatic brain neoplasms, epidural and subdural empyema, meningitis, acute focal necrotising encephalitis, inflammatory granuloma or tuberculoma, neurocysticercosis, toxoplasmosis, cryptococcosis, haematoma, septic cerebral emboli with associated infarction, septic dural sinus thrombosis, mycotic cerebral aneurysm and hydatid cyst.^{2,8}

There is no definite rule for the treatment of brain abscess. Treatment should be tailored according to individual cases and it includes antibiotic therapy and surgical management. It is directed towards the relief of mass effect if present, identification

of pathogen and eradication of infection accordingly, reduction or prevention of occurrence of neurological sequelae and provision of adequate supportive care.^{2,7} Antibiotics are considered the first line of treatment and should be started immediately. Different empiric antibiotic regimens have been proposed. Broad-spectrum antibiotics to be initiated include third or fourth generation cephalosporins, vancomycin and metronidazole for a duration of 4–6 weeks in surgically treated abscesses and 6–8 weeks in conservatively treated abscesses. Longer course is also indicated for necrotic, multiloculated and brainstem lesions and in immunocompromise. Penetration of the antimicrobial through the blood–brain barrier should be considered as higher doses might be required.^{8,9} Our patient received vancomycin, meropenem, rifampicin and liposomal amphotericin B for 4 weeks with good response.

The prophylactic use of anticonvulsants is recommended in children who develop seizures for prevention of further episodes. First-line drugs include phenytoin, carbamazepine and valproic acid. Levetiracetam is also being increasingly used due to its advantageous safety profile. Recommended duration of use is 3 months if no further episodes take place and according to EEG studies.^{4,7} Our patient did not develop any seizures but due to the abnormal EEG study, she was started on levetiracetam prophylactically. The use of corticosteroids in patients with brain abscess is controversial. Corticosteroids cause a rapid reduction in vasogenic oedema and slow the encapsulation process; however, they are often avoided due to their effect on immune response and the blood–brain barrier which interferes with the penetration of antibiotics into the abscess.^{7,8} Due to the presence of massive oedema and mass effect, dexamethasone was started and benefit was obvious within few days.

Medical treatment alone is not recommended for pyogenic abscesses greater than 2.5–3 cm in diameter and for refractory smaller abscesses. Surgical options include open craniotomy with complete excision and stereotactic aspiration. Open surgery is indicated for large and multiloculated lesions, cerebellar lesions which obstruct CSF flow and fungal abscesses. It is contraindicated in multiple and deep-seated lesions. Aspiration is associated with less morbidity; however, up to 70% of patients require a repeat procedure due to factors such as incomplete aspiration and inadequate antibiotic coverage. When multiple abscesses are present, a successful strategy dictates aspiration of lesions >2.5 cm and treating other lesions conservatively for 6–8 weeks. In suspected fungal abscess, patients are treated with antibiotics until the diagnosis is confirmed. Due to the poor penetration of antifungals, medical treatment is rarely indicated. Parasitic abscesses are treated with antiparasitics or specific antibiotics.⁷ In line with guidelines, our patient underwent multiple aspiration procedures.

Brain abscess can often result in permanent neurological sequelae such as epilepsy, motor deficits, cranial nerve palsies, intellectual and behavioural disorders, hydrocephalus and death. However, early diagnosis and intervention have led to reduced mortality rates and improved outcomes. Poor prognosis is seen

in immunocompromised patients, children younger than 1 year of age, brainstem, multiple and deep abscesses, delayed diagnosis, presence of coma or severe mental status change at the time of diagnosis, rupture into ventricles and surgical management complicated by haemorrhage, among other factors.^{1,8} In the presented case, despite presenting with unresponsiveness and low GCS, the patient recovered dramatically with minor deficits.

This case represents a fine example of multidisciplinary approach and team work. Specialties including paediatrics, paediatric neurology, neurosurgery, radiology, intensive care and anaesthesia, otolaryngology, oral and maxillofacial surgeons and infectious disease specialists contributed to the management of this critical case and in minimising adverse outcomes and events.

Learning points

- ▶ Dental infection is an uncommon source of multiple brain abscesses, and these are often seen in immunocompromised individuals.
- ▶ A detailed history taking and physical examination are of utmost importance for early diagnosis and hence successful management of brain abscess.
- ▶ A multidisciplinary approach is essential in the management of brain abscess.

Contributors RAA has prepared the manuscript. HMA was the consultant in charge of the concerned patient and has supervised the writing of the manuscript. RHSJ has supervised the writing of the manuscript. DFH has participated in preparing the manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent Parental/guardian consent obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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