Bacterial Brain Abscess Caused by *Klebsiellae Pneumoniae* in an Adult

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Introduction

Bacterial brain abscess is still a disease that challenges neurosurgeons in its diagnoses and treatment, in both adults and children because of variations in the microbiological features, and altered immune status (for example, due to HIV infection, treatment with chemotherapy or organ transplantation). The incidence of brain abscesses is ~ 8% of intracranial masses in developing countries, whereas in the West the incidence is ~ 1–2% [Moorthy, et al.[11], 2008]. Despite a wide spectrum of antibiotics, morbidity and mortality is none the less higher about 27% and 6.6-12.7% respectively. The overall mortality rate is higher (26.7%) in Klebsiella brain abscess [Liliang, et al.[8], 2001]. It should also be kept in mind that the signs and symptoms of brain abscess can be non-specific, therefore a high index of suspicion is necessary [Lobato[9], 2009].

Case Presentation

A previously healthy 51-year old adult male had been admitted to the department of neurology with a week history of headache, nausea, disturbed speech, a slight right-sided weakness and a hypodense lesion on the CT scans, not seemingly a mass lesion. Several days later, the patient was referred to the department of neurosurgery because of sudden increase in his right-sided hemiparesis as well as a decrease in his level of consciousness and a left fronto-parietal lesion what was revealed to be a mass lesion through repeated neuroradiological imaging scans. On neurological examination, the patient's Glasgow Coma Scale score was 13, there was severe dysphasia and muscle strength was 1/5 on the right-sided extremities. His medical history revealed no recent dental problems, sinusitis, otitis media or respiratory tract infections. However, plain X-ray studies showed a pulmonary lesion.

Additional to the non-contrast axial computed tomography (CT) scans (**Figure 1**) and contrast enhanced magnetic resonance imaging scans (**Figure 2**) which were done previously, a diffusion-weighted imaging (DWI) (**Figure 3**), and a magnetic resonance spectroscopy (MRS) study (**Figure 4**) of the patient were taken.

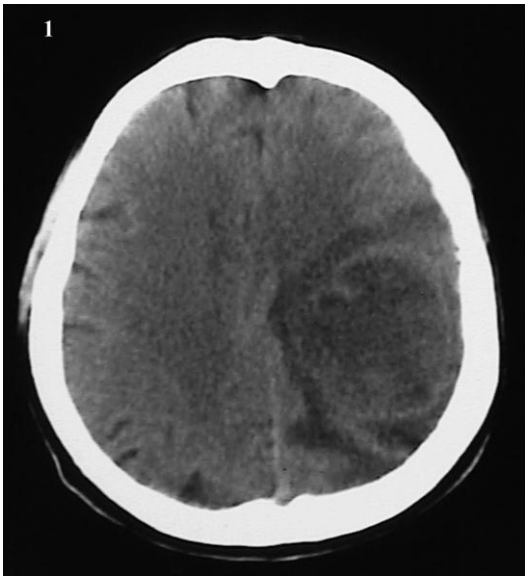
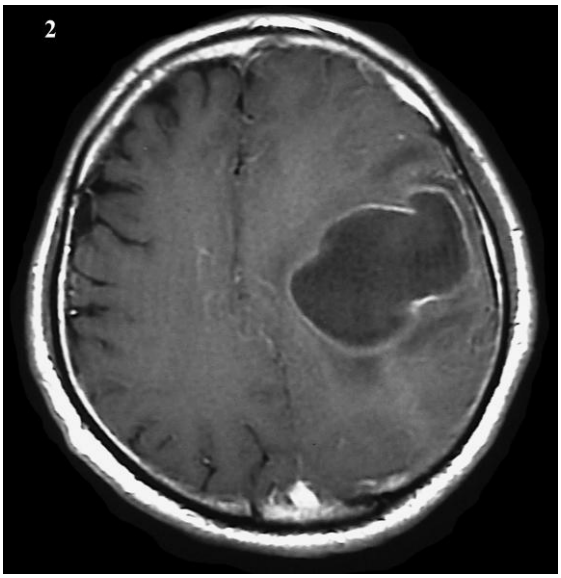


Figure 1.



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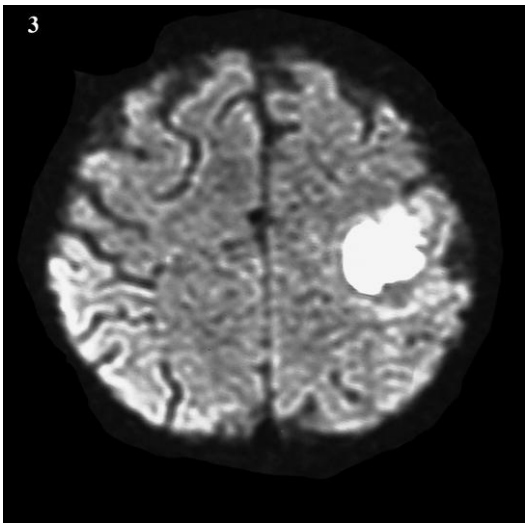

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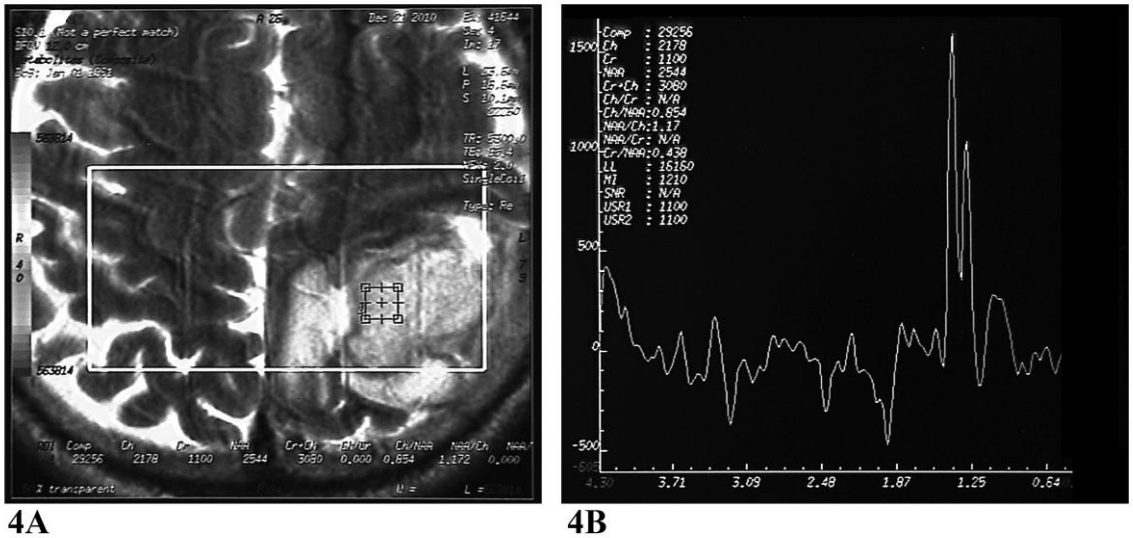
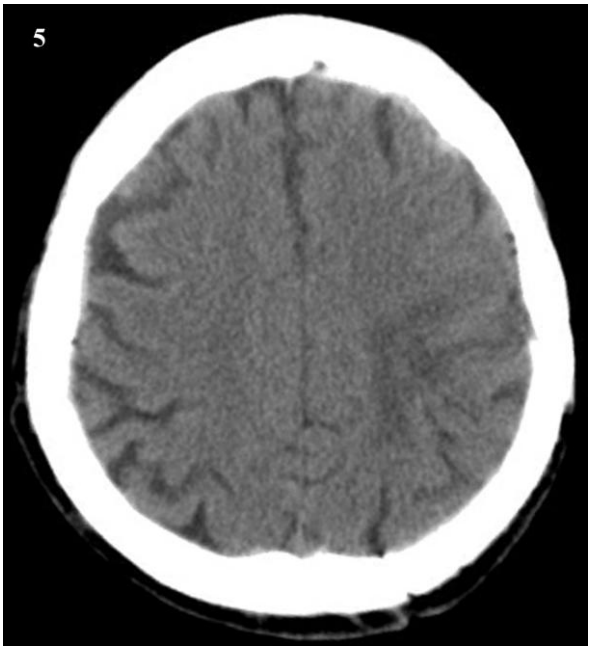


4A 4B

Figure 4.

A fronto-parietal craniotomy was performed and the lesion, which was composed of pus and a capsule, was excised with its capsule using microsurgical techniques and intra-operative ultrasound guidance. On microbiological studies, *Klebsiellae Pneumoniae* was isolated from the cultures obtained during the craniotomy procedure. Significant neurological improvement was noted after the surgery. The patient continued to be treated with a regimen of antibiotics according to the result of the culture sensitivity tests. Post-operative CT and MR follow up scans two month after the operation can be seen in **Figure 5** and **Figure 6**. After the surgery, the patient has shown significant improvement and has returned to work. At follow up one year after the operation, he has continued working without any neurological deficits.



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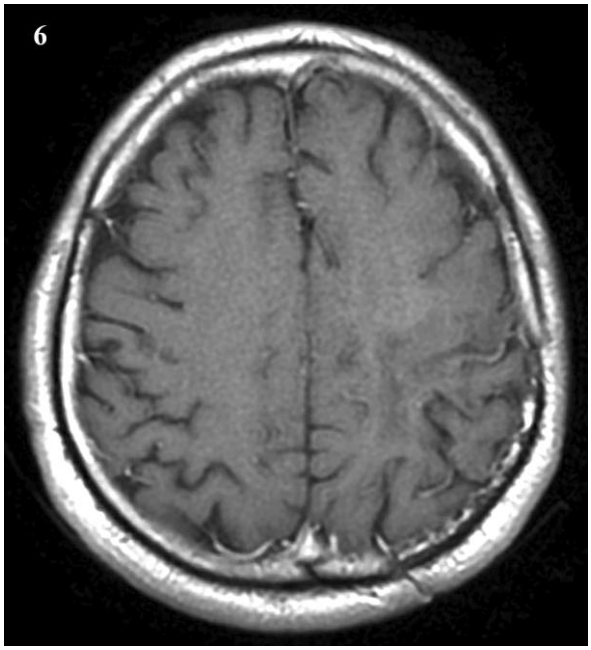

Figure 6.

Questions

1. **What is the differential diagnosis for the lesion seen in the figures?**

   The axial non-contrast CT scan (Figure 1) shows a hypodense mass with moderate oedema and mass effect. The axial contrast enhanced T1-weighted MR scan (Figure 2) shows a ring-enhancing mass lesion. This could be a primary tumour, a metastatic lesion, an abscess, a resolving hematoma, demyelinating process or a subacute infarct. Although, there are no clinical signs and laboratory findings of infection, such as fever or leukocytosis, the most probable diagnosis is a cerebral abscess since there is a bright signal due to diffusion restriction on the DWI scan. Additionally, magnetic resonance spectroscopy (MRS) demonstrates prominently elevated levels of lactate and lipids, a decrease in NAA and in the level of choline. Only 40−55% of the patients present with fever [Spreer[17], 2009]. Blood examinations may reveal inflammatory signs, and C-reactive protein is increased in 80−90% of cases; however, normal laboratory findings do not exclude a brain abscess. In most cases it is not possible to isolate the pathogens from the cerebrospinal fluid (CSF), because

there is no communication of the abscess with the CSF spaces; rather, lumbar puncture should be avoided because of the high risk of brain herniation in cerebral abscesses. However, it may be possible to perform ventricular taps in neonates with cerebral abscesses for both CSF analysis and following of treatment [Heep, et al.[3], 2004]. The intracerebral abscess presented in this case was likely the result of a pulmonary infection.

Metastases as well as abscesses are preferentially located in the border zone between gray and white matter (the corticomedullary junction). All cerebral lesions with central necrosis and peripheral contrast enhancement may mimic brain abscesses. However, in most cases the rim enhancement of primary brain tumours will be more irregular, with focal thickenings, and will be less well demarcated than the enhancement of an abscess capsule. Primary or metastatic neoplasm would have low signal intensity on diffusion- weighted images.

A resolving hematoma usually has an associated history of trauma and would demonstrate the presence of hemosiderin. A demyelinating process would usually show incomplete ring enhancement, would usually manifest with multiple brain lesions, instead of a single focus, and would show little or no mass effect. A subacute infarct would demonstrate a vascular distribution and gyriform enhancement [Kingsley, et al.[4], 2006, Salzman[16], 2004].

On MRS, the spectra of pyogenic abscesses often include metabolites not normally seen in brain parenchyma, including acetate, succinate, lactate, alanine, and lipids, and there is no choline elevation [Kingsley, et al.[4], 2006, Salzman[16], 2004]. In astrocytic tumours, MRS shows an elevated choline, increased Cho/Cr ratio and decreased NAA. In metastatic tumours, a strong choline peak without elevation in the surrounding peritumoural oedema is characteristic.

Susceptibility-Weighted Imaging (SWI), a novel MR technique that exploits the magnetic susceptibility differences of various tissues, such as blood, iron, and calcification, may provide additional information valuable in the diagnosis of pyogenic brain abscesses. [Lai, et al.[6], 2012]

2. What are the pathologic stages of cerebral abscess?

The development of brain abscesses may be divided into four stages [Salzman[16], 2004, Spreer[17], 2009]:

1-Early cerebritis (days 1−3);

2-Late cerebritis (days 4−9);

3-Early capsule formation (days 10−13);

4-Late capsule formation (days 14 and later).

The early cerebritis stage (days 1−3) is characterized by perivascular infiltration of inflammatory cells, exudation of protein-rich fluid, excessive oedema, petechial haemorrhages, and necrosis. On plain CT or MRI studies, the early cerebritis stage is characterized by an ill-defined area of low attenuation (CT) or high signal on T2-weighted images, respectively. On non-enhanced T1-weighted images the early inflammatory changes are difficult to discriminate and may present with an isointense or a slightly hypointense signal. Mass effect in the form of the narrowing of sulci and ventricular compression may be present. Following contrast injection there is no, or only sparse, inhomogeneous enhancement.

In the late cerebritis stage (days 4−9) the blood−brain barrier (BBB) becomes disrupted in the tissue adjacent to the emerging necrotic centre

(abscess cavity), resulting in a ringlike enhancement on imaging studies. The mass effect increases. The CT density of the emerging necrosis may vary between strong hypodensity and near isodensity compared with normal brain parenchyma. On T1-weighted images the signal of the liquid centre is higher than that of CSF, depending on the content of proteins and other macromolecules. On T2-weighted images the signal of the core may be similar to that of the surrounding oedema or slightly lower.

During early capsule formation (day 10−13) the necrotic centre decreases and the number of fibroblasts forming the capsule increases. The amount of reticulin produced by the fibroblasts is larger on the cortical side (directed to the brain surface) compared with the ventricular side of the abscess. Whereas the oedema decreases, the reactive astrocytosis advances. On contrast enhanced T1-weighted MT scans, a well-defined, thin-walled enhancing rim is seen.

In the late capsule stage (day 14 and later) the volume of the necrotic centre and the number of inflammatory cells decrease. The capsule becomes thicker and the cavity collapses. The oedema and mass effect diminish.

3. How do causative organisms reach the brain parenchyma?

Infective pathogens can reach brain parenchyma by one of the following mechanisms [Lobato[9], 2009]:

1- Extension in contiguity: Direct extension from infections affecting the paracranial sinuses or ear remains the main pathophysiologic mechanism in the formation of brain abscesses. This occurs through the invasion and destruction of the skull and cerebral envelopes by pathogens, although it can also proceed through septic thrombophlebitis of intra-extracranial venous channels. These infections are frequently polymicrobial.

2- Haematogenous spread: It is the result of bacteremic episodes secondary to infectious pathologies in other organs (endocarditis), or breaches (i.e. dental extractions, or invasive diagnostic studies) results in the introduction of microorganisms into the blood stream, especially when there are underlying conditions shunting the pulmonary filter such as arteriovenous fistulas or persistent foramen ovale. The haematogenous introduction of pathogens is a frequent source of brain abscesses that tend to be monomicrobial and multiple.

3- Direct inoculation by means of trauma or surgery: The increment of neurosurgical procedures added to the relative decrease in other sources of infection resulting from improvement in their medical management (mainly of otic infections), has increased the relative incidence of this mechanism that nowadays equals that of contiguous extension in some series. Infections following open traumatic injuries are infrequent.

4- The origin of some brain abscesses still remains unknown in 20–30% of the cases (“cryptic” abscess without an obvious source).

4. Which are the most common causative organisms?

The spectrum of pathogens of bacterial infections of the brain depends on several extrinsic and intrinsic factors: local and/or regional distribution of pathogens, route of infection, and patient characteristics (age, medical conditions, status of the immune system). Generally, the most common pathogens in bacterial brain abscesses in Western Europe and the U.S. are

Streptococci, followed by Staphylococcus, Pseudomonas, Enterobacteriaceae, and Bacteroides species. Infections with several different pathogens are common [Spreer[17], 2009].

5. What are the risk factors for invasive *Klebsiella Pneumoniae* infection?

Klebsiella pneumoniae is responsible for hospital-acquired urinary tract infections, septicaemia, pneumonia, and intra-abdominal infections. In addition, since the mid-1980s, a distinct clinical syndrome of liver abscess and metastatic infections due to *K. pneumoniae* has emerged, with a predominance of cases in Taiwan. In addition, K. pneumoniae can cause severe pneumonia, bacteraemia, and meningitis. These severe infections are usually community acquired in patients with host risk factors, including diabetes mellitus and possibly an Asian ancestry. The *K. pneumoniae* isolates from severe invasive infections are often hypermucoviscous and frequently belong to the capsular serotype K1 or K2. The majority of invasive infections with hypermucoviscous *K. pneumoniae* have been reported in Asia and in Asian patients living abroad. The basis for this apparent ethnic specificity remains unknown. Host genetic susceptibility, limited geographical distribution of particular strains, or contamination through unique dietary elements may play a role in the epidemiology of invasive infection [Decre, et al.[1], 2011, McCabe, et al.[10], 2010].

6. What are the treatment options?

The management of brain abscesses aims to reduce the space-occupying activity, to reduce intracranial pressure, and eradicate the pathogenic organisms by their correct identification. The strategy for management includes surgical (primarily aspiration and excision) and conservative (e.g., antibiotic, steroid, and anticonvulsant treatment) methods. The choice depends on several factors such as the anatomic location, the stage of abscess formation, and the neurological status of the patient [Ratnaike, et al.[15], 2011]

7. What are the surgical options?

Surgical intervention has been broadly classified into two groups [Grossman, et al.[2], 2012, Ratnaike, et al.[15], 2011]:

1- Aspiration

2- Excision

Recent studies show progressively improving outcomes, irrespective of the intervention used. There are advantages for both methods. The group “aspiration” includes the techniques of single aspiration, repeated aspirations, stereotactic aspiration, stereotactic-endoscopic aspiration and irrigation, ultrasound-guided and free-hand drainage. These techniques have different outcomes, with some expected to produce better survival rates, particularly stereotactic aspiration. The choice of surgical approach usually depends on surgeon preference, the patient’s ability to tolerate the procedure, and the characteristics of the abscess (e.g., aspiration is useful for deep-seated lesions and excision for posterior fossa abscesses) [Kocherry, et al.[5], 2008]. Aspiration is less likely to cause neurological deficit than excision and it is simpler to perform. It can be done easily using a burr hole at any stage of the abscess, even in severe cases. It is minimally invasive and can be used in less accessible sites (e.g., brainstem using microsurgical techniques) or in dangerous sites (e.g.,

paraventricular regions preventing more serious sequelae)[Ratnaike, et al.[15], 2011].

Excision of brain abscesses is useful in some clinical scenarios including large (more than 2.5 cm) abscesses, superficial abscesses, multiloculated abscesses,failure of resolution after several aspirations, posterior fossa lesions, some fungal abscesses, post-traumatic abscesses with retained foreign bodies, and gas-containing abscesses [Grossman, et al.[2], 2012]. Immediate primary excision seems to improve outcome, as aspiration does not completely eliminate oedema (the space-occupying effect of oedema causes mortality) and some loculi can be missed in multilocular abscesses [Mut, et al.[12], 2009]. There is no need for pus to be collected repeatedly, no expense for repeated imaging, and hospital stays are shorter. In the case of an autogenic brain abscess, the middle ear disease can be operated on at the same time. Excision also reduces recurrence of the abscess. Excision after unsuccessful repeated aspiration often improves outcomes, as it allows more complete abscess removal. Open debridement is also necessary when foreign material is present [Pamir[13], 2010].

Neuronavigation has become an established technology that provides objective data for localization in 3D space and thus decreases uncertainties regarding tumour localization, relation to vasculature, safe trajectories, and craniotomy design during surgery. It is possible to use operative neuronavigation based on intraoperative ultrasound without relying on preoperative navigational imaging.[Peredo-Harvey, et al.[14], 2012]

Immunosuppression, haematogenous spread and advanced age have been reported as predictors of poor prognosis. [Landriel, et al.[7], 2012]

Conclusions

It should be remembered that the classical triad of fever, headache, and focal neurological deficits in bacterial brain abscesses is present in less than 50% of the cases. The clinical course of a patient with a bacterial abscess is unpredictable. Therefore, an emergent and proper treatment is necessary in patients with these lesions.

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