Non operative management of cerebral abscess

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Abstract. Cerebral abscess is a focal intracerebral infection that begins as a localized area of cerebritis and develops into a collection of pus surrounded by a well-vascularized capsule. Patients typically present with varying combinations of headache, progressive neurologic deficits, seizures, and evidence of infection. Computed Tomography and Magnetic Resonance Imaging are the most important diagnostic tools in diagnosing cerebral abscess. The treatment of cerebral abscess has been a challenge. Small cerebral abscesses (< 2.5 cm) have been treated empirically with antibiotics. Elevation of intracranial pressure and threatening herniation can be managed by the use of intravenous mannitol (or hypertonic saline) and dexamethasone. Acute seizures should be terminated with the administration of intravenous benzodiazepines or by intravenous fosphenytoin. Anticonvulsants prophylaxis must be initiated immediately and continued at least one year due to high risk in the cerebral abscesses. Easier detection of underlying conditions, monitoring of the therapeutic progress, and recognition of complications have probably contributed to the improved prognosis.

1. Introduction
Cerebral abscess is a focal intracerebral infection that begins as a localized area of cerebritis and develops into a collection of pus surrounded by a well-vascularized capsule.[1] There is no clear data on the epidemiology of cerebral abscess in Indonesia.[2] Populations in low-resource settings have a higher burden of brain abscess. It accounts for less than 1% of intracranial lesions in the developed world, as opposed to roughly 8% in developing countries.[3] There is a wide range of pathogens that can cause acerebral abscess. The microbial cause depends on how it develops and whether the patient is immunocompromised or not. Streptococci (both aerobic and anaerobic) are the most common pathogens, comprising about 70% of isolates cultured from abacterial cerebral abscess.[4] The others cause includes fungal (Candida, Aspergillus, Actinomycetes) and parasites (Entamoebahystolitica, Cysticercosis, Schistosomiasi).[5]

A cerebral abscess can develop from three sources. The first source is a spread of infection from pericranial contiguous focus in 25-50% of cases (such as the sinuses, middle ear, or dental infection), interestingly dental infections, ethmoid or frontal sinusitis (usually spreads to the frontal lobe), and subacute or chronic otitis media or mastoiditis (preferentially spreads to the inferior temporal lobe and cerebellum). The second form is hematogenous spread from a distant focus of infection (such as lung abscess or empyema, bacterial endocarditis, skin infections, and intraabdominal (including pelvic)) in 15-30% of cases. In some of the patients with cryptogenic cerebral abscess, it can be possible to find a cardiac source, a congenital heart disease, like a patent foramen ovale or a pulmonary arteriovenous fistula. Third, from direct inoculation (such as head trauma or neurosurgery) in 8-19% of cases. The
origin of cerebral abscess formation remains elusive (cryptic cerebral abscess) in up to 40% of cases, but they are a known complication of intracranial surgery.[4,6] (See table 1). Brain abscess development has four stages: 1) early cerebritis (1-4 days); 2) late cerebritis (4-10 days); 3) early capsule formation (11-14 days); and 4) late capsule formation (>14 days).[7]

| Source                  | Frequency | Probable Focus                                           | Comments                                           |
|-------------------------|-----------|----------------------------------------------------------|----------------------------------------------------|
| Spread from pericranial | 25-50%    | Paranasal sinuses, middle ear or dental infection        | • Dental infections, ethmoid, or frontal sinusitis usually spreads to the frontal lobe  
| contiguous focus        |           |                                                          | • Subacute/ chronic otitis media or mastoiditis preferentially spreads to the inferior temporal lobe and cerebellum  
|                         |           |                                                          | • The causes a solitary cerebral abscess  
| Hematogenous spread     | 15-30%    | Lung abscess or empyema, bacterial endocarditis, skin infections, intra-abdominal (including pelvic) | Many are multifocal and located in the distribution of middle cerebral artery |
| Direct inoculation      | 8-9%      | Mainly due to head trauma or neurosurgical procedures   |                                                    |

Table 1. Sources characteristics of cerebral abscess [4].

2. Diagnosis of Cerebral Abscess
A cerebral abscess can present with such focal signs, often associated with headaches and spiking temperatures. The focal signs of brain dysfunction can be hemiparesis, hemianesthesia, language disturbance, seizures, etc.[8] Patients typically present with varying combinations of headache, progressive neurologic deficits, seizures, and evidence of infection. However, fever and leukocytosis are absent in about half of the patients harboring a brain abscess.[9]

Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) is the most important diagnostic tools. In the CT scan, the capsule of the abscess enhances, and the center of the abscess and surrounding edematous white matter are hypodense.[10] The enhancing rim typically has a smooth inner margin with thinning of its medial aspect (as the white matter has less perfusion than the grey matter). The abscess center never enhances on delayed images (compare to cerebritis).[11] With MRI, in T1-weighted images, the capsule enhances, and the interior of the abscess is hypointense and shows restricted diffusion; in T2-weighted images, the surrounding edema is apparent, and the capsule is hypointense, and there is variable diffusion restriction within the lesion. There is almost no likelihood of cerebral abscess if enhanced CT and MRI studies are negative.[10]

3. Management of Cerebral Abscess

3.1. Antibiotics
The treatment of brain abscess has been a challenge. Small brain abscesses (< 2.5 cm) have been treated empirically with antibiotics.[7] During the stage of cerebritis and early abscess formation, which is an acute focal encephalitis, the adequate administration of high-dose antibiotics might cure. Even before bacteriologic examination of the intracerebral mass, certain antibiotics can be given, with the choice based on the predisposing condition (vancomycin, a second- or third-generation cephalosporin such as ceftriaxone, and either meropenem or metronidazole). These drugs are given intravenously in divided daily doses. Metronidazole has a good absorption from the gastrointestinal tract that it can be administered orally, 500 mg q6h.[10] Metronidazole readily penetrates brain abscesses; intraleSIONAL concentrations have been found to be 40 mg/mL. This drug has excellent bactericidal activity against many anaerobes but is not active against aerobic organisms including microaerophilic streptococci. Given the excellent intraleSIONAL concentrations and the high probability of anaerobes, many experts recommend administering this agent to most patients with brain infections.
abscess.[7] The regimen is altered once culture and sensitivity data are available. Antimicrobial treatment is usually continued parenterally for 6–8 weeks, followed by orally for 2–3 months. The patient needs an observation by serial CT scans or MRI every two weeks and at deterioration.[12] (See table 2)

Opportunistic organisms which are not pathogenic to humans, cause brain abscess in immunocompromised patients. Antibiotics are given for 3–12 months. In patients with reduced lymphocytic function, infection with Nocardia asteroides or Toxoplasma gondii is common, and sulfonamide and pyrimethamin are most effective. In those with a T-lymphocytic defect, Candida neoformans is common; therefore, 5flucytosine and amphotericin-B are used. In renal transplant recipients, patients with blood cancer and those on steroid therapy, Listeria is common and ampicillin is most effective. In patients with leukemia and lymphoma, Pseudomonas infection is common and aminoglycosides are most effective.[7]

**Table 2.** The empiric treatment of cerebral abscess [13].

| Source                  | Pathogens                                | Preferred  | Alternative for Serious Penicillin Allergy |
|-------------------------|------------------------------------------|------------|-----------------------------------------|
| Unknown                 | S. aureus, Streptococci,                 | Vancomycin PLUS | Vancomycin PLUS |
|                         | Gram-negatives, Anaerobes                 | Ceftriaxone PLUS | Ciprofloxacin PLUS |
| Sinusitis               | Streptococci (incl. S. pneumoniae),      | Metronidazole | Metronidazole |
|                         | Anaerobes                                | (Penicillin OR Ceftriaxone) PLUS | Metronidazole |
| Chronic otitis          | Gram-negatives, Streptococci, Anaerobes  | Metronidazole | Aztreonam PLUS |
| Post neurosurgery       | Staphylococci, Gram Negatives            | Vancomycin PLUS | Vancomycin PLUS |
| Cyanotic heart disease  | Streptococci (esp. S. viridans)          | Penicillin OR Ceftriaxone | Ciprofloxacin |

- Aztreonam 2 g IV Q6H
- Cefepime 2 g IV Q8H
- Ceftriaxone 2 g Q12H
- Ciprofloxacin 400 mg IV Q24H
- Metronidazole 500 mg IV Q6H
- Penicillin 4,000,000 IUs IV Q4H
- Vancomycin load with 25-35 mg/kg, then 15-20 mg/kg Q8-12H (minimum 1 g Q12H)

3.2. Management of Intracranial Pressure

The edema around the abscess cavity is usually very pronounced, it may be greater in volume than the abscess itself.[1] The edema can cause the increasing of intracranial pressure. The initial elevation of intracranial pressure and threatening temporal lobe or cerebellar herniation can be managed by the use of intravenous mannitol (or hypertonic saline) and dexamethasone 10 mg IV, then 4 mg q6hr until clinical improvement is observed, may be reduced after 2-4 days and gradually discontinued over 5-7 days. If improvement does not begin promptly, it becomes necessary to aspirate the abscess stereotactically or remove it by an open procedure that also allows precise etiologic diagnosis (Gram stain and culture).[3,10]

The use of corticosteroids in cerebral abscess is controversial. Intravenous steroids are usually reserved for patients who have severely increased intracranial pressure, either from mass effect or substantial edema around the periphery of the abscess. Steroids are thought to reduce intracranial pressure by decreasing edema via their anti-inflammatory properties. It may decrease inflammation by suppressing migration of polymorphonuclear leukocytes and reversing increased capillary permeability. However, steroid use may also decrease antibiotic penetration, as well as slow the
encapsulation of the suppurative fluid, thus potentially offsetting the beneficial effects. Significant and potentially serious metabolic adverse effects can occur with high dosages.[3] Corticosteroids decrease enhancement of abscess wall on CT. Therefore reduction of ring enhancement should not be interpreted as theresorlution of abscess and indication of theeffectiveness of therapy. Change in volume of the abscess is more reliable for evaluating theeffectiveness of therapy. Steroids, when used, are tapered as rapidly as possible.[7]

3.3. Anticonvulsants
On admission, seizures are reported in up to 34% of patients with acerebral abscess. Acute seizures should be terminated with the administration of intravenous benzodiazepines, such as lorazepam or midazolam, or by intravenous fosphenytoin.[1] Prophylaxis with anticonvulsants is a recommendation for all patients with brain abscesses. It is a belief that posterior fossa lesions are less likely to cause seizures, although reports have failed to demonstrate a correlation between abscess location and the likelihood of seizures. First-line agents include phenytoin (1000 mg orally as a single dose on day one, followed by 300-600 mg/day given in 3 divided doses), carbamazepine (200-400 mg orally twice daily), and valproate (15 mg/kg/day orally given in 3-4 divided doses). Additionally, levetiracetam (750 mg orally twice daily) is increasingly used, due to its favorable adverse-effect profile.[13]

Anticonvulsants prophylaxis must be initiated immediately and continued at least one year due to high risk in the brain abscesses. The treatment can be discontinued if no significant epileptogenic activity appears in electroencephalogram (EEG). The treatment management of the abscess plays one of the most important factors both in the seizure and neurological outcome. The location of the abscess has no predisposition to seizure. However, the hypo-dense areas surrounding the cavity of the abscess were wider in surgically treated patients. These areas are thought to be the harmed brain parenchyma causing neurological deficits and epileptically activities. Epilepsy is also a key sequel in these patients. The rate of epilepsy is 5.2-25%.[7]

4. Prognosis of Cerebral Abscess
The least satisfactory results are when the patient is comatose before treatment starts; more than 50% of such patients in the past have died. If treatment starts while the patient is alert, the mortality is in the range of 5-10%, and even multiple metastatic abscesses may respond. Approximately 30% of surviving patients have aneurologic sequel. Of these, focal epilepsy is the most troublesome.[10] Easier detection of underlying conditions (e.g., sinusitis, head trauma), monitoring of the therapeutic progress, and recognition of complications have probably contributed to the improved prognosis.[1]

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