Etiology, pathology and diagnosis of brain abscess - Review article

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ABSTRACT

Brain abscess is a rare and life-threatening disease which has serious complications. It is important to differentiate between a pyogenic brain abscess and a necrotic neoplasm, as both have different treatments and prognoses. The signs and symptoms of brain abscess vary and are nonspecific. The microbiology has less value in the diagnosis of this disease, which makes radiology the only method of significance for diagnosis known yet. Notably, CT and MRS coupled with structural MRI, DWI and MRS are effective in diagnosing and differentiation of the etiologies of abscesses.

Key words: Brain abscess, CT, Diagnosis, MRI, radiology.

INTRODUCTION

Brain abscess is a focal supportive process within the brain parenchyma (Garg et al., 2004). It is a rare and life-threatening disease which has serious complications. Usually, it occurs due to contiguous purulent spread (for example, frontal sinus infection leading to frontal lobe abscess); hematogenous or metastatic spread, head trauma and neurosurgical procedure (Erdog and Cansever, 2008). Notably, it begins as localized areas of cerebritis in the parenchyma and evolves into collections of pus enclosed by a well-vascularized capsule. Although there have been breakthrough advances in neuro-imaging, neurosurgical techniques, neuro-anesthesia, microbiological isolation techniques and antibiotic therapy; bacterial brain abscesses can be fatal (Lu et al., 2006; Takeshita et al., 1998; Tekkök and Erbengi, 1992; Yang, 1981). In a significant proportion of cases, an etiology cannot be identified. Besides, the clinical presentations vary and the results of laboratory tests are lack sensitivity (Lu et al., 2006). Computed tomography (CT) and magnetic resonance imaging (MRI) offers timely and sensitive methods for assessing abscess (Kevin and Clifford 2014). Brain abscess may lead to serious disability, or even death if misdiagnosed or managed improperly. However, the advent of modern neurosurgical techniques including stereotactic brain biopsy and aspiration, better anaerobic culture techniques, newer generation antibiotics, and modern non-invasive neuro-radiological imaging procedures have revolutionized the treatment and outcome of brain abscess (Lu et al., 2006; Xiao et al., 2005; Osenbach and Loftus 1992). Moreover, the difficulty of collecting samples and the possibility of contamination during collection made brain CT or MRI the only methods used to obtain sensitive diagnosis (Miranda et al., 2013). This review is aimed at gathering the last published information related to brain abscess and their diagnosis and discuss the value of radiology (CT and MRI) in emergency and rapid diagnosis and differentiation of bacterial brain abscess.

EPIDEMIOLOGY

Recently, the incidence of brain abscess has decreased in the United States and all worlds. Brain abscesses account for 1-2% of brain occupying space lesions in western countries and 8% in developing countries (Faraji-Rad and Samini, 2007). In general, brain abscess may occur at any age, but the majority of cases occur between the third and fifth decades of life. Recent case series demonstrate a significant variance in mean age at presentation ranging from 24 to 57 years (Faraji-Rad and Samini 2007; Hakan et al., 2006; Song et al., 2008; Jansson et al., 2004; Kuo et al., 2003; Nathoo et al., 2011; Sarmast et al., 2012; Tattevin et al., 2003; Tseng et al., 2006; Lu et al., 2002). Brain abscesses were more frequent in adults, while only 15-30% of the cases reported in young patients (< 15 years) (Carpenter et al., 2007). Furthermore, it is most predominant in males...
than females and has male to female ratios ranging from 1.5:1 to 4.5:1 (Faraji-Rad and Samini, 2007; Hakan et al., 2006; Song et al., 2008; Sarmast et al., 2012; Tattevin et al., 2003; Tseng and Tseng, 2006; Lu et al., 2002).

ETIOLOGY AND PATHOLOGY

The etiology of bacterial brain abscess includes both aerobic and non-aerobic bacteria but usually occurs as a mixed infection. The most common isolated organism includes *Staphylococcus*, *Streptococcus* and *Pneumococcus* (Muccio et al., 2014). Brain abscesses develop in response to a parenchymal infection with pyogenic bacteria. It begins as a localized area of cerebritis and evolves into a supportive lesion surrounded by a well-vascularized fibrotic capsule (Britt et al., 1984). The staging of brain abscesses has been based on findings obtained during CT scans or MR imaging sessions (Britt et al., 1984). The early-stage or early cerebritis occurs from day 1 to 3 and is typified by neutrophil accumulation, tissue necrosis, and edema. Microlaial and astrocyte activation is also evident at this stage and persists throughout abscess development. The intermediate, or late cerebritis stage, occurs from day 4 to 9 and is associated with a predominant macrophage and lymphocyte infiltrate. The final or capsule stage occurs from day 10 onward and is associated with the formation of a well-vascularized abscess wall, in effect sequestering the lesion and protecting the surrounding normal brain parenchyma from additional damage. Early capsule formation develops from day 10 to 13 and tends to be thinner on the medial or ventricular side of the abscess and prone to rupture in this direction. After day 14, late capsule formation develops, with gliotic, collagenous, and granulation layers (Britt et al., 1984). The most common localization of a pyogenic abscess in the brain is the supratentorial region, in the subcortical white matter especially, if they come from the hematogeneous spread of a distant infection (Luthra et al., 2007; Osborn, 2004). Abscesses secondary to middle ear otitis are typically located in the temporal lobe or in the cerebellum, and localization of a pyogenic abscess in the basal ganglia is possible but rare (Nowak et al., 2003). The abscess is often an isolated lesion but, in immune compromised patients, it is frequent the finding of multiple lesions (Domingo, 1994). The presence of air into the abscess is not frequent and is associated with *Clostridium*, *Klebsiella*, *Enterobacter*, *Peptococcus*, or *Pseudomonas* (Liliang et al., 2001). A single organism was isolated in the majority of bacterial brain abscess and multiple pathogens are uncommon (4-23 %) (Kao et al., 2003; Nathoo et al., 2011; Sarmast et al., 2012). Isolated organisms vary significantly according to etiology of the abscess, for example, an otogenic abscess is most often associated with *Proteus*, *Streptococcus* milleri group organisms, and *S.pneumoniae* (Kao et al., 2003; Nathoo et al., 2011; Sennaroglu and Sozeri, 2000).

DIAGNOSIS

Clinical

The presenting signs of brain abscess are variable and nonspecific. Patients most commonly present with headache, fever, altered mental status, focal neurologic symptoms, neck stiffness, nausea, vomiting, and seizures are less common (Roche et al., 2003; Menon et al., 2008).

Microbiological

It has low value in diagnosis, as a result of the difficulty in the collection of samples from abscess for diagnosis, as well as, it also mainly depends on blood culture and CSF analysis (Kao et al., 2003; Muralidhar et al., 2011; Radoi et al., 2013). Moreover, there is difficulty in obtaining samples from abscess itself and Lumbar puncture (LP) has been considered hazardous in patients with brain abscess and it yields only about 10-30% positivity rate in the cerebrospinal fluid (CSF) cultures (Unnikrishnan et al., 2011; Schliamser et al., 1988). In addition, approximately 20% of the patient’s microbiological cultures of abscess material remain sterile. The polymerase chain reaction (PCR) provides a new alternative, but the data reporting the specific use of broad-spectrum PCR assays to detect the causative pathogens in brain abscesses are infrequent in literature (Tsai et al., 2004).

Imaging

Radiologic diagnosis of brain abscess usually performs by using Computed Tomography (CT) and Magnetic Resonance Imaging (MRI).

Computed tomography

In the earlier phases, a non-contrast CT may show only low-attenuation abnormalities with mass effect. In later phases, a complete peripheral ring may be seen. On contrast CT, uniform ring enhancement is virtually always present in later phases (Salzman and Tuazon, 1987). In early phases, the capsule will be difficult to visualize via conventional techniques, but double-contrast CT and Thallium-201 single-photon emission computed tomography is helpful in defining encapsulation of abscess (Salzman and Tuazon, 1987; Haimes et al., 1989; Desprechins et al., 1999).

Magnetic resonance imaging

MRI features recognize pyogenic abscesses accurately. A central area of liquefaction gives high signals while the
sparing edematous brain tissue gives low signals on T1-weighted images, whereas, the necrosis shows higher signals similar to the grey matter on T2-weighted images (Haines et al., 1989). The maturity of the abscess is indicated by the rim that is formed probably by the collagen and inflammation due to free radicals and microhemorrhages in the abscess wall (Haines et al., 1989). The zone of inflammation is significantly thicker in tubercular as compared to a pyogenic abscess in morphometric analysis of histologic sections (Haines et al., 1989). Thickness, irregularity, and nodularity of the enhancing ring are suggestive of the tumor (in the majority of cases) or, possibly, fungal infection (Tsai et al., 2004). The external capsule of abscess appears typically as a complete hypointense on T2-w and hyperintense on T1-w images rim (Smith, 1992).

**Advanced MR imaging for the diagnosis of brain abscess**

It includes Diffusion-weighted imaging (DWI-ADC), Magnetic resonance spectroscopy (as 1 H-MRS), and Perfusion techniques (PMR). Diffusion-weighted imaging (DWI) is also useful to improve the diagnosis of an intraventricular rupture of a pyogenic abscess, as the purulent fluid appears hyperintense in DWI (Rana et al., 2002). Abscesses tend to grow toward the white matter, away from the better-vascularized gray matter, with thinning of the medial wall (Karampekios and Hesselink, 2005). Diffusion-weighted imaging (DWI) has a sensitivity and specificity of over 90% for distinguishing abscess (low ADC) from the necrotic tumor (high ADC). DWI usually shows restricted diffusion (bright signal) that helps to differentiate abscesses from necrotic neoplasms, which are not usually restricted (Muccio et al., 2014; Desprechins et al., 1999; Guzman et al., 2002). Also, fungal disease, toxoplasmosis, and necrotic portions of the tumors usually show lower signal intensity on DWI and higher ADCs (Muccio et al., 2014; Muralidhar et al., 2011; Mishra et al., 2004; Chong-Han et al., 2003). Cerebral toxoplasmosis MRI usually demonstrates multiple lesions in different stages (Muccio et al., 2014; Chong-Han et al., 2003; Chinn et al., 1995). In addition, the center of the toxoplasma abscess has a hypointense signal in DWI with ADC values higher than in pyogenic abscesses (Chinn et al., 1995; Burtsche and Holtás, 1999). Magnetic resonance spectroscopy uses for the detection of products of bacterial metabolism and neutrophil proteolysis. The distinction of abscess from a rim-enhancing tumor is done by demonstrating amino acids within the contents of the cyst, a finding that is essentially diagnostic of the presence of activated polymorphonuclear leukocytes, and thus of bacterial or, less likely, parasitic infection (Burtsche and Holtás, 1999; Sheila-Dave et al., 2001). On MR-spectroscopy (1 H-MRS), typically, the central necrotic area of pyogenic abscesses shows peaks corresponding to lipids (0.8—1.2 ppm), lactate (1.3 ppm) and amino acids (0.9 ppm) without peaks corresponding to the normal spectrum of nervous tissue (Grand et al., 1999). H-MRS is useful in distinguishing between different bacteria responsible for the abscess and in choosing an appropriate therapy (Lai et al. 2005).

Three different spectroscopic patterns of pyogenic cerebral abscesses have been recognized. In pattern A, lactate, cytosolic amino acids, alanine, acetate, succinate, and lipids are associated with 138 D was commonly linked to obligate anaerobes or a mixture of obligate and facultative anaerobes [50] (Lai et al. 2005). Spectroscopic pattern B is characterized by the presence of lactate, cytosolic amino acids and the occasional presence of lipids was mostly associated with obligate aerobes and facultative anaerobes (Lai et al. 2005). Pattern C is characterized by the presence of lactate and is associated with *Streptococcus* species (Lai et al. 2005). Spectroscopic analysis can also provide information regarding the exact histological stage of the studied abscess (early vs. late cerebritis and early vs. late capsular formation) (Akutsu et al., 2002). In only one paper, Harris found that rCBV values higher in the abscess capsule than in the normal white matter (Harris et al., 2008). On 1 H-MRS, the presence of amino acids, acetate, and succinate is typical for cerebral abscess (Luthra et al., 2007). Furthermore, Tuberculoma and tubercle abscesses typically show a hypointense T2 peripheral rim and a “ring-like” contrast enhancement after injection of gadolinium (Batra and Tripathi, 2004). Tuberculoma associated with tubercular meningitis that typically involves basal meninges (Bernaerts et al., 2003). A tubercular abscess is rare, more commonly in immuno-compromised patients (Gupta et al., 2005). As seen, tubercle abscess on 1 HMR shows only peaks of lipids (Luthra et al., 2007). Perfusion techniques (PMR) can aid in the distinction of intra-cranial abscess from cystic glioma by demonstrating an rCBV lower than or equal to the surrounding white matter in the abscess. An abscess due to *Staphylococcus* has characteristic peaks from lipids and lactate (Muccio et al., 2014; Fabiola et al., 2004). A pyogenic abscess can be differentiated from fungal and tubercular abscesses on PMRS by the presence of acetate and succinate as it is seen only in pyogenic abscess (Grand et al., 1999). Furthermore, tubercular cerebral abscesses show increased concentrations of lipids along with an increased concentration of phosphoserine (Lai et al. 2005).

**DISCUSSION**

A ring-enhancing lesion in the brain is a nonspecific finding, and a variety of inflammatory and neoplastic processes can have a similar appearance. Moreover, it is important to differentiate between a pyogenic brain abscess and a necrotic neoplasm, as both have different treatments and prognoses (Fabiola et al., 2004). These data suggest that CT
facilitates the early detection, exact localization and accurate characterization of brain abscess. Likewise, it provides information about the number, size and stage of the abscess. However, it is difficult to distinguish cerebral abscesses from necrotic tumors inflammatory granuloma (tuberculoma), neurocystercerosis, toxoplasmosis, metastasis, glioma, infarct, resolving hematoma, hydatid cyst lymphoma, and radionecrosis. As well as, it is unable to differentiate between the etiologies of brain abscess. In our review, the differential diagnosis between pyogenic abscesses and other brain lesions with a “ring-like” enhancement is not always possible with MRI only. DWI-ADC, 1 H-MRS, and PWI, together with morphological MRI, can give information about structural, metabolic, and hemodynamic features of abscesses that is helpful in the differential diagnosis.

CONCLUSIONS

CT and MRS coupled with structural MRI, DWI and MRS are effective in diagnosing and differentiation of the etiologies of bacterial abscesses. Metastatic tumors, high-grade gliomas, cerebral infarction, resolving cerebral contusion or hematoma, lymphoma, toxoplasmosis, demyelinating disease, and radiation necrosis must be kept in mind in the different diagnosis for brain abscesses as they appear as ring-enhancing lesions. Particularly the combined use of morphological and advanced techniques together is critical in the diagnostic approach to abscess-like masses in the brain. Magnetic resonance (MR) imaging has greater sensitivity and specificity than CT in identifying pyogenic infection.

REFERENCES


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