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Review

Brain abscess: An overview

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ABSTRACT

Intracranial abscess is a formidable entity. Despite the advent of newer antibiotics and surgical strategies, the overall outcome and quality of life issues in brain abscess patients still remain a continuous challenge for the neurosurgical community. It is a direct interplay between the virulence of the offending microorganism and the immune response of the host. An analysis of our experience in the 289 cases of surgically treated pyogenic brain abscess is presented along with an *overview of intra-cranial abscess of varied etiology and in different locations*. The etiology, pathogenesis, radiological advances and treatment modalities of brain abscess are discussed in light of current literature.

1. Introduction

A brain abscess is an intraparenchymal collection of pus. The incidence of brain abscesses is approximately 8% of intra-cranial masses in developing countries and 1–2% in the western countries.[1,2] They begin as localized areas of cerebritis in the parenchyma and evolve into collections of pus enclosed by a well vascularized capsule. Although there have been breakthrough advances in neuroimaging, neurosurgical techniques, neuroanesthesia, microbiological isolation techniques and antibiotic therapy, bacterial brain abscesses can be fatal.[3–6] The changes in the epidemiology and clinical spectrum of the brain abscess, the predisposing factors and the prevalence of implicated bacterial pathogens contribute to this mortality in different rates.

A multidisciplinary approach is paramount to the successful management of bacterial brain abscesses and is a team approach. The neurosurgeon is the nucleus of the team working in close association with a neurologist, an infectious disease specialist, and neuroradiologist. Intracranial abscess formation is a direct interplay between the virulence of the offending microorganism and the immune response of the host. It is still a serious, life-threatening disease and remains a potentially fatal entity.[3,7] It 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 neuroradiological imaging procedures have revolutionized the treatment and outcome of brain abscess. Eradication of the primary foci of infection is paramount.[3,8,9] The success of treatment is best when the etiologic agent is identified and antimicrobial therapy is targeted. The causative pathogens of bacterial brain abscesses vary according to geographic location, age, underlying medical and/or surgical condition, and mode of infection.[5,8,10–12] Over the period of last 10–15 years, the incidence of otogenic abscess has reduced while the posttraumatic or postoperative brain abscess has increased.[13–15]

2. History

The first successful operation for brain abscess was performed by French surgeon S.F. Morand in 1752 on a temperoethmoidal abscess.[16] In his classic work, Pyogenic Disease of the Brain and Spinal Cord, Meningitis, Abscess of the Brain, Infective Sinus Thrombosis, published in 1893, William Macewen[17] advised draining the abscess and treating the underlying causative sinus infections. In 1918, Warrington[18] investigated the etiological factors in 2 groups: 1) infections from foci in the contiguous structures; 2) infections spread through the bloodstream from a distant site. King[19] introduced marsupialization in 1924 and Dandy[20] introduced aspiration in 1926. Sargent[21] considered the procedure of enucleation of an encapsulated brain abscess in 1928. Vincent[22] popularized complete excision and proved its value in 1936. In 1971,

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Heineman[23] and colleagues became the first to report the successful medical management of a brain abscess.

3. Demographic profile

The incidence of brain abscesses in the western population is approximately 1500–2500 cases/year. It is higher in developing countries.[24] The male to female ratio varied from 1.3:1 to 3.0:1 in the literature.[3,7,13,25] The patients ranged from infancy to elderly ages.[3,7,14,26,27] Most brain abscesses occurred in the first two decades of life.[27] However, the observations are based on the literature during the past several decades, when intra-cranial complications of paranasal sinuses and otogenic infections were more evident.[3,25,28] Roche et al.[29] found the incidence of brain abscess in children to be lower than they had expected from earlier reports.[13] The incidence in patients <15 years of age was between 15 and 30%.[7,13,30]

4. Clinical presentation

An abscess can primarily present in four basic syndromes viz. focal mass expansion, intra-cranial hypertension, diffuse destruction, focal neurological deficit. There are marked variation in clinical symptoms and signs. Headache, changes in level of consciousness, nausea and/or vomiting, and high fever are the most common manifestations.[5,8,13,31] Seizure is also not uncommon as an initial symptom, occurring in 25–34% of patients.[30,32] Brain abscesses may be unicentric or multifocal. Majority, about 90% result from pericranial infection (sinusitis, mastoiditis, otitis media) and many who are hematogenous-borne (those from bacterial endocarditis) are multifocal, especially from cyanotic congenital heart disease. The clinical syndrome will be caused by the forces involved in the host organism interaction, number and size and distribution of abscess, specific brain structures involved and the neighbourhood anatomy disturbances involving cisterns, ventricles, and the dural venous sinuses. A pontine abscess may bulge posteriorly compressing the aqueduct of sylvius causing obstructive hydrocephalus or an occipital abscess may rupture into ventricle causing ventriculitis or ependymitis or it may cause septic thrombophlebitis of the transverse sinus causing venous hypertension, edema, seizures and raised intra-cranial pressure. In our series of 715 cases of brain abscess treated at the Seth G.S. Medical College and King Edward VII Memorial hospital over past 7 years (1999 to 2006), 425(60%) were having tuberculosis and 289 (40%) were pyogenic suggesting that tuberculous abscess was more common (Table 1). 407 (57%) were males and 308 (43%) were females. Out of 407 males 204 (50%) had pyogenic abscess while 203 (50%) had tuberculous abscess and out of 308 females 86 (28%) had pyogenic abscess and 222 (62%) had tuberculous abscess. The age of presentation was common in the second and third decade (Table 2). Fever, headache and vomiting were common symptoms which is consistent with that observed in literature. Majority of the abscesses were in the frontal, temporal and posterior fossa region.

5. Etiology

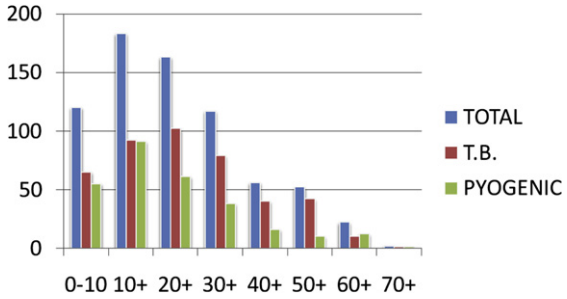
The primary source of infection or predisposing factors to brain abscess, the age of the patient, underlying disease or immune status and previous use of antibiotics determine the ultimate outcome in a patient with brain abscess. The formation of cerebral abscess occurs in contiguous, hematogenous or metastatic manner. The paranasal sinuses are a common source of purulent spread occurring through the frontal sinus infection into the frontal lobe, sphenoid sinus infection extending to the cavernous sinus and middle ear/mastoid air sinus infection spreading into the temporal lobe and cerebellum. Bacteroides, Peptostreptococcus and Streptococcus are mostly identified in brain abscesses due to contiguous spread. The risk of developing a brain abscess in an adult with active chronic otitis media is 1/10,000 per year.[33] Peptostreptococcus and Streptococcus (esp. viridians and microaerophilics) are mostly identified in patient with cardiac origin (cyanotic heart disease) and right-to-left shunts. In CHD diminished arterial oxygen saturation and increased blood viscosity may cause focal cerebral ischemia, often in middle cerebral artery (MCA) distribution.[4,5,30,34] CHD was a significant predisposing factor in children's, but there is a decline due to advances in cardiac surgery and usage of broad spectrum antibiotics. Staphylococci, Streptococcus are identified in patients with prior neurosurgical procedures while Staphylococcus, Streptococcus, Clostridium and Enterobactericea are identified in patients with open head trauma. Recently, hematogenous or metastatic spread is more common due to increase in immunosuppression, organ transplantation, and prolonged life expectation on HIV and chemotherapy usage in cancer.

Fungal infections, Toxoplasma, Staphylococcus spp, Streptococcus spp and Pseudomonas are identified in immunocompromised patients with HIV infections, organ transplantation, chemotherapy or steroid usage.[35] Branched hyphal-form fungal infections obstruct large and intermediate size vessel, causing cerebral arterial thrombosis and infarction. Sterile infarct may be converted to septic infarcts with associated formation of the abscess.[36–38] The mortality rates due to fungal abscesses range from 75 to 100%, despite intensive treatment with amphotericin B.[37,39]

Table 1
Intracranial location of abscess.

	Frontal	Temporal	Parietal	Post.fossa	Occipital	Multiple
Total	175	146	95	138	7	154
T.B.	114	35	76	64	0	137
Pyogenic	61	111	19	74	7	17

Table 2
Age distribution.



6. Pathogenesis

Brain abscess development can be divided into 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).[40] Staging of brain abscess in humans has been based on findings obtained during CT or MRI scans. The glial cell activation in brain abscesses is through parenchymal microglia and astrocytes. Activated microglia has the potential to influence the type and extent of antibacterial adaptive immune response through upregulation of MHC class II and costimulatory molecule expression. The continued release of proinflammatory mediators could damage the surrounding brain parenchyma.[41] Cytokines IL-1 and TNF-alpha individually dictate essential functions for establishment of an effective antibacterial response in the CNS parenchyma. Recent

studies support persistent immune activation associated with experimental brain abscesses with elevated levels of interleukin-1beta (IL-1), tumor necrosis factor-alpha (TNF- and macrophage inflammatory protein-2 (MIP-2)) detected from 14 to 21 days following Staphylococcus aureus exposure. It suggests that intervention with anti-inflammatory compounds subsequent to sufficient bacterial neutralization may be an effective strategy to minimize damage to surrounding brain parenchyma during the course of brain abscess development, leading to improvements in cognition and neurological outcomes.[42]

6.1. Diagnosis

CT facilitates early detection, exact localization, and accurate characterization, determination of number, size and staging of the abscess. It also detects hydrocephalus, raised ICP, edema and associated infections like subdural empyema, ventriculitis and thus helps in treatment planning. It is invaluable in assessment of adequacy of treatment and sequential follow up. Hematogenous abscesses, which can be seen in the setting of endocarditis, cardiac shunts, or pulmonary vascular malformations, are usually multiple, identified at the grey–white junction, and located in the middle cerebral artery territory. 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. On early phases the capsule will be difficult to visualize via conventional techniques, and double contrast CT often is helpful in defining encapsulation of abscess.[43] Positive labelling in radionuclide imaging with III-Indium labelled leukocytes, C-reactive protein, 99m TC-hexamethylpropylene amine oxime leukocyte scintigraphy, diffusion weighted MR imaging, Thallium-201 single photon emission computed tomography and proton magnetic resonance spectroscopy (MRS) help in differentiating abscess from tumor.[44–50]

MRI features recognize pyogenic abscesses fairly accurately. A central area of liquefaction gives high signals while the surrounding edematous brain tissue gives low signals onT1 weighted images. On T2 weighted images, the necrosis shows higher signals similar to the grey matter. The maturity of the abscess is indicated by the rim, which is formed probably by the collagen and inflammation due to free radicals and micro hemorrhages in the abscess wall. The zone of inflammation is significantly thicker in tubercular as compared to pyogenic abscess in morphometric analysis of histologic sections. MRI findings also depend on the stage of the infection. In the early phase, MRI can have low T1-weighted images (T1WI) signal and high T2-weighted images (T2WI) signal with patchy enhancement. In later phases, the low T1WI signal becomes better demarcated, with high T2WI signal both in the cavity and surrounding parenchyma. The abscess cavity shows a hyperintense rim on non-contrast T1-weighted images and a hypointense rim on T2WI.[44] As on CT, MRI usually demonstrates a ring of enhancement surrounding the abscess.[38] Abscesses tend to grow toward the white matter, away from the better-vascularized grey matter, with thinning of the medial wall. However, the enhancing-ring sign is nonspecific and must be evaluated in the context of the clinical history. Thickness, irregularity, and nodularity of the enhancing ring are suggestive of tumor (majority of cases) or, possibly, fungal infection.[44] Vascularity of the wall was not significantly different in abscesses of varied etiology. Differential diagnosis of abscesses on MR imaging is hematomas, metastases and granulomas since a similar low signal rim is obtained on the T2 images in such cases.[43] Brain abscesses are life threatening and detection and identification of the causative pathogens is crucial to substantiate the diagnosis and select the optimal antibiotic regimen. It is known that in approximately 20% of the patients microbiological cultures of abscess material remain sterile. The polymerase chain reaction (PCR) provides a new alternative, but data reporting the specific use of broad-spectrum PCR assays to detect the causative pathogens in brain abscesses are infrequent in literature. PCR is an excellent tool to detect hardy and obligate organisms that require stringent growth conditions like Fusobacterium species and Aspergillus. PCR is rapid, sensitive, and does not depend on the viability of tubercle bacilli in the samples.[51]

7. Advanced MR imaging for diagnosis of brain abscess

Diffusion-weighted imaging (DWI) has a sensitivity and specificity of over 90% for distinguishing abscess (low ADC) from necrotic tumor (high ADC). DWI has a high sensitivity to detect early acute ischemic changes in cortical and deep white matter that can occur in the setting of infectious vasculitis. The viscous cellular pus in abscess produce a very low ADC that distinguishes these lesions from increased diffusivity in necrotic tumor and from normal or slightly low diffusivity in demyelinating plaque. On immediate postoperative MRI, ischemia at the margin pyogenic infection can produce a focally reduced ADC.[38,44] DWI usually show restricted diffusion (bright signal) that helps to differentiate abscesses from necrotic neoplasms, which are not usually restricted,[45,46] although not all abscesses follow this rule. Fungal and tuberculous abscesses may have elevated diffusivity and low signal on DWI.[44] Several studies demonstrate the utility of DWI to differentiate between necrotic or cystic lesions and brain abscesses.[45,46] The latter demonstrates increased signal on the trace images and reduced apparent diffusion coefficient (ADC), while necrotic neoplasms demonstrate decreased signal on the trace image and high ADC values. Brain abscess cavity shows regions of increased fractional anisotropy (FA) values with restricted mean diffusivity compared with other cystic intra-cranial lesions.

7.1. Magnetic resonance spectroscopy

The distinction of abscess from 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.[52] Perfusion techniques (PMR) can aid in distinction of intra-cranial abscess from cystic glioma by demonstrating an rCBV lower than or equal to the surrounding white matter in abscess. Intracerebral abscesses are characterized by specific resonances on MRS that are not detected in normal or sterile pathologic human tissue. MRS has been shown to be specifically beneficial in differentiating between brain abscesses and other cystic lesions,[49] which can be used to expedite implementation of the appropriate antimicrobial therapy. Metabolic substances, such as succinate (2.4 ppm), acetate (1.9 ppm), alanine (1.5 ppm), amino acids (0.9 ppm), and lactate (1.3 ppm), can all be present in untreated bacterial abscesses or soon after the initiation of treatment.[48]

1HMRS is a safe, non-invasive imaging modality and could accurately differentiate between necrotic/cystic tumor and cerebral abscesses. In combination with DWI, it can significantly increase the diagnostic accuracy of conventional MRI and provide valuable preoperative information regarding the nature of a space occupying, ring enhancing intra-cranial lesions. Moreover, 1HMRS can also provide valuable information regarding the etiology of an abscess, as well as, its response to any medical or surgical treatment. However, the promising role of 1HMRS in delineating the specific etiology of intra-cranial abscesses requires though further clinical investigation and validation of the existing results.

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

obligate anaerobes or a mixture of obligate and facultative anaerobes.[53] Spectroscopic pattern B is characterized by the present of lactate, cytosolic amino acids, and the occasional presence of lipids was mostly associated with obligate aerobes facultative anaerobes.[53] Pattern C is characterized by the presence of lactate and is associated with Streptococcus species.[53] Abscesses due to Staphylococcus has characteristic peaks from lipids and lactate.[54] This finding has apparent clinical impact in the early preselection of the appropriate antibiotic treatment for these patients. Tubercular cerebral abscesses show increased concentrations of lipids along with increased concentration of phosphoserine.[55] The spectral characteristics of fungal abscesses are still illdefined. Cytosolic amino acids and lactate are detected in the majority of their fungal abscesses while lipids and lactate or lactate alone is found less consistently. Interestingly, a peak at 3.6 and 3.8 ppm representing trehalose is observed in the majority of the fungal abscesses (a component of the fungal wall). 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).[56]

Lumbar puncture (LP) has been considered hazardous in patients with brain abscess.[57,58] It is usually performed under a strong suspicion of concomitant meningitis and/or ventriculitis in the absence of increased intra-cranial pressure. It yields only 10–30% positive cerebro-spinal fluid (CSF) cultures compatible with abscess cultures.[57,58]

7.2. Differential diagnosis

Radiological features alone are inadequate to differentiate pyogenic brain abscess from fungal, nocardial or tuberculous abscess, inflammatory granuloma (tuberculoma), neurocysticercosis, toxoplasmosis, metastasis, glioma, resolving haematoma, infarct, hydatid cyst lymphoma and radionecrosis. However, fever, meningism, raised ESR, multilocularity, leptomeningeal or ependymal enhancement, reduction of ring enhancement in delayed scan and finding of gas within the lesion favor a diagnosis of abscess.

7.3. Treatment

There are no pragmatic rules for treatment of brain abscess and each case must be individualized and treated on its own merits. The main stay of the treatment includes prompt action and institution of antibiotic therapy.

7.4. Antibiotics

Initial therapy should be commenced with broad spectrum antibiotics which cross blood–brain and blood–CSF barriers in adequate concentrations. After the pus is drained and the antibiotic sensitivity reports become available, specific bactericidal agents for the organism cultured should be administered. If the culture is negative for organism, then the broad spectrum antibiotics should be continued according to the likely predisposing cause (primary source) and the anatomic location of abscess.[59] The complexity of microbial flora in brain abscess necessitates empirical antibiotic therapy against both aerobic and anaerobic organisms. More than one third otogenic and metastatic abscesses are polymicrobial[59] (aerobic and/or anaerobic). Bacteroides, Peptostreptococcus and Fusobactrium are common anaerobes and are sensitive to metronidazole. Rhinogenic abscess is generally streptococcal. Staphylococcus is common in posttraumatic and postoperative cases. In infants and neonates, post meningitic abscess is caused by gram negative organisms. Sulpha drugs are most effective in Nocardia and vancomycin against Staphylococcus. Usually 'triple high dose' antibiotics intravenously for 2 weeks followed by four weeks of oral therapy is recommended.

In our experience, Penicillin and chloramphenicol have long been the main stay of empiric antimicrobial therapy. They have now been replaced by Cefotaxime/Ceftriaxone/Ceftazidime, Vancomycin and metronidazole.

Opportunistic organisms which generally 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 pyrimethanium are most effective. In those with T-lymphocytic defect, Candida neoformans is common; therefore, 5 flucytosine 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 leukaemia and lymphoma, Pseudomonas infection is common and aminoglycosides are most effective.

Metronidazole readily penetrates brain abscesses; intralesional concentrations have been found to be 40 μg/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 abscess.

Steroid administration should be generally avoided unless the patient demonstrates signs of meningitis or disproportionate cytotoxic edema posing a life threatening problem. Corticosteroids decrease enhancement of abscess wall on CT. Therefore reduction of ring enhancement should not be interpreted as resolution of abscess and indication of effectiveness of therapy. Change in volume of abscess is more reliable for evaluating effectiveness of therapy. Steroids when used are tapered as rapidly as possible. Corticosteroids decrease enhancement of abscess wall on CT. Therefore reduction of ring enhancement should not be interpreted as resolution of abscess and indication of effectiveness of therapy. Change in volume of abscess is more reliable for evaluating effectiveness of therapy. Steroids when used are tapered as rapidly as possible.

7.5. Anticonvulsant therapy

Legg advocated anticonvulsant therapy for 5 years to all patients with cerebral abscess.[60] Discontinuation of antiepileptic drugs can be considered when patient is seizure free for at least 2 years after surgery and EEG shows no epileptic activity.

8. Surgery

In our experience, pyogenic abscess required surgical intervention while most of the tuberculous abscesses were managed conservatively. The initial approach is to drain the abscess through a twist drill craniotomy. If the pus is thick or there is inadequate drainage of abscess suspected, the next procedure would be therapeutic burrhole drainage. Deep seated abscess like a thalamic abscess should be drained by a CT guided stereotactic procedure.

Adequate drainage of the pus produces an immediate clinical improvement and helps the patient to stabilize hemodynamically. It is our aim to drain the entire pus with a single attempt but to a large extent, the burhole drainage is seldom complete. This could be achieved with intraoperative radiography or using neuronavigation. However, the patient is kept under close neurological and radiological monitoring. The residual pus can evacuated if the patient does not exhibit significant improvement or serial radiography or CT imaging reveals moderate to large residue. About 90% of the supratentorial hemispheric abscesses resolve with burhole drainage. We have seldom felt the need to perform a craniotomy. The indications for

craniotomy are multiloculated abscess and thick pus. In case of otogenic abscesses, urgent otolaryngological consultation is mandatory and mastoidectomy should be performed at the earliest.

The treatment of brain abscess has been a challenge. Small brain abscesses have been treated empirically with antibiotics.[61] Patients presenting with rapidly progressive neurological deficits due to the mass effect of the neuroradiologically verified brain abscess are strict candidates for urgent decompression both for the neurosurgeons and internists. The choice of procedure is a matter of debate.[2,6,39] Craniotomy was advocated in the pre CT era but is now rarely practiced as the first line of treatment. Aspiration repeated as necessary or with drainage, has widely replaced attempts at complete excision. However, open surgical procedure is still preferred by the treatment of the brain abscess with the combination of medical treatment, if there is an evidence of increased intra-cranial pressure due to significantly mass effect of the brain abscess, if there are difficulties in diagnosis, if the abscess is traumatic and, if the lesion is located in the posterior fossa and if there is any presumption of fungal infection. Excision is recommended for the multiloculated abscesses, post-traumatic abscesses containing foreign bodies or contaminated retained bone fragments, and abscesses due to fistulous communication. Several reports have advocated excision as the procedure of choice because it is often followed by a lower incidence of recurrence and shorter hospitalization.[1,26,35] Even the decompression with the craniotomy or craniectomy will be helpful for the patients with poor neurological condition. As diagnosis based only on clinical and neuroradiological findings can be erroneous, nonsurgical therapeutic decisions should not be taken without positive pathological diagnosis. Xiao et al[8] reported that favorable outcome was not significantly different between the patients treated by excision or aspiration however, the mortality rate was significantly lower in the patients treated with excision than the patients treated with aspiration. This is probably due to the better general condition and/or more favorable location of abscess that could be excised surgically in such patients.

Stereotactic management of brain abscess, allowing both confirmation of the diagnosis and institution of therapy by aspiration of its contents and identification of the offending organism, has become widespread with the introduction of CT-guided stereotaxy.[2,26,62] A review of the recent literature shows several series of brain abscesses primarily treated with stereotactic techniques. Stereotactic aspiration should be considered the treatment of choice in all but the most superficial and the largest cerebral abscesses. Kondziolka et al.[63] related the failure of stereotactic treatment of brain abscesses in a series of 29 cases, because of either inadequate aspiration, lack of catheter drainage, chronic immunosuppression, or insufficient antibiotic therapy. Neuroendoscopic technique with free hand stereotaxy has also been practiced.[64] Both Hellwig and Kamikawa[65,66] reported their experiences with a flexible scope (free-hand or stereotactic-guided), while Fritsch[67] opted for a rigid one in a pediatric series. Longatti et al.[64] reported the usefulness of flexible endoscope in certain crucial surgical actions, such as aspirating and inspecting the abscess in all space directions or in firm and elastic membrane requires scissors or other instruments for its perforation.[64,65] The use of drainage catheters inside the abscess cavities is controversial.[65,67] Longatti et al.[64] reported that no significant difference could be obtained in the length of hospital stay, number of postoperative CT scans, and duration of the antibiotic therapy between traditional and endoscopic stereotactic aspiration. Intraoperative imprint-smear diagnosis of brain abscess is fraught with pitfalls viz. abscess related necrosis must be differentiated from tumor necrosis. In deep seated, multiloculated and periventricular abscesses, a reduction of 1 mm in the distance between the ventricle and brain abscesses will increase the rupture rate by 10%.[68] Surgical therapy can be preferred for the patients with neurological deterioration and/or radiological unresolved lesions.

The surgical technique of choice for intra-cranial abscess should be specific to each patient. A combination of the surgical aspiration or removal of all abscesses larger than 2.5 cm in diameter, a six weeks or longer course of intravenous antibiotics, and weekly CT or MRI imaging should result in a cure rate of more than 90%. It is important to follow the patient carefully by CT or MR imaging until the abscess has completely resolved. If any abscess enlarges after two weeks of antibiotics or fails to resolve after three to four weeks of antibiotics, further surgical aspiration or excision should be performed.

9. Intraventricular rupture of abscess

Intraventricular rupture of abscess can herald significant morbidity and potential mortality. Treatment has been controversial. A combination of intrathecal and intravenous antimicrobial treatment has been recommended.[11] Urgent craniotomy with rapid evacuation of the abscess,[69] emergent evacuation with lavage of the ventricles and ventriculostomy placement accompanied by the administration of intraventricular antibiotics[70,71] and a five-component therapeutic regimen, including open craniotomy with debridement of the abscess cavity, lavage of the ventricle system, intravenous administration of antibiotics for 6 weeks, intraventricular administration of gentamicin twice daily for 6 weeks and intraventricular drainage for 6 weeks has also been advocated.[72]

10. Outcome

In the pre CT era, the mortality was ranged 40–60% ad has been reduced to between 17% and 32%.[3–7,29,72,73] This discrepancy may be mainly due to the drastic changes in epidemiology taking place nowadays. Poor prognosis is reported in patients who are immunocompromised, having diabetes mellitus or cirrhosis and a low GCS score. Xaio et al[8] reported 2.8-fold risk of poor outcome in immunocompromised patients. A much poorer prognosis was reported from patients presenting with lower Glasgow coma scale.[2,4,8] Intraventricular rupture is a devastating and often fatal complication of brain abscess, associated with high mortality.[69] Lee et al.[68] have reported a series, 48% (30/62) of the patients having poor outcome (severe disabilities, vegetative states and death) due to intraventricular rupture of the brain abscess. Pretreatment neurological state of the patient is the most influential independent factor related with the outcome. Patients with deep-seated infection (basal ganglion or thalamus) have worse outcome caused by the higher incidence of intraventricular rupture in these patients. Intraventricular rupture of brain abscess is believed to be associated with an extremely high mortality rate. In our experience, majority of the tuberculous abscess responded to conservative treatment with antituberculous drug therapy while most of the pyogenic abscesses required surgical intervention.

10.1. Seizure and cognitive dysfunction

Seizure is the longterm risk from 30 to 50% of the patients suffering from brain abscess.[9,13] The latency period can be as long as 5 years, but is shorter in older patients.[9] Carey et al[74] and Morgan et al[28] reported that epilepsy is more frequent in the patients treated with excision than the patients treated with aspiration only. Some longterm effects following brain abscess resolution include seizures, loss of mental acuity, and focal neurological deficits that are likely attributed to the loss of neurons during infection. Following long-term evaluation, the incidence of subsequent seizures after brain abscess approached 70%. Therefore it is recommended that seizure prophylaxis or antiepileptic medication should be given in every case and continued for extended periods.

Antiepileptic prophylaxis must be initiated immediately and continued at least 1 year due to high risk in the brain abscesses. The treatment can be discontinued if no significant epileptogenic activity can be shown in electroencephalogram (EEG). The treatment management of the abscess plays one of the most important factors both in seizure and neurological outcome. Cansever et al.[75] reported that after surgical excision more focal neurological deficits (5.2–0%) and seizures (47.7–31.2%) were seen according to stereotactic aspiration. 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 an important sequel in these patients: The rate of epilepsy is 5.2–25%.[6,11,30]

Rates of recurrence are estimated to be 10–50%. The period of surveillance should be continued at least 1 year. The resolution of the surrounding edema and loss of the enhancing rim must be documented in this period which can take up to 6 months.[76] If the patients show no neurological deterioration the imaging can be obtained at 1-week intervals with and without contrast in the first 6 weeks. Lesions that do not show any regression should be aspirated.

11. Cerebellar abscess

Cerebellar abscesses comprise 6–35% of all brain abscesses. Despite widespread use of antibiotics, brain abscess following chronic suppurative otitis media (CSOM) remains a major problem for the pediatrician, neurologist, otologist and neurosurgeon. Brain abscesses constitute about 8% of all intra-cranial lesions.[9,24] Otogenic brain abscess may constitute about 70% of brain abscess.[28] Middle ear suppurative disease may extend to temporal lobe or cerebellum via various routes. Intracranial abscess follows a typical evolution in its formation[46] and its management differs at various stages of its formation.[40] They are more dangerous than sinogenic abscesses (frontal and parietal) and are more often resistant to antibiotics. Some authors reported that otogenic abscesses have worse outcome than others.

Antibiotics are very effective in early and late cerebritis stages. The ineffectiveness of antibiotics in the stage of capsule formation is due to the acidic medium within the abscess cavity and the inability to have adequate therapeutic concentration of the antibiotic within the abscess. Therefore, surgical intervention is essential once the capsule is well formed.[2,4,9,73] Nadvi et al[77] adopted aggressive policy of immediate CSF diversion in presence of overt or incipient hydrocephalus by means of an external ventricular drain. Persistent hydrocephalus is treated with a shunting procedure. Presence of periventricular lucency is an absolute indication for immediate ventricular drainage regardless of level of consciousness i.e. even if patient is fully conscious. Most of the patients have well formed abscess at the time of presentation. Surgical intervention can be either by repeated aspiration or excision. It is, therefore, very essential to diagnose an abscess at an early stage of its evolution, as it avoids surgical intervention. Steroids reduce brain edema but diminish the effectiveness of the host defense mechanisms that assist in containment of infection. Steroids inhibit collagen capsule formation and also inhibit migration of leucocytes. They are therefore, avoided in the stages of early and late cerebritis.

In 1980's it was suggested that cerebellar abscess should be managed by primary excision, but in recent years burr-hole aspiration has emerged as a satisfactory method.[78] Radical or cortical mastoidectomy with preservation of hearing is performed concurrently with abscess drainage under same anesthesia or as soon as possible afterwards. There can be various modes of surgical management. Stereotactic aspiration and endoscopic drainage are some of the newer modalities. Burr-hole aspiration is still used with 2.7% mortality. Drainage via a twist drill (2–3 mm) craniostomy is as effective as a burrhole in draining the pus. This can even be done under local anesthesia at the bedside. In our experience, burrhole and twist drill drainage are best avoided except in life threatening situation or as a salvage procedure. There is a potential significant morbidity associated with residual abscess and additional risk of bleed within the abscess cavity. Cerebellar abscess should be completely excised through a suboccipital craniectomy or a craniotomy. Excision of abscess significantly helps to reduce the cerebellar edema and relieves brainstem compression. During the course of recovery from the cerebellar abscess, simultaneous otolaryngological consultation should be sought for mastoidectomy on an urgent basis to prevent reformation of abscess. If treated within reasonable time period, the prognosis following evacuation of cerebellar abscess is excellent. The longterm outcome of patients with cerebellar abscess is directly proportional to their preoperative consciousness level. Cerebellar abscess is often ominously silent and can have significant mortality. Associated supra or infra tentorial abscess or empyema may be present. The cerebellar abscess needs to be regarded differently from supratentorial abscess because of their ability to cause sudden total occlusion of CSF pathways early in the course of disease. A high index of suspicion and an aggressive surgical approach becomes mandatory in these cases. Brain abscess following CSOM can be effectively managed if the evolution pattern is known, as the treatment is now mainly based on the stage of abscess formation.

11.1. ***Delayed "Glue" abscess*** *complicating an embolized cerebral arteriovenous malformation*

Complications of arteriovenous malformation (AVM) embolization are well known but development of a delayed multiloculated abscess after embolization of AVM nidus is extremely rare.[79–82] The duration of the procedure and repeated handling of the catheters along with use of large amount foreign material or Hysto-acryl "glue" can precipitate infection. Cure of the lesion can only be obtained by surgical excision of the infected and partially embolized AVM. Antibiotic prophylaxis with all endovascular procedures is recommended.[78–80]

12. Cyanotic heart disease and brain abscess

Brain abscess can develop in 5–18% population with cyanotic heart disease (CHD). Individuals with CHD are 10 times more prone to develop brain abscess than those with no CHD. Fallot's tetralogy is the most common cause.[73,83] Intracardiac right to left shunt by-pass allows direct entry of blood containing bacteria to the cerebral circulation without pulmonary filtration. Hypoxaemia, metabolic acidosis and increased blood viscosity from compensatory polycythemia results in low perfusion areas (microinfarcts) in the brain. Microinfarcts provide a milieu where seeded microorganism can sustain growth and multiply to form abscess. Anaerobic streptococci are most common agents. Sterile cultures are reported in 16–68% of brain abscesses with CHD.[84] These patients possess cardiopulmonary risk, wide variety of coagulation defects and variable degree of immunodeficient states increasing the risk of anesthesia and surgery. Thus, a less invasive surgical procedure such as aspiration should be chosen. A deeply located parieto-occipital abscess larger than 2 cm diameter which causes mass effect, should be aspirated immediately even in late cerebritits stage using stereotactic or CT guided methods to decrease intra-cranial pressure and avoid intraventricular rupture of brain abscess.[85] Intravenous Beta-lactam antibiotics are started immediately.

13. Multiple abscesses

Multiple abscesses account for 5–50% of all brain abscesses. They are frequently diagnosed due to the easy availability of CT and MR imaging. They are a result of hematogenous spread from systemic infections and the organisms may be found in peripheral source. Streptococcus and Staphylococcus are common organisms. Multiple abscesses are found more often in immunocompromised patients as compared to solitary abscess. The frequency of intraventricular rupture is also more in these cases. Risk factors include AIDS, organ transplant recipients, IV drug abuse, chemotherapy for lymphoma, cardiac anomaly or prosthetic cardiac valves, diabetes, and regional enteritis. However, in India, ear infection remains an important cause of multiple abscesses. Broad spectrum antibiotics should be instituted along with follow-up CT scans to assess response to treatment. However, in cases where the antibiotic sensitivity of organisms is unknown, aspiration of most superficial or larger lesions producing neurological deficit and treating the remaining lesions with antibiotics and biweekly CT scan is advocated. If abscess recollects or fails to decrease or previously small abscess enlarges, serial or staged stereotactic aspiration can be performed.[85] All abscesses, >3 cm diameter and those causing mass effect particularly deeply located in brain stem or close to ventricular wall should be aspirated with stereotactic technique. If all the abscesses are of <2.5 cm size, still most accessible abscess should be aspirated. This permits aspiration of several lesions in a single sitting with minimal morbidity even in patients who are at poor risk for surgery or anesthesia. In multiple abscesses antibiotics are continued for 3 months.

14. Analysis of our series of 289 cases of pyogenic abscess

14.1. Clinical material and methods

A retrospective analysis of 289 cases of pyogenic abscess treated at the Seth G.S. Medical College and King Edward VII Memorial hospital over past 7 years (1999–2006) is presented. The clinical and radiological records were searched and information was retrieved with respect to age, sex, duration of symptoms, clinical presentation, laboratory tests, radiological imaging, abscess site, surgical therapy, microbiological information, clinical and radiological outcome. The clinical profile was assessed using the modified Rankin scale. CT scan was performed in all patients as initial and follow-up exam. The diameter of the abscess, abscess wall, perifocal edema was assessed on CT scan. MR exam was not performed in any patient. Abscesses measuring less than 2 cm in mean diameter were treated by medical regimen. Surgery was performed for abscess greater than 2 cm, poor response to medical treatment, sequential increase in the abscess size and deterioration in neurological function. Empirical intravenous broad spectrum antibiotics were immediately instituted upon diagnosis and were further modified according to microbiological isolation and antibiotic sensitivity. Antibiotic therapy was continued for a total period of 6 weeks. Steroids were administered under antibiotic cover if the patient showed clinical signs of meningeal involvement or impending cerebral herniation. They were gradually tapered over a period of 4 weeks. Most of the patients underwent aspiration of the abscess through single burrhole. Craniotomy was performed for cerebellar, postoperative and posttraumatic abscesses. Stereotactic guided aspiration was performed for deep seated abscesses. Follow-up CT imaging was performed within 24 h of aspiration and then weekly as a part of therapeutic monitoring. Further CT imaging was advised at interval of 1, 3, 6 and 12 months interval. The surgical outcomes were assessed in all patients according to the modified Rankin score. Statistical analysis was performed using the SPSS 13 program for Windows and the statistical significance was established at a probability value 0.05.

15. Results

The average follow-up duration was 15 months (range 9–21 months). There were 204 male (71%) and 86 female (29%) patients, ranging in age from 18 months to 62 years (median 32 years) at the time of diagnosis. At the time of admission, 252 patients complained of headaches and 46 had nausea and vomiting. One hundred and forty-six patients had fever or signs of meningeal irritation, and neurological deficits were present in 142. Two hundred and thirty-three patients were alert, and fifty seven were somnolent or confused at admission. Sixty two patients presented with seizures. The mean duration of symptoms was 6 days (range 3–10 days). In our series, the initial neurological condition showed a strong correlation with the overall outcome ($p < 0.001$).

One hundred and twenty patients had chronic otitis media, fifteen patients had paranasal sinusitis and two patients had adjacent localized cranial infection as a predisposing factor. Seventeen patients had pulmonary or heart disease. Twelve patients had posttraumatic or postoperative abscesses. Four patients had no identifiable predisposing cause. There was no identifiable cause in 137 patients.

The temperoparietal region was the most common location in 130 patients (Table 1). The diameter of abscesses on CT imaging ranged from 1.8 cm to 7.2 cm (mean 4.5 cm) at diagnosis. Seventeen patients had multiple brain abscesses. Cerebellar abscess was seen in 74 patients (25%).

Majority of the patients underwent aspiration as a primary modality of treatment. Craniotomy or craniectomy was performed in cerebellar, postoperative and posttraumatic abscesses as a primary form of treatment. Deep seated (thalamic, brain stem) and hemispheric eloquent area abscesses underwent frame based stereotactic or neuronavigation guided aspiration. 196 patients underwent aspiration via single burrhole. Repeated aspirations were required in forty-four patients. Inspite of repeated aspirations and/or failure to respond to antibiotic therapy, nineteen patients required craniotomy for excision of the abscess. The interval of repeated aspirations ranged from 4 to 18 days. In our series, a significant number of patients treated with burr-hole aspiration had a favorable outcome ($p < 0.05$).

Intravenous steroids were used only in 15 patients, who presented with severely meningitic at presentation and had significant perifocal edema on imaging. They were tapered over 2 weeks. The edema markedly reduced following resolution of the abscess cavity. Nine patients presented with ventriculitis and hydrocephalus which responded to repeated aspirations of CSF and broad spectrum antibiotics. No patient needed ventriculoperitoneal shunt procedure.

Microorganisms were isolated in only seventy six patients. Streptococcus was identified in nineteen patients, Staphylococcus spp. in eighteen patients, Pseudomonas aeurginosa in sixteen and Klebsiella in seventeen patients. Microbial culture was obtained in forty-six patients. Broad spectrum intravenous antibiotics were administered on admission, and specific antibiotic therapy as per the sensitivity report was instituted once it was available. Antibiotic therapy was administered for 6 weeks. In six patients, therapy was continued for 6 more weeks since imaging revealed residual small abscess measuring <1.3 cm in diameter. In patients in whom no organisms were cultured, broad spectrum antibiotic therapy was continued and response was favorable. In our series, there was no statistical significiance between causative organisms and clinical outcome ($p > 0.05$).

The overall clinical outcome at the end of one year was assessed using the modified Rankin scale (mRS). A good outcome was noted in 82.4% patients (mRS score 0–2) and poor outcome (mRS score >2)

was seen in 18.6% patients. The neurological condition at admission and the early institution of treatment strongly correlated with clinical outcome ($p \leq 0.001$). A moderate residual disability was seen in nine patients and 2 patients had severe neurological deficit. Eight patients out of 289 patients died out of which three patients presented in a comatose state with transtentorial herniation. Two patients died of exacerbation of diffuse meningitis and encephalitis. Amongst eight patients who died, three had diabetes mellitus and immunosuppression. In the follow-up period ranging from 9 to 21 months, no recurrence of abscess cavity was noted, none of the patients who survived showed clinical or neuroimaging signs of recurrence.

In conclusion, pyogenic brain abscess should be treated on an emergent basis. Abscess diameter more than 2 cm need surgical intervention and most of them show an excellent clinical and radiological response to single burr-hole aspiration. Craniotomy is required in selected cases and is a primary procedure in cerebellar, postoperative and posttraumatic abscesses. Intravenous broad spectrum antibiotic therapy should be administered for a period of minimum 6 weeks to prevent relapse. The long term outcome is gratifying if prompt treatment is instituted in appropriate time period.

Conflict of interest statement

None declared.

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