Brain abscess in children with Cyanotic Congenital Heart Disease- clinical presentation and outcome

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ABSTRACT

BACKGROUND: Brain abscess is a serious life threatening infection of brain parenchyma. Cyanotic congenital hearth disease is important predisposing factor for brain abscess.

OBJECTIVE: This study was conducted to evaluate the clinical profile and outcome of children with brain abscess and underlying Cyanotic congenital hearth disease.

MATERIALS & METHODS: The study was carried out at The Department of Paediatric Cardiology, Hayatabad Medical Complex, Peshawar. This study was conducted from June 2015 to May 2016. All children presenting with brain abscess and having an underlying Cyanotic congenital hearth disease were prospectively entered into this study. Data was collected on a written Performa and later on shifted to and analysed by SSPS 18 program.

RESULTS: Thirty children with underlying Cyanotic congenital hearth disease were confirmed to have a brain abscess during this period. There were 22 (73%) males and 8 (27%) females. Majority (22 pts-73%) were in the age group 6 to 10 years. Mean duration of illness related to the brain abscess at the time of presentation was 15.2±18.6 days. All patients had a variable degree of fever while headache (25 pts-83%), vomiting (19 pts-63%) and seizures (19 pts-63%) were other common presenting features. Tetralogy of Fallot was the commonest underlying Cyanotic congenital hearth disease present in 23 patients (76.6%). The abscesses were large and required surgical drainage in 21 (70%) children while 9 (30%) patients had small abscesses requiring medical management only. A positive pus aspirate culture was present in 11/21 (52%) with commonest organism being Staphylococcus aureus (3/11). Surgical intervention consisted of single or repeated needle aspiration through burr hole and excision of abscess was done in two patients. There were 5 deaths (16.7%) and all died of severe cerebral oedema and tentorial herniation. Unconsciousness, focal neurological signs, papilledema and Glasgow Coma Scale less than 8 at the time of presentation were associated with poor outcome (p < 0.05). Seven children (23%) had long-term sequelae like hemiparesis & seizures.

CONCLUSION: Majority of children presented with fever and headache. Other presenting features included vomiting and seizures. Brain abscess in children with underlying cyanotic congenital heart disease carries a high mortality and morbidity despite surgical treatment. Presence of fever and headache in any such patient shall alert the physician about this possibility.

Key Words: Brain abscess, congenital heart disease, Tetralogy of Fallot

INTRODUCTION

Brain abscess is a serious life threatening infection of brain parenchyma.¹ It is an important cause of morbidity and mortality arising from central nervous system (CNS) infections all over the world. It results from spread of infection from contiguous non-neuronal tissue, haematogenous seeding or a direct introduction into brain from cranial trauma and surgery.²³

Cyanotic congenital heart disease (CCHD) is an important predisposing factor for brain abscess and haematogenous spread to brain parenchyma through a right to left shunt or common mixing leads to often multiple and deep seated abscesses.⁴ Early repair of CCHD has led to a marked decrease in its incidence in the West⁵. In developing countries, however, the children with CCHD still present late, surgical facilities are inadequate and not uncommonly brain abscess may be the first presentation. In this report we describe the clinical presentation, microbiology, management protocol, outcome and prognosis of brain abscess in children with underlying CCHD presenting in our set up.

The aim of this study is to educate and alert the primary physicians, paediatricians and paediatric cardiologists about this important complication. This will help in referral of suspected cases at early stage of the disease, which in turn will lead to early diagnosis and management. Moreover, this will reduce the morbidity and mortality related with this devastating illness.

MATERIAL AND METHODS

This is a prospective study conducted in a single tertiary care referral centre. The study period was from June 2015 to May 2016. All children having an underlying CCHD who were admitted with brain abscess were enrolled.
Intravenous benzyl penicillin, ceftriaxone and metronidazole were used as empiric therapy in all these patients. Antibiotics were changed according to culture and sensitivity report of pus as well as the clinical response. Osmotic diuretic therapy in the form of 20% mannitol was used if clinical signs and symptoms of raised intracranial pressure (ICP) present along with radiological evidence in the form of brain oedema and midline shift on CT scan brain. Mannitol was given in a dose of 0.5 grams per kilogram as a bolus followed by 0.25 to 0.5 g/kg 6 hourly. Corticosteroid in the form of dexamethasone was used intravenously, only when severe raised ICP was present and child was critically ill. Dose of dexamethasone used was 0.5 milligram per kilogram (mg/kg) body weight 8 hourly for 3 days followed by tapering over next 2 days.

Surgical management consisted of aspiration and or excision of abscess depending upon site, size, nature, multiplicity and its effects on surrounding tissues. Pus aspirated was sent for microscopy and culture. Antibiotics were continued for 4 to 8 weeks depending upon the clinical and radiological response. Longer therapy (up to 16 weeks) was required depending on clinical response and repeat CT brain reports.

Immediate outcome comprised of death, partial recovery with sequelae or complete recovery of patients. Those surviving were followed up by a multidisciplinary team at 1 week, 4 weeks, 3 months, 6 months and 12 months after leaving the hospital. Earlier review was arranged where necessary.

Data was collected on a written performa and later shifted to SPSS 18 program. Variables of the study included demographic details, duration of stay in the hospital, clinical signs and symptoms which included headache, vomiting, seizures, focal neurological signs, unconsciousness, Glasgow coma scale and papilledema. Other variables included Echocardiographic findings of underlying cardiac lesion and the presence or absence of vegetations and CT scan findings consisting of number and location of abscess/abscesses. Vegetations are described as oscillating intracardiac mass on valve or supporting structures, in the path of regurgitant jets, or on implanted material in the absence of an alternative anatomic explanation.

An abscess has a stereotyped appearance on contrast-enhanced CT: A ring or doughnut representing the spherical wall or capsule of the abscess, the contrast enhancement being the result of breakdown of the blood-brain barrier and, in addition, hypervascularity of the granulation tissue. The nonenhancing abscess centre is pus or nonviable debris, and there is commonly extensive oedema of vasogenic type in the surrounding white matter.

The patients were divided into two groups. One of the groups comprised of the patients who had full recovery while the other consisted of the patients who sustained morbidity/mortality. Variables were analyzed for both the groups using Pearson Chi-Square test.

Data was analyzed using SPSS 18 program. A p value less than 0.05 was considered statistically significant.

**RESULTS**

Thirty children with underlying CCHD were admitted with brain abscess over the study period. Among them 22 (73.3%) were males and 8 (26.7%) females. The mean age at presentation was 7.1 ± 6.2 years (range 15 months to 17 years). Majority of children (93%) were over 5 years of age, 73% in 6-10 years age group and 20% in 11-17 years.

The mean duration of illness at the time of presentation was 15.2 days (range 03-90 days). Most common presenting feature was fever; often low grade, present in all children (100%) followed by headache in 25 (83.3%). Other symptoms at presentation included vomiting, lethargy, seizures, focal neurological deficit and coma.

Tetralogy of Fallot was the commonest underlying CCHD present in 23 children (76.6%). Other CCHD included double outlet right ventricle with pulmonary stenosis (3 pts), transposition of great arteries with ventricular septal defect and pulmonary stenosis (2 pts) and univentricular heart with pulmonary atresia (2 pts). Previous palliative procedure in the form of Blalock Taussig shunt was done in 5 (20%) children. Concomitant evidence of infective endocarditis on echocardiography was present in 12 (40%) children. Only two of these patients had a positive blood culture, both being staphylococcus aureus.
Polycythemia was present in 17 (56.7%) patients with mean hemoglobin and hematocrit levels being 17.8 ± 4.2 gm/dl and 56 ± 7% respectively. Leucocytosis was present in 19 children (63.3%) where mean white blood cell count was 18.6 ± 8 thousands /dl. ESR was raised in 22 (73.3%) children where mean ESR was 32 ± 20 mm in 1st hour. CRP was raised in 19 (63.3%) where mean CRP was 24 mg/l.

The diagnosis of brain abscess was confirmed on CT scan brain in all children. Repeat scan was done once in 4 (13.3%), twice in 17 (56.7%), thrice in 7 (23.3%) and four times in 2 (6.7%) children. A solitary brain abscess was detected in 15 (50%) while multiple abscesses were found in rest of 15 (50%) children. In majority of cases i.e., 28 (93.3%) abscesses were unilateral (Fig 1), while bilateral abscesses were found in only 2 (6.7%) cases. Single lobe involvement was seen in 15 children (50%) while in other 15 (50%) multiple lobes were involved. The commonest lobe involved was parietal which was affected in 26 (86.6%) children (Table II).

Twenty-one children (70%) were having large abscesses (> 2 cm diameter) and they required combined medical and surgical management. Only 9 (30%) were having small abscesses (< 2 cm diameter) and were treated medically. Empirical antibiotics in the form of benzyl penicillin, ceftriaxone and metronidazole were initially used in all children. Adequate response to first line antibiotics was seen in 17 children (56.7%) and benzyl penicillin was replaced by vancomycin in the remaining 13 (43.3%) patients. Mannitol was used in 21 (70%) children and steroids were used in 18 children (60%). Surgical management in the form of needle aspiration through a burr hole was done in 21 cases (70%). Out of those who required needle aspiration, it was done once in 16 (72.6%), twice in 3 (14.2%) and thrice in 2 (9.6%) cases. Excision of abscess cavity was required in only 2 (9.6%) cases. Culture of pus from abscess was positive in 11 out of 21 cases (%). Staphylococcus aureus was the commonest organism found (3/11 27%), followed by Streptococcus pyogenes (2/11 19%), alpha hemolytic streptococcus (2/11 19%), Pseudomonas (2/11 19%), Escherichia coli (1/11 9%) and Bacteroides fragilis (1/11 9%). Majority of children, (70%) reached the study centre at the end of 2nd week and all of them had used a number of antibiotics (oral and intravenous) before hospitalization.

The hospital stay was 5-8 weeks in 23 (76.7%) patients while 2 patients (6.7%) stayed for 12 weeks or more.

Life threatening complications encountered included cerebral edema with deteriorating GCS seen in 11 children (36.6%), tentorial herniation in 5 (16.7%) and bleeding into abscess cavity in 2 (6.6%). No case of syndrome of inappropriate secretion (SIADH) was encountered. None of children had intraventricular rupture of abscess (IVROBA). Immediate outcome in the form of full recovery was seen in 18 children (60%) and partial recovery in 7 (23.3%).

Five children (16.7%) died and all died of severe cerebral edema and tentorial herniation. The hospital stay was < 4 weeks in all these patients. Neurological sequelae in the form of hemiparesis while bilateral abscesses were found in only 3 children, persistent seizures in 3 while one child was having cortical blindness and was aphasic.

Unconsciousness, focal neurological signs, papilledema and GCS less than 8 at the time of presentation were associated with poor outcome (p = < 0.05). The children with multiple and/or bilateral abscesses had high morbidity and mortality (p = < 0.05). The gender, age, headache, vomiting, seizures and antibiotics use prior to hospitalization were statistically insignificant factors regarding prognosis (Table II).

Children surviving this serious illness were followed up in outdoor department after 1 week, 4 weeks, 3 months, 6 months and thereafter as needed. Those having hemiparesis recovered very well. Seizures persisted in 3 children at one; three and six months follow up. They had abnormal electroencephalograms (EEGs) and were continued on anticonvulsant therapy.

**DISCUSSION**

Brain abscess is a serious life threatening infection in children. Un-operated CCHD is an important predisposing risk factor for brain abscess, accounting for 25-46% of cases. The underlying pathophysiology in CCHD includes persistent hypoxia which leads to polycythemia and hyperviscosity. This state of hyper viscosity causes sluggish blood flow in cerebral microcirculation which leads to micro thrombi and focal infarcts. These infarcted areas in brain are seeded by microorganisms, which bypass...
pulmonary phagocytosis due to right to left shunting in heart. This leads to focal cerebritis, which is the first stage in development of brain abscess. Though Staphylococcus aureus is commonly encountered in traumatic brain abscesses, our study showed it to be the predominant organism with underlying CCHD as the predisposing factor. This may be related to the fact that there is a high incidence of associated infective endocarditis (30%) in our study population and same organism was grown in the blood culture in 2 of these patients. The association of brain abscess with infective endocarditis is well recognized and multiple abscesses are associated with infective endocarditis.

Patients who have symptoms for less than a week have a more favourable response to medical therapy than those with symptoms more than one week. Unfortunately in our setup majority of children are diagnosed late. Medical therapy is usually initiated before results of bacteriology are available. Knowledge of the aetiological agents can allow for appropriate selection of antimicrobials. Because of the difficulty involved in penetration of various antimicrobial agents through blood brain barrier, the choice of antibiotics is restricted. Penicillin penetrates well into abscess cavity and is active against non-beta lactamase producing anaerobic and aerobic organisms. Metronidazole penetrates blood brain barrier and covers penicillin resistant anaerobic organisms. Administration of a beta lactamase resistant penicillin or vancomycin for treatment of Staphylococcus aureus is generally recommended. In this series 57% patients responded to first line therapy i.e., benzyl penicillin, ceftriaxone and metronidazole. Benzyl penicillin was replaced by vancomycin in 43% patients. Duration of antibiotic therapy ranged from 4 to 12 weeks. Majority of children required 8 weeks of antimicrobial therapy. Measures to control the increase in intracranial pressure (ICP) are essential to decrease morbidity and mortality. Hyperosmolar therapy is used for treatment of intracranial hypertension and mannitol is the most commonly used agent as was used in our study. The use of corticosteroids for treatment of brain abscess is however, controversial. They can reduce antibiotic penetration into abscess cavity, retard encapsulation and increase necrosis. However, use of steroids can be life saving and should be given to those with increased ICP and/or neurologic deterioration. Therapy should be for short duration when steroids are used to reduce cerebral edema.
Surgical intervention is required for abscesses which are larger than 2 cm in diameter or situated in critical areas of the brain or causing significant mass effect. It can take the form of needle aspiration through a burr hole, CT-guided stereotactic aspiration or excision of abscess. Some advocate stereotactic aspiration as the method of choice, while others favour complete excision of abscess cavity. In our series 70% of children required surgical intervention. Needle aspiration through burr hole was done in 60%, while excision of abscess cavity was performed in the rest 10% children.

Seizures were the commonest long term sequelae observed in this study. Similar high incidence of seizure disorder sequelae has been reported. This might be related to severe local inflammation or infection resulting in a more severe local cerebral reaction. Immediate outcomes depend on early diagnosis and appropriate therapy. Presence of low GCS score, multiple abscesses, critical site of abscess and severe cerebral edema are associated with poor outcome. In our study unconsciousness, presence of focal neurological signs, papilledema and low GCS score at the time of presentation were associated with poor outcome (p<0.05). Children with multiple and/or bilateral abscesses had bad prognosis (p<0.05). Immediate outcome depends on early diagnosis and appropriate therapy. Over all mortality observed in this study was 16.7%. Over all mortality observed in this study was 16.7%. This is comparable to other studies.

CONCLUSION
Brain abscess is a serious life threatening infection in children with underlying cyanotic congenital heart disease. A high index of suspicion is required for early diagnosis. Presence of fever, headache, vomiting and seizures in any such patient shall alert the physician about this possibility. Majority is large, unilateral in parietal lobe and despite surgical intervention there is a high mortality and morbidity. Early correction of the underlying CCHD can prevent this devastating complication.

REFERENCES