ORIGINAL ARTICLE

CLINICAL PROFILE, MICROBIOLOGY, MANAGEMENT, AND OUTCOME OF PEDIATRIC BRAIN ABSCESS AT THE UNIVERSITY OF THE PHILIPPINES - PHILIPPINE GENERAL HOSPITAL: A 5-YEAR RETROSPECTIVE STUDY (2012-2016)

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The authors declare that the data presented are original material and has not been previously published, accepted or considered for publication elsewhere; that the manuscript has been approved by all authors, and all authors have met the requirements for authorship.

ABSTRACT

Objective: To determine the clinical profile, microbiology, management, and outcome of pediatric brain abscess at a tertiary hospital in the Philippines from 2012 to 2016.

Methods: A retrospective study and review of medical records of 50 patients aged 18 years old and below diagnosed with brain abscess from 2012 to 2016 was performed.

Results: Majority of patients affected were 10 years old and below (74%), with no gender predilection, and mostly underweight/wasted (68%). Coverage for common vaccine-preventable pathogens was low (38% for *H. influenzae* type b, 2% for *S. pneumoniae*). Most common signs and symptoms on admission were fever (62%), vomiting (50%), and headache (50%). The top pre-disposing condition was congenital heart disease (46%), mostly Tetralogy of Fallot (33%). Methicillin-resistant *Staphylococcus aureus* (MRSA) was isolated in 38%) of cases. Sterile cultures comprised 68% of cases. There were two cases of tuberculous abscess. Empiric antibiotics administered for patients seen in 2012 were penicillin G and chloramphenicol, with a shift to a third-generation cephalosporin and metronidazole in the succeeding years. Aspiration with or without drainage was performed in majority of cases (85%). Six underwent complete excision and had a shorter mean length of stay of 57 days, and a lower morbidity rate of 17% with no mortalities. The overall mean length of hospital stay was 65 days. Residual neurologic deficit was observed in 28%, mostly extremity weakness. Mortality rate was 6.8%. No statistical association was found between a predisposing condition and affectation of a particular area of the brain using the Fisher exact test.

Conclusion: There should be a high index of suspicion for brain abscess among patients with pre-disposing conditions (i.e. paracranial infection, cyanotic congenital heart disease) presenting with fever, headache, and vomiting. Common etiologic agents in this study were MRSA and Enterococcus. The isolates were sensitive to the antibiotics recommended for empiric therapy, particularly parenteral third generation cephalosporin + metronidazole for 6 to 8 weeks. Patients with sterile cultures were also continued on this regimen. With the high resistance rates to oxacillin, vancomycin should be considered for abscesses arising from paracranial infections and for those with breaks in the skull post-trauma. There was an overall reduction in mortality due to improved imaging studies and identification of pathogens for definitive treatment, as well as improved surgical techniques over time. A considerable number of affected children however had neurologic deficits upon discharge.

KEYWORDS: *Pediatric brain abscess*

INTRODUCTION

Brain abscess is a focal, intracerebral infection that begins as a localized area of cerebritis and eventually ends in a collection of pus surrounded by a well-vascularized capsule[1]. Seeding to the brain occurs by hematologic transit of microbes from contiguous site infections (e.g. chronic otitis), disruption of the pulmonary vascular bed which filters out bacteria (e.g. cyanotic congenital heart disease), direct inoculation after penetrating head injury or neurosurgical procedure, or from a cryptogenic source[1,2]. A high index of suspicion commonly arises from a good review of possible predisposing conditions such as paracranial infections, history of head trauma, or presence of congenital heart disease. Management of brain abscesses pose a challenge in clinical practice, owing to its complex bacteriology, as well as changing patterns of antibiotic resistance. In our setting, the problem is further confounded by the presence of sterile cultures brought about by late microbiologic testing and delay in surgery, which usually occurs several weeks into treatment. Antibiotic therapy with source control thru immediate surgery (aspiration, drainage, or excision), and management of associated complications are the mainstays of treatment.

Indirect seeding to particular areas within the brain has been postulated to be largely dependent on the underlying predisposing condition. For brain abscess that is not associated with direct inoculation thru instrumentation or trauma, this study explored a possible association between the location of the lesion and the predisposing condition.

Although brain abscess is a relatively uncommon condition owing to the protection provided by the impermeable blood-brain barrier, a significant percentage of children who recover have residual deficits including epilepsy, permanent sensory and motor deficits, visual defects, and personality changes[2]. Local mortality rates of children with brain abscess range from 4.8% to 12.8% based on studies done from 1990-1999[4,5].

This life-threatening condition calls for timely diagnosis and treatment. This study aims to aid the clinician increase his index of suspicion thru a better knowledge of common diagnostic and clinical features of brain abscesses. The nutritional and vaccination status of affected children, antimicrobial susceptibility patterns of isolates, response to local empiric antibiotics, and outcomes of children with brain abscess will be the focus of this paper.

MATERIALS AND METHODS

A retrospective study was performed by review of medical records of charity patients aged 18 years old and below, diagnosed with brain abscess from January 2012 to December 2016 at a tertiary hospital in the Philippines. In this institution, all pediatric patients diagnosed with brain abscess are referred to the Section of Pediatric Neurology, thus a list of patients diagnosed consecutively within this time period was generated from the monthly in-patient database of the Section of Pediatric Neurology. To verify completeness, supplemental data was gathered from the records of the Section of Infectious and Tropical Diseases in Pediatrics, which also co-manages patients with this diagnosis.

After excluding patients with extra parenchymal pus collection (intraventricular, subdural, or epidural empyema), a total of 80 patients diagnosed with intraparenchymal brain abscess remained. Several attempts were made to completely gather patient records for data analysis, but despite such efforts, only 50 charts were retrieved from the 80 identified cases.

To ensure the privacy of patients, names, addresses, hospital case numbers or other identifying data were excluded from the data collection sheets, and informed consent to access patient charts was requested to be waived in accordance with the Data Privacy Act of 2012 and the 2017 National Ethical Guidelines for Health-Related Research (NEGHHR).

Each patient was evaluated in terms of demographic data (age, gender, nutritional status using WHO Child growth standards, and vaccination coverage for *Haemophilus influenzae* type b and *Streptococcus pneumonia*), clinical data (presenting signs and symptoms and co-morbidities), radiographic data (Cranial CT scan results), cultures and resistance pattern of isolates, antibiotic treatment regimen, surgical approach, and patient outcome (including residual neurological deficits on discharge). A definite diagnosis of brain abscess was made with the finding of a ring-enhancing lesion within the brain parenchyma via neuroimaging, or an intra-operative finding of intraparenchymal collection of pus[6]. Microbiologic cultures and imaging results were verified thru the records of the Department of Laboratories and Department of Radiology, respectively.

RESULTS

DEMOGRAPHIC DATA

There were 50 patients included in the study, 29 (58%) males and 21 (42%) females, with a male to female ratio of 1.4:1. The mean age of patients in this study was 7 years old, with a range

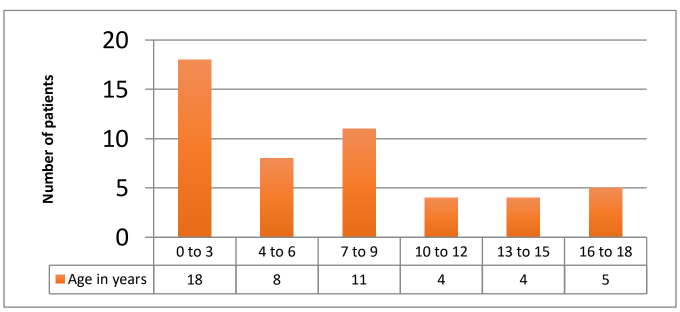

Figure 1. Age distribution of children with brain abscess (n=50)

of 2 months to 18 years old (Figure 1). Majority of patients were 10 years old and below (72%), and 36% (n=18) were < 3 years old.

NUTRITIONAL STATUS

Based on assessment of weight for length or height, majority of affected children were poorly nourished using the WHO growth curves as standard. Figure 2 shows that for the 41 patients with complete data, 36% were underweight, while 32% were severely underweight. Due to lack of data on length, the status of nine patients could not be assessed. However, these nine were all poorly nourished with a weight-for-age less than the 5th percentile using the CDC growth curve standards.

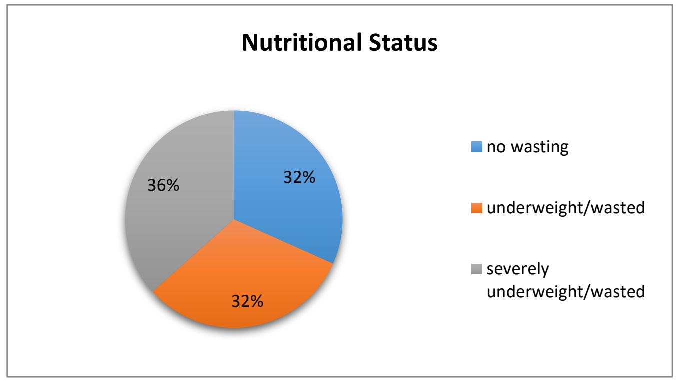

Figure 2. Nutritional status of children with brain abscess (n=41). As per WHO standards, underweight/wasted for z score below -2, severely underweight/wasted for z score below -3.

VACCINATION STATUS

Vaccination status was known in 66% of cases (n=33). Of these, only 19 patients received age-appropriate doses of *H. influenzae* type b (Hib) vaccine, and only one received age-appropriate doses of *S. pneumoniae* vaccine.

CLINICAL FEATURES

Presenting Signs and Symptoms

The classic triad of headache, fever, and focal neurologic deficit was seen in 28% of patients (n=14). The most common presenting symptom was fever in 62% followed by vomiting and headache, both seen in 50% of subjects. The most prominent neurologic symptom was vomiting, followed by altered state of consciousness, mostly drowsiness. Two (4%) came in stuporous. Seizure was mostly generalized (n=10, 20%), and only three patients came in with focal seizures (6%). The rest of the constitutional and neurologic signs and symptoms are listed in Table 1.

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Table 1. Presenting signs and symptoms of children with brain abscess, (n=50).

Signs and Symptoms	Number of patients	Percentage (%)
I. Constitutional		
Fever	31	62
Headache	25	50
Poor appetite	6	12
Irritability	4	8
II. Neurologic		
IIa. Altered consciousness	24	48
IIb. Seizure	13	26
IIc. Meningeal signs	11	22
IId. Increasing head diameter	5	10
IIe. Increased intracranial pressure		
Vomiting	25	50
Papilledema	2	4
IIf. Focal Neurologic deficits		
Extremity weakness	12	24
Clonus	6	12
Facial asymmetry	4	8
Babinski	3	6
Limited Extraocular movement	3	6
Visual field defect	3	6
Spasticity	2	4
Loss of balance	2	4
Wide-based gait	2	4
Posturing	2	4
No verbal output	2	4
Dysmetria	1	2

PREDISPOSING CONDITION

The leading predisposing condition for brain abscess was uncorrected cyanotic congenital heart disease (46%), mostly Tetralogy of Fallot (22%). Other pathologies seen were Pentalogy of Fallot, double outlet right ventricle, tricuspid valve atresia, pulmonary valve atresia, and tricuspid valve atresia with pulmonary valve atresia and non-restrictive ventricular septal defect. There was one case of acyanotic heart disease - ventricular septal defect with chronic suppurative otitis media (CSOM).

Paracranial infections comprised 40% of cases leading to indirect seeding to the brain. Majority of these consisted of ear infections, followed by various types of oral and perioral infections. There was one case of nasal carbuncle, while another patient presented with scalp abscess.

Another distant site of seeding to the brain was the respiratory tract (n=3), with two cases of bacterial pneumonia and one case of sputum-positive pulmonary tuberculosis.

There were 5 cases which arose from direct inoculation. Three patients presented with traumatic brain injury, one patient presented with a retained foreign body, while another patient had a concomitant shunt infection. The primary source of infection was unknown in 5 cases.

Table 2. Predisposing condition in children with brain abscess.

Pre-disposing condition	Number of patients	Percentage (%)
I. Uncorrected Congenital Heart Disease	22	44
Tetralogy of Fallot	11	22
Pentalogy of Fallot	6	12
Double outlet right ventricle with ASD, VSD	2	4
Tricuspid valve atresia with non-restrictive ASD secundum, MAPCAS	1	2
Pulmonary valve atresia with myocardial sinusoids	1	2
Isolated ventricular septal defect	1	2
II. Paracranial infection	20	40
Ear infection	11	22
• Acute Otitis Media	9	19
• Chronic Otitis Media	1	2
• Otitis Externa	1	2
Oral infection	7	14
• Dental carries	6	12
• Peri-oral furunculosis	1	2
Nasal infection (carbuncle)	1	2
Scalp abscess	1	2
III. Distant infectious source		
Pulmonary infection	3	6
• Bacterial pneumonia	2	4
• Pulmonary tuberculosis	1	2
III. Direct inoculation and instrumentation	5	10
Intracranial Foreign Body (Metallic rod)	1	2
Traumatic brain injury secondary to fall	3	6
Ventriculoperitoneal shunt infection	1	2
IV. Cryptogenic (unknown)	5	10

**ASD Atrial septal defect; VSD Ventricular septal defect; MAPCAS Major aortopulmonary collateral arteries*

Table 2 shows the complete list of identified pre-disposing conditions for brain abscess in children.

RADIOLOGIC FEATURES

Cranial computed tomography (CT) scan was still the diagnostic imaging of choice, which manifests as a ring-enhancing lesion in the brain parenchyma. In majority of patients (n=29), multiple lesions were seen. The most frequently involved area of the brain was the parietal lobe, followed by the frontal and temporal lobe. Table 3 summarizes the different areas of involvement as seen on imaging.

Majority of patients (96%) presented as surgical candidates on initial CT scan, with an aggregate abscess diameter >2.5 cm. The largest aggregate diameter documented was 7.8 cm, with a mean of 4.7 cm.

Table 3. Abscess location on initial cranial CT-scan.

Abscess location	Frequency	Percentage (%)
Parietal	26	52
Frontal	23	46
Temporal	19	38
Occipital	9	18
Cerebellar	7	14
Thalamus	2	4
Sellar-suprasellar	1	2

ASSOCIATION BETWEEN PREDISPOSING CONDITION AND ABSCESS LOCATION

No significant association was found between predisposing condition (excluding those from direct inoculation) and area of the brain affected using Pearson Chi, with a correction value using Fisher's exact test, with a level of significance of $p<0.05$ (Table 4).

Table 4. Association between predisposing condition causing indirect seeding to the brain and area of the brain affected using Pearson Chi and Fisher's exact test. Level of significance < 0.05.

Predisposing condition	Frontal	Temporal	Occipital	Parietal	Cerebellar	Thalamus	Sellar-suprasellar	Pearson chi p(X2)	Fisher's exact	**p-value**
Nasal infection	1	-	-	1	-	-	-	0.691	1.000	p>0.10
Ear infection	4	3	1	4	4	-	-	0.024	0.054	p>0.05
Oral infection	11	6	2	14	-	1	-	0.955	0.963	p>0.10
Scalp abscess	1	-	-	-	-	-	-	-	-	-
Pulmonary tuberculosis	-	-	-	-	-	-	1	-	-	-
Pneumonia	2	1	-	2	1	-	-	0.478	0.851	p>0.10
Congenital Heart Disease	9	9	3	13	1	1	-	0.656	0.639	p>0.10

MICROBIOLOGIC STUDIES

Specimen for abscess culture and sensitivity were obtained from 41 patients. Majority (68%) had no growth on aerobic cultures, and a microbiologic diagnosis was established in only 32% of cases (Table 5). The isolates were gram-positive bacteria, mainly Methicillin-resistant *Staphylococcus aureus* (MRSA) from patients with paracranial infections (nose and scalp) and breaks in the skull post-trauma.

Gram-negative isolates included *Proteus mirabilis*, Enterobacter spp., *Escherichia coli*, *Acinetobacter baumanii,* Pseudomonas *putida*, and *Klebsiella pnuemoniae*, and were mostly seen in patients with ear (CSOM) or shunt infection.

Only three of 13 cases had polymicrobial isolates consisting of combinations of Enterococcus spp + *Escherichia coli*, MRSA + *Acinetobacter baumannii*, and MRSA + Mycobacterium spp. (based on acid fast bacilli smear of abscess fluid).

Table 5. Microorganisms isolated from brain abscess fluid stratified according to pre-disposing condition.
**CSOM (Chronic suppurative otitis media), **Acid fast bacilli*

Organism Isolated	Frequency	Percentage	Associated condition(s)
Methicillin resistant Staphylococcus aureus (MRSA)	5	38	Nasal carbuncle Lip carbuncle Scalp abscess Traumatic brain injury Cryptogenic
Enterococcus	2	15	Tetralogy of Fallot with periodontitis Cryptogenic
Proteus mirabilis	1	8	CSOM*
Enterobacter	1	8	Traumatic brain injury with CSOM
Escherichia coli	1	8	Cryptogenic
Streptococcus viridans	1	8	Pentalogy of Fallot
Methicillin resistant Staphylococcus epidermidis (MRSE)	1	8	Traumatic brain injury
Acinetobacter baumannii	1	8	Nasal carbuncle
Pseudomonas putida	1	8	Cryptogenic
Klebsiella pneumoniae	1	8	Ventriculoperitoneal shunt infection
*Tuberculosis***	1	8	Pulmonary tuberculosis

(AFB) +1/30 on AFB smear of abscess fluid

The sensitivity and resistance pattern of isolates are shown in table 6. Notably, Staphylococcus isolates were 100% resistant to Oxacillin and Penicillin G. Majority of gram-positive isolates (MRSA, *Streptococcus viridans*, Enterococcus) were 100% susceptible to Vancomycin. Most gram-negative isolates were sensitive to Meropenem, Piperacillin-Tazobactam, and third generation Cephalosporins (Ceftriaxone, and Ceftazidime). Notably, one *Klebsiella pnuemoniae* isolate was multi-drug (extended spectrum penicillin, cephalosporin, sulfonamide) resistant.

Table 6. Sensitivity and resistance pattern of isolates from brain abscess fluid in children.

Isolates	Type of resistance	Percent resistant	Susceptibility	Percent susceptible
Staphylococcus sp. (n=6)	Methicillin-resistant (MRSA, MRSE); Oxacillin and Penicillin G resistant	100 %	Vancomycin Ciprofloxacin	100% 33%
Gram positive (*Streptococcus viridans, Enterococcus sp.; n=3)*	—	—	Vancomycin	100%
Gram negative (*Acinetobacter baumannii, Proteus mirabilis, Enterobacter sp., Pseudomonas putida, Eschericia coli*; n=5)	Ceftazidime resistant Ceftriaxone resistant Ciprofloxacin	20% 20% 20%	Piperacillin-tazobactam Meropenem Ampiillin-sulbactam Ceftriaxone Ceftazidime Gentamicin Ciprofloxacin Aztreonam	80% 80% 60% 60% 60% 60% 60% 40%
Klebsiella pnuemoniae (n=1)	Multi drug resistant (Piperacillin-Tazobactam, Ceftazidime, Trimetophrim-sulfamethoxazole resistant)	100%	Meropenem	100%

**Methicillin-resistant Staphylococcus aureus (MRSA)*
**Methicillin-resistant Staphylococcus epidermidis (MRSE)*

TREATMENT AND OUTCOMES

Medical Management

Empiric antibiotics prescribed for patients with brain abscess diagnosed in 2012 consisted of Penicillin G and Chloramphenicol. Subsequently in 2013, third generation cephalosporins (ceftazidime or ceftriaxone) combined with metronidazole, with or without an aminoglycoside (amikacin) were prescribed. Oxacillin was given for cases resulting from direct inoculation (post-surgical/post-traumatic). A 6 to 8-week course of directed therapy was given for microbiologically confirmed cases. For AFB smear positive cases, a 12-month regimen of anti-tuberculosis drugs, with 2HRZE 10HR, was started.

Surgical Management

The table below (Table 7) lists the different surgical procedures done on 39 patients. Abscess aspiration ± drainage was done in majority of cases (n=33). Only six patients underwent complete excision of abscess. Serial aspiration/drainage of abscess was done in five cases. As for the 11 remaining patients, surgery was deferred due to marked clinical improvement with significant decrease in abscess size on Cranial CT scan, no consent for surgery with subsequent decision to go home against medical advice, or mortality before the scheduled surgery.

Table 7. Surgical procedure performed on children with brain abscess, (n=39)

Surgical Procedure	Number of patients	Percentage
Complete excision	6	15
Aspiration and drainage		
Burrhole + Tube drainage	13	33
Craniectomy + Tube drainage	7	18
Needle drainage	1	3
Ultrasound guided aspiration	6	15
Marsupialization	1	3
Serial aspiration and drainage	5	13

OUTCOME

The mean reduction in the size of the abscess on discharge was 76%, while a complete resolution of the lesion was observed in eleven patients (22%) who were treated surgically with concomitant antibiotics (culture guided in 5 cases) for 6-8 weeks. Overall mean length of hospital stay was 65 days.

For those who underwent abscess aspiration ± drainage, mean length of hospital stay was 70 days, with a morbidity rate of 30%, and mortality rate of 6%. For the six patients who underwent complete excision of abscess, mean length of hospital stay was shorter at 54 days, morbidity rate was lower at 17%, with no mortalities.

Morbidity, defined as having residual neurological deficit on discharge, was seen in 14 patients (28%). Majority (50%) were observed to have extremity weakness, and almost one-third had epilepsy.

Table 8. Residual neurological deficits observed upon discharge, (n=14).

Neurological deficit	Number of patients	Percentage %
Epilepsy	4	29
Spasticity	2	14
Facial asymmetry	2	14
Extremity weakness	7	50
Slurred speech	1	7
Bitemporal hemianopsia	1	7
Pronator drift	1	7

Of the 44 patients who stayed on to complete treatment, three died, with a mortality rate of 6.8%. Two patients died of healthcare associated pneumonia, while one patient with shunt infection died of brain herniation from probable reaccumulation of abscess. Six patients went home against medical advice.

DISCUSSION

Brain abscess, although uncommon in the pediatric age group, is a life-threatening condition that could progress rapidly, leading to devastating and permanent neurologic sequelae. A high index of suspicion, timely surgical intervention, and administration of appropriate antibiotics are essential in its management.

As in other studies focusing on children with brain abscesses[2,3,7], no gender predilection was seen. The predominant age group is comparable with findings from other studies[3,4,7,20] . Predilection of the disease for this age group may be partly explained by the higher prevalence of paracranial infections particularly ear infections with contiguous spread[20], as well as the <60% survival of children with critical congenital heart diseases up to 15 y/o[6].

As for contributory factors predisposing children to develop brain abscess, it was observed that a primary immunodeficient condition as well as secondary immunodeficient states such as *leukemia*[7] was not a common cause of brain abscess in local studies[3,4]. This study however supports the idea that a secondary immunocompromised state in the form of malnutrition can be a major risk factor for morbidity and mortality due to infectious agents. Strong associations between malnutrition and mortality from gastrointestinal and acute respiratory infections were reported [14,15], but its association with infections affecting the central nervous system is yet to be investigated. Leptin plays a central role in the speculated mechanism that connects nutrition and immunity. Under conditions of protein-energy malnutrition and low leptin concentrations, there is a decrease in the immune response in the form of decreased activation of naive T cells, memory T cells, and activation markers (CD69, CD25, and CD71)[16], as well as dysregulation of the hypothalamic-pituitary-adrenal axis with increase in serum levels of glucocorticoids, impairing macrophage function in animal studies[17].

As for protective factors, this study also supports the need to address vaccine preventable causes, and particularly immunize against *Streptococcus pneumoniae* and *Haemophilus influenza* type b (Hib)[4]. Studies on the brain abscess-specific protective effects of immunity against these pathogens is still lacking, but it is important to note that their protective effects on conditions which pre-dispose children to brain abscesses, particularly, pneumonia and middle ear infections is indisputable.

Similar to other studies, [3,4,10,15] the classic triad of fever, headache, and neurologic deficits was observed in less than 30% of children in this study. This is an observation, which may indicate that this triad is more specific, rather than sensitive in detecting brain abscess on initial presentation[19]. For the patients seen in this study, seizure on admission was mostly generalized rather than focal. This is in contrast to a study by Chuang in 2010, where seizures were mostly focal in 52% of cases, majority of which had solitary lesions[18]. The predominance of generalized seizures in this study may be explained by the fact that majority of cases had multiple lesions involving multiple lobes.

Previous studies have suggested that some predisposing conditions are associated with abscess predilection for particular areas of the brain. Infections arising from the middle ear, paranasal sinuses, and teeth presumably allows microbe transit thru the emissary veins serving these regions, explaining a tendency towards frontal lobe involvement for sinusitis and dental infection, and temporal lobe involvement in patients with chronic otitis and mastoiditis[1,8]. Infections associated with metastatic inoculation from distant extracranial sources (e.g. pulmonary infection, endocarditis), as well as conditions where there is disruption of pulmonary vascular bed filtration of bacteria (e.g. cyanotic congenital heart disease), tend to be associated with multiple cerebral abscesses, with a distribution that reflects the regional cerebral blood flow of the middle cerebral artery[1,8]. The findings in our study are comparable to that of available local data[3,4], which showed no significant association between predisposing factor and the area of the brain affected. The lack of association however may be partly explained by the small sample size.

Most paracranial infections including post-traumatic inoculation, except that of the middle ear, were caused by Methicillin-resistant *Staphylococcus aureus*. This is in contrast with the study of Ablaza-Medalla et. al. done in the same institution in 1999, where most cases were caused by Methicillin-sensitive *Staphylococcus aureus*[4]. For patients with congenital heart disease, the isolates noted were Enterococcus and *Streptococcus viridans,* sensitive to Vancomycin, and cephalosporins (Cefepime or Ceftriaxone). Gram-negative organisms (*Escherichia coli*, *Pseudomonas putida, Proteus mirabilis*), were mostly sensitive to third-generation cephalosporins (ceftriaxone or ceftazidime) and carbapenems (meropenem), and were isolated from patients with infections of the middle ear, as with cryptogenic cases. These findings support the basis for subsequent change in the choice of empiric antibiotics from penicillin G to third generation cephalosporins in 2013. Only five cases had specimens sent for anaerobic cultures, and none of them had positive growths. Starting 2013, most patients were started on metronidazole than chloramphenicol, as the former has a better margin of safety with fewer side effects. By 2014, empiric antimicrobial coverage proposed by the institution's Section of Infectious and Tropical Diseases in Pediatrics (INTROP)[13] included a combination of third generation cephalosporin (ceftriaxone or ceftazidime) and metronidazole, with the addition of oxacillin in cases of head trauma, post-operative infections, or endocarditis.

What has remained constant is the high incidence of sterile cultures, with rates as high as 60%[12]. Notably in this study, 50% of those with negative cultures had previous antibiotic exposure, mostly intravenous cephalosporins, prior to surgical excision of the abscess. The practice of not routinely sending aspirates for anaerobic cultures may also be contributory. This parallels the local data where sterile cultures are reported in as many as 68% of cases, attributed to previous antibiotic intake and the inability to properly collect and culture for strict anaerobes[3,4,5].

In this study, patients with sterile cultures were evaluated for improvement following a regimen of empiric antibiotics (penicillin G + chloramphenicol, or ceftriaxone / ceftazidime + metronidazole), with the basis for improvement being clinical response and imaging studies. If after 14 days, imaging results did not show an interval decrease in the size of the abscess, escalation to meropenem was done and given for 6-8 weeks. With concomitant surgical intervention, interval decrease in size of the abscess was seen in 96% of patients with sterile cultures, with as much as 19-100% (mean of 66%) decrease from the largest aggregate diameter of the parenchymal lesion upon discharge.

A local study by Tongco and Domingo (1983) done in this same institution compared serial aspiration or drainage of pus from the abscess against total excision[9]. It was found that although total evacuation led to lower mortality rates, this was associated with an extended hospital stay. These findings were comparable to those in the present study, in terms of lower morbidity rate (17% vs 30%) and no mortalities (vs 2 mortalities). However, this study differs in terms of shorter mean length of hospital stay (54 vs 70 days) for those who underwent total excision compared to abscess aspiration ± drainage.

Comparable to other studies[5,12], morbidity, defined as having residual neurological deficit on discharge, was seen in 28% of patients in this study. Mortality rates prior to the 1980s ranged from 11-53%. Available data on local mortality between 1990-1998 [3,5] showed significantly lower rates, due to availability of improved imaging studies, microbiologic techniques for definitive treatment, as well as improvement in surgical techniques[1,2,11].

CONCLUSION

Brain abscess in children, although rare, is a life-threatening condition that requires prompt recognition, diagnosis, and treatment. There should be a high index of suspicion for this complication among patients with pre-disposing conditions (i.e. paracranial infections, cyanotic congenital heart disease), presenting with fever, headache, and neurological deficits. The likelihood of a brain abscess increases among patients with malnutrition, and among those who lack protection against vaccine preventable pathogens, such as *Streptococcus pneumoniae* and *Haemophilus influenza* type b (Hib). No significant association was found between predisposing condition and the area of the brain affected.

Organisms isolated in this study were sensitive to antibiotics recommended for empiric therapy[13], particularly parenteral third generation cephalosporins (ceftriaxone or ceftazidime) and metronidazole given for 6 to 8 weeks. Patients with sterile cultures were also continued on this regimen.

With the high rates of Methicillin-resistant *Staphylococcus aureus* (MRSA) in our present setting, vancomycin should be considered for abscesses arising from paracranial infections and for those with breaks in the skull post-trauma, with appropriate guidance from the infectious disease specialists. Optimal management calls for surgical evacuation, preferably complete excision of abscess. Morbidity and mortality rates decreased over time, which could be attributed to improved imaging studies, improved identification of pathogens for definitive treatment, as well as improved surgical techniques[1,2,11].

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