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BRAIN ABSCESS IN CHILDREN AT THE PHILIPPINE GENERAL HOSPITAL: A PROSPECTIVE EPIDEMIOLOGIC STUDY

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Abstract: **Even with the advances in microbiology and radioimaging studies, intracranial abscesses remain to pose a threat to the pediatric population, particularly in those with known predisposing factors in developing countries. Twenty one patients less than 18 years of age who were diagnosed to have brain abscess by CT scan, were seen at the Philippine General Hospital from February to September 1999. Seventy six percent were less than 10 years old (25% were 2 years of age). The most common presenting symptoms were fever, weakness, vomiting and headache with 67% presenting with focal neurologic deficit on admission. Ten (47.6%) had cyanotic congenital heart disease as their predisposing condition, the most common of which was due to Tetralogy of Fallot. Chronic suppurative otitis media was only seen in 28.6%. Eight (44.4%) of the 18 patients who underwent surgery yielded no growth on both aerobic and anaerobic cultures but half of these patients had previous antibiotic intake. A microbiologic diagnosis was established in 55.5% and only one patient grew an anaerobic organism (Bacteroides spp.) on culture of the brain abscess. There was no specific organism associated with certain predisposing factor although gram negative bacteria were more commonly seen in patients with CSOM (*Proteus vulgaris, Proteus mirabilis, Acinetobacter anitratum, Morganella morgagni). Staphylococcus aureus* was isolated in 2 patients with no known predisposing factor. All aerobic gram negative organisms and *Streptococcus viridans* isolated were sensitive to chloramphenicol and Penicillin G, respectively. All *staphylococcus aureus* isolated were sensitive to oxacillin. Thus, the empiric antibiotics of choice remain to be penicillin G and chloramphenicol or metronidazole in the treatment of brain abscess. In cases of chronic otitis media wherein gram negative aerobes are usually implicated, a third generation cephalosporin or an anti-pseudomonal antibiotic is recommended . Although antimicrobial therapy may play a major role in the treatment of brain abscess, surgical evacuation, either by aspiration, tube drainage or excision is essential for optimum management.**

INTRODUCTION:

Brain abscess is considered an uncommon yet serious and life threatening infection in children[5]. With the advent of more effective antibiotic regimen and

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improvement of neuroimaging studies in diagnosing brain abscess, the morbidity and mortality rate of brain abscess have dramatically declined. However, this remains a significant problem in developing countries.

Brain abscess has been shown to develop from hematogenous spread from a primary focus of infection (e.g. cyanotic heart disease), contiguous spread from an adjacent focus (e.g. ear infection, sinusitis), from meningitis or after trauma or head surgery. The most common organism involved usually depends on the focus of infection or predisposing factor which led to the development of an abscess. The most common source of infection are the ears and sinuses in several series[2, 4, 8, 11, 13, 15, 16, 19, 22, 23, 28]. However, a study done by Pathucheary and Parasakthi in Malaysia showed that Tetralogy of Fallot and other congenital cyanotic heart diseases were the predominant factors, with infections of the ear and mastoids occurring only second.

The most common organisms isolated in children with brain abscess in a review of several studies done on its microbiology by Brook are aerobic and anaerobic *Streptococcus* species (isolation frequency, 60-70%), gram negative anaerobic rods (20-50%), Enterobacteriaceae (20-30%), *S. aureus* (10-15%) and fungi (10-15%)[3]. In the preantibiotic era, around 50% of cultures from brain abscess did not grow any organism. With advances in anaerobic microbiology, recent studies have shown that anaerobic organisms play a major role in intracranial abscesses. Since the introduction of CT scan, mortality rate has declined from an estimated rate of 40-80% in the pre-antibiotic era to 0-24% in several series. This may be attributed to earlier diagnosis and treatment of brain abscesses. Management of brain abscess include appropriate antimicrobial therapy, drainage of pus by aspiration or excision of the abscess.

Reports on the most common predisposing factors as well as the microorganisms commonly implicated in relation to the source of infection have been done long before the advent of the CT scan. Studies done in the Philippines were usually retrospective, wherein specimen collection was not well-controlled and others were done in more developed countries. The last local extensive prospective study on brain abscess was done by Rama in 1990. Since the bacteriology of brain abscess remains complex and varies from center to center through time, the purpose of this study is to (1) to determine the prevalence of brain abscess in a tertiary hospital in the Philippines, (2) to describe its clinical presentation, causative organism based on the presumed origin of infection and eventually evaluate the empiric antibiotic regimen for brain abscess based on the data obtained.

PATIENTS AND METHODS:

Twenty one patients less than 18 years of age diagnosed to have brain abscess were seen at the Philippine General Hospital from February 1999 to September 1999. All patients were either admitted to the Department of Neurosurgery or to the Department of Pediatrics. Each patient was evaluated in terms of age, sex, presenting signs and symptoms, predisposing condition, radiographic and microbiologic findings, treatment regimen and duration and outcome. The clinical diagnosis of brain abscess based on signs and symptoms was confirmed by visualization of localized lesions on computerized axial tomography (CT scan). Pus from the abscess was obtained either by aspiration or drainage and was sent for gram stain, aerobic and anaerobic culture with the use of standard methods. Initial complete blood count, blood culture and aerobic culture of the ear discharge, if any, were also obtained. Two-dimensional echocardiogram was also requested as part of the cardiac assessment in patients with congenital heart disease.

Empiric antibiotic therapy was administered while awaiting culture and sensitivity result of the brain abscess. Repeat CT scan was done to assess the resolution or reaccumulation of the abscess post-evacuation, in order to evaluate the need for reaspiration. Specimens obtained from repeat aspirations were also sent for gram stain, culture and antibiotic susceptibility studies.

RESULTS:

Demographic Data:

Out of the 21 patients included in the study, there were 11 males and 10 females (male/female ratio : 1/1). The majority (76%) of the patients were less than 10 years old (mean age=7 years; range, 2-17 years) (Fig. 1). Twenty five percent of the cases were two (2) years of age.

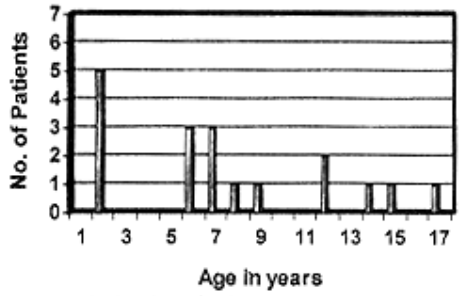

Fig. 1 Age distribution of children with brain abscess (n=21)

Presenting Signs and Symptoms:

The most common presenting symptoms were fever, weakness (preferential movement, facial asymmetry), vomiting, headache and increased sleeping time (Table 1). The duration of symptoms ranged from 4 days to 4 months. On physical examination, fourteen (67%) presented with focal neurological signs such as hemiparesis and eleven (52%) patients presented with cranial nerve deficits usually involving the 7th cranial nerve . Neurologic exam was normal in 3 (14%) patients and 4 (19%) showed signs of increased intracranial pressure within the first 24 hours after admission.

Table 1: Presenting Signs and Symptoms in children with brain abscess (n=21)

SIGNS AND SYMPTOMS	Patients	Percent (%)
Fever	15	71
Neurologic deficit*	14	67
Vomiting	12	57
Headache	11	52
Increased sleeping time	11	52
Cough	7	33
Seizures	5	24
Focal	3	
Generalized	2	
Behavioral changes	3	14
Loss of consciousness	2	10
Nausea	2	10
Dizziness	1	5
Poor feeding	1	5
Blurring of vision	1	5
Difficulty of breathing	1	5

*Includes ptosis, hemiparesis,loss of balance, facial asymmetery

Predisposing Condition and Location of the Abscess:

Ten (47.6%) out of twenty one patients had congenital heart disease as their predisposing condition, the most common of which was due to Tetralogy of Fallot (seven patients). Six were due to chronic suppurative otitis media while 3 of the patients had no known underlying cause (Table 2). One patient had both cyanotic heart disease (Double outlet right ventricle with subaortic VSD) and chronic otitis media.

Table 2: Predisposing Condition of brain abscess (n=21)

	Patients	Percent %
Congenital cyanotic heart disease	10	47.6
Tetralogy of Fallot	8	38.1
PVA with ASD, PDA	1	4.7
TVA with VSD	1	4.7
Chronic suppurative otitis media	6	28.6
Unknown	3	14
Post-traumatic	1	5
Skin infection	1	5
Shunt infection	1	5

ASD = Atrial septal defect; PDA = Patent ductus arteriosus
VSD = Ventricular septal defect.

Although there was no definite association between the predisposing factor and the location of the abscess, the most frequently involved sites were the parietal area and the cerebellar area in patients with congenital cyanotic heart disease and chronic suppurative otitis media, respectively (Table 3). Multiple abscesses were more commonly observed in patients with a hematogenous route of infection (eg. Congenital heart disease) than that from a contiguous spread of infection from an adjacent site (e.g. ear infection).

Table 3: Location of brain abscess in relation to the predisposing condition

	P	FP	TP	T	C	TOF	O
CHD	3	1	2	2	1	1	
CSOM				1	3	1	
Unknown		2					1
Trauma	1						
Skin infection		1					
Shunt infection		1					

P = parietal, FP = fronto, T = temporal; TP = temporo-parietal,
C = cerebellar, TOF = temporo-occipital-frontal; O = occipital

Laboratory Findings:

White blood cell count (WBC) on admission ranged from 6,800 to 26,700/mm^3 with 75% having a WBC count of more than 10,000/mm^3 . Most of the patients showed presence of monocytes on complete blood counts. Patients with CHD were noted to have an elevated hematocrit ranging from 0.40 to 0.63.

CT scan was solely done to diagnose brain abscess in all cases. This was later supplemented by cranial ultrasound through the burr hole to assess re-accumulation or improvement after evacuation and antibiotic therapy but this was still confirmed by repeat CT scan.

Forty seven percent (10 patients) had a single abscess while 8 had multiple abscesses on CT scan.

Multiloculated abscesses were detected in 3 patients. Most patients with CSOM had single abscess while patients with CHD equally had single and multiple abscesses on CT scan (Table 4).

Table 4: Characteristics of brain abscess seen on CT scan

	Multiple	Patients	Percent %
CHD	5	4	1
CSOM	1	4	0
Unknown	1	1	1
Trauma	0	1	0
Skin infection	0	0	1
Shunt infection	1	0	0

Microbiological Findings:

Eight patients (44.4%) yielded no growth on both aerobic and anaerobic cultures of the brain abscess but gram stain was positive for both gram positive cocci and gram negative bacilli in 2 cases while three showed only gram positive cocci in pairs. Four patients (50%) had been started on empirical antibiotics for at least 2 days prior to surgery. However, two of these patients had positive cultures on other sites. One patient had brain abscess secondary to TOF and grew *Acinetobacter* on blood culture which was resistant to the antibiotics being given. Patient however, improved with Penicillin G and chloramphenicol for 4 weeks and do not need re-aspiration of the abscess. The second patient on the other hand, with CSOM as the predisposing condition, yielded *Pseudomonas aeruginosa* on culture of the ear discharge. Patient had to undergo repeat aspiration and eventually excision of the abscess due to reaccumulation. Antibiotics were later on shifted from penicillin, chloramphenicol and metronidazole to ceftazidime, oxacillin and metronidazole with improvement.

A microbiologic diagnosis was established in 10 (55.5%) out of 18 patients who underwent drainage or aspiration of the brain abscess. There were 9(90%) aerobic organisms and 1 (10%) anaerobic organism (Bacteroides spp) isolated. Gram stain results were reflective of the growth on culture. There was no specific organism associated with certain predisposing factors although gram negative bacteria were more commonly seen in patients with CSOM (*Proteus vulgaris, Proteus mirabilis, Acinetobacter anitratum, Morganella morgagni*). *Staphylococcus aureus* was isolated in a patient with a history of cellulitis/skin infection. *Streptococcus viridans* was isolated from a case of TOF and 2 cases with no known predisposing condition grew *Staphylococcus aureus*. Only one (10%) case had multiple organisms (2) isolated from the culture. The organism that was isolated from the ear discharge/cholesteatoma was comparable to that isolated from the brain abscess in two patients.

All aerobic gram negative organisms and *streptococcus viridans* isolated were sensitive to chloramphenicol and penicillin G, respectively. All *staphylococcus aureus* isolated were resistant to penicillin G but sensitive to oxacillin.

Table 5. Gram stain and culture results of brain abscesses

Underlying Condition	Organism(s)	Gram Stain
CSOM	*Proteus vulgaris, Acinetobacter anitratum*	Gm (−) cocci in pairs, Gm (-) bacili - TNTC
CSOM	*Morganella morgagni*	Gm (-) bacilli
CSOM	*Proteus mirabilis, Enterococcus*	Gm (-) bacilli, (+) cocci in pairs
CSOM	*Staphylococcus aureus*	Gm (−) cocci in clusters
CHD (TOF)	*Diphteroids*	Gm (+) cocci in pairs
CHD (DORV)	*Klebsiella pneumonia*	no organism seen
CHD (TOF)	*Streptococcus viridans*	
CHD (TVA)	*Bacteroides spp*	Gm (+) cch, Gm (-) bacilli
Skin infection	*Staphylococcus aureus*	Gm (+) cocci in clusters
Unknown	*Staphylococcus aureus*	Gm (+) cocci in clusters
Unknown	*Staphylococcus aureus*	Gm (−) in clusters

Table 6. Results of sensitivity testing of the organisms isolated

Organisms	Sensitive	Resistant
I. Gram Positive *Streptococcus viridans*	Ampicillin, Ciprofloxacin, Gentamycin, Penicillin G	
Staphylococcus aureus	Oxacillin, Chlorampenicol, Ciprofloxacin, Gentamycin, Cotrimoxazole	
Staphylococcus aureus	Oxacillin, Erythromycin, Clindamycin, Gentamycin, Chlorampenicol, Ciprofloxacin, Cefoxitin, Vancomycin	Penicillin G
Staphylococcus aureus	Oxacillin, Chlorampenicol, Cefoxitin, Cotrimoxazole	Penicillin G
Staphylococcus aureus	Oxacillin, Chlorampenicol, Ciprofloxacin, Contrimoxazole, Gentamycin	Penicillin G
II. Gram Negative *Morganella morgagni*	Chlorampenicol, Cotrimoxazole, Ciprofloxacin, Gentamycin, Netilmycin, Imipenem, Pipertazo	
Klebsiella pneumonia	Ampicillin-sulbactam, Cefoxitin, Chlorampenicol, Gentamycin, Netilmycin, Chlorampenicol	
Proteus mirabilis	Ampicillin, Cefoxitin, Chloramphenicol, Ciprofloxacin, Gentamycin, Netilmycin, Contrimoxazole	

Treatment:

Nineteen patients underwent surgery with 7 (33%) undergoing more than one surgical procedure: 11 aspirations (40.7%). 15(55.5 %) tube drainage and 1 (3.7 %) excision of the abscess were performed. Three patients with CSOM also underwent radical mastoidectomy. The mean delay between the time of admission and the surgical intervention was 2.8 days.

Penicillin G (300,000 units/kg/day) and chloramphenicol (100 mg/kg/day), with or without metronidazole (30 mg/kg/day) were started on all except for one patient. Four patients were later shifted to a penicillinase-resistant penicillin (oxacillin) after cultures grew *Staphylococcus aureus* which was sensitive to the antibiotic. Four patients were shifted to a third generation cephalosporin (ceftazidime or ceftriaxone) after there was no improvement despite aspiration or drainage of the pus with conventional empiric antibiotics. Three of these patients had CSOM. Intravenous antibiotics were given for a duration of 4 to 6 weeks. The patient who completed only 2 weeks of intravenous antibiotics was transferred to another hospital for completion of the medications for another 2 weeks. One case who completed only 3 days of antibiotic therapy was brought home against medical advise. Only one patient died in this series because of related complications (candidemia). This patient was stuporous on admission.

DISCUSSION:

Even with the advances in microbiology and radioimaging studies, intracranial abscesses remain to pose a threat in the pediatric population particularly in those with known predisposing factors.

Males are more commonly affected than females with a 2-3:1 ratio in several series[5, 13, 16, 22, 25]. However, recent local studies, including our study, showed equal preponderance of both males and females[6, 26].

In comparison to the other series previously done in the Philippines and abroad (0.2 to 1 admission per month)[4, 6, 10, 14, 15, 17, 20, 23,24, 27], the admission rate was higher in our study. In a span of 8 months, there was an average of 2.6 admissions per month. But unlike most of the studies reviewed with the incidence of CHD only at 6 to 32%[2,4,8,11,13,15,16,19,22,23,28], our study showed that cyanotic congenital heart disease (47%) was the most common predisposing condition leading to the development of an intracranial abscess. Eighty percent were due to Tetralogy of Fallot. This was comparable to the study done by Puthucheary and Parasakathi in Malaysia which also showed a predominance of cyanotic congenital heart disease in 32% of the cases. These findings could probably be due to a more aggressive approach in treating upper respiratory tract infections including otitis media and less corrective procedures done on patients with congenital heart disease primarily due to financial constraints.

Patients with brain abscess may present with varying symptoms depending on the patient's immunologic status, number and location of the abscess(es) and the presence of accompanying complications such as ventriculitis[27]. The classic triad of fever, headache and focal neurologic deficit were seen in less than 50% of the cases[9, 22, 27]. However, fever was noted to be the most common presenting symptom in our study. Papilledema was observed in 19-45% of the patients[9, 19, 22] while seizures were reported in 10-40%[9, 13, 19, 22, 26].

The classification of brain abscess is based on the possible origin of infection to predict the most likely causative organism(s). Aerobic and anaerobic streptococci, Bacteroides, Enterobacteriaceae, *Staphylococcus aureus* and *H. influenzae* were the common organisms isolated in frontal lobe abscesses secondary to sinusitis. The first 3 organisms were likewise commonly associated with temporal abscess secondary to middle ear or mastoid disease[27]. A local study by Rama et al. showed that *Peptostreptococcus* species was the dominant anaerobe isolated and that 60% of these were due to chronic otitis media. Other studies support that chronically infected ears predominantly yielded anaerobes and gram negative aerobes on culture[19, 23, 27]. A study done by Del Rosario et al on patients with CSOM at the Philippine General Hospital showed that the top organisms isolated from cholesteatoma were *Proteus* and *Pseudomonas*. Two more recent retrospective studies done in the same institution also showed a predominance of gram negative organisms from brain abscess specimens and did not yield any anaerobes[6, 26]. In congenital heart disease, the predominant organisms are *Streptococcus viridans*, anaerobic and microaerophilic streptococci and *Haemophilus* species[27]. Takeshita et al reported that the most common aerobic bacteria associated with CHD were *Staphylococcus* species, *Streptococcus* species and

Gram-positive cocci, whereas the most common anaerobic bacteria were *Peptostreptococcus*. *Staphylococcus aureus* remains to be the predominant organism associated with brain abscess as a result of a head trauma[5]. *Staphylococcus aureus, Staphylococcus epidermidis*, gram negative enteric rods and *Pseudomonas aeruginosa* were the most common organisms implicated in intracranial abscesses caused by ventriculoperitoneal shunt infections[5]. The organisms isolated from our patients were mostly aerobic gram negative (*Proteus spp., Klebsiella, Morganella, Acinetobacter*) and gram positive bacteria (*Staphylococcus, Streptococcus*). Only one anaerobe was isolated. These findings are consistent with the organisms isolated from other studies although we had a low yield for anaerobic organisms due to technical difficulties in isolation.

Sterile cultures from several studies ranged from 0% to as high as 70%. This discrepancy in isolating organisms may be due to previous antibiotic intake, improper sampling techniques and the inability to culture for strict anaerobes . No organism was isolated in 44% of the specimens cultured in this study. No organism was seen on gram stain in 3 (42%) of the patients whose cultures yielded no organism. Fifty seven percent of the cases with sterile cultures had previous antibiotic intake for an average of 2.8 days prior to the surgery. This may explain the sterile cultures obtained. However, according to Seydoux and colleagues, treatment with an antibiotic for less than 10 days does not reduce the rate of positivity of the cultures. Another factor which may have contributed to obtaining sterile cultures may be the failure to observe strict adherence to proper collection of specimen for anaerobic culture. A review of several studies showed that anaerobes were only isolated in 0 to 42% of the cases[2, 6, 11, 13, 19, 24, 26]. However, Brook demonstrated that anaerobic organisms play an important role in the etiology of brain abscess. He recovered pure anaerobes in 63% of the cases and had a yield of 100% (both aerobe and anaerobe) from all the specimens cultured.

Based on the previous studies done on brain abscess, the use of high dose penicillin G and chloramphenicol or metronidazole to cover for anaerobes was recommended. The organisms obtained in our study were all sensitive to the conventional antibiotics being given and thus, there is no need to modify the present antibiotic regimen. An exception may be in cases of chronic otitis media wherein gram negative aerobes such as *Proteus* and *Pseudomonas* have been found to be common. An addition of a third generation cephalosporin or an anti-pseudomonal antibiotic may be warranted especially in cases who do not seem to respond to the recommended antibiotic regimen. This may also be applicable in cases where culture sensitivity testing shows resistance to the antibiotics at hand. In cases of unknown etiology, Brook recommended giving antibiotics with anti-staphylococcal coverage (oxacillin and nafcillin), antibiotics against anaerobes (metronidazole, chloramphenicol) and gram negative organisms (third generation cephalosporin), particularly Enterobacteriaceae. Once culture and sensitivity results are in, antibiotics are then modified accordingly. The recommended duration of the parenteral antibiotics is 4 to 6 weeks.

Medical management alone is only advocated in patients whose abscess is less than 2 centimeters in diameter, patients with multiple abscesses, when there is evidence suggestive of cerebritis, when the abscess is located in a critical area or when patient is a poor surgical risk[21-22].

The choice between aspiration and excision of an intracranial abscess as the best surgical procedure remains controversial. There is still no conclusive evidence in the literature to support which is more superior than the other in terms of operative risk and mortality.

A mortality rate of 4.8% was observed in our study which is comparable to the 0-20% mortality rate reported in other series after the introduction of the CT scan[6,10, 17, 20,23, 27].

CONCLUSION:

Although brain abscess in children is uncommon compared to other forms of intracranial infections, the clinician should have a high index of suspicion when patients with a history of chronic ear discharge or cyanotic heart disease present with fever and a focal neurologic deficit. Organisms isolated in our series show that aerobic gram negative bacilli and gram positive organisms, particularly Staphylococci and Streptococci, are still the predominant microbial flora in brain abscess. However, our study failed to isolate a significant number of anaerobes probably due to technical

difficulties. The empiric antibiotics of choice remain to be Penicillin G and metronidazole or chloramphenicol in the treatment of intracranial abscesses. An addition of a third generation cephalosprin in patients with CSOM is recommended. Though antimicrobial therapy plays a major role in the treatment of brain abscess, surgical evacuation either by aspiration, tube drainage or excision is essential for optimum management.

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