

INTRACRANIAL ABSCESS DUE TO STREPTOCOCCUS MILLERI: A REPORT OF SEVEN CASES

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SYNOPSIS

Streptococcus milleri was isolated from the pus in seven patients with intracranial abscess, but in the three of them aerobic and obligate anaerobes were also isolated as mixed growth together with *Str. milleri*. Predisposing factors to infection were present in six of the patients. Therapy consisted of penicillin, chloramphenicol, metronidazole, diphenhydantoin as well as surgical drainage. Four patients recovered fully without neurological deficits and three died. Brain abscess is an emergency and vigorous therapy with suitable antimicrobials as well as surgical drainage is necessary.

INTRODUCTION

A variety of pyogenic organisms give rise to brain abscesses which are localized infections of the brain substance. These lesions are characterised by progressive stages of purulent exudate formation and encapsulation.

The pathogenesis of brain abscess is complex but it has important implications for therapy, for the original focus of infection determines the causative bacteria and the location of the abscess within the brain. The lesions may arise as the result of direct spread from contiguous anatomical structures, following injury or local infection; alternatively, they may occur as the result of metastatic spread from a distant focus (1).

In the pre-antibiotic era, brain abscess was almost universally attributable to aerobic organisms such as the staphylococci, streptococci as well as the gram negative rods (2). Recent focus has been on the growing aetiological role of the anaerobic and the microaerophilic bacteria in brain abscess formation, in particular *Streptococcus milleri*.

The management of intracranial abscesses depends on relieving the space occupying effect of a brain abscess as well as finding suitable antimicrobials that will attain therapeutic levels in the brain tissue after crossing the blood-brain barrier (1).

This report reviews seven consecutive cases of brain abscess seen at the University Hospital, Kuala Lumpur, Malaysia, over a period of eight months (March - October 1979).

PATIENTS AND METHODS

Seven patients were admitted to the surgical unit of the University Hospital and diagnosed as having intracranial abscesses. The diagnosis was confirmed and localised either by isotope brain scan, computerised axial tomography or by carotid angiogram. Table 1 summarises the relevant clinical data such as presenting symptoms and signs, associated illness and the outcome. Twist drill drainage of the abscess was performed on five patients, operative drainage in one and surgical excision in one.

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All patients were routinely started on phenytoin (diphenylhydantoin) which was continued for one year. The dose for adults was 300 mg per day. Antimicrobials were also given routinely at the time of diagnosis. These were chloramphenicol 4 gm per day, crystalline penicillin 12 mega/day and metronidazole 1200 mg/day. The chloramphenicol and penicillin were continued for up to six weeks - initially intravenously and subsequently orally.

Bacteriological investigations:

Pus was examined as soon as it was received, and details of the gram-stained appearance and subsequent microbial findings were telephoned to the surgeon in charge. The pus was inoculated on to plates of 5% sheep blood agar incubated aerobically and anaerobically with added carbon dioxide, to sheep blood agar with added kanamycin and vancomycin incubated anaerobically; to chocolate blood agar incubated in 10% carbon dioxide, to Robertson's cooked meat medium and to MacConkey's medium. Plates were incubated at 37°C for up to five days. Subcultures were made from Robertson's cooked meat medium after preliminary incubation at 37°C for 48 hours. Antibiotic sensitivities were determined by the disc diffusion method as described by Bauer and associates (3).

Anaerobiasis was achieved by the use of anaerobic jars (BTL) with two catalysts which were replaced after each use. A 10% carbon dioxide environment was produced by Gaspaks (Oxoid) in anaerobic jars from which the catalyst had been removed.

Aerobes and facultative anaerobes were identified specifically using the methods of Cowan and Steel (4).

All isolates growing anaerobically were subcultured aerobically and those failing to grow were further examined to determine their sensitivity to metronidazole when grown anaerobically by means of a diffusion test using a 5 µg metronidazole disc. These obligate anaerobes were identified according to the methods described by Willis (5).

The streptococci isolated were provisionally identified by using the methods described by Parker and Ball (6), Poole and Wilson (7) and subsequently confirmed by the Streptococcus Reference Centre, Colindale, England. Lancefield grouping was performed by using a rapid latex test kit (Streptex, Wellcome Reagents Ltd., England).

RESULTS

Age and sex distribution: The ages ranged from 12 to 37 years, the mean being 22. There were five males and two females, the ethnic composition being four Chinese, two Indians and one Malay.

Clinical features: A summary of the major clinical features is presented in Table 1. All seven patients presented with fever, nausea/vomiting, and headache which is the universal symptom for brain abscess (8). The presenting signs were - all seven had altered state of consciousness, six had focal neurologic signs, three had papilloedema and three had neck rigidity. Duration of symptoms prior to admission to the University Hospital consisted of four weeks or

more in three patients, three weeks in one patient and two weeks in three patients.

Organisms isolated: The bacteriological results of the samples of pus are presented in Table 2. The salient finding is that *Str. milleri* was isolated from all seven samples. The gram-stained smear of the pus showed organisms in six of the seven specimens and pus cells were visible in all seven of them. This is a valuable procedure as it may provide useful therapeutic information. Of the seven strains of *Str. milleri* isolated, two belonged to Lancefield group F, one to group G and four were ungroupable. One additional organism was present in three samples, the organisms being bacteroides species, *Haemophilus influenzae* type b and diphtheroids. This study augments previous reports that streptococci are the most frequently isolated organisms from brain abscesses (9) and of the streptococci, *Str. milleri* is the commonest (10).

Predisposing factors and infection: There were four frontal lobe abscesses of which two were post-traumatic, one patient had mitral stenosis with cyanotic heart disease and in another no predisposing factors were evident. We could not find any association between abscesses of the frontal lobe and sinusitis as described by de Louvois *et al* (10). The one case of temporal lobe abscess had a severe cyanotic heart disease. The patient with the parieto-occipital abscess had several lumbar punctures performed and treated with antibiotics elsewhere for suspected purulent meningitis.

Antibiotic sensitivity: All the seven strains of *Str. milleri* were uniformly sensitive to penicillin and chloramphenicol. None of them were sensitive to metronidazole and rightly so as they are not considered to be obligate anaerobes.

Diagnostic procedures: Brain abscess diagnosis is often made possible by specialised diagnostic procedures. Radioisotope scan was used in confirming the diagnosis in five patients and computerised axial tomography (CAT) in one patient. These two methods were found to be the most useful investigations in localization of the abscess by McCann *et al* (11). The CAT scan is a non-invasive procedure and can be repeated. It may indicate the necessity for repeated aspiration or help in assessing the result of therapy. Carotid angiogram was used only on one patient.

Treatment and outcome: Therapy in cases of cerebral abscess is a combination of antimicrobial agents and surgical drainage. Intravenous penicillin and chloramphenicol were given as soon as the diagnosis was made together with phenytoin. Intravenous antimicrobials were continued for four weeks and subsequently for two weeks via the oral route. Therapy with phenytoin which was started together with the antimicrobials was continued for a year. The patients were also started on metronidazole but it was discontinued after 3 - 4 days in two patients, 8 - 9 days in another two and after 12 - 13 days in three patients.

Surgical aspiration of the pus by the twist drill method was performed on five patients, operative drainage in one and surgical excision in another. Four patients recovered completely without any neurologic deficit or seizures. There was one operative mortality and two deaths were probably due to the primary cardiac lesion.

TABLE 1
CLINICAL DATA OF 7 PATIENTS WITH BRAIN ABSCESS

Case No.	Age (yrs.) Sex	Presenting Symptoms	Presenting signs	Associated illness	Site of Abscess	Outcome
1.	37 F	(R) frontal headache 1 month. Nausea, vomiting & decreased visual acuity on (R) side 7 days	Febrile, lethargic, (L) hyper-reflexia with extensor plantars	Mitral stenosis with cyanotic heart disease	(R) Frontal lobe	Died
2.	12 M	Headache, fever, nausea & vomiting 7 days	Lethargic but rousable. (R) central 7th nerve paresis. (R) upper extremity weakness	Tetralogy of Fallot with cyanotic heart disease	(L) Temporal lobe	Complete recovery
3.	29 M	Headache, vomiting, confusion	Febrile, neck rigidity.	Involved in motor vehicle accident. (R) maxillary & parietal skull fractures. Open repair of maxilla via Caldwell-Luc incision	(R) Frontal lobe	Complete recovery
4.	14 F	Fever & rigors - 10 days Headache, lethargy, nausea & vomiting - 5 days	Febrile, obtunded, neck rigidity, (R) papilloedema, (R) extensor plantar	Severe cyanotic heart disease. Mute.	(R) Occipital lobe	Died
5.	17 M	Bifrontal headache, fever, nausea, vomiting 4 weeks. One major generalized seizure	Febrile. Both pupils dilated & fixed. Bilateral papilloedema with extensor plantars	Involved in motor vehicle accident 2 months ago. Was hospitalized and discharged well	(L) Frontal lobe	Died
6.	26 M	Headache & fever 2 weeks. Vomiting & coma 1 day p l a n	Febrile, obtunded (L) hyper-reflexia with extensor plantars	Initially diagnosed as meningitis. Lumbar punctures (3) performed. Treated with antibiotics	(R) Parieto-occipital lobe	Complete recovery
7.	16 M	Headache, fever 1 month	Febrile, lethargic but rousable. Bilateral papilloedema. Mild paresis upper extremity	—	(R) Frontal lobe	Complete recovery

TABLE 2
BACTERIA ISOLATED FROM INTRACRANIAL ABSCESSSES

Case	Smear for organisms	Causative organisms	Lancefield group
1	Gm + ve cocci	<i>Str. milleri</i>	G
	Gm - ve rods	Bacteroides species	
2	Gm + ve cocci	<i>Str. milleri</i>	ungroupable
3	Gm + ve cocci	<i>Str. milleri</i>	F
4	Gm + ve cocci	<i>Str. milleri</i>	ungroupable
5	Gm + ve cocci	<i>Str. milleri</i>	ungroupable
6	No organisms seen	<i>Str. milleri</i>	ungroupable
		Diphtheroids	
7	Gm + ve cocci	<i>Str. milleri</i>	F
		<i>H. influenzae</i> type b	

DISCUSSION

Brain abscess is a curable form of focal intracranial suppuration in the brain substance. The effects of an expanding mass lesion characteristically overshadow signs of infection unless the primary site is obvious. This has been clearly demonstrated by all our seven patients presenting with headaches but the presence of fever in all of them was an indication of infection.

The predominance of male patients in our study is in conformity with other published reports (2, 8). In one report (9) peak incidence was in the first two decades of life and four of our seven patients were in the second decade of life. But brain abscesses can occur through all ages and this is probably a reflection of the underlying predispositions. Carey *et al* (12) distinguished four aetiological groups of brain abscesses:

1. Haematogenous or metastatic abscesses in normal individuals
2. Haematogenous or metastatic abscesses in cyanotic patients having right-to-left shunts because of congenital heart disease or pulmonary A-V malformations
3. Abscesses secondary to sinus or mastoid infection
4. Abscesses consequent to trauma or osteomyelitis of the skull

Examples of category one, two and four can be found amongst the seven patients in our study group.

The bacterial flora of intracranial abscesses is usually complex consisting of a mixture of aerobes and obligate anaerobes. If meticulous attention is paid to microbiological technique, bacteria can be cultured from all abscesses on primary investigation contrary to some reports of pus from brain abscesses being sterile (13). Streptococci form the largest group of organisms to be isolated from abscesses of the central nervous system (13) and of these *Streptococcus milleri* heads the list of being the commonest.

Str. milleri is an invasive and pyogenic streptococcus and is characterised by an ability to cause large and usually solitary collection of pus in many different internal organs. It is widely distributed on the body being found in the oral cavity, the upper respiratory tract, the gut and the vagina (13).

The computerised axial tomographic equipment has revolutionised the method of confirming the diagnosis and accurately pinpointing the location of brain abscesses. It may also be used to monitor the progress of the patients and assess the therapeutic efficiency of current treatment.

Therapy is a combination of surgical drainage and antimicrobial agents. The method of twist drill aspiration is fairly simple compared to open surgical drainage. There is also less likelihood of soiling the operative area by the use of this method.

Penicillin penetrates the blood-brain barrier and is active against all streptococci, virtually all haemophilus species and some anaerobes as well. Chloramphenicol is concentrated in brain tissue, penetrates brain abscesses and is active against all anaerobes as well as aerobic streptococci, haemophilus species,

staphylococci as well as many Enterobacteriaceae (8). Antibiotic therapy should generally be prolonged for six to eight weeks even if excision has been performed.

Oral or intravenous administration of metronidazole results in high concentrations of the active agent in the pus of cerebral abscesses. But this agent is effective only against obligate anaerobes and both penicillin and chloramphenicol will act against most anaerobes and the addition of metronidazole to the regimen of penicillin and chloramphenicol may be questionable. The overall mortality of brain abscesses is about 50 percent, but it is 20 percent in patients treated with surgery and antibiotics (8). The numbers in our study are too small to be statistically significant with regard to mortality. Brain abscess is an emergency for both the neurosurgeon as well as the microbiologist. Therefore prompt diagnosis, surgical intervention, good microbiological techniques and vigorous antimicrobial therapy are the pillars of success in the treatment of this condition.

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