BACTERIAL INTRACRANIAL ANEURYSMS

by

A R Aspoas MBBCh, FCS (Neurosurgery)

Supervisor: Professor JC de Villiers FRCS

Professor and Head of Department of Neurosurgery

University of Cape Town

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"Bacterial intracranial aneurysm" is the term that should be used nowadays to describe "septic embolic" or "mycotic aneurysms". This is an important form of intracranial aneurysms since to date there has been no large series reported, but the clinical experience has revealed a type of aneurysm with a great propensity to rupture[31], an event previously reported to be associated with a high mortality[6,18,24].

Infected aneurysms were initially described by Virchow in 1847 and Koch in 1851[27], but the term "mycotic aneurysm" was first used by Sir William Osler in 1885 in his Gulstonian Lecture[25], when he describe a mycotic endarteritis resulting in aneurysm formation. To-day the term mycotic should be reserved for infected aneurysms caused by fungi, which is an extremely rare condition with only a total of fifteen reported in the literature[19].

In First World Countries with advances in health care and the increase in intravenous drug abuse[11,31] there has been a significant alteration in the clinical presentation of bacterial intracranial aneurysms. However in Third World Countries where rheumatic heart disease is still rife, the complications of bacterial endocarditis occur fairly frequently. Other rare causes of bacterial intracranial aneurysms are secondary to infection as with meningitis[14,30], otitis media[7], osteomyelitis[15], cavernous sinus thrombophlebitis[2,7,8,29] and skin abscess[6,8,27].

Malignant Endocarditis was the term Osler[25] used to describe the fungating valvular vegetations of bacterial

endocarditis, from which septic emboli (consisting of platelet aggregations and bacteria) are dislodged into the circulation. Dissemination to various parts of the body may occur for example the kidney, where they may present with haematuria; the spleen, causing multiple sub-capsular infarcts, the subcutaneous tissues where Osler's nodes may be formed. Rarely abscess formation may occur in the various organs[26].

The natural history of bacterial intracranial aneurysms is unknown, although 30% to 50% of patients with bacterial endocarditis present with neurological symptoms and signs[3,13,16,22,26], which include cerebral infarcts, haemorrhage, toxic encephalopathy, meningitis, headache and convulsions[16].

The patho-physiology of infected aneurysms has been studied in dogs, with fusiform aneurysms developing secondary to septic emboli lodging in the vasa vasora[23] of the aorta, resulting in intimal thickening and atrophy of the muscularis and elastic layers. The absence of the vasa vasora in the intracranial arteries requires a different pathogenesis to be postulated.

Septic emboli lodge in perforating vessels, totally occluding them thus causing a focal endarteritis which spreads to the Virchow-Robin spaces and there initially involve the adventitia of the parent vessel[20,28]. The infection spreads from without inwards resulting in weakening of the vessel wall and the formation of a false aneurysm. This mechanism is supported by the fact that

infected aneurysms have been documented in patients with meningitis (focal arteritis may result in saccular dilatation whilst circumferential arteritis results in fusiform dilatation[28]). Secondly, the intact intima is highly resistant to infection so that direct seeding onto the endothelium only occurs when the septic embolus occludes a parent vessel. The endarteritis results in the infection spreading from within outwards. When this weakened segment, proximal to the obstruction, is exposed to the normal pulse pressure the vessel may dilate.

Finally experimental evidence in dogs shows that septic emboli into the internal carotid artery result in rapid general clinical deterioration due to subdural and subarachnoid haematomas following rupture of aneurysms which formed within 48 hours of embolization[20]. Those dogs that were given penicillin immediately after the injection of the septic emboli had aneurysms present on day 7 or 8, but none had ruptured. Thus experimentally septic emboli cause an extremely rapid formation of aneurysms and with antibiotics there appears to be some protection from haemorrhage in the early stages of the disease process. What provides this protection? The bacteriocidal or bacteriostatic effect of the antibiotics enhances the acute inflammatory reaction resulting in less necrosis and a superior fibroblastic response.

Clinical Material(Appendix 1)

The study consists of a retrospective analysis of patients treated by the Department of Neurosurgery, Groote Schuur Hospital and the University of Cape Town over a 20 year period, from 1971 to 1990 inclusive. Information was retrieved from hospital records, the departmental discharge summaries, records of the department of Neuroradiology. One patient had no clinical records but the information was gained from the radiological notes and the operating theatre register. Over this period twenty five patients with bacterial intracranial aneurysms were treated by the department and these patients were drained from as far north as Northern Namibia and as far east as East London, a radius of about 2000 km; this resulted in two patients being partially treated for their bacterial endocarditis with intravenous antibiotics for a period of 2 and 4 weeks prior to being referred to the Department of Neurosurgery. (A summary of the patients treated is listed in Appendix 1).

TABLE 1:CLINICAL MATERIAL

Number of Patients		25
Age		11 to 67 years
Sex	males 13	females 12

Age (Table 1)

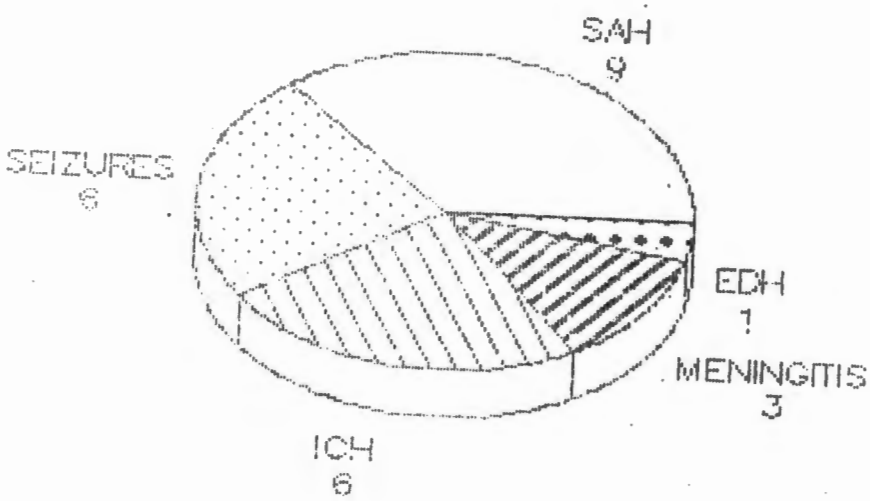
The average age of patients admitted to the department was 23.36 years with a range of 11 to 67 years.

Sex (Table 1)

The ratio of males to females were fairly evenly matched with 13 males to 12 females.

Presentation (Figure 1)

Figure 1 : Clinical Presentation



SAH-Subarachniod Haemorrhage; EDH-Extradural Haematoma; ICH-Intracerebral Haematoma.

The majority of patients presented with haemorrhage :- subarachnoid haemorrhage occurred in nine patients, intracerebral haemorrhage in six patients and extradural haematoma in one; thus sixteen out of twenty five or 64% of patients presented with haemorrhage. Of the remaining nine patients, six presented with seizures and three with meningitis.

TABLE 2:SOURCE OF INFECTED EMBOLI

Mitral valve	18
Mitral & aortic valves	2
Aorta	2
Aorta & Tricuspid	1
Coarctation of Aorta	1
Normal Heart (otitis media)	1

The Source of the Septic Emboli (Table 2)

Eighteen patients had mitral valve disease, two had aortic and mitral valve disease, one had aortic valve disease, one aortic and tricuspid valve disease, one patient had congenital coarctation of the aorta and one patient had a normal cardiovascular system, although on admission was

found to have bilateral chronic otitis media (a rare cause of infected aneurysms in an area where chronic ear sepsis is very common) . This distribution of the site of infection merely parallels the commoner sites of valvular damage with rheumatic heart disease[16].

TABLE 3:CARDIAC DISEASE.

Known prior to admission	9
Diagnosis on admission	11
Diagnosis on subsequent admission	3
Normal cardiovascular system	1
Unknown	1

It is well documented in the literature that the neurological presentation may be the first presentation of bacterial endocarditis[5,12,16,28]. Only nine of our patients were known to have rheumatic heart disease or bacterial endocarditis prior to admission. Ten patients had their cardiac pathology diagnosed on admission, and three patients had a positive diagnosis made on later admissions by positive blood cultures. These three patients were not treated with antibiotics but were operated on shortly after admission.

Organisms Culture

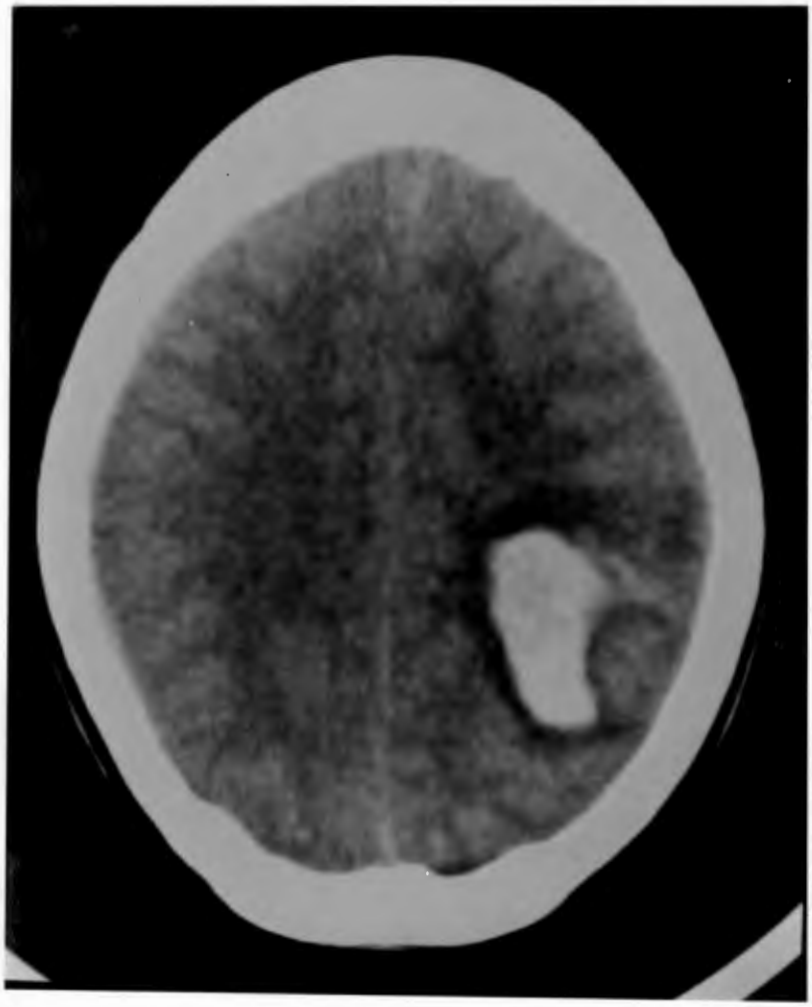
Blood cultures were performed on all patients admitted to Groote Schuur Hospital and only eleven positive cultures were obtained from those twenty five patients.

Eight of the cultures grew streptococci with three Streptococcus mitior, two alpha haemolytic Streptococcus, one group B Streptococcus, one group C Streptococcus and one Streptococcus mutans. The other bacteria were all staphylococci, one Staphylococcus albus and two Staphylococcus aureus.

Radiological Investigation

The Computer Tomographic(CT) Scanner was only introduced to the Department of Neuroradiology at Groote Schuur Hospital in 1977 and as a result of this, only eighteen patients had CT Scans as the first investigation with intravenous contrast used in four patients. The majority of scans revealed evidence of haemorrhage (as a result of which finding contrast was not used by the radiologist) with nine intracerebral haematomas(figure 2),

Fig. 2: Case 25 CT Scan(without contrast)- Left Parietal Intracerebral Haematoma



one subdural haematoma and one extradural haematoma (this extradural haematoma was found to be due to an infected aneurysm of the middle meningeal artery, proven angiographically and confirmed histologically). Three patients showed evidence of infarction and one patient showed an infarct with luxury perfusion(a term used by our radiologists to describe the radiological appearance of a low density infarct surrounded by an area of enhancement). Three patients had normal CT scans, only one of which was done with contrast enhancement. The new generation, high resolution CT scan has now become the initial investigation in patients with bacterial endocarditis who present with a neurological symptom.

Angiography was performed on only twenty four patients, since one patient died within 24 hours of admission before an angiogram could be performed. This patient had a postmortem which revealed a large subdural haematoma with an infected intracranial aneurysm of the middle cerebral artery. Of the twenty four patients who were subjected to angiography, one had a middle meningeal artery aneurysm, while twenty three patients had a total of twenty seven intracranial intradural aneurysms identified.

The distribution of these aneurysms were mainly in the more peripheral vessels. One patient had a distal anterior cerebral artery aneurysm. A second patient had two aneurysms, one involving the distal anterior cerebral artery and one middle cerebral artery aneurysm. The middle cerebral artery was the most common site for an

aneurysm[4,10,17,28,31] with fifteen patients having single aneurysms (figure 3) and two with double aneurysms of the middle cerebral artery(figure 4) and fifteen of all twenty one middle cerebral artery aneurysms occurred on the right side. One patient had a middle cerebral artery aneurysm and a basilar artery aneurysm and the remainder had single aneurysms of posterior communicating artery in two patients, one basilar and one distal posterior cerebral artery(figure 5). This gave us a result of 82.6% of patients having single aneurysms and 17.4% having multiple aneurysms.

Fig.3 : Case 21 Left Middle Cerebral artery Aneurysm

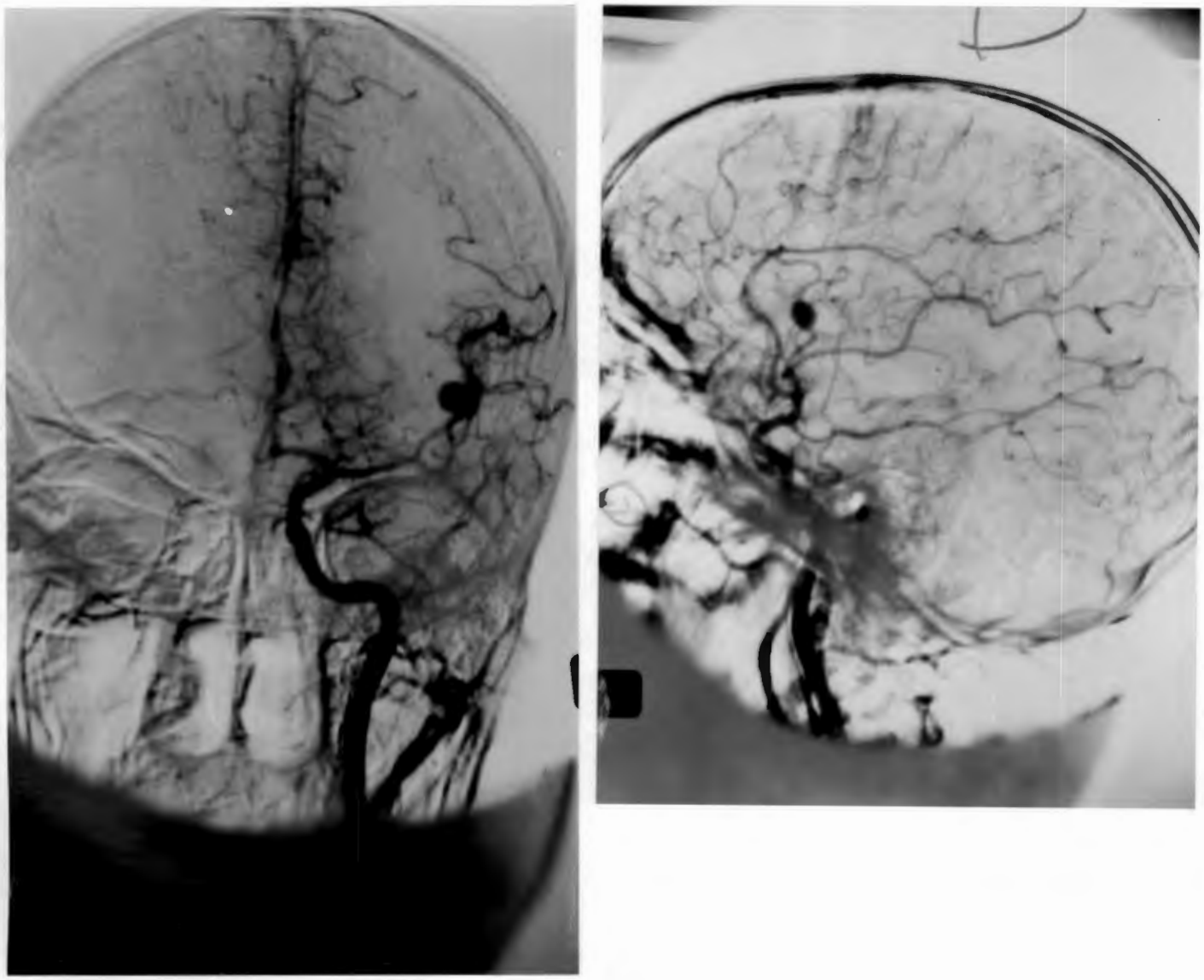


Fig. 4 : Case 25 Two Left Middle Cerebral Artery Aneurysms

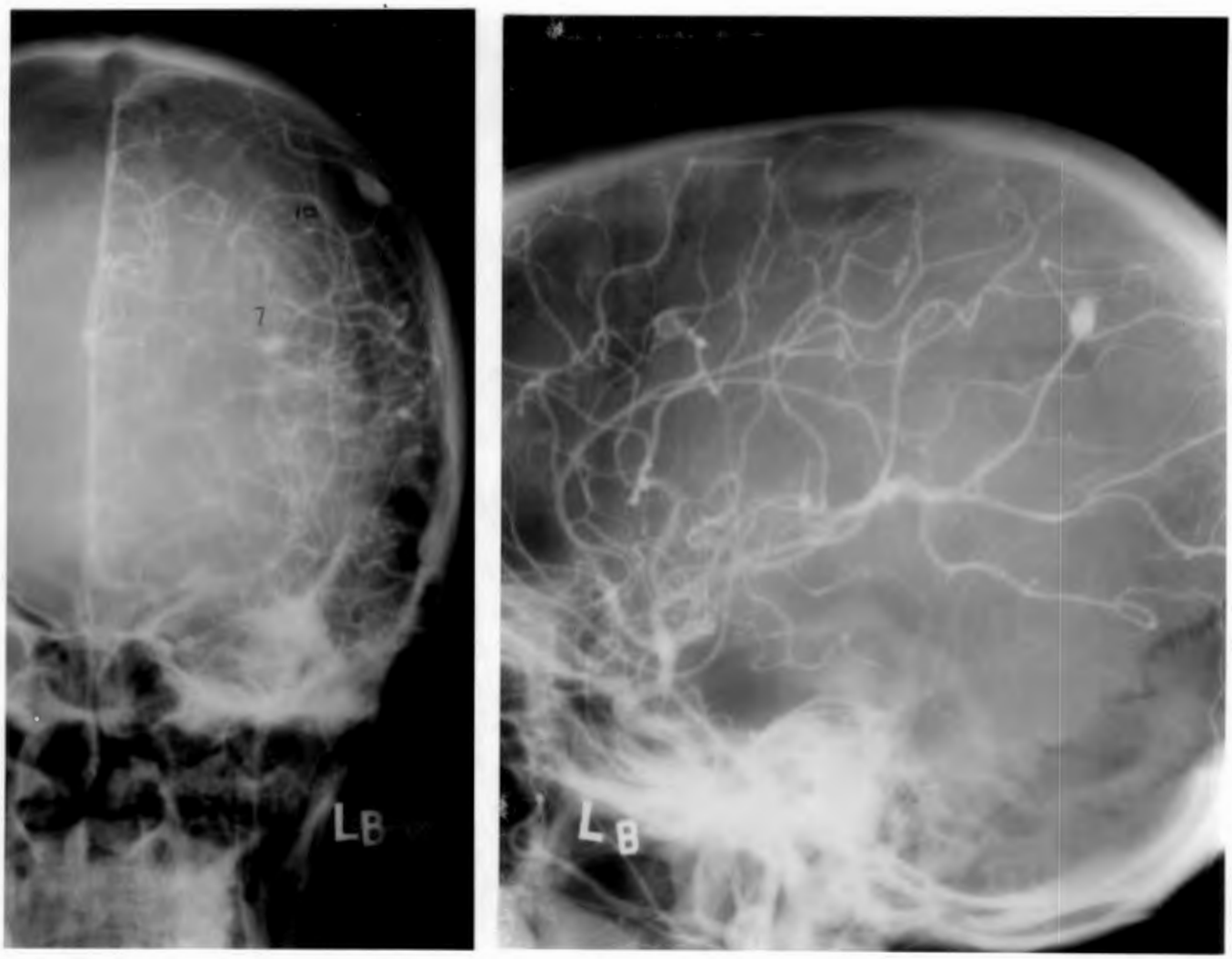
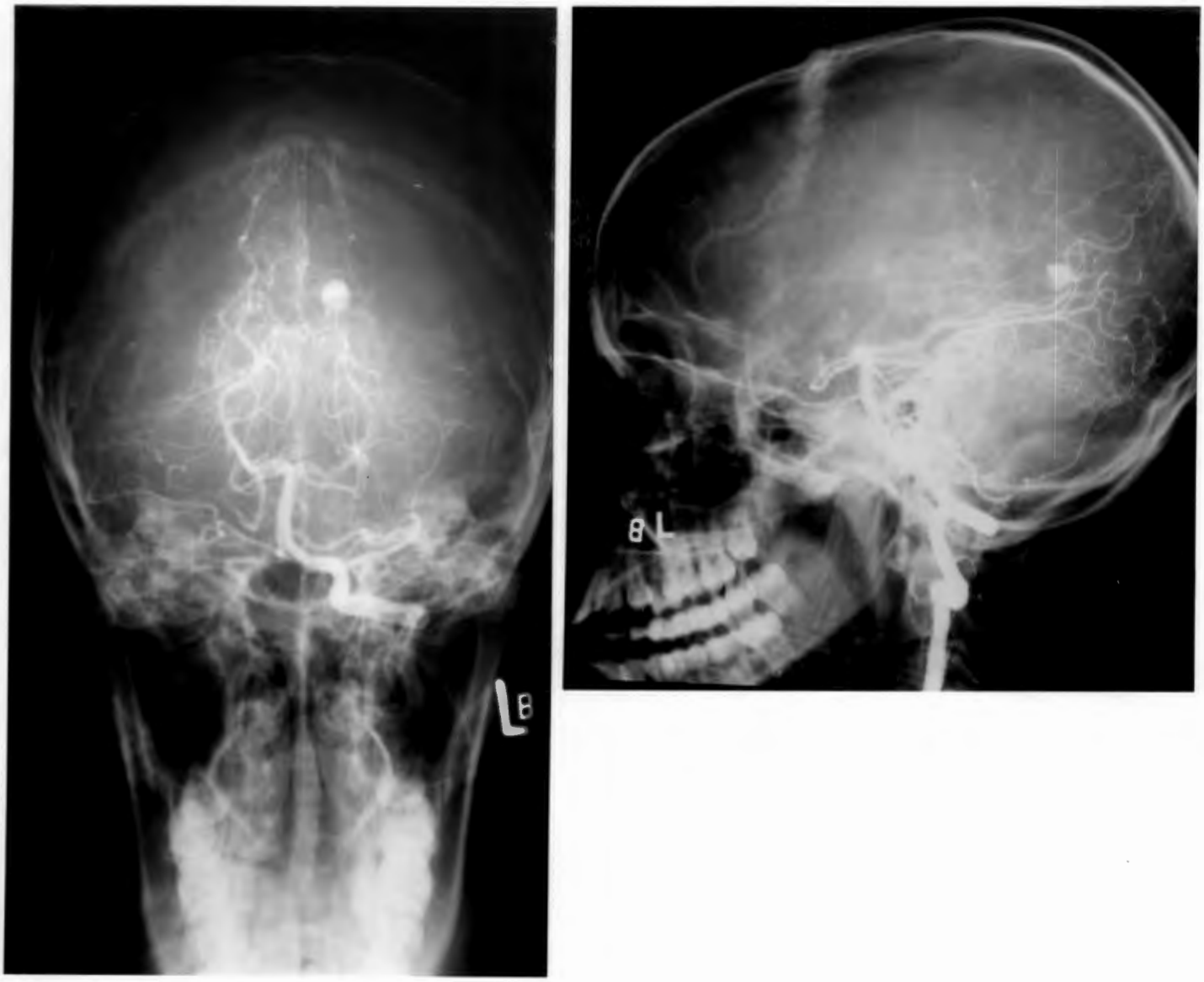


Fig. 5 : Case 24 Distal Left Posterior Cerebral Artery Aneurysm



Repeat angiography

Authors[6,10,22] have suggested that angiography should be repeated due to the dynamic pathology of the bacterial intracranial aneurysms. In our study thirteen repeat angiograms were performed i.e. a repeat angiogram rate of 56.5% and these thirteen patients had a total of seventeen aneurysms.

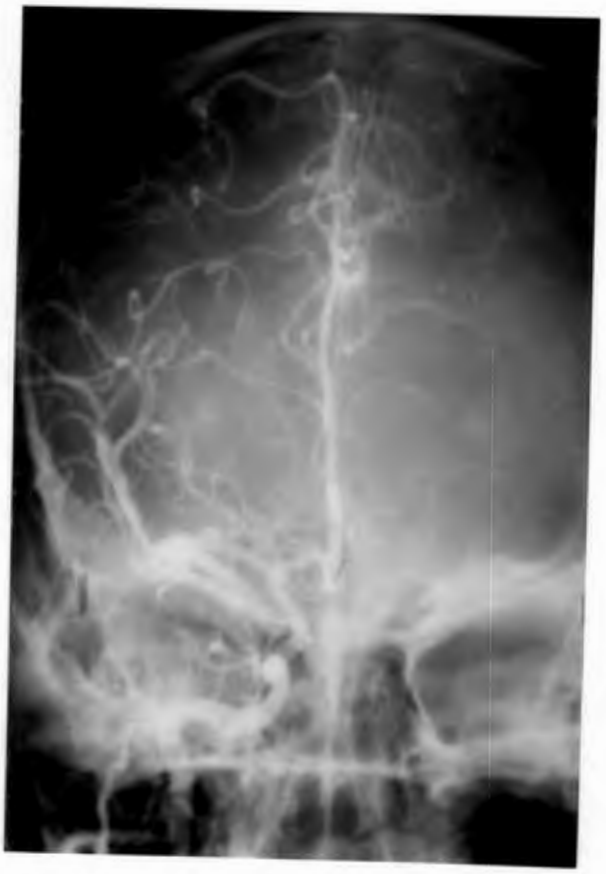
The results of these seventeen aneurysms

Eight increased in size, the most significant finding was three enlarged within two weeks (figure 6) and the remainder within 12 weeks. The aneurysm size was unchanged in five instances. One aneurysm decreased in size and three aneurysms disappeared entirely. The timing of the repeat study varied from two weeks to twelve weeks, with the initial angiogram done soon after admission. Just less than half of the patients whose aneurysms enlarged, increased within a 2-week period

Fig. 6 : Case 18 Right Middle Cerebral Artery Aneurysm

a) Angiogram-29/03/85 aneurysm with associated spasm.

b) Repeat Angiogram-16/04/85 Enlarging Aneurysm and absence of spasm



(The above case illustrates an increase in the size of the aneurysm; for the vasospasm to affect the size of the aneurysm by dropping the pressure in the aneurysm it could theoretically also cause an ischaemic neurological deficit which was, however, not present.)

Management

The patients were treated with a full course of antibiotics for six weeks. The patients were treated with various antibiotic regimes as advised by the cardiologists and the bacteriologists, and included: penicillin, chloramphenicol, erythromycin, aminoglycosides, cloxicillin and fusidin. (Alpha haemolytic Streptococci - penicillin & chloramphenicol; Streptococcus mitior - erythromycin, penicillin and gentamycin, penicillin and vancomycin; Streptococcus group B & C and mutans - penicillin; Staphylococus albus - penicillin & gentamycin and cloxicillin & fusidin.)

Surgery

If aneurysms were present after a full six weeks of antibiotic therapy or if the aneurysms were increasing in size then the patients were operated on. Out of the total study of twenty five patients, one patient died prior to angiography, while in three patients the aneurysms disappeared on medical therapy. Twenty one patients were operated on. One of these had a craniotomy with drainage of an extradural haematoma and excision of middle meningeal artery aneurysm. The remaining twenty patients had a total of twenty three aneurysms. The most common surgical procedure was clipping of the aneurysms (seven patients),

followed by excision of aneurysm (five patients), wrapping of aneurysm (four patients), trapping (two patients), wrapping and clipping (one patient). In one patient the aneurysm could not be found despite two craniotomies, and repeat angiography following the first operation which demonstrated the aneurysm still to be present. In the wrapping procedures muslin gauze was used, with particular care taken to ensure that the parent vessel and aneurysm were completely surrounded by the gauze.

Multiple aneurysms posed a particular problem. In two patients the aneurysms could be approached through a single craniotomy whilst in one patient two craniotomies were performed three months apart, with a pre-operative angiogram showing enlargement of the second aneurysm prior to the second procedure. In the final case with multiple aneurysms one disappeared and one increased in size requiring surgery.

Intra-operative angiography has a valuable roll in the anatomical localisation of the aneurysm which is usually on the distal branches of the parent vessel, often in the depths of a sulcus. In one patient(no.6) the superficial temporal artery was catherised at the beginning of the procedure so that a retrograde carotid angiogram could be performed as a mode of intra-operative localisation.

Outcome

The outcome of this group of patients includes the surgically and the medically treated patients is indicated in Table 4.

TABLE 4:OUTCOME of Twenty five Patients.

Normal	14
Died	1
Neurological deficit	9
Unknown	1

From this study the lowest mortality is 4% but if the unknown patient is presumed dead and added to this group there is a 8% mortality, and a 36% morbidity while 56% had a normal outcome.

TABLE 5:NEUROLOGICAL DEFICIT

On Admission		On Discharge	
Hemiplegia	4	Hemiplegia	4
Hemiplegia	1	Monoplegia	1
Dysphasia	1	Dysphasia	3
Third Nerve Palsy	2	Third Nerve Palsy	1

The neurological deficit consisted of hemiplegia in four patients and interestingly enough, in three of the four patients the aneurysms disappeared on conservative treatment. The fourth patient presented with a hemiplegia but an aneurysm was not found at surgery. Thrombosis of the aneurysm must have extended into the lumen of the parent vessel to account for this disappearance as well as the neurological deficit. One monoplegia occurred in a patient who had presented with a hemiplegia. One third nerve palsy due to a basilar artery aneurysm persisted. One preoperative third nerve palsy in the patient with the extradural haematoma resolved postoperatively. Three patients developed dysphasia (two postoperative complications, one lasting only 24 hours, one commencing 48 hours post-operatively but improving after two months and the permanent dysphasia was a deficit present on admission).

Discussion

The true incidence of bacterial intracranial aneurysms is unknown[2], but 2-10% of patients with endocarditis develop aneurysms[4,13,18,27] and 1.5-30% of intracranial aneurysms are of infective origin[6,7,18,22,28].

In view of the great geographic distances between the Department of Neurosurgery and some of the referring hospitals combined with the reluctance of some physicians to investigate young patients with a stroke, there is clearly a "pre-selection" of patients admitted and treated by us(only 19 of the patients treated were from the greater Cape Town area). The average age of these patients treated by our department is younger than those documented in the literature[2,23,26] and this is probably related to the young age at which rheumatic heart disease occurs in this country. The presentation is similar to that of patients reported in the literature and that is subarachnoid haemorrhage, a seizure or a sudden onset of a neurological deficit[2,10]. Although bacterial culture was attempted the yield was very poor due to the fact that patients were treated on intravenous antibiotics at their referring hospitals prior to admission to our department, secondly the rather liberal use of antibiotics in the community[20] and thirdly, the inadequate anaerobic culture technique. Interestingly intravenous drug addicts have multiple exposures to multiple organisms and a variety of bacteria may , therefore be cultured[11]. (An important word of caution, this group of patient may well be HIV positive)[9].

Angiography is important in bacterial intracranial aneurysms for two reasons:

Firstly as with any aneurysms it shows the site of the aneurysm, the morphology of the neck and fundus, and the number of aneurysms.

Secondly certain angiographic pointers towards the bacterial origin of the aneurysms may be present namely :

i) distal aneurysms[4,17,28](figure 3,4&5), in one reported series all 19 aneurysms were distal to the first major bifurcation[10].

ii) multiple aneurysms[6,10,16](figure 4), in a review of the English literature in 1977 nine of thirty nine patients were found to have multiple aneurysms[1].

iii) most commonly saccular in shape in the distal vessels and fusiform in proximal vessels(with only two out of five being described as fusiform, one proximal to the middle cerebral bifurcation and one distal)[28].

Multiple aneurysms are not synonymous with bacterial aneurysms since 15% of congenital Berry aneurysms are multiple but these are more proximal, saccular in shape and often "mirror image" aneurysms.

Angiography in our series revealed a far fewer patients

with multiple aneurysms than have been reported by other studies and this may well be related to the underlying pathology. In South Africa one deals mainly with rheumatic heart disease and subacute bacterial endocarditis as the cause of bacterial aneurysms. Rheumatic heart disease has not disappeared from the scene in first world countries, in fact, a study by the British Cardiological Society revealed that 43% of patients in the United Kingdom treated for bacterial endocarditis had "normal hearts or previously unrecognized cardiac abnormality"[21]. In first world countries bacterial infected aneurysms are becoming more and more frequent amongst intravenous drug abusers. Proximally situated aneurysms can not be excluded from the diagnosis of infective origin as two of our posterior communicating artery aneurysms and one terminal basilar aneurysms all had clinical evidence of valvular disease with proven endocarditis. One posterior communicating artery aneurysm disappeared on repeat angiography, whilst the other two required surgery).

The middle cerebral artery dominance is due to the fact that the middle cerebral artery is the larger and more direct terminal branch of the internal carotid artery.

The role for repeat angiography

In view of the fact that this is a dynamic disease[2,22] where aneurysms may shrink and even disappear repeat angiography is called for. New aneurysms may develop on treatment, since poor antibiotic penetration of avascular heart valves results in repeated embolization of septic particles well after the commencement of antibiotic therapy. Therefore angiograms should be repeated to indicate the exact natural history of the aneurysms being treated. The timing of the repeat angiogram is debatable. Experimental evidence shows that rapid development of aneurysms is retarded with antibiotics[20]. Our study demonstrates that almost half the aneurysms enlarge within two weeks. Patients should, therefore have angiography repeated every 14 days until the six weeks of antibiotics have been completed.

Surgical Procedures

With any saccular aneurysm the ideal surgical procedure is to isolate the aneurysm completely from the intracranial circulation to prevent recurrent haemorrhage. This may, however be difficult if one is dealing with a false aneurysm and in such circumstances it is easier to trap the aneurysm, but bearing in mind total occlusion of even a small vessel in an eloquent area will result in a post operative neurological deficit.

Some authors advise that in proximal aneurysms surgery should be delayed while early surgery is recommended for distal ones[28]. In this series the policy for both proximal and distal aneurysms has been delayed surgery if there was no aneurysm enlargement for the following reasons :

If one looks at the dynamic pathology in the development of bacterial aneurysm[27], there is destruction of the vessel wall with acute inflammatory reaction in the early stages which then progresses to healing by fibrosis with thickening of the wall with the passage of time[27].

Early surgery is fraught with the hazards of trying to clip a false aneurysm which is formed by fibrinous/reticulin fibres. Under these circumstances the aneurysm will not readily allow the application of a clip so that it must rather be trapped. Elective delayed surgery after a full course of antibiotics has the best outcome[2].

In patients with multiple aneurysms each lesion must be dealt with on its own merits; if accessible through a single craniotomy then they should all be dealt with however if this is not possible then staged procedures should be timed according to the growth of the individual aneurysms.

The outcome of patients in this series is slightly different to those reported[1,6] by others. Of the patients treated medically three out of four aneurysms disappeared but were associated with a persistent neurological deficit. The mortality from the first haemorrhage has been described as high as 60%[1,2]. In this study only one patient is known

to have died from the initial haemorrhage and no recurrent haemorrhage occurred.

The lower mortality rate may well be due to the patients not being admitted to hospital in rural communities, and the nature of intracranial pathology not being recognized in patients who demise prior to transfer to this department.

There are certain special problems that may occur with bacterial intracranial aneurysms such as rupture of an aneurysm in a patient with severe cardiac failure. Under such circumstances any neurosurgical procedure can only follow valvular replacement surgery[3]. The risk of intracranial haemorrhage from anticoagulation for extracorporeal circulation is high. The risk of rupture of an infective intracranial aneurysm after any surgery is at its highest at about two weeks post operatively when the antifibrinolytic activity is at its greatest [3].

IN CONCLUSION

i) Any patient known to have rheumatic heart disease who presents with seizures, subarachnoid haemorrhage, neurological deficit or meningitis should be investigated for bacterial intracranial aneurysm[9,28,32].

ii) Any patient who presents with a proximal fusiform or peripheral aneurysm must be investigated for bacterial endocarditis or intravenous drug abuse.

iii) Blood cultures must be done and the appropriate antibiotic therapy commenced.

iv) Urgent angiography for baseline assessment is essential.

v) Repeat angiography at 14 day intervals is mandatory unless the patients neurological status deteriorates.

vi) Surgery is performed electively after six weeks of antibiotic therapy if the aneurysms are still present on repeat angiography

OR

urgent surgery is indicated if repeat angiography shows enlargement of the aneurysms.

vii) Clipping of the aneurysm is the procedure of choice.

viii) Cardiovascular surgery is only to precede neurosurgical intervention if progressive cardiac failure due to valve damage[3] occurs.

ix) Finally, a prospective study should be done to assess the true incidence of bacterial intracranial aneurysms in bacterial endocarditis.

ARA August 1990.

APPENDIX 1

BACTERIAL INTRACRANIAL ANEURYSMS (DEPARTMENT OF NEUROSURGERY GSH AND UCT)

CASE	AGE	SEX	PRESENTATION	SOURCE	ORGANISM
1 CF	30	M	Seizures	M	Str a haem
2 TN	18	M	SAH	M	---
3 GJ	13	F	ICH	M	---
4 PO	14	M	Meningitis	A&T	St albus
5 AO	32	M	SAH	A	Str a haem
6 NS	47	F	Seizures	M	---
7 JB	17	F	SAH	M	Str b
8 EK	16	F	SAH	M	---
9 AA	67	F	SAH	M	St aureus
10 MB	20	F	EDH	EAR	---
11 JH	11	M	Seizures	M	Str group c
12 AP	33	F	SAH	M	---
13 SO	23	F	ICH	M	Str mitior
14 MT	7	M	Meningitis	Coarct	---
15 BN	20	M	ICH	M	---
16 CA	15	F	SAH	M	---
17 CK	15	M	ICH	M	---
18 SJ	18	F	Meningitis	M	Str mutans
19 MM	45	M	ICH	M	---
20 GC	22	M	Seizures	A	St aureus
21 LF	18	M	ICH	A&M	---
22 SP	13	M	Seizures	M	---
23 BB	27	F	Seizures	M	Str mitior
24 MM	21	M	SAH	A&M	---
25 GC	22	F	SAH	M	Str mitior

ICH-Intracerebral Haemorrhage; SAH-Subarachnoid Haemorrhage; EDH-Extradural Haemorrhage; M-Mitral Valve; A-Aortic Valve; Coarct-Coarctation of the Aorta.

APPENDIX 1

CASE		ANGIO	REPEAT ANGIO	SURGERY	OUTCOME
1	CF	ACA	Nil	Nil	Hemiplegia & Dysphasia
2	TN	MCA	Increase	Wrap	Normal
3	GJ	MCA	Increase	Wrap	Unknown
4	PO	MCA	Nil	Excised	Monoplegia
5	AO	MCA	Unchanged	Wrap	Normal
6	NS	MCA	Increase	Trap	Normal
7	JB	ACA&MCA	Increase	Clip	Normal
8	EK	MCA&BA	Unchanged	Clip	IIIrd Palsy
9	AA	PCoA	Nil	Clip	Normal
10	MB	MMA	Nil	Excised	Normal
11	JH	MCA	Disappear	Nil	Normal
12	AP	MCA	Nil	Clip	Normal
13	SO	MCA	Nil	Excised	Normal
14	MT	MCA	Nil	Clip	Normal
15	BN	MCA	Increase	Excised	Dysphasia
16	CA	MCA	Nil	Excised	Normal
17	CK	MCA&MCA	Increase	Not Found	Hemiplegia
18	SJ	MCA	Increase	Wrap	Normal
19	MM	MCA	Disappear	Nil	Hemiplegia
20	GC	MCA	Nil	Clip & wrap	Normal
21	LF	MCA	Nil	Clip	Dysphagia
22	SP	-	-	-	Died
23	BB	PCoA	Disappear	Nil	Hemiplegia
24	MM	PCA	Nil	Trap	Normal
25	GC	MCA&MCA	Unchange	Clip	Dysphasia

ACA-Anterior Cerebral Artery; MCA-Middle Cerebral Artery; PCA-Posterior Cerebral Artery; PCoA-Posterior Communicating Artery; MMA-Middle Meningeal Artery; BA-Basilar Artery. ANGIO-Angiogram

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