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Author(s)	高橋, 睦正; Killeffer, Fred; Wilson, Gabriel
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特別掲載

Cerebral Mycotic Aneurysms<sup>1)</sup>

Mutsumasa Takahashi<sup>2)</sup>, Fred Killeffer<sup>3)</sup> and Gabriel Wilson<sup>4)</sup>

<sup>1)</sup> From the Department of Radiology and Neurosurgery, UCLA School of Medicine, Los Angeles, California 90024 and the Department of Radiology, Kyushu University School of Medicine, Fukuoka, Japan.

<sup>2)</sup> Acting Assistant Professor of Radiology; currently Instructor at Kyushu University School of Medicine, Fukuoka, Japan.

<sup>3)</sup> Assistant Professor in Residence, Division of Neurosurgery; currently at Veterans Administration Hospital, Los Angeles, California.

<sup>4)</sup> Assistant Professor of Radiology and Chief, Neuroradiology, Department of Radiology.

細菌性脳動脈瘤

九州大学医学部放射線科学教室

高橋 陸 正

UCLA医学部脳外科学教室

Fred Killeffer

UCLA医学部放射線科学教室

Gabriel Wilson

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細菌性脳動脈瘤は比較的稀な疾患であるが、われわれが経験した4例と過去10カ年間に英文文献に報告された19例の合計23例について臨床的、神経放射線学的検討を行なった。脳動脈瘤が、全身

性感染症、心雑音、脾腫、血尿、出血斑を伴っている場合には、まず、細菌性脳動脈瘤を考慮すべきである。さらに、脳血管造影による経過観察、早期の外科的摘出の利点を強調した。

The term mycotic aneurysm refers to aneurysms caused by an invading organism which has an origin inside or outside the vessel wall. Such aneurysms were first described by Osler (10) in 1885 who coined the term in focussing attention on their inflammatory nature. Eppinger (3) considered these lesions to be the result of infected emboli lodging in the vessel wall with resultant weakening and bulging of the vessel.

Mycotic aneurysms occur most frequently with acute or subacute bacterial endocarditis, and involve bifurcations of the major arterial branches and small peripheral arteries. Intracranial arteries are involved in a high percentage of cases, preceded only by involvement of the aorta and abdominal branches such as the superior mesenteric and celiac arteries. In 1923 Stengel and Wolferth (14) collected 217 cases of mycotic aneurysms from the world literature and 42 (19.4%) had intracranial aneurysms. Schnider and Cotisona (13) reviewed the literature from 1923 to 1954 and found 17 cases of subarachnoid hemorrhage in 69 mycotic aneurysms of all varieties (24.6%). Although the incidence of intracranial aneurysms and subarachnoid hemorrhage is relatively low in patients with

bacterial endocarditis, 33 of 116 patients (28.4%) presented neurologic difficulties in association with bacterial endocarditis (4) in spite of treatment with effective antibiotics.

The purpose of this paper is to review cerebral mycotic aneurysms in the English literature in order to emphasize the importance of making the early diagnosis of a mycotic aneurysm on the basis of clinical and radiologic findings, and to report on 4 additional cases.

#### Review of the Literature

In the English literature of the last 10 years, we have selected 19 cases with mycotic aneurysms which had detailed clinical and radiologic descriptions (1, 2, 5, 8, 9, 11, 12). Four cases of our own were added. Thus 23 cases with mycotic aneurysms form the basis of this review. One patient had two episodes of subarachnoid hemorrhages.

Sex and Age: There were 12 males and 11 females. Table 1 gives the age incidence by decades. Although spread over all decades through the 7th, the highest incidence was noted in the 5th decade. The youngest patient was 4 years of age and the oldest 67 years of age. It has been reported that the majority occur before the age of 40 when all locations are considered (13, 14). It is interesting to note that cerebral mycotic aneurysms more frequently occur between the ages of 40 and 50.

Table 1. Age by Decades

0—9	3
10—19	3
20—29	3
30—39	3
40—49	8
50—59	2
60—69	1
Total	23

Table 2. Underlying Disease

1. Rheumatic heart disease	17
2. Congenital heart disease	5
3. Otitis media	1
Total	23

Underlying Disease: Acute or subacute bacterial endocarditis was present in all but one patient. Rheumatic heart disease was the most common underlying cardiac condition, being present in 17 patients. Congenital heart disease was implicated in 5 patients. The remaining patient developed a mycotic aneurysm following meningitis secondary to otitis media (Table 2).

Rupture of mycotic aneurysms occurred prior to diagnosis of their cardiac disease in 6 of 22 patients with endocarditis, although heart murmur was heard in most patients. In the remaining 16 patients a diagnosis of endocarditis had been made before neurological symptoms appeared.

Causative Organism: Organisms were demonstrated on blood culture or in the resected aneurysms in 21 patients (Table 3). Histologic examination of the resected specimen showed an inflammatory process in the wall of the aneurysm. In one patient the diagnosis of mycotic aneurysm was made

Table 3. Bacteriological Findings

1. Streptococcus	12
2. Staphylococcus	3
3. Enterococcus	2
4. Pneumococcus	1
5. Micrococcus	1
6. Unknown type	2
7. Negative	2
Total	23

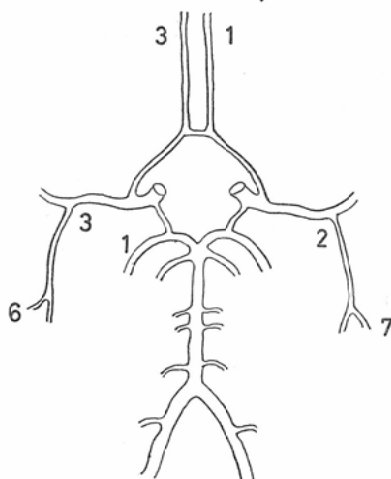
Table 4. Presenting Neurologic Symptoms

	Primary	Associated
1. Focal lesions	5	9
2. Meningitis and meningoencephalitis	1	0
3. Impairment of consciousness	7	3
4. Mental symptoms	2	0
5. Headaches	7	0
6. Seizures	1	2
7. Others	1	0
Total	24	14

on microscopic examination of the resected specimen alone. When the various organisms causing endocarditis were taken into consideration (6, 15), there was no single organism which produced cerebral mycotic aneurysms in a higher frequency.

Clinical Findings: Neurological symptoms were the presenting feature in 20 patients at the time of admission, while general symptoms of infection were the primary reason for admission in 3 patients. Primary and associated neurologic symptoms are tabulated in Table 4. Most common symptoms were severe headaches, impairment of consciousness and focal neurologic signs and symptoms.

Fig. 1. Schematic diagram showing sites of mycotic aneurysms in 22 patients. The case with 4 aneurysms was not included.



**Radiologic Findings:** Mycotic aneurysms were usually demonstrated in the small peripheral branches or at the bifurcations of the cerebral arteries. Five of 23 aneurysms involved the bifurcation of the middle cerebral artery. In 13 patients peripheral branches of the middle cerebral artery was involved, while involvement of the peripheral anterior cerebral artery was observed in 4 patients. (Fig. 1).

The infection of the artery was circumferential. Approximately half of the mycotic aneurysms showed fusiform dilatation of an arterial segment, but the remaining aneurysms were saclike in appearance. In general aneurysms below 6 mm in diameter were fusiform while larger aneurysms were sac-like.

In 21 patients there was a single aneurysm, 2 patients had multiple aneurysms. One patient had 4 fusiform dilatations in peripheral branches of the anterior cerebral artery and in the other patient saccular aneurysms were noted on the right posterior communicating and posterior cerebral arteries (9).

Intracranial hematomas were demonstrated angiographically in 6 patients.

**Treatment:** Surgical intervention was attempted on 10 patients and in 8 there were good surgical results with improvement of neurologic deficits. Conservative therapy with antibiotics was the sole treatment in the remaining 13 patients, and 4 survived.

#### Case Reports

**Case 1:** A 52-year-old male was in good health until approximately four weeks prior to admission when he started having intermittent headaches, alterations in behavior and occasional confusion. He also had occasional chills and fever. Two weeks prior to admission he had an episode of severe back pain which required him to remain in bed for five days. Two days prior to admission he had an acute onset of severe headache which persisted in spite of mild analgesics. He was taken to another hospital where a lumbar puncture was performed. Opening pressure was 120 mm H<sub>2</sub>O. The fluid was cloudy. There were 950 cells/mm of which 85% were polymorphonuclear neutrophils. No organisms were seen on gram stain or on culture of the fluid. Sugar was 40 mg per cent. At this time the patient was conscious and able to give a history of his present illness. Several hours after the lumbar puncture the patient had a generalized seizure and became comatose. He was transferred to UCLA the following day.

**Physical Examination:** The patient was deeply comatose, responding to sharp pain with decerebrate movements. The pupils were equal, 2–3 mm in diameter and reactive. He moved the left extremity less well than the right when an endotracheal tube was being placed. Examination of the fundi revealed mild blurring of the disc and two small hemorrhages in the right fundus. The deep tendon reflexes were 3+ on the left and 2+ on the right throughout. Both plantar responses were extensor. There was no nuchal rigidity, splenomegaly, or petechiae. There was a grade II/IV cardiac murmur at the apex.

**Hospital Course:** An echoencephalogram was done immediately which revealed a shift toward the left side. A lumbar puncture revealed an opening pressure of 430 mm H<sub>2</sub>O and grossly bloody fluid, the supernatant of which was xanthochromic. An emergency bilateral carotid arteriogram was performed which revealed an aneurysm arising from a branch of the right middle cerebral artery ap-

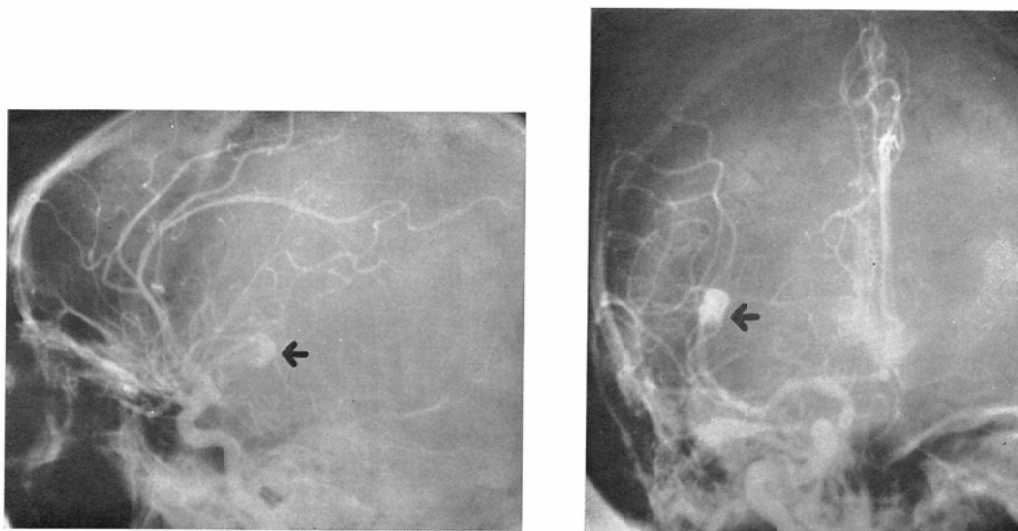


Fig. 2. A and B. Case I. Right carotid angiogram in lateral and frontal projections showing a 1.0 cm aneurysm at a branch of the middle cerebral artery. There is stretching of the anterior cerebral artery and midline shift to the left which indicate intracerebral and intraventricular hemorrhage.

proximately 1 cm beyond the trifurcation (Fig. 2 A & B). The aneurysm appeared approximately 10 mm in size. There was evidence of moderate ventricular dilatation bilaterally with a shift of the midline structures of approximately 6 mm from right to left. Both posterior cerebral arteries were displaced downward. Multiple blood cultures were obtained, several of which grew *Streptococcus viridans*. The patient ran a febrile course and it was felt that he was probably discharging emboli from a cardiac focus. The peripheral blood smear revealed a white blood count of  $23,000/\text{mm}^3$  with a considerable shift toward the left. He was maintained on large doses of intravenous penicillin as well as other supportive measures. His general condition progressively deteriorated and he expired 5 days following admission.

**Autopsy Findings:** An autopsy limited to the brain revealed a large intracerebral and intraventricular hemorrhage.

An aneurysm was identified in the distribution of the middle cerebral artery which had the histologic features of a mycotic aneurysm.

**Case II:** A 28-year-old male was well until approximately 8 days prior to admission, when he developed sudden onset of shaking chills and a fever of  $102^\circ\text{F}$ , with associated myalgia and vomiting. The symptoms responded to a 5 day course of tetracycline, but recurred with development of anorexia. He denied edema, chest pain, shortness of breath or dyspnea. Significant past history revealed an asymptomatic ejection murmur documented since 4 years of age and a 2 week episode of "strep" throat and malaise at 12 years.

**Physical Examination:** The patient was a well developed, thin, moderately ill-appearing male in no acute distress. Funduscopic examination was normal. There was a grade III/IV systolic ejection murmur, heard loudest in the 3rd and 4th intercostal space 2 or 3 cm to the left of the sternal border.

Neurologic examination was within normal limits.

**Hospital Course:** The patient was febrile with temperatures varying between 102° and 103°F. Penicillin-Streptomycin therapy was started which resulted in symptomatic improvement but intermittent spiking fever continued. For the last 10 days of his illness, Kanamycin was tried with good suppression of febrile episodes. Despite numerous blood cultures, no organism could be recovered. In spite of a subjective feeling of well being, the patient continued to have conjunctival petechiae, slight splenomegaly, anemia and thrombocytopenia. Six days prior to his death, he developed confusion, lethargy and marked personality change, without other neurologic deficits. These mental signs fluctuated over the next five days at which time he suddenly became opisthotonic, incontinent, and his respiration became stertorous. His head and eyes were deviated to the left and the left pupil was dilated and fixed. Funduscopic examination revealed unilateral papilledema on the left with a small hemorrhage. The neck was moderately stiff.

Bilateral carotid angiography was performed which demonstrated an 0.7 cm aneurysm of a branch of the ascending fronto-parietal branch of the left middle cerebral artery within the Sylvian fissure (Fig. 3 A & B). The Sylvian triangle was depressed and the opercular branches were

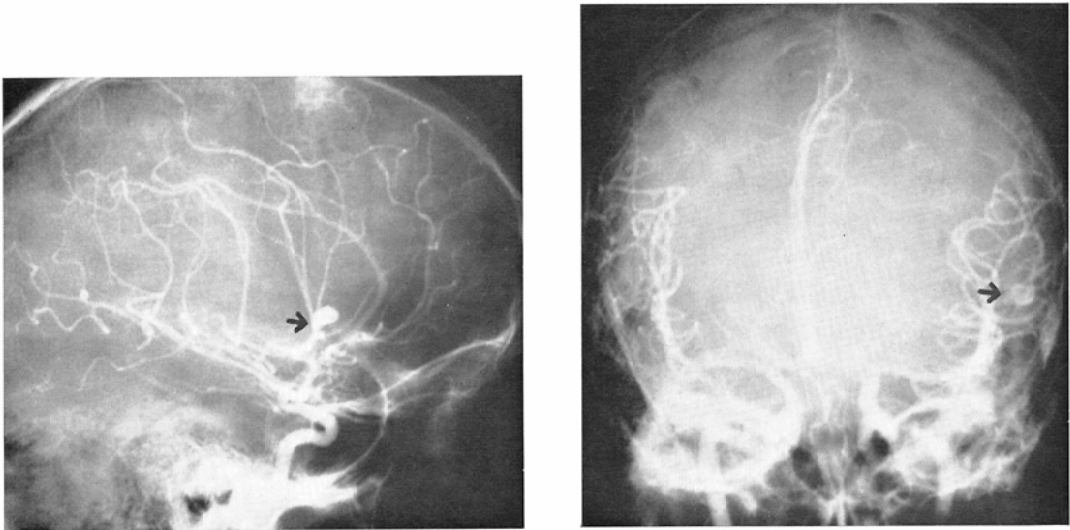


Fig. 3. A and B. Case II. Left carotid angiogram in lateral and frontal projections, demonstrating a 0.7 cm saccular aneurysm of a branch of the ascending frontoparietal branch of the left middle cerebral artery. The middle cerebral arteries are depressed and opercular branches are stretched, indicating intracerebral hematoma. There is moderate midline shift to the right.

stretched. There was a moderate midline shift from left to right. It was thought that the patient had an intracerebral hemorrhage secondary to a ruptured mycotic aneurysm. He remained comatose and expired in spite of intensive medical treatment.

**Autopsy Findings:** There was subacute bacterial endocarditis involving the mitral valve, from the verrucae of which a *Streptococcus viridans* was cultured. A mycotic aneurysm of the left middle cerebral artery was present. There was associated focal malacia and gliosis as well as massive in-

traventricular hemorrhage. The aneurysm had the histologic features of a mycotic aneurysm.

Case III: A 47-year-old male was admitted to UCLA Hospital for the third time because of fever and mental confusion. Six weeks prior to the present admission the patient developed chills and a fever of 103°F with malaise, headache, myalgia and vomiting. His two previous admissions to UCLA Hospital had included complete work-ups, but no underlying disease had been found. Physical examination at that time had been essentially normal with the exception of a temperature of 102.8°F. Complete blood count, sedimentation rate, urinalysis, chest X-ray, repeated blood cultures, and febrile agglutinins were all within normal limits. Cerebrospinal fluid examination was normal. Electrocardiogram revealed premature ventricular contraction and first degree heart block. He was placed on Aspirin and occasional Chlorpromazine tablets.

One day prior to this admission the patient developed mental confusion, disorientation, and expressive aphasia in addition to elevated temperature. In the emergency room a lumbar puncture was performed. Opening pressure was 220 mm H<sub>2</sub>O, protein 92 mg per cent, glucose 58 mg per cent, 729 white cells per mm<sup>3</sup>, 75% of which were polymorphonuclear, and 220 red cells.

Physical Examination: Temperature was 103.8°F. He was confused and disoriented. There was an expressive aphasia and slight nuchal rigidity. A grade II to III apical systolic murmur was heard for the first time. There was an Osler's node on the plantar surface of the left great toe.

Hospital Course: Repeat lumbar puncture showed essentially similar findings to the one performed in the emergency room. Gram stain smears and cultures were all negative. Because of the strong evidence of endocarditis and the focal neurologic deficit, a mycotic aneurysm was strongly suspected. A left carotid angiogram was performed which demonstrated a small peripheral aneurysm of an anterior branch of the ascending front-parietal branch of the left middle cerebral artery (Fig. 4 A). Treatment was started with penicillin and streptomycin with marked improvement in the aphasia and con-

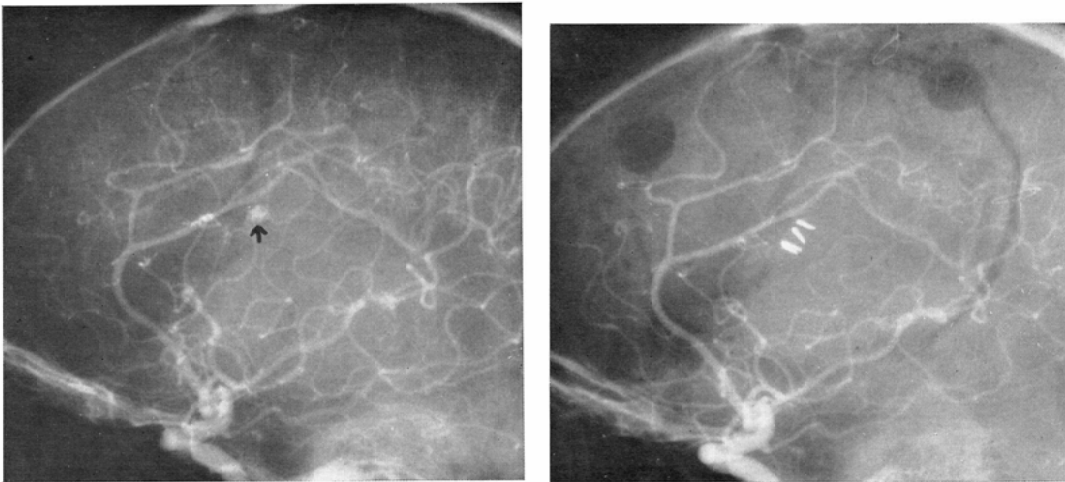


Fig. 4. A and B. Case III. A: Preoperative left carotid angiogram showing a small fusiform dilatation of an opercular branch of the middle cerebral artery. No evidence of intracerebral hematoma is seen. B: Postoperative angiogram with resection of aneurysm. The artery from which the aneurysm arose is not visible probably due to thrombosis.



fusion.

Three days following angiography the patient underwent a left frontal craniotomy. There was noted a small area of infarction in the frontal cortex with a small overlying subdural hematoma. Dissection of the cortex in this area revealed a 5 mm mycotic aneurysm which was excised. Microscopic examination of the resected specimen showed the aneurysm to be mycotic in type. Culture of the specimen grew *Micrococcus*.

The patient made a slow recovery on antibiotic therapy. Six weeks after surgery, he became afebrile and had no mental or neurological impairment. Carotid angiography was performed which showed no evidence of aneurysm (Fig. 4 B). He was able to return to his occupation, and 2 years later remained asymptomatic.

Case IV: A 32-year-old female was admitted to UCLA Hospital with a diagnosis of a right middle cerebral artery aneurysm. She had been in excellent health until 10 weeks prior to admission when she developed a temperature of 103°F following a prolonged labor and delivery of a full term infant at a local hospital. She responded well to antibiotic therapy. She was admitted to the same hospital again 7 weeks prior to this admission because of another temperature elevation and a positive blood culture which grew out beta hemolytic *Streptococcus*. At that time she was found to have a heart murmur and was felt to have subacute bacterial endocarditis which responded to antibiotic therapy.

Two weeks prior to the present admission she developed a fever and became confused. She also noted left upper extremity weakness. She was again hospitalized at the other hospital where she was noted to have a left hemiparesis and a left inferior quadrantanopsia. A lumbar puncture revealed 600 white blood cells without xanthochromia. A carotid angiogram showed a right middle cerebral

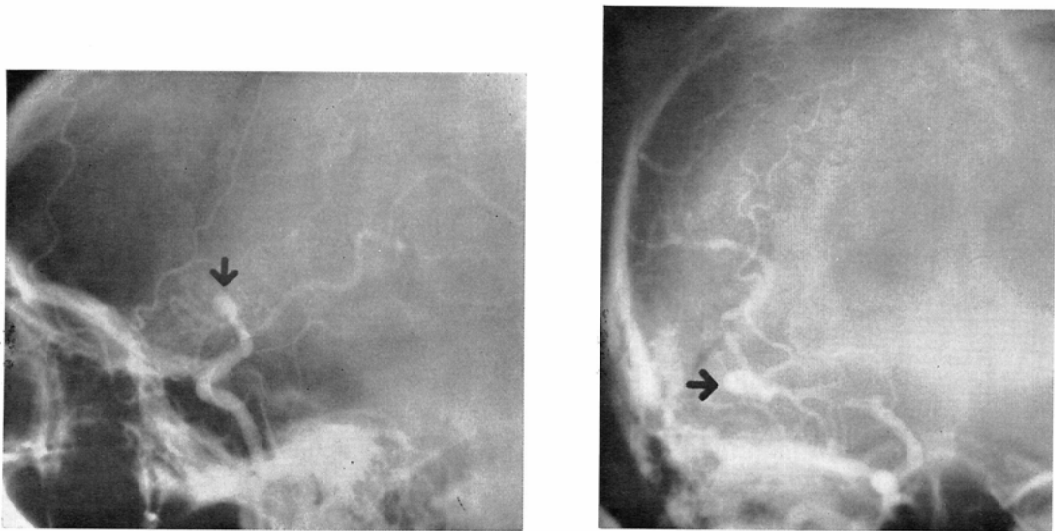


Fig. 5. A and B. Case IV. Right carotid angiogram in frontal and lateral projections, showing a 1.0 cm  $\times$  0.8 cm aneurysm from the trifurcation of the middle cerebral artery. The distal middle cerebral arterial branches are occluded with the exception of the enlarged angular artery.

aneurysm near the trifurcation. She was placed on Ampicillin and transferred to UCLA for further treatment.

**Physical Examination:** The patient was alert and oriented. There were no petechiae or hemorrhages. Auscultation of the heart revealed a grade III/IV systolic murmur best heard over the apex and along the sternal border. Neurologic examination revealed normal cranial nerves except for a slight left facial weakness. There was diffuse weakness of the left lower and upper extremities. Deep tendon reflexes on the left were slightly hyperactive. Plantar reflex was extensor on the left.

**Hospital Course:** The patient was continued on Ampicillin therapy and was afebrile on admission to this hospital. Bilateral carotid angiography was performed which again demonstrated the right middle cerebral aneurysm with non-filling of most of the middle cerebral arterial branches (Fig. 5 A & B). The only branch patent was the angular branch. The patient underwent a right temporal craniotomy for attempted removal of the aneurysm. The aneurysm was exposed, but could not be ligated because of its complicated anatomy and therefore was wrapped with muscle. Postoperatively, she gradually returned to ambulatory status without evidence of neurologic deficit.

### Discussion

The incidence of cerebral mycotic aneurysms was reported by McDonald and Korb (7) who found 70 mycotic aneurysms of 1125 cerebral aneurysms (6.2%) in the literature to 1938. In Roach and Drake's series (12) in 1965, there were 5 mycotic aneurysms of 191 ruptured intracranial aneurysms (2.6%). This statistical decrease may reflect widespread use of effective antibiotics. It should be noted, however, that unruptured cerebral mycotic aneurysms may not be identified and undergo spontaneous healing with appropriate antibiotic therapy.

Mycotic aneurysms may develop on any artery of the body. Frequent involvement is seen at arterial bifurcations and at the segment where an artery suddenly narrows or turns sharply. The aorta is the most frequent site of involvement and its branches are involved in a high frequency, followed by involvement of the intracranial arteries.

The most common underlying conditions are acute and subacute bacterial endocarditis. Other sources of infection are uncommon, although otitis media, septicemia of whatever source, or thrombophlebitis may be the source of infection. Roach and Drake (12) reported that five cerebral mycotic aneurysms developed in 130 patients with bacterial endocarditis (4.6%). As high as 26.4% of patients with bacterial endocarditis developed neurologic symptoms and signs in the entire course of the disease (4).

Angiographic diagnosis of cerebral mycotic aneurysms is not always easy. Small peripherally located cerebral aneurysms should suggest mycotic aneurysms, but one-third of mycotic aneurysms in this review arose at the bifurcations or branching sites of the middle and posterior cerebral arteries. These are indistinguishable from non-infected aneurysms on angiographic findings alone. Fusiform dilatation of the arterial segment is suggestive of a mycotic aneurysm, but this finding may be difficult to appreciate on angiograms when the aneurysms become larger or when they develop at arterial segments of greater diameter. Mycotic aneurysms are usually small when first seen, le-

cause of the tendency for early rupture, but the size cannot be considered a reliable criteria. Clinical correlation with the angiographic findings is most important in the diagnosis of mycotic aneurysms. Subarachnoid hemorrhage or cerebral aneurysm in association with findings of infection, splenomegaly, petechiae, hematuria, elevated sedimentation rate, and cardiac murmur should strongly suggest the possibility of mycotic aneurysm.

The prognosis of patients with ruptured mycotic aneurysms has been considered poor (16). In this review of 23 patients, however, surgical treatment of aneurysms and associated hematomas was attempted in 10 patients, 8 of whom showed good recovery from their potentially fatal illness. The more peripherally located aneurysms may be excised, as in our third case, and aneurysms of the proximal arterial bifurcations can be either ligated or treated with a wrapping procedure, as in our fourth case. Cantu et al. (2) advocated massive antibiotic therapy. It is our opinion that peripheral mycotic aneurysms should be surgically treated as early as possible, and that unresectable aneurysms be treated with massive antibiotic therapy. Further angiographic evaluation following antibiotic therapy may demonstrate changes which make surgical treatment feasible.

The likelihood of early rupture and the frequency with which rupture results in an intracerebral hematoma make mycotic aneurysms unusually dangerous lesions. On the other hand, if detected prior to rupture, effective surgical treatment can often be carried out.

For these reasons we feel that early angiography should be performed in patients with bacterial endocarditis or a variety of other systemic infections in whom neurologic symptoms suggestive of mycotic aneurysms are present.

### Summary

Clinical and angiographic data on 19 cerebral mycotic aneurysms in the literature and four of our own have been reviewed. Cerebral mycotic aneurysm should be considered a strong possibility when there is a systemic infection, murmur, splenomegaly, hematuria, and petechiae in association with peripherally located aneurysms. The importance of follow-up angiography and early surgical removal is also emphasized.

Notes: Medical aspects of Cases I, III and IV have been reported elsewhere (17).

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