Treatment Strategy Based on Experience of Treating Intracranial Infectious Aneurysms

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■ OBJECTIVE: **Intracranial infectious aneurysms (IIAs) are a rare but unique subtype of potentially life-threatening vascular lesion. However, there is no widely accepted standard protocol for their management. We reviewed our treatment experiences of IIAs from 2001 to 2015 and proposed a treatment strategy for future use.**

■ METHODS: **We retrospectively reviewed 25 patients with 33 IIAs. All patients had predisposing infectious disease for which the causative organism had been identified.**

■ RESULTS: **There were 12 patients with ruptured IIAs and 13 with unruptured IIAs. Of these patients, 17 (68%) had infective endocarditis, and viridans group streptococci (40%) were the most common causative organisms. All patients underwent antibiotic therapy, and 17 IIAs in 13 patients resolved with intravenous antibiotic therapy. However, 16 IIAs in 12 patients required neurosurgical treatment, including parent artery occlusion with glue or coils, endosaccular coiling, or microsurgery. The mean size of IIAs that responded to intravenous antibiotics (4.1 ± 2.2 mm) was smaller than that for IIAs with no response (7.5 ± 3.1 mm) ($P = 0.01$). Two patients had treatment-related complications: an acute cerebral infarction after parent artery occlusion and a rupture of the IIA during antibiotic therapy. There was no recurrence or mortality.**

■ CONCLUSIONS: **All patients with IIAs should undergo appropriate antibiotic therapy. In cases with unruptured IIA, patients can be managed using medical therapy with antibiotics alone for 4–6 weeks. However, neurosurgical treatment should be considered in cases of ruptured IIA or unruptured IIA that do not respond to antibiotic therapy.**

INTRODUCTION

Intracranial infectious aneurysms (IIAs) are rare, accounting for 0.7%–6.5% of all intracranial aneurysms.[1,2] Infection of the intracranial arterial wall that leads to IIA can occur either via hematogenous spread of a causative organism or via direct extravascular invasion from existing predisposing infection.[1,2] Although several bacterial, fungal, and viral organisms can cause IIAs, most cases are caused by bacterial infections, typically a viridans *Streptococcus* or *Staphylococcus aureus*.[1,3] In addition, most IIAs are related to infective endocarditis, but cavernous sinus phlebitis, bacterial meningitis, subdural empyema, poor dental hygiene, intravenous (IV) drug abuse, and orbital cellulitis are also considered causative.[2-4] Typical radiologic characteristics of IIAs include multiplicity, distal location, fusiform or irregular shape, size change, and the appearance of a new IIA during follow-up.[2]

Previous studies have reported that 56%–72% of patients with IIAs present with intracranial hemorrhage, including intracerebral hemorrhage, intraventricular hemorrhage, and subarachnoid hemorrhage.[2-4] The overall mortality associated with IIAs has also been reported to be as high as 18.7%–46%, and a previous study separately reported the mortality of IIAs to be 30% in patients with

Key words
- Antibiotics
- Endovascular procedures
- Infected
- Intracranial aneurysm
- Microsurgery
- Mycotic

Abbreviations and Acronyms
CSF: Cerebrospinal fluid
CT: Computed tomography
GCS: Glasgow Coma Scale
GOS: Glasgow Outcome Scale
IIA: Intracranial infectious aneurysm
IV: Intravenous
MRA: Magnetic resonance angiography
MRI: Magnetic resonance imaging
NBCA: *N*-butyl-2-cyanoacrylate
PAO: Parent artery occlusion
TFCA: transfemoral cerebral angiography

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unruptured IIAs and 80% in patients with ruptured IIAs.[3,5,6] However, there is no widely accepted standard protocol for the management of IIAs because of their low incidence, disparate causes, unusual locations, unusual shapes, and differing clinical presentations. Therefore, tailored management is necessary for each case of IIA, with the need to ensure accurate diagnosis and multidisciplinary approaches, including medical, neurosurgical, and endovascular treatments, as necessary.

In this study, we aimed to review our treatment experiences with IIA and to discuss the implications of these experiences for future treatment strategies.

METHODS

This study was approved by our institutional review board before data collection began. All consecutive patients treated for intracranial aneurysm at our institution between January 2001 and September 2015 were identified by retrospective chart review. The diagnosis of IIAs was based on the following criteria: 1) the presence of intracranial aneurysms on imaging, 2) the presence of predisposing infections, and 3) confirmation of the causative organism by blood culture or cerebrospinal fluid (CSF) culture. We used other clinical, radiologic, and laboratory findings as supporting criteria, such as fever, leukocytosis, increased erythrocyte sedimentation rate, increased C-reactive protein levels, and the type of intracranial hemorrhage, as well as the shape, number, and location of the aneurysms.

The following details were extracted from the records of patients with IIAs: demographic characteristics, initial presentation, initial Glasgow Coma Scale (GCS) score, neurologic status during treatment, predisposing infectious disease, causative organism, aneurysm characteristics (including the number, morphology, size, and location), type of intracranial hemorrhage, presence of combined cerebral infarction as a result of septic emboli, delayed appearance of the IIA, and the response of the IIAs to antibiotics and neurosurgical treatments. The sizes of IIAs before treatment were determined by transfemoral cerebral angiography (TFCA) or magnetic resonance imaging (MRI). Treatment outcomes were analyzed, including aneurysm obliteration, aneurysm recurrence, morbidity, and mortality. The clinical outcomes 6 months after treatment were analyzed using the Glasgow Outcome Scale (GOS) in the medical records. The Mann-Whitney test was used for comparing group means.

In our institution, all patients with possible or proven IIAs received empiric IV antibiotic therapy immediately after obtaining blood and CSF samples for bacterial, tuberculosis, and fungal staining and culture. The antibiotic prescription was changed, if needed, following the results of the microbial culture and sensitivity testing.

Blood pressure and circulating blood volume were maintained in the normal range with adequate use of fluid, antihypertensive medication, or inotropic agents to sustain adequate perfusion pressures in major organs and to avoid rupture and rebleeding of IIAs. In addition, avoidance of unnecessary anticoagulation was instituted. In cases of infective endocarditis, detailed cardiac evaluation and serial echocardiograms were performed to monitor changes in endocardial lesions during antibiotic therapy. Appropriate monitoring and management of other predisposing infectious diseases were also instituted. In cases of subarachnoid hemorrhage as a result of ruptured IIA, oral nimodipine was administered, and transcranial Doppler was performed to detect vasospasm for 2 weeks after rupture. IIAs initially managed conservatively were monitored closely with serial MRI and computed tomography (CT) angiography for 4–6 weeks after initial TFCA. A follow-up TFCA was also performed after this period to evaluate the changes in IIAs.

The type of neurosurgical treatment and the interval between diagnosis and neurosurgical treatment were determined by the initial presentation, initial GCS score, medical status for general anesthesia, location and shape of the aneurysm, rupture status, amount of intracranial hemorrhage, and response to IV antibiotics.

RESULTS

Characteristics of Patients and IIAs

We diagnosed and treated 6285 patients with 7229 intracranial aneurysms during the study period. Of these patients, only 25 (0.4%) with 33 IIAs (0.5%) were included in this study; 19 patients had only 1 IIA, but 4 patients had 2 IIAs, and 2 patients had 3 IIAs. The series comprised 18 men and 7 women, and the mean (± standard deviation) age was 48.0 ± 17.5 years. At presentation, radiologic findings showed that 12 patients had intracranial hemorrhage as a result of ruptured IIAs, 8 had acute cerebral infarction because of septic emboli and IIAs, 3 had unruptured IIAs only, and 2 had intracranial hemorrhage with unruptured IIAs. The mean GCS score at initial presentation was 12.4 ± 2.3, and the mean GCS scores of patients with ruptured and unruptured IIAs were 11.4 ± 2.8 and 13.2 ± 1.3, respectively. Among the 33 IIAs, 3 had a delayed appearance.

At the widest diameter, the mean size of the IIAs was 5.2 ± 2.7 mm. The locations of the IIAs were as follows: middle cerebral artery ($n = 25$; 75.8%), posterior cerebral artery ($n = 4$; 12.1%), anterior cerebral artery ($n = 3$; 27.3%), and recurrent artery of Heubner ($n = 1$; 3.0%). Among the middle cerebral artery IIAs, 7 were located in the M2 segment, 5 in the M3 segment, 1 at the M3-4 junction, and 12 in the M4 segment. Among the posterior cerebral artery IIAs, 1 was in the P2 segment, 1 was in the P3 segment, and 2 were in the P4 segment. Among the anterior cerebral artery IIAs, 1 was in the A2 segment and 2 were in the A4 segment. The shape was fusiform and irregular in 26 IIAs and saccular in 7 IIAs.

Predisposing Infectious Disease and Causative Organism

All patients had underlying infectious diseases known to be related to IIAs (Table 1). In 17 patients (68%), infective endocarditis was present, including mitral valve, aortic valve, or tricuspid valve regurgitation with vegetations. However, in 4 patients (16%), the cause was opportunistic infection related to immunosuppressant use after liver transplantation (invasive lung aspergillosis = 2; bacterial pneumonia = 2). The other underlying infectious diseases were orbital cellulitis ($n = 1$; 4%), bacterial meningitis ($n = 1$; 4%), bacterial pneumonia ($n = 1$; 4%), and opportunistic sepsis during chemotherapy for primary lymphoma of the central nervous system ($n = 1$; 4%). The causative organisms were verified by blood culture in 24 patients