Unruptured Intracranial Aneurysms

Christopher S. Ogilvy, MD, Deidre A. Buckley, NP, Ajith J. Thomas, MD

Unruptured intracranial aneurysms are being detected with higher frequency because of more generalized utilization of noninvasive cranial imaging in the form of MRI/MRA and CT angiography. Autopsy studies have documented the prevalence of intracranial aneurysms to be on the order of 3 to 5% of the general population. As less invasive and more accurate imaging studies are obtained, many unruptured aneurysms are now being discovered. Many of these are incidental and as they are discovered it raises the question of who needs treatment and who can be left alone and observed. If an aneurysm patient is "followed," the question of how frequently to obtain imaging and what imaging to use is raised as a concern.

There are certain risk factors that increase the chance of harboring an unruptured intracranial aneurysm. A family history is noted in approximate 25% of patients with intracranial aneurysms. Therefore, if there are two or more blood relatives affected, it is recommended that the family undergo screening. A major modifiable risk factor associated with intracranial aneurysms is cigarette smoking. Cigarette smokers have a significantly increased risk of subarachnoid hemorrhage compared to a control population. Hypertension is also thought to be related to ruptured aneurysms, but given the fact that so many smokers are hypertensive, it's hard to dissociate these two factors. There are other less common risk factors of certain connective tissue disorders such as Ehlers – Danlos syndrome and pseudoxanthoma elasticum. Autosomal dominant polycystic kidney disease is associated with a 6.9 times higher risk of intracranial aneurysm and patients with this disorder are now routinely studied to evaluate for the presence of intracranial aneurysms.

Once an aneurysm is detected there is often great concern as to whether or not the aneurysm should indeed be treated. In the past, the majority of aneurysms in patients presented with subarachnoid hemorrhage. Currently, approximately 70% of aneurysms diagnosed are discovered incidentally or with minimal symptoms in the unruptured condition. There have been two large prospective studies that have been designed to evaluate the natural history of unruptured intracranial aneurysms. The "International Study of Unruptured Intracranial Aneurysms" (ISUIA) study prospectively assessed 1692 patients with 2686 unruptured aneurysms in the United States, Canada and Europe (1). A more recent study conducted in Japan, the Unruptured Cerebral Aneurysm Study (UCAS), followed 6669 aneurysms and 5720 patients (2). In both of these studies, size was found to be significantly related to the risk of subarachnoid hemorrhage. With increasing size over 7 mm, the risk of aneurysmal subarachnoid hemorrhage increased correspondingly. In the ISUIA study, for anterior circulation aneurysms five-year rupture rates of aneurysms 7 to 12 mm was 2.6%, for those 13 to 24 mm it was 14.5%, and for those greater than 25 mm it was 40%. With a larger

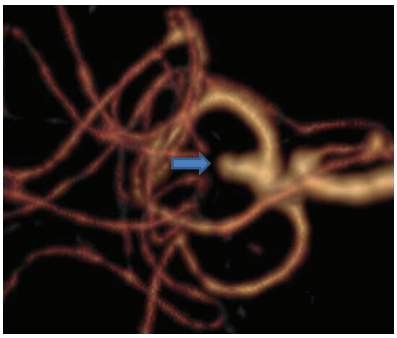

Figure 1A: CT Angiogram shows a right 6mm middle cerebral artery (MCA) aneurysm (arrow) in a 63-year-old man with a strong family history of aneurysm. After discussion with the patient, surgical clipping was chosen for treatment.

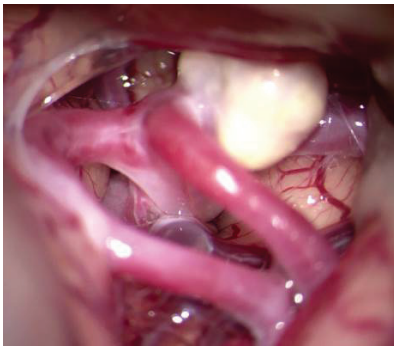

Figure 1B: MCA aneurysm prior to clipping as seen through the operating microscope.

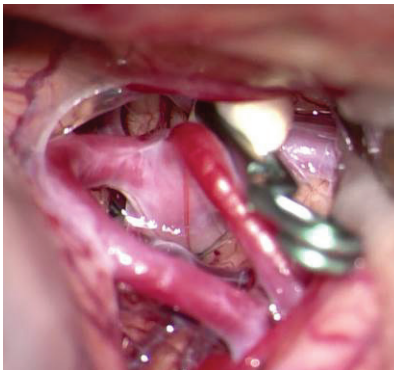

Figure 1C: MCA aneurysm after clipping.

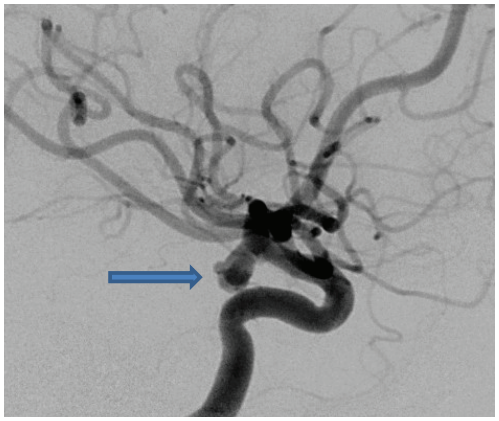

Figure 2A: Before Coiling – Patient is a 56-year-old woman with a 9mm, irregular shaped posterior communicating artery aneurysm. Lateral angiogram shows the aneurysm (arrow).

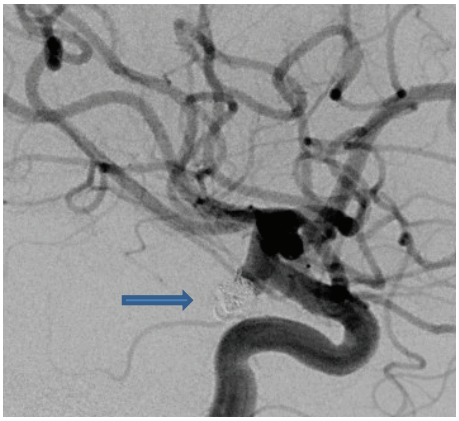

Figure 2B: Post Coiling – Follow up lateral angiogram shows the lesion remains well occluded one year following coil embolization.

number of patients, the UCAS study was able to evaluate rupture rates in aneurysms as small as 3 to 4 mm in size. Indeed the larger an aneurysm, the more likely it was to hemorrhage. While the overall annual risk of rupture was relatively low, there is certainly a cumulative effect of the rupture rate. While these studies demonstrate a lower risk of hemorrhage for smaller aneurysms, it must be remembered that 75% of patients who present with subarachnoid hemorrhage have intracranial aneurysms that are smaller than 10 mm. Therefore, small size does not infer protection from hemorrhage. However, with improved imaging there are many lesions that are more of a "bulge" of a vessel or "protruberance" that are 1-3 mm in size and appear to have a very low risk of rupture. These are generally followed clinically or radiographically. The question for these patients is how often to study the lesion and with what imaging modality. At the BIDMC Brain Aneurysm Institute, we are working on stratifying follow up with noninvasive imaging based on lesion specific- and patient-specific risk factors. Some patients may need a scan only every 10 years while others with multiple risk factors (smoking, family history, multiple aneurysms, young age, females) may need scans annually or every other year.

Treatment considerations

Once an unruptured aneurysm is detected, there must be a detailed analysis of the lesion and patient-specific factors to try to estimate risks of leaving the aneurysm alone and living with the natural history versus the risks of endovascular or surgical management of the lesion. Patients and families have time to obtain information and learn about unruptured brain aneurysms. At the BIDMC Brain Aneurysm Institute, we utilize a weekly neurovascular conference to discuss as a team the options of continued observation versus intervention in patients with unruptured aneurysms. The first step is to understand the morphology of the aneurysm in terms of size and location, which have bearing on potential risks of endovascular management. In addition patient age and other comorbidities factor into the potential risks and benefits of treating the individual. It is only by carefully considering the natural history risks and comparing these to the treatment-related risks for each individual patient that a recommendation or decision can be made as to how to manage a given patient with an unruptured intracranial aneurysm. In general, treatment of patients with unruptured aneurysms have a significantly lower risk than patients who suffered a subarachnoid hemorrhage secondary to the sequela of that subarachnoid hemorrhage. Figures 1 and 2 demonstrate typical patients who had an open surgical clipping and a coil embolization.

One factor that has a large impact on whether an unruptured aneurysm is treated or not is the patient's anxiety. As patients learn more about their intracranial aneurysm, they also come to understand that there is no guarantee that hemorrhage will not occur, despite the fact that the data as noted above suggest the chance of this is very low. There is increased information available on the Internet and the information available can be quite confusing. At the BIDMC Brain Aneurysm Institute we take these issues into consideration when trying to counsel a patient on how to manage an unruptured aneurysm. Indeed, in many patients continued observation is the favored alternative. The question then arises, if the lesion is not treated, how should the patient be followed? Typically we opt for less invasive imaging in the form of MRI or MRA studies. These are usually obtained one year after diagnosis to determine whether the lesion has changed. In the great majority of patients no change will be observed. Thereafter, follow-up imaging can be spaced out at intervals that take into account the individual patient's risk factors. Patients with a family history of aneurysm, multiple aneurysms, polycystic kidney disease, fibromuscular dysplasia, young age, or smokers are monitored more frequently than those patients without these risk factors.

When patients with intracranial aneurysms are not treated, we tend to recommend full and normal activity. This includes normal physical activity, sexual activity, and social activities. We feel it would be unfair to tell patients that their aneurysms are low risk of hemorrhage, but need to modify their behavior or activities. At the BIDMC Brain Aneurysm Institute, we are involved in a number of projects designed to elucidate risk factors for which patients in the population should be studied for intracranial aneurysms. If an aneurysm is detected, the decision about which of these should be treated needs determination. Using a multidisciplinary approach, we care for patients with unruptured intracranial aneurysms whether they engage in treatment or not.

There are support resources available at the BIDMC Brain Aneurysm Institute through a monthly support group that features a speaker and clinicians to answer questions; but more importantly consists of patients and family members who have been affected by a brain aneurysm, either ruptured or unruptured, treated and untreated. This forum provides a warm environment and opportunity to share experiences, and to help others who are in the process of treatment. The Brain Aneurysm Foundation (www.bafound.org) is another resource for patients and their loved ones. The Brain Aneurysm Foundation is the nation's premier nonprofit organization solely dedicated to providing critical awareness, education, support, and research funding to reduce the incidence of brain aneurysm ruptures. There are monthly educational webinars, as well as a listing of over 60 support groups in the USA and Canada. Informational booklets are available online to provide details about the treatment options and the recovery process. The Brain Aneurysm Foundation has become the world's leading source of private funding of brain aneurysm research.

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Dural Arteriovenous Fistulae and Dural Arteriovenous Malformations

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Dural arteriovenous fistulae (dAVF) are acquired vascular lesions involving intracranial dural sinuses. They comprise 10-15% of all adult cerebrovascular lesions(1). Initially, they were thought to be a subset of arteriovenous malformations; however, today they are recognized as separate entity. They usually occur in adults with a prior history of trauma, craniotomy, or venous thrombosis. Management is directed by symptomatology, location, and angioarchitecture.

There are two hypothesis regarding the development of dAVF: One hypothesis is based on the assumption that there is an enlargement of existing physiologic arteriovenous fistulae due to elevated local venous pressure from trauma or craniotomy. The second hypothesis states that there is pathological new arterial ingrowth of meningeal arteries into a thrombosed venous sinus, creating an AV fistula.

Carotid cavernous fistulas (CCF) are a subset of dAVFs and represent an abnormal communication between the internal (ICA) and external carotid arteries (ECA) or their branches and the cavernous sinus. They comprise around 35% of all dAVF(2). They are frequently classified as direct and indirect fistulas. Direct fistula results from a defect in the wall of the ICA, from trauma or rupture of an ICA aneurysm. While direct fistulas are usually high flow fistula, indirect fistulas are low-flow fistulas and comprise the majority of CCFs. Recently, the team at the BIDMC Brain Aneurysm Institute has published an updated five-tier classification system that captures symptomology, and treatment approach, and outcomes in the prestigious journal *Neurosurgery* (Figure 1)(3).

Treatment of CCFs is indicated in patients presenting with ophthalmologic symptoms, cranial nerve

deficits, cortical venous drainage, and hemorrhage. Manual compression and endovascular embolization are two available treatment modalities for CCFs. Endovascular transvenous embolization is an established treatment modality for most CCFs.

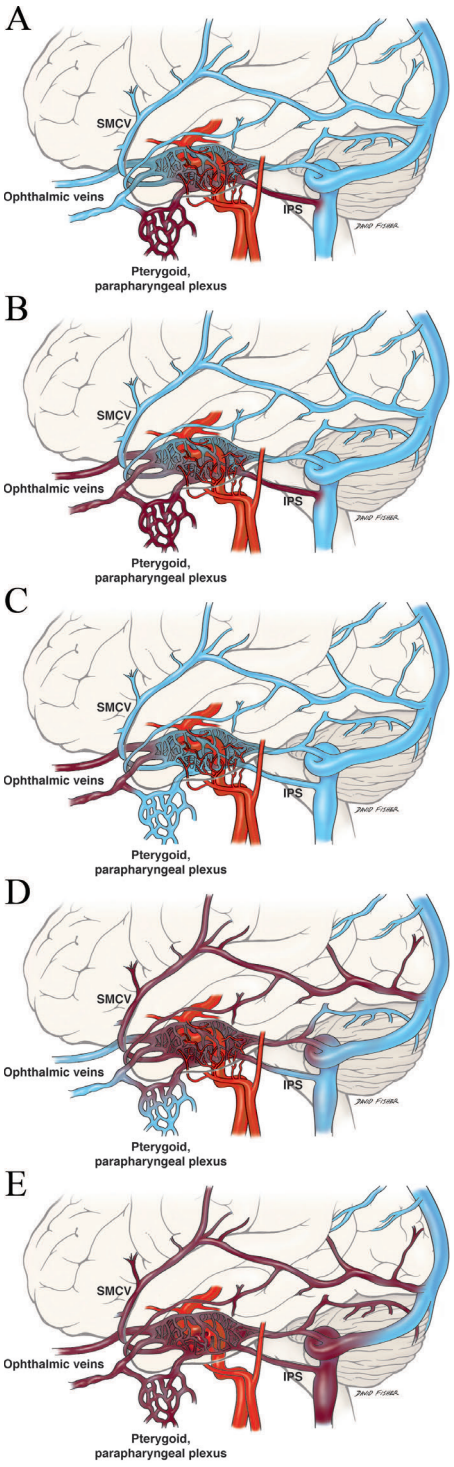
Other dAVFs (Figure 2) are commonly located at the junction of the transverse-sigmoid sinus, superior sagittal sinus, involving deep venous structures (straight sinus, torcula, and the vein of Galen), and tentorium-incisura region. Patients with dAVFs may present with headache, seizures, hemorrhage, increased intracranial pressure, cranial neuropathy, dementia, or focal neurologic deficits. Tinnitus is another common presenting symptom of dAVFs. Transverse-sigmoid sinuses are the most common location of dAVF and associated with a low risk of hemorrhage(4). Dural arteriovenous fistulae of the superior sagittal sinus and the deep venous structures are rare and frequently associated with retrograde venous drainage. Tentorial-incisura region dAVFs frequently present with subarachnoid or intraparenchymal hemorrhage.

According to Borden classification, types II and III, considered as higher-risk lesions, reported annual mortality and annual intracranial hemorrhage rates of 10.4% and 6.9%, respectively(5). Prompt further imaging and workup is required if patients present with either changes in symptoms or new neurologic changes.

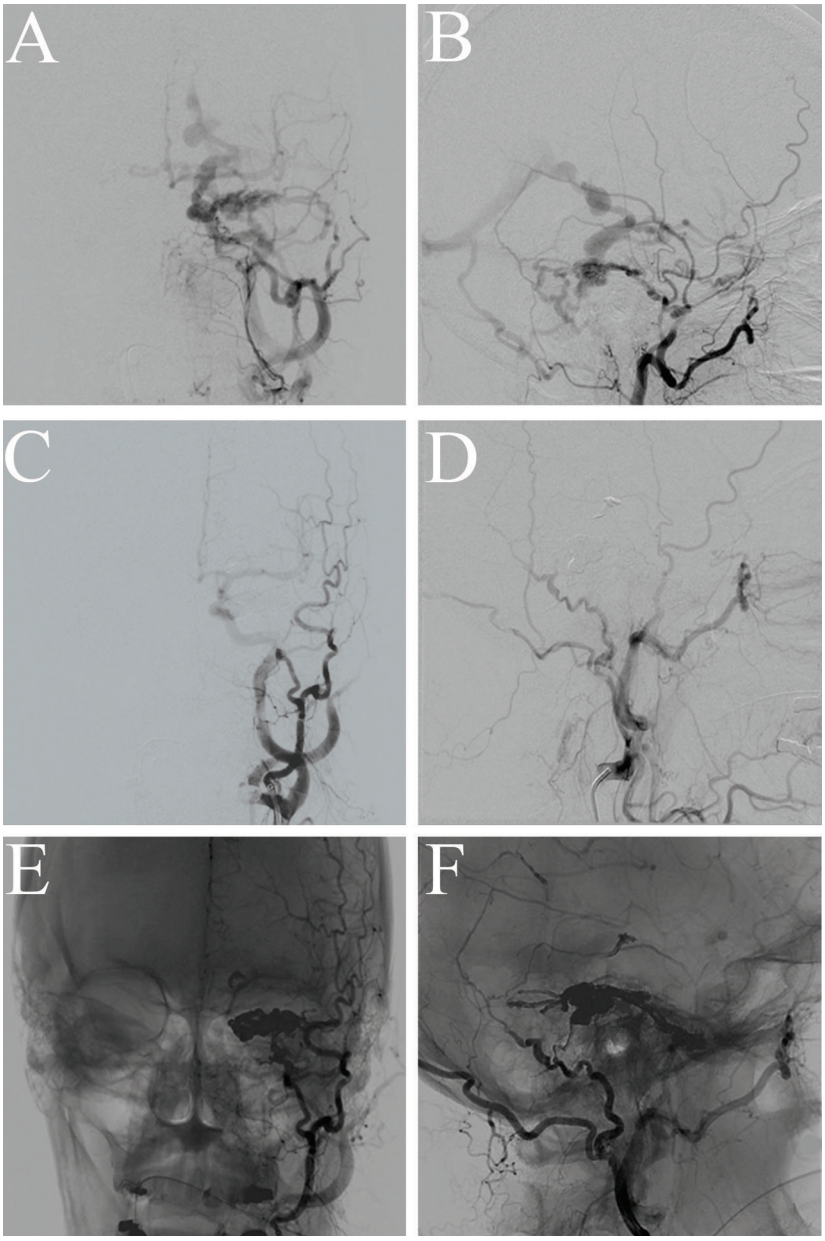
Treatment of dAVF is usually considered for patients who present with cortical venous drainage as these lesions have a higher risk of hemorrhage and warrant treatment. Treatment modalities include endovascular embolization or open surgical ligation.

With endovascular embolization, the goal of the procedure is to occlude the fistulous region. Onyx or n-Butyl Cyanoacrylate (n-BCA), also known as glue, are agents frequently used for embolization. Either transarterial or transvenous routes can be pursued. During transarterial embolization, the feeding arteries are catheterized and used for injection of the embolic agent. During the transvenous approach, the dural sinus or cortical veins are catheterized in a retrograde fashion and platinum coils or liquid embolic agents are injected.

In current day practice, surgical ligation is usually reserved for cases where endovascular treatment has failed or endovascular embolization carries a higher risk. In such conditions, identification of fistulous connection followed by either clip ligation or bipolar cautery is required.



▲ **Figure 1:** Schematic illustration of the venous drainage-based classification system for carotid cavernous fistulas. Normal venous anatomy is colored light blue. Preferential drainage of the individual fistula types are colored dark red. *Panel A:* Type I. *Panel B:* Type II. *Panel C:* Type III. *Panel D:* Type IV. *Panel E:* Type V. (IPS = inferior petrosal sinus, SMCV = superficial middle cerebral vein)



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◀ **Figure 2:** A patient presented with hearing loss and posterior fossa dAVF (Cognard IV, Borden III). Antero-posterior (AP) (Panel A) and lateral (Panel B) projections of left external carotid artery pre-embolization. There was a robust left middle meningeal artery supply and early venous drainage into the straight sinus. Post-embolization of the left middle meningeal artery there was of lack of filling of the dAVF in both the AP (Panel C) and lateral projections (Panel D). AP (Panel E) and lateral (Panel F) projections show the Onyx cast. Embolization of the left middle meningeal artery alone resulted in robust Onyx penetration along the entirety of the fistulous connection and obliteration.

Current Management of Intracranial ("Mycotic") Infectious Aneurysms

Christopher S. Ogilvy, MD, Apar S. Patel, MD, Christopher Griessenauer, MD

The diagnosis and management of infectious intracranial aneurysms has changed dramatically in the last 10 years with the advent of improved imaging modalities and management techniques. Although often referred to as mycotic aneurysms, the majority of infectious intracranial aneurysms are, in fact, bacterial. A variety of neurologic symptoms can occur in patients with endocarditis including infectious intracranial aneurysms, which occur in 3 to 10% of patients (1).

While bacterial endocarditis is the major cause of intracranial infectious aneurysms, other causes such as meningitis, orbital cellulitis, immunosuppression, and intravenous drug abuse are less common causes. While infectious intracranial aneurysms may be caused by bacterial, fungal, or viral organisms, the majority result from bacterial infections. Staphylococcus aureus and Streptococcus species are leading gram-positive organisms. Gram-negative pathogens include salmonella and Pseudomonas aeruginosa. Other pathogens such as Aspergillus, enterococci, Canadida, Mycobacterium tuberculosis and cardio bacterium hominis have been reported. Rarely, viral causes from varicella zoster virus have been reported (2).

When patients experience a rupture from an infectious aneurysm, symptoms can include severe headache, dizziness, seizures, altered mental status, or focal neurologic deficits related to subarachnoid hemorrhage. In addition, large hematomas can result from the hemorrhage. Unruptured lesions can be discovered. Patients with endocarditis can have a variety of transient neurologic events which may represent septic embolization. The pathogenesis of infectious intracranial aneurysms is thought to be secondary to an infective embolus with colonization of the arterial wall by bacteria. This sets the stage for wall weakening and aneurysmal formation. It is felt that roughly 40% of infectious intracranial aneurysms are saccular while the majority are fusiform. The aneurysm morphology has implications when considering treatment. Given the high risks associated with infectious aneurysms, many feel that patients with endocarditis should undergo cerebral imaging even if neurologic manifestations are not evident.

Typically, noncontrast CT scans can be used to evaluate if a subarachnoid or intraparenchymal hemorrhage is present. CT angiography will often show infectious aneurysms even down to the size range of 2 to 3 mm. Once an infectious aneurysm is suspected, cerebral angiography should be performed to delineate the details and anatomy of the aneurysm. If antibiotics are used as the initial treatment of the infectious aneurysm then follow-up imaging is required. Both CTA and angiography can be used. Angiography will more clearly delineate multiplicity, distal location, fusiform shape, and a change in the size or the appearance of a new aneurysm during treatment.

Given the lack of any randomized controlled trials, there are currently no standards to guide the decision-making and therapeutic approach to intracranial infectious aneurysms. Overall management of patients with infectious intracranial aneurysms requires close collaboration between the neurosurgical team and specialists from infectious disease, cardiac surgery, and cardiology. Many believe that infectious aneurysms should be treated regardless of absence of hemorrhage and that unlike congenital saccular aneurysms, size does not seem to relate to risk of subsequent hemorrhage. For unruptured infectious aneurysms in patients with high surgical risk, treatment with antibiotic therapy is often the mainstay of therapy. Antibiotic treatment is guided by blood and cerebrospinal fluid cultures. In patients with unruptured infectious aneurysms without high surgical risk, endovascular surgical treatment is often advised. On the other hand, ruptured aneurysms should be secured as soon as possible by surgical or endovascular techniques. Which technique is chosen is often dictated by the aneurysm morphology, the comorbidities of the patient, or the presence of associated intracerebral hemorrhage. The choice between endovascular or open surgery is complex and should be individualized.

Endovascular techniques are rapidly gaining ground in the management of mycotic aneurysms. Complete occlusion of fusiform lesions can be accomplished with liquid embolic agents or coil embolization. In cases of more saccular aneurysms, parent vessel preservation can be achieved with endovascular coiling. At the BIDMC Brain Aneurysm Institute, patients are managed with either surgical or endovascular techniques (2). Figure 1 shows imaging from a 55-year-old woman with bacterial endocarditis who developed an intense headache. Her noncontrast CT scan showed subarachnoid hemorrhage over the parietal region (Figure 1A, arrow). Cerebral angiography confirmed a distal middle cerebral artery infectious aneurysm measuring approximately 2.5 mm (Figure 1B, arrow). Careful analysis revealed that the branch vessel distal to the aneurysm supplied the motor cortex. It was therefore decided to proceed with endovascular coil embolization. Figure 1C demonstrates placement of a micro catheter adjacent to the aneurysm with coil embolization of the lesion. Complete obliteration of the aneurysm was achieved with a single coil with excellent preservation of distal branch vessels. The patient remained completely intact neurologically and underwent successful treatment of her endocarditis with antibiotics. Follow-up CT angiography did not demonstrate any new infectious aneurysms. Once an aneurysm is detected, repeat CT angiography is often performed several days to a week later. Infectious

aneurysms can grow, shrink, or appear in new locations while under antibiotic therapy. While the aforementioned patient was treated with endovascular techniques, open surgery is also used in carefully selected patients. Surgical clipping is often more difficult than clipping of congenital saccular aneurysms because of wall fragility secondary to infection. One consideration that may favor an endovascular approach is the patient's cardiac function. Given its less invasive nature, endovascular therapy may be safer in patients with deteriorating cardiac function or severe valvular disease facing potential cardiac surgery (3).

Clinical outcomes from intracranial infectious aneurysms are often determined by the neurologic status of the patient at the time of diagnosis and treatment. This emphasizes the importance of early diagnosis and aggressive treatment of both ruptured and unruptured aneurysms. Collaboration of the medical, infectious disease, cardiology, cardiac surgery, neurosurgery, and nursing teams involved in these complex patients can lead to excellent outcomes.

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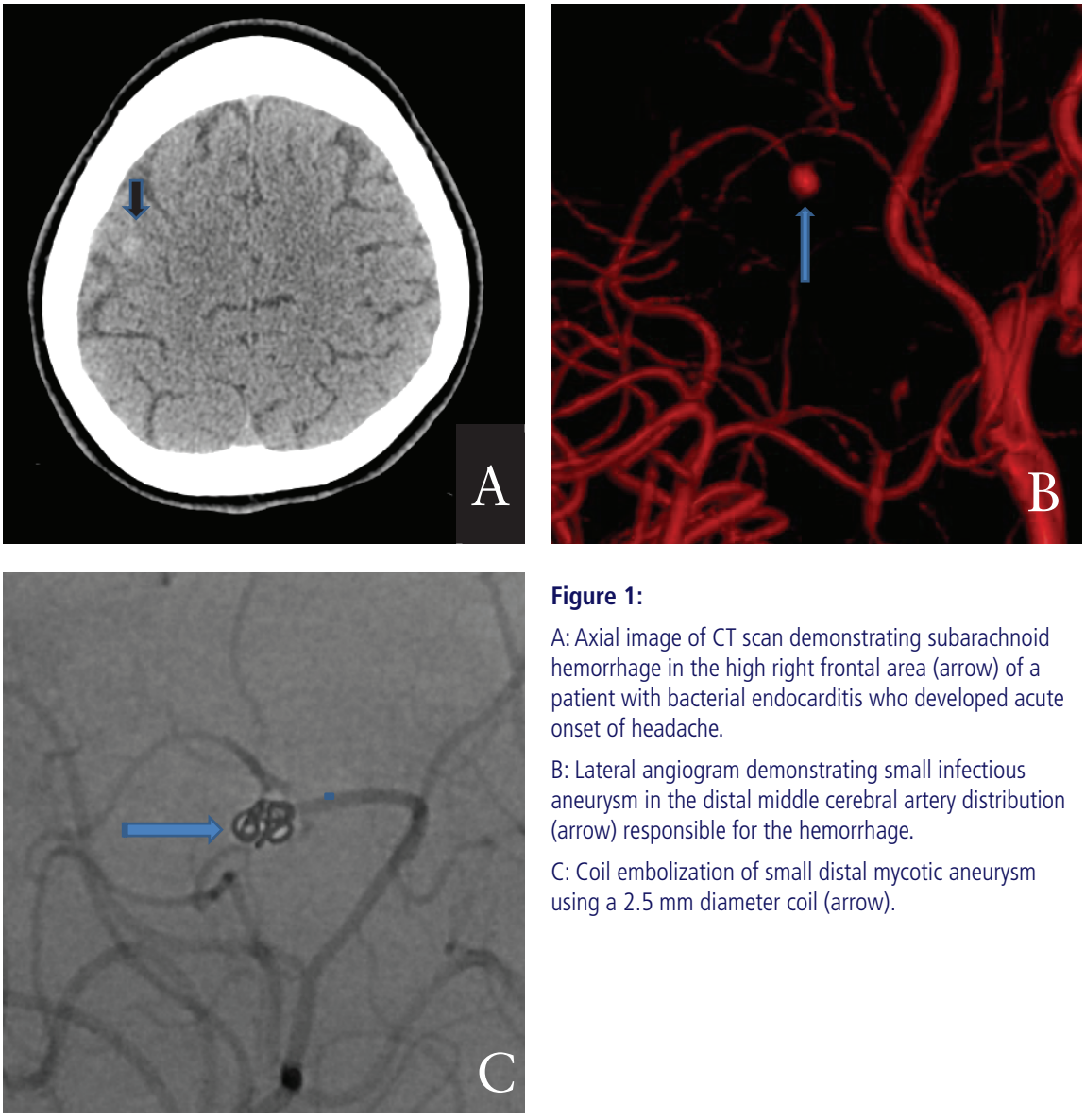

Figure 1:

A: Axial image of CT scan demonstrating subarachnoid hemorrhage in the high right frontal area (arrow) of a patient with bacterial endocarditis who developed acute onset of headache.

B: Lateral angiogram demonstrating small infectious aneurysm in the distal middle cerebral artery distribution (arrow) responsible for the hemorrhage.

C: Coil embolization of small distal mycotic aneurysm using a 2.5 mm diameter coil (arrow).

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