Cerebral Ischemia Complicating Intracranial Aneurysm: A Warning Sign of Imminent Rupture?


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BACKGROUND AND PURPOSE: Patients harboring nongiant cerebral aneurysms may rarely present with an ischemic infarct distal to the aneurysm. The aim of this case series was to report clinical and radiologic characteristics of these patients, their management, and outcome.

MATERIALS AND METHODS: We undertook a single-center retrospective analysis of consecutive patients admitted during an 8-year period with an acute ischemic stroke revealing an unruptured nongiant (<25 mm) sacciform intracranial aneurysm. Clinical, radiologic, therapeutic, and follow-up data were analyzed.

RESULTS: Nine patients were included. The mean size of aneurysms was 9.6 ± 6 mm, and 5 were partially or totally thrombosed. Two patients had a fatal SAH within 3 days after stroke-symptom onset, whereas asymptomatic meningeal bleeding was diagnosed or suspected in 2 others. Most of the patients with unthrombosed aneurysms were successfully treated by endovascular coiling in the acute phase. Thrombosed aneurysms were usually treated with antithrombotics, and most recanalized secondarily, requiring endovascular treatment or surgical obliteration. No recurrence of an ischemic event or SAH was observed during the 31 ± 12 months of follow-up (from 4 to 53 months).

CONCLUSIONS: In this single-center series, the frequency of early SAH in patients with ischemic stroke distal to an unruptured intracranial aneurysm was high. Acute management should be undertaken with care regarding antithrombotic use, and early endovascular coiling should be considered.

ABBREVIATIONS: MCA = middle cerebral artery; mRS = modified Rankin Scale; NIHSS = National Institutes of Health Stroke Scale; PCA = posterior cerebral artery; PICA = posterior inferior cerebellar artery; SAH = subarachnoid hemorrhage.

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From the Departments of Neurology (B.G., M.S., F.H.), Neuroradiology (B.D.-D., K.W.-F., E.A.-C., H.D.), and Biochemistry (O.D.), University Hospital of Nantes, Nantes, France.
Address correspondence to Benoît Guillon, MD, Stroke Unit, Department of Neurology, Hopital Laennec, Centre Hospitalier Universitaire de Nantes, 44093 Nantes Cedex 1, France; e-mail: benoit.guillon@chu-nantes.fr
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Materials and Methods
Patients admitted in our stroke unit from October 2001 to October 2009 with an ischemic stroke and an unruptured <25-mm sacciform intracranial aneurysm were selected from our data base. To be included, patients should have had the following: 1) an ischemic event in a distribution distal to a nongiant intracranial aneurysm; 2) no history of intracranial aneurysm and no symptoms of SAH such as thunderclap headache before stroke symptom onset; 3) CT scans, MR imaging studies, and 4-vessel angiography performed, ruling out vasospasm secondary to SAH, a large infundibulum of a lenticulostriate artery, or features of intracranial dissection (defined as fusiform aneurysm, double lumen, intramural hematoma, stenosis with or without dilation); and 4) an extensive work-up excluding other causes of infarction (standard blood tests, electrocardiography, and echocardiographic and cervical artery sonographic studies).

CSF obtained from lumbar puncture between 12 hours and 10 days after stroke onset was analyzed for red and white blood cell counts, the presence of xanthochromia, and the detection of bilirubin by using spectrophotometry, in accordance with published guidelines. The demographics, clinical presentation, site, size and management of the aneurysm, and data regarding the use of antithrombotics were collected. Clinical outcome by using the mRS (0, no symptoms at all; 1, no significant disability despite symptoms; 2, slight disability; 3, moderate disability; 4, moderately severe disability; 5, severe disability; 6, death) and radiologic follow-up data were recorded between 2 and 4 months after presentation and the last visit for each patient.

Results
Nine patients fulfilled our selection criteria (5 women; mean age, 50.8 ± 7.4 years; range, 38–63 years). These patients represented 0.2% of all patients admitted in our stroke unit dur-
ing the 8-year study period and 1.4% of the population of patients with symptomatic intracranial aneurysms managed in our hospital. Baseline characteristics, acute management, aneurysm pattern, and patient outcome are presented in Online Tables 1 and 2. All presented with an ischemic stroke distal to a small or large sacciform intracranial aneurysm. Infarctions were located free of the MCA territory in 4 and in the posterior circulation in 5. Work-up did not identify atherothrombotic or cardioembolic origin or small vessel disease. Headache or orbital pain or both were noted at presentation in 2 patients and appeared at 24 hours in another. No patient had neck stiffness or meningeal syndrome, and there was no sign of SAH on the initial CT scan or MR imaging. Aneurysms were <25 mm in their greatest diameter, with a mean size of 9.6 ± 6 mm (range, 3–20 mm).

Digital angiography and MR imaging studies showed partial or complete aneurysm thrombosis in 5, whereas the aneurysmal sac was free of thrombus in the others. The parent artery was occluded or narrowed in 4 (Fig 1A, -B). Lumbar puncture was performed in 5 patients from 24 hours to 10 days after the onset of symptoms. Four had a spectrophotometry analysis, which depicted an unexpected and asymptomatic SAH in 1 (patient 7). In the last one (patient 2), lumbar puncture suggested an SAH with an increased red cell count, but there was no spectrophotometry to confirm this suggestion. Two patients (patients 1 and 5) had a severe and acute headache during hospitalization, and their conditions rapidly deteriorated with a loss of consciousness 2 and 3 days after their first ischemic symptoms, revealing a massive SAH (Fig 2A – C). Both died a few days later.

Antithrombotics were used on admission in 4 patients (aspirin in 1, heparin in 3) and within the first week in 6. Four patients had an unthrombosed aneurysm; 3 were successfully treated during the acute stage by endovascular coiling and the last one died early from SAH.

The mean length of follow-up in surviving patients was 31 ± 17 months (from 4 to 53 months). The overall prognosis was excellent for these patients (mRS, 0–2 at 3–4 months). No recurrence of ischemic stroke or SAH was observed. One patient with early aneurysm embolization showed partial recanalization of the aneurysm on imaging at 4 months, and the aneurysm was then successfully re-embolized (patient 8). Three of the 4 patients with complete aneurysm thrombosis showed partial or complete reopening at the first follow-up imaging (2 days to 4 months, Fig 1C). The aneurysm of last patient who also had parent vessel occlusion did not recanalize during follow-up. For those whose aneurysms secondarily re-canalized, 2 were treated by endovascular embolization or surgical obliteration and the other refused any invasive treatment. Four patients remained on long-term antiplatelet therapy; 3 had no treatment with antithrombotics.

Discussion

In our series of ischemic strokes revealing unruptured intracranial aneurysm, an early SAH occurred in 2 patients leading to death, diagnosed by CSF spectrophotometry in 1 and suspected by CSF analysis in another. This complication was excluded in 3 by using CSF spectrophotometry and could not be ruled out in the last 2 patients (no lumbar puncture). To our knowledge, this consecutive series is the first to report such a high frequency (at least one-third) of early subarachnoid bleeding in the context of ischemic stroke distal to a small or large unruptured intracranial aneurysm.

Several case series have reported cerebral ischemia as a presenting feature of a nongiant unruptured intracranial aneurysm, but there are very few reports describing such a symptom as a warning sign of subsequent aneurysm rupture. Ideally, when CT or MR imaging depicts an intracranial aneurysm without bleeding, an SAH should be ruled out by CSF spectrophotometric analysis in accordance with published guidelines before a treatment decision. However, in the context of
intravenous thrombolysis, such a procedure is difficult to per-
form because of the short time window allowed with this treat-
ment and also because it increases the risk of epidural hema-
toma. The alteplase product license states that an intracranial
aneurysm is a contraindication to thrombolysis for acute isch-
emic stroke even if the data that inform this statement are
limited.20 However, guidelines for thrombolytic therapy in
acute stroke usually do not retain this condition as an exclu-
sion criterion. Our experience strongly supports a contraindi-
cation when an aneurysm may be the source of distal emboli-
zation and brain infarct.

The second practical implication when confronted with an
aneurysm that embolizes distally is that its status evolves from
an asymptomatic to symptomatic state. Because of the risk of
subsequent SAH or stroke recurrence within the following
days, endovascular or surgical aneurysm exclusion should be
considered as early as possible.5,14-21 Medical treatment with
aspirin or perhaps with heparin seems to be a reasonable al-
ternative for patients who are not good candidates for endo-
vascular/surgical procedure or while waiting for this treat-
ment.5,6,12 Surgical treatment of aneurysms in the presence of
cerebral infarcts seems to be a high-risk procedure, with in-
creased morbidity and mortality.5,6,9 This poorer outcome was
significantly demonstrated compared with that of good-grade
aneurysms.9 So, whenever possible, endovascular coiling
should be offered as the first-line management in these pa-
tients and should be performed by experienced teams.

The follow-up of patients with ischemic stroke distal to an
aneurysm should be undertaken with caution even if the data
suggest that the risk of recurrent ischemic events or rupture
after the acute stage is very low, regardless of therapy.3-5 How-
ever, considering that even totally thrombosed aneurysms
may recanalize, close radiologic follow-up is strongly recom-
ended to detect further reopening,7 and if it occurs, it should
be treated adequately and quickly.14 In our experience as in
previous studies, none of the patients with ischemic events had
additional ischemic episodes after aneurysm treatment.

The relationship between distal embolization from an an-
eurysmal thrombosis and SAH is unclear. Factors associated
with aneurysmal thrombosis are size and, particularly, the ra-
tio of chamber volume to orifice area, blood stagnation, slow
flow, and increased blood viscosity.12 Furthermore, turbulent
flow within the aneurysmal sac may result in endothelial in-
jury, with exposure of the subendothelial matrix favoring
platelet deposition and thrombus formation.13 Brain infarct
may result from subsequent distal embolization or parent ves-
sel occlusion due to local extension from the intrasaccular thrombosis. Subendothelial exposure may also induce intramural thrombus and damage of the aneurysmal wall with fragmentation of the elastic lamina and then wall fragility. Resolu-
tion of fresh intramural thrombus associated with the altered wall may lead to rupture or blood extravasation.

Our study has several limitations owing to its retrospective nature and the small number of patients. It is thus difficult to draw any definite recommendations regarding acute management of aneurysms associated with ischemic stroke, particularly because the occurrence of subsequent SAH has rarely been reported previously. It is possible that we have missed, in our patient selection, those patients with an ischemic stroke distal to an aneurysm not depicted by imaging (for example aneurysms beyond an occluded artery or patients without an MR imaging study). Another concern is whether the aneu-
rysms are the source of embolization or are present incidentally, particularly in those without intrasaccular or arterial thrombosis. We applied strict selection criteria to reduce the risk of an incidental aneurysm.

Conclusions
Ischemic stroke distal to an unruptured intracranial aneurysm is a rare condition. Our case series indicates that the frequency of early SAH in these patients is high. Therefore, acute management should be undertaken with care regarding anti-
 thrombotic use and with asymptomatic meningeal bleeding ruled out by imaging or CSF analysis. To reduce the risk of subsequent bleeding, early endovascular coiling seems a safe and effective treatment and should be considered as the first-
line management. Long-term outcome is good for surviving patients. Close radiologic follow-up is required to detect re-
opening after acute aneurysmal thrombosis.

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