AJNR

# Multiple cerebral aneurysms in identical twins.

T Hagen, K Neidl and U Piepgras

*AJNR Am J Neuroradiol* 1997, 18 (5) 973-976
http://www.ajnr.org/content/18/5/973

# Multiple Cerebral Aneurysms in Identical Twins

T. Hagen, K. Neidl, and U. Piepgras

**Summary: We report the finding of multiple cerebral aneurysms in a pair of identical twins. One twin had subarachnoid hemorrhage and intracerebral hematoma; her sister had subarachnoid hemorrhage and intraventricular bleeding. Angiography in both cases showed multiple cerebral aneurysms. It is appropriate to recommend a cerebral angiographic examination of an asymptomatic twin after the other twin has suffered an aneurysmal subarachnoid hemorrhage.**

**Index terms: Aneurysm, cerebral; Familial conditions**

The familial occurrence of cerebral aneurysms implies the presence of such aneurysms in two or more first- to third-degree family members. The highest association occurs among siblings. We present a pair of monozygotic twins with subarachnoid hemorrhage. Angiography, performed after subarachnoid hemorrhage, showed multiple cerebral aneurysms.

## Case Reports

*Case 1*

A 39-year-old woman reported acute onset of severe headache and emesis in November 1990. Examination upon arrival at the hospital showed the patient to be somnolent (Hunt and Hess grade IV). No risk factors, such as smoking, hypertension, or other associated vascular disease, were known. Computed tomography (CT) revealed a large right-sided temporal intracerebral hematoma with mass effect and a right-sided hemorrhage. Four-vessel angiography showed a 7-mm right supraclinoidal internal carotid artery aneurysm pointing posterolaterally (between the anterior choroidal artery and the posterior communicating artery). In addition, a 5-mm bilobular aneurysm projecting posteriorly and a 2-mm aneurysm pointing inferoposteriorly at the trifurcation of the right middle cerebral artery were found. The measurements were corrected for magnification. Arterial vasospasm was present in the middle cerebral artery (Fig 1).

After external ventricular drainage, the patient's level of consciousness improved slowly. On day 24, rehemorrhage occurred. The three aneurysms were clipped, and the patient's postoperative course was uncomplicated.

*Case 2*

The identical twin sister of the patient in case 1 was admitted to the hospital with severe headache and rapid deterioration of her level of consciousness in August 1992. As with her sister, no risk factors for vascular disease were known. A CT scan showed intraventricular and subarachnoid hemorrhage. Four-vessel cerebral angiography revealed a 5-mm aneurysm pointing posteriorly at the trifurcation of the right middle cerebral artery, a 4-mm right posterior communicating artery aneurysm projecting laterally, and a fusiform enlargement of the infraclinoidal internal carotid artery (Fig 2). Additionally, a 3-mm left posterior communicating artery aneurysm pointing posteriorly was found. To prevent repeat hemorrhage, we performed an early clipping of the two right-sided aneurysms. Postoperatively, the patient's neurologic status deteriorated progressively. She died 3 days after admission and surgical clipping. An autopsy revealed the aneurysms and a general vasospasm, with multiple infarcted regions of the brain stem.

## Discussion

Only a few cases of identical twins with intracranial aneurysms have been reported (Table). The highest rate of familial aneurysms seems to be in twins, but they do not necessarily have a higher frequency of aneurysmal occurrence than that of the general population (1). Thirty-two (6.7%) of 485 patients with subarachnoid hemorrhage have a first- to third-degree relative who had a subarachnoid hemorrhage. On the basis of chance alone, one would expect the frequency of such an occurrence to be 5.6% (2). Hence, familial aneurysms can be explained by accidental aggregations. However, familial aneurysms have to be distinguished from sporadic, nonfamilial aneurysms, because they show some specific differences. Like aneurysms in twins, they appear to rupture at an earlier age, 41.9 years for the eight reported cases and 42.3 years for familial aneurysms (3), in contrast to an average age of 51.4 years

Received May 20, 1996; accepted after revision September 24.

From the Department of Neuroradiology, Saarland University Hospital, D-66421 Homburg-Saar, Germany. Address reprint requests to Dr T. Hagen.

AJNR 18:973–976, May 1997 0195-6108/97/1805–0973 

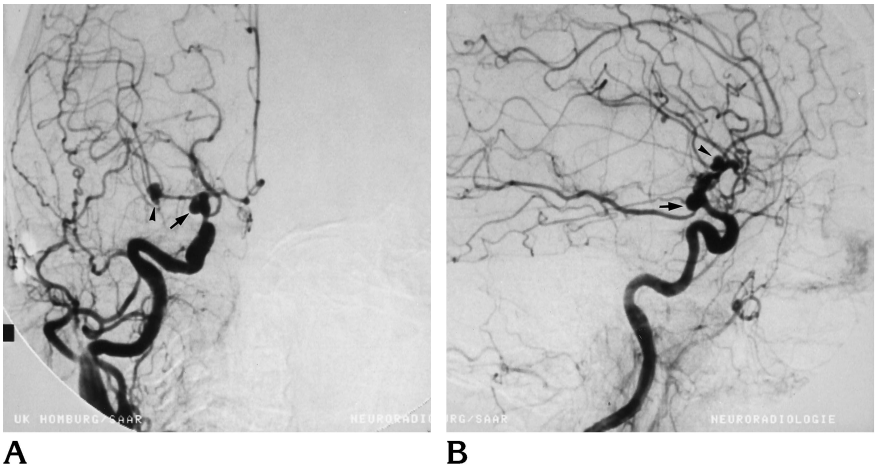


Fig 1. Case 1.

*A*, Right carotid angiogram, anteroposterior view, shows a 7-mm supraclinoidal internal carotid artery aneurysm (*arrow*) and a 2-mm aneurysm pointing inferoposteriorly (*arrowhead*) at the trifurcation of the right middle cerebral artery.

*B*, Lateral view shows the internal carotid artery aneurysm between the anterior choroidal artery and the posterior communicating artery (*arrow*) and a 5-mm bilobular aneurysm projecting posteriorly (*arrowhead*). Vasospasm is present in the middle cerebral artery.

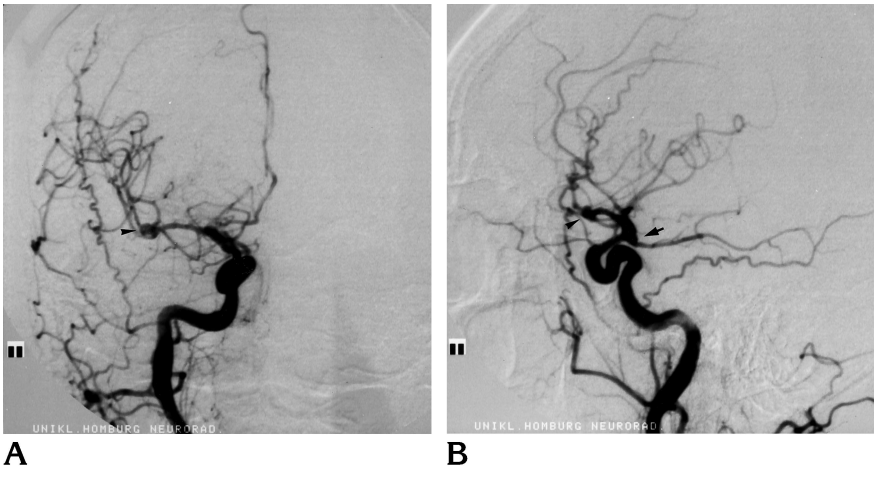


Fig 2. Case 2.

Cerebral angiograms in anteroposterior (*A*) and lateral (*B*) views show a 5-mm aneurysm pointing posteriorly (*arrowheads*) at the trifurcation of the right middle cerebral artery, a 4-mm right posterior communicating artery aneurysm (*arrows*), and a fusiform enlargement of the infraclinoidal internal carotid artery.

for the rupture of sporadic nonfamilial aneurysms. The difference in age at presentation among the pairs of twins reported ranges from 2 to 8 years. Familial aneurysms seem to rupture at a smaller size and to occur less frequently in the anterior communicating artery (3).

In identical twins, aneurysms are located more frequently at the same site or at mirror sites than in randomly selected patients. Andrews (4) found that the frequency of occurrence at the same site was over twice the expected frequency. In a retrospective study of familial intracranial aneurysms, 15 of 38 pairs of siblings had at least one aneurysm in the ipsilateral vessel and 26 of 40 pairs had aneurysms at mirror sites (5). Among the sets of twins listed in the Table, aneurysms occurred in the same location in four pairs (6–8), including ours, and in mirror sites in two pairs (9, 10).

The findings of aneurysms in identical twins make a genetic predisposition probable. An autosomal mode of inheritance is most likely (11); however, polygenic multifactorial transmission may be possible (3, 12, 13). Cerebral aneurysms have been reported in association with Ehlers-Danlos syndrome type IV (14, 15), Marfan syndrome (16, 17), pseudoxanthoma elasticum (18–20), Anderson-Fabry disease (21), polycystic kidney disease (22–25), and coarctation of the aorta (26, 27). Arterial hypertension may contribute to the development of aneurysms in the latter two diseases. Besides arterial hypertension, arteriosclerosis has been implicated as an acquired factor in the pathogenesis of cerebral aneurysms. Ostergaard et al (28) postulated an association of the *C3F* gene with arteriosclerotic vascular disease. This gene was suggested to be a risk factor for early aneurysmal rupture.

Collagen type III deficiency results in an abnormal extensibility of the arterial wall (29). Such deficiency has been reported in patients

**Eight pairs of identical twins with cerebral aneurysms**

| Study | Year | Age, y/Sex | Signs and Symptoms | Site of Aneurysm |
|---|---|---|---|---|
| O'Brian (34) | 1942 | 26/M | Sudden death | Unknown |
| | | 34/M | SAH, fatal | L MCA |
| Brisman and Abbassioun (33) | 1971 | 30/F | SAH, aneurysms clipped | L and R MCA |
| | | 35/F | SAH, fatal | L and R ICA |
| Wilson and Cast (7) | 1973 | 42/F | SAH, no surgical treatment | L MCA |
| | | 45/F | SAH, fatal | L MCA |
| Fairburn (9) | 1973 | 44/F | SAH, ligation of ICA | R ICA |
| | | 46/F | SAH, no surgical treatment | L ICA |
| Schon and Marshall (6) | 1984 | 39/M | SAH, fatal after clipping | ACoA |
| | | 43/M | SAH, fatal | ACoA |
| Weil et al (8) | 1988 | 43/F | SAH, two aneurysms clipped | L and R ICA, L PCoA, basilarA |
| | | 43/F | Headaches, one aneurysm clipped | L and R ICA, L PCoA, basilarA |
| Parekh et al (10) | 1992 | 36/F | Epilepsy, two aneurysms clipped | L MCA, L PICA |
| | | 37/F | SAH, fatal | R MCA |
| Present report | 1997 | 39/F | SAH, three aneurysms clipped | R ICA, two in R MCA |
| | | 41/F | SAH, two aneurysms clipped | R ICA (fusiform), R PCoA, R MCA |

Note.—ACoA indicates anterior communicating artery; basilarA, basilar artery; ICA, internal carotid artery; MCA, middle cerebral artery; PCoA, posterior communicating artery; PICA, posterior inferior cerebellar artery; and SAH, subarachnoid hemorrhage.

with sporadic aneurysms, but we found no abnormalities of collagen type III reported in patients with familial cerebral aneurysms.

Not only are the genetics and pathogenesis of intracerebral aneurysms controversial but also the screening of relatives in families with two or more members with subarachnoid hemorrhage. Ter Berg et al (11) devised a decision tree, taking into consideration the age of the patient, the risks of intraarterial digital subtraction angiography (IA-DSA) (30), and the postoperative morbidity related to the size of the aneurysm(s) (31). However, the risks of diagnostic procedures play only a minor part in the resulting gain for the patient. Use of magnetic resonance (MR) angiography as the screening method for calculations based on the decision tree and the assumption of a sensitivity of 100% would only result in a slight increase in the benefits. In conclusion, Ter Berg et al recommended screening of asymptomatic relatives only for those between the ages of 35 and 65 years (11). Clinical factors, like familial history or associated medical conditions, and morphologic parameters, such as the size, shape, and location of an aneurysm, are subjects of intense interest to those engaged in refining the characteristics of patients with unruptured aneurysms who are at risk for subarachnoid hemorrhage. The risk of hemorrhage has to be compared with the total risk of diagnostic screening and treatment of the aneurysm, such as surgery or endovascular intervention.

Less invasive imaging studies such as MR angiography or CT angiography may be used for the screening of relatives of patients with intracerebral aneurysms. Owing to its higher sensitivity, IA-DSA remains the definitive study for the diagnosis and preinterventional delineation of aneurysms.

Whether the risk of subarachnoid hemorrhage in an asymptomatic twin after the other twin has had an aneurysmal subarachnoid hemorrhage is increased or decreased, we believe that an angiographic examination should be offered to the asymptomatic twin. We found one pair of monozygotic twins who did not have identical intracranial aneurysms reported (32). In this case, one twin had aneurysmal subarachnoid hemorrhage and MR angiography and IA-DSA could not detect intracranial aneurysms in his asymptomatic brother. In the set of twins reported by Brismann and Abbassioun (33), one sister had normal angiographic findings after her twin sister died of a subarachnoidal hemorrhage. However, 4 years later, cerebral angiography of the same vessels revealed bilateral middle cerebral artery aneurysms, which have been clipped. Thus, normal findings at cerebral angiography do not preclude later development or visualization of an aneurysm. The development of aneurysms in arteries that were previously reported to be normal is not unusual. MR angiography may be used as a tool to study the natural course in patients with risk factors for vascular disease.

## References


1. Norrgard Ö, Ängquist KA, Fodstad H, Forsell A, Lindberg M. Intracranial aneurysms and heredity. *Neurosurgery* 1987;20:236–239
2. Dippel DWJ, Ter Berg JWM, Habbema JDF. Screening for unruptured familial intracranial aneurysms: a decision analysis. *Acta Neurol Scand* 1992;86:381–389
3. Lozano AM, Leblanc R. Familial intracranial aneurysms. *J Neurosurg* 1987;66:522–528
4. Andrews RJ. Intracranial aneurysms: characteristics of aneurysms in siblings (letter). *N Engl J Med* 1977;297:115
5. Fox JL. Associated conditions: I. In: Fox JL, ed. *Intracranial Aneurysms.* New York, NY: Springer Verlag; 1983;1:chap 13
6. Schon F, Marshall J. Subarachnoid haemorrhage in identical twins. *J Neurol Neurosurg Psychiatry* 1984;47:81–83
7. Wilson PJE, Cast IP. "Twin" intracranial aneurysms (letter). *Br Med J* 1973;1:484
8. Weil SM, Olivi A, Greiner AL, Tobler WD. Multiple intracranial aneurysms in identical twins. *Acta Neurochir (Wien)* 1988;95:121–125
9. Fairburn B. "Twin" intracranial aneurysms causing subarachnoid haemorrhage in identical twins. *Br Med J* 1973;1:210–211
10. Parekh HC, Gurusinghe NT, Sharma RR. Cerebral berry aneurysms in identical twins: a case report. *Surg Neurol* 1992;38:277–279
11. Ter Berg HWM, Dippel DWJ, Limburg M, Schievink WI, Gijn van J. Familial intracranial aneurysms: a review. *Stroke* 1992;23:1024–1030
12. Bannerman RM, Ingall GB, Graf CJ. The familial occurrence of intracranial aneurysms. *Neurology* 1970;20:283–289
13. Graf CJ. Spontaneous carotid-cavernous fistulae: Ehlers-Danlos syndrome and related conditions. *Arch Neurol* 1965;13:662–672
14. Lack B, Nair SG, Russel NA, Benoit BG. Spontaneous carotid-cavernous fistulae and multiple arterial dissections in type IV Ehlers-Danlos syndrome: case report. *J Neurosurg* 1987;66:462–467
15. Schievink WI, Limburg M, Oorthuys JWE, Fleury P, Pope FM. Cerebrovascular disease in Ehlers-Danlos syndrome type IV. *Stroke* 1990;21:626–632
16. Finney HL, Roberts TS, Anderson RE. Giant intracranial aneurysm associated with Marfan's syndrome: case report. *J Neurosurg* 1976;45:342–347
17. Speciali JG, Lison MP, Junqueira GL. Aneurisma intracranio na sindrome de Marfan. *Arq Neuropsiquiatr* 1971;29:453–457
18. Kito K, Kobayashi N, Mori N, Kohno H. Ruptured aneurysm of the anterior spinal artery associated with pseudomyxoma elasticum. *J Neurosurg* 1983;58:126–128
19. Munyer TP, Margulis AR. Pseudoxanthoma elasticum with internal carotid artery aneurysm. *AJR Am J Roentgenol* 1981;136:1023–1024
20. Scheie HG, Hogan RF. Angoid streaks and generalized arterial disease. *Arch Ophthalmol* 1957;57:855–868
21. Maisey DN, Cosh TA. Basilar artery aneurysm and Anderson-Fabry disease. *J Neurol Neurosurg Psychiatry* 1980;43:85–87
22. Ditlefsen EM, Tönjum AM. Intracranial aneurysms and polycystic kidneys. *Acta Med Scand* 1960;168:51–54
23. Schievink WI, Torres VE, Piepgras DG, Wiebers DO. Saccular intracranial aneurysms in autosomal dominant polycystic kidney disease. *J Am Soc Nephrol* 1992;3:88–95
24. Wakabayashi T, Fujita S, Ohbora Y, Suyama T, Tamaki N, Matsumoto S. Polycystic kidney disease and intracranial aneurysms: early angiographic diagnosis and early operation for the unruptured aneurysm. *J Neurosurg* 1983;58:488–491
25. Dalgaard OZ. Bilateral polycystic disease of the kidneys: a follow up of two-hundred and eighty-four patients and their families. *Acta Med Scand* 1957;328(suppl):186–190
26. Stehbens WE. Cerebral aneurysm and congenital abnormalities. *Aust Ann Med* 1962;11:102–112
27. Tyler HR, Clark DB. Neurologic complications in patients with coarctation of aorta. *Neurology* 1958;8:712–718
28. Ostergaard JR, Bruun-Petersen G, Kristensen BO. The C3-F gene in patients with saccular aneurysms. *Tissue Antigens* 1986;28:176–181
29. Ostergaard JR, Oxlund H. Collagen type III deficiency in patients with rupture of intracranial saccular aneurysms. *J Neurosurg* 1987;67:690–696
30. Dion JE, Grates PC, Fox AJ, Barnett JM, Blom RJ. Clinical events following neuroangiography: a prospective study. *Stroke* 1987;18:997–1004
31. Wirth FP, Laws ER, Piepgras D, Scott RM. Surgical treatment of incidental intracranial aneurysms. *Neurosurgery* 1983;12:507–511
32. Puchner MJA, Lohmann F, Valdueza JM, Siepmann G, Freckmann N. Monozygotic twins not identical with respect to the existence of intracranial aneurysms: a case report. *Surg Neurol* 1994;41:284–289
33. Brisman R, Abbassioun K. Familial intracranial aneurysms. *J Neurosurg* 1971;34:678–682
34. O'Brian JG. Subarachnoid haemorrhage in identical twins. *Br Med J* 1942;1:607–609