Acta Medica Okayama

Volume 48, *Issue* 5 1994 *Article* 5

OCTOBER 1994

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Abstract

The growth and rupture of 40 cerebral aneurysms was studied in 36 patients (14 men, 22 women; were average age, 51.8 years). Aneurysms were classified into five types according to the intraoperative findings: type 1, uniformly thin, smooth surface; type 2, thin neck and thick wall, smooth surface with or without red and/or transparent portions; type 3, uniformly thick wall, smooth surface with or without red portions; type 4, thick neck, bubbled or loculated thin wall at dome with or without red and/or transparent portions; type 5, thick wall in entirety, irregular surface with or without red portions. Five were type 1, six type 2, and 12 type 3. In four of the type 2 aneurysms, turbulence could be seen at the neck. In seven of the type 3 aneurysms, red and/or transparent portions were observed in the wall. Thirteen were type 4; nine of which had a bubbled or loculated wall with or without red and/or transparent portions. Four were type 5, with scattered red portions but a thick wall. Type 1 aneurysms were 2-5 mm, most of types 2 and 3 were 3-6 mm, type 4 were 3-13 mm, and type 5 were more than 9 mm. Types 1 and 2 had few local changes in the wall, suggesting that aneurysms at this stage are stable. Type 3 is considered to be a transitional stage to type 4 from type 2. Type 4 aneurysms had some local changes within the wall including bubbles or loculi. We concluded that aneurysms exceeding 4 mm have local pathologic changes in the wall and are critical.(ABSTRACT TRUNCATED AT 250 WORDS)

KEYWORDS: unrupturesd cerebral aneurysm, growth, rupture, pathologic change

*PMID: 7863797 [PubMed - indexed for MEDLINE]

ACTA MED OKAYAMA 1994; 48(5): 257-262

Growth and Rupture of Unruptured Cerebral Aneurysms Based on the Intraoperative Appearance

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The growth and rupture of 40 cerebral aneurysms was studied in 36 patients (14 men, 22 women; were average age, 51.8 years). Aneurysms were classified into five types according to the intraoperative findings: type 1, uniformly thin, smooth surface; type 2, thin neck and thick wall, smooth surface with or without red and/or transparent portions; type 3, uniformly thick wall, smooth surface with or without red portions; type 4, thick neck, bubbled or loculated thin wall at dome with or without red and/or transparent portions; type 5, thick wall in entirety, irregular surface with or without red portions. Five were type 1, six type 2, and 12 type 3. In four of the type 2 aneurysms, turbulence could be seen at the neck. In seven of the type 3 aneurysms, red and/or transparent portions were observed in the wall. Thirteen were type 4; nine of which had a bubbled or loculated wall with or without red and/or transparent portions. Four were type 5, with scattered red portions but a thick wall. Type 1 aneurysms were 2-5 mm, most of types 2 and 3 were 3-6 mm, type 4 were 3-13 mm, and type 5 were more than 9 mm. Types 1 and 2 had few local changes in the wall, suggesting that aneurysms at this stage are stable. Type 3 is considered to be a transitional stage to type 4 from type 2. Type 4 aneurysms had some local changes within the wall including bubbles or loculi. We concluded that aneurysms exceeding 4 mm have local pathologic changes in the wall and are critical. To prevent subarachnoid hemorrhage, aneurysms of this size should be detected and surgically treated.

Key words: unruptured cerebral aneurysm, growth, rupture, pathologic change

Once a cerebral aneurysm ruptures, about 50% of patients die or are permanently disabled as a result of the initial hemorrhage, and another 25 to 30% die after a subsequent hemorrhage (1-5). Because of these statistics, unruptured cerebral aneurysms garner a great deal of attention, and neurosurgeons cannot be indifferent to these lesions (4-6). The best way to improve mortality and morbidity is to discover and treat these aneurysms before they rupture. Most importantly, understanding the process by which unruptured cerebral aneurysms grow has significant implications in preventing subarachnoid hemorrhage. We approached this process with two questions in mind: What type of aneurysm is liable to rupture? Is the rupture of an aneurysm predictable? In this report, we try to clarify the growth process of unruptured cerebral aneurysms, according to the relation between their shape, size and wall properties, through direct observation during surgery.

Subjects and Methods

Subjects. We experienced 72 unruptured cerebral aneurysms in 69 patients undergoing surgery over a 12-year period. The 40 unruptured cerebral aneurysms (36 patients) which were observed in entirety intraoperatively are the subject of this study. The patients included 14 men and 22 women ranging in age from 36 to 74 years (average, 51.8 years). Twenty aneurysms were multiple in 17 patients with subarachnoid hemorrhage, 5 were discovered during investigations for other diseases, 4 were symptomatic unruptured lesions presenting with oculomotor nerve palsy, and 11 were detected on noninvasive screening tests of the brain in outpatients.

Classification of aneurysms based on the macroscopic observation. We examined the macroscopic appearance of each aneurysm in detail during

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surgery. Based on these observations, we classified the aneurysms into five types: type 1, uniformly thin wall, smooth surface; type 2, thin neck and thick dome, smooth surface with or without red and/or transparent portions; type 3, uniformly thick wall, smooth surface with or without red portions; type 4, thick neck, and bubbled or loculated thin wall at dome with or without red and/or transparent portions; and type 5, thick wall in entirety, irregular surface with or without red portions. The red portion suggests the infiltration of intra-aneurysmal blood into the wall or intramural hemorrhage. The term of "transparent portion" describes the section where turbulent flow in the aneurysm could be seen through the thin wall. This study does not include the autopsy case because there was no operative mortality.

Grouping of aneurysms based on the sizes. The size of the aneurysm indicated the greatest diameter of the aneurysmal sac measuring during intraoperative view or on the angiogram. Based on sizes, 40 aneurysms were divided into two groups; less than 4 mm at the maximum diameter (n = 11), and 4 mm or greater (n = 29), because 4 mm was considered to be the critical size of the aneurysmal rupture (7, 8). The differences between these two groups were analyzed statistically using the chi-square test and the ridit analysis in the following two points: firstly, the existance of the abnormal findings including a red and/or transparent portion, and secondly the type of aneurysm.

Results

Classified aneurysms. Five aneurysms were classified as type 1 (Fig. 1A) and six were type 2 (Fig. 1B). In four of type 2 aneurysms, turbulent flow in the aneurysmal sac could be seen through the thin wall of the neck. Twelve aneurysms were classified as type 3 (Fig. 1C); seven of these showed one or more red and/or transparent portions in the wall. Thirteen aneurysms were classified as type 4 (Fig. 1D); nine of these had red and/or transparent portions in the bubbled or loculated wall. There were four aneurysms of type 5. (Fig. 1E).

Types and sizes of aneurysms. Fig. 2 shows the relation between the type and size of aneurysms: type 1 ranged from 2 to 5 mm (average 3.2 mm), type 2 were from 3 to 6 mm (average 4.5 mm), and type 3 ranged from 3 to 9 mm (average 4.8 mm). The size varied in type 4 from 3 to 13 mm (average 7.8 mm). Type 5 aneurysms were large; all were more than 9 mm (average 16.0 mm). In types 1-3, as a whole, 10 of 23 aneurysms (43.5 %) were less than 4 mm, and in types 4 and 5, 16 of 17 aneurysms (94.1 %) were 4 mm or greater. The percentage of aneurysms with red and/or transparent portions was as follows: 0 % in type 1, 66.7 % in type 2, 58.3 % in type 3, 69.2 % in type 4, and 100 % in type 5.

Table 1 shows the relation between the two groups of aneurysmal size and each type. The distribution was significantly different between the two groups ($\chi^2 = 11.3$, $P = 0.0234$). The ridit analysis showed the large aneurysm group (4 mm or greater) tended to be of the higher type ($P < 0.0001$). Table 2 shows the relation between the two groups of aneurysmal size and the existance of red and/or transparent portions in the wall. The large sized aneurysms 4 mm or greater seemed to have more red and/or transparent portions than those less than 4 mm in diameter. However, there was no significant difference ($\chi^2 = 2.304$).

Table 1 Relation between the aneurysmal size distribution and type of aneurysm

Maximum diameter (mm)	Type 1	Type 2	Type 3	Type 4	Type 5
4 >	4	2	4	1	0
4 ≤	1	4	8	12	4

chi-square: $\chi^2 = 11.3$, $P = 0.0234$
ridit analysis: $P < 0.0001$

Table 2 Relation between aneurysmal size distribution and existence of a red and/or transparent portion in the wall

Maximum diameter (mm)	Existence of a red and/or transparent portion	
	Yes	No
4 >	4	7
4 ≤	20	9

chi-square: $\chi^2 = 2.304$

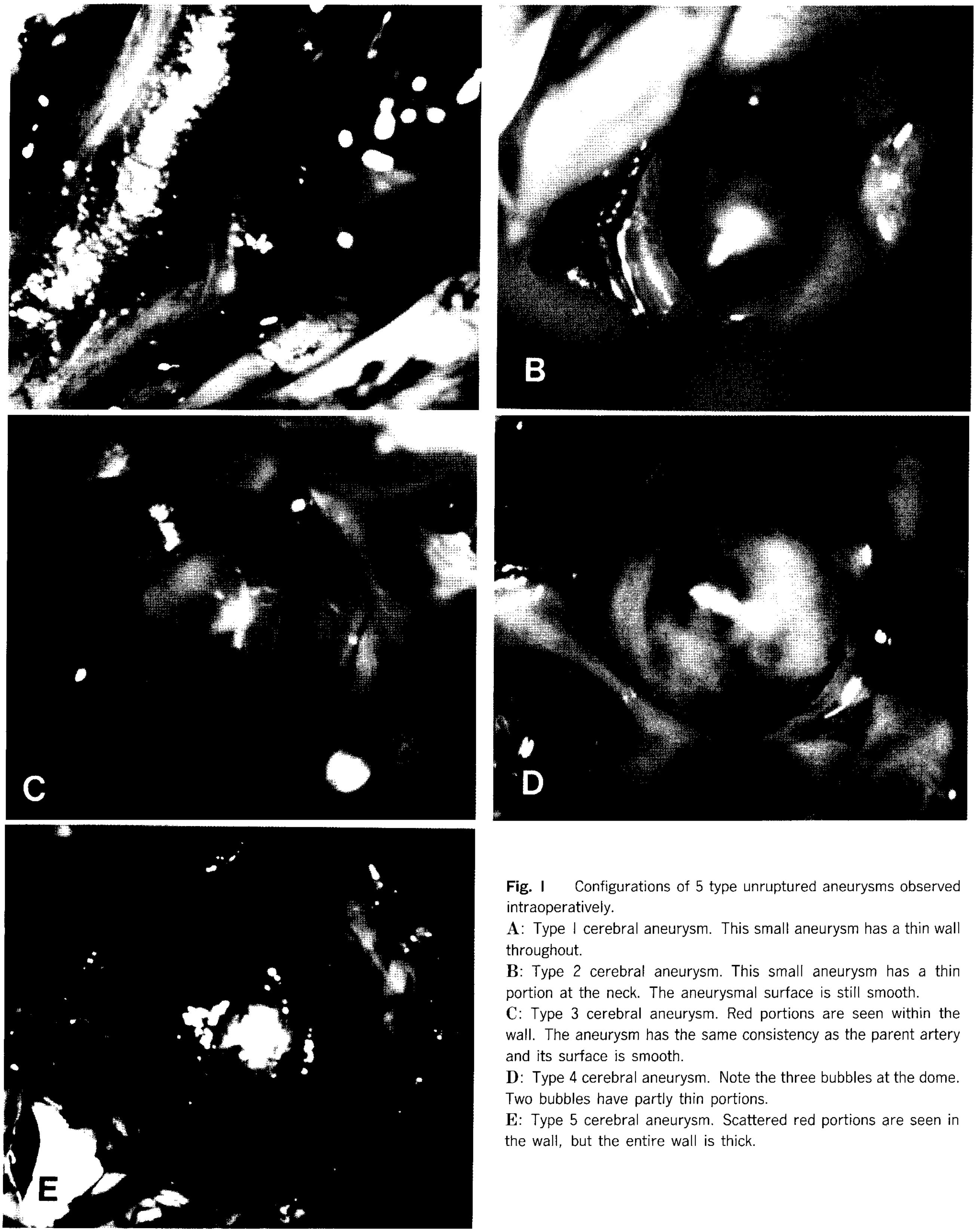

Fig. 1 Configurations of 5 type unruptured aneurysms observed intraoperatively.
A: Type 1 cerebral aneurysm. This small aneurysm has a thin wall throughout.
B: Type 2 cerebral aneurysm. This small aneurysm has a thin portion at the neck. The aneurysmal surface is still smooth.
C: Type 3 cerebral aneurysm. Red portions are seen within the wall. The aneurysm has the same consistency as the parent artery and its surface is smooth.
D: Type 4 cerebral aneurysm. Note the three bubbles at the dome. Two bubbles have partly thin portions.
E: Type 5 cerebral aneurysm. Scattered red portions are seen in the wall, but the entire wall is thick.

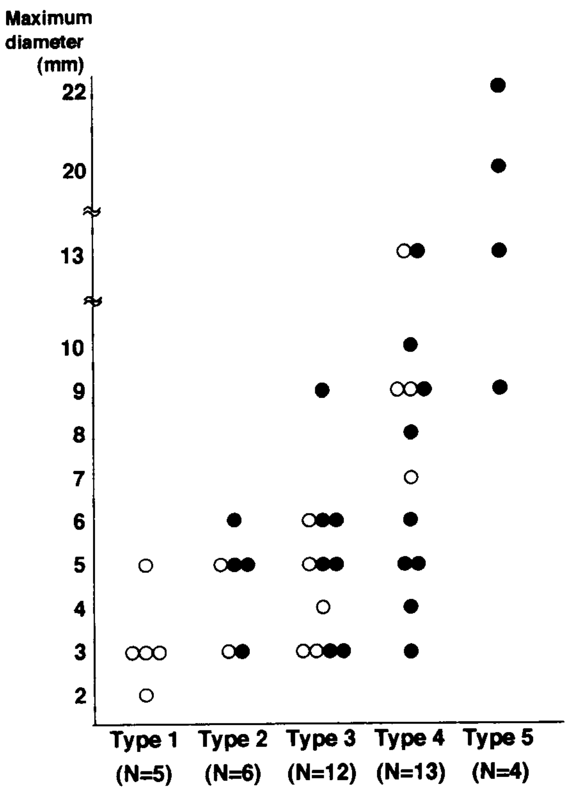

Fig. 2 Relation between the type and size of unruptured cerebral aneurysms. Closed circle indicates the aneurysm with a red and/or transparent portion in the wall.

Discussion

Histopathological changes, such as medial defects, degeneration of the internal elastic lamina of the arterial wall, and hemodynamic stress play an important role in the pathogenesis of cerebral aneurysms (9–12). Once an aneurysm forms, further pathologic changes that promote its growth occur in the aneurysmal wall.

The mechanisms of growth and rupture of an aneurysm have been studied from the standpoints of hemodynamics (10, 13) and histopathology (7–9, 14). We studied cerebral aneurysms from the standpoint of their intraoperative appearance. In our series, 10 of 11 lesions less than 4 mm in diameter were classified as types 1, 2, and 3. Type 1 aneurysms develop when a weak point at the apex of the arterial bifurcation can no longer resist the pulsatile blood pressure and impact of the blood stream (8, 12). These aneurysms are the earliest stage detected clinically, and the wall of the lesion at this stage is thin. In an autopsy study, Suzuki and Ohara (8) noted that the wall of an early aneurysm was thin and consisted of loose fibrous tissue similar to the adventitia of the parent artery. Although few aneurysms may rupture at this stage, we have seen the rupture of a very small aneurysm (15). For some reason, this aneurysm grew rapidly, hyperextending the thin wall.

Generally, however, tissue proliferates in the intima and adventitia of the dome wall as a result of mechanical stimulation from the bloodstream (8) and results in a type 2 aneurysm. In type 2, the thin portion of the neck appears to contribute to the growth of aneurysm through its extension or dilation of the orifice. In four of the six type 2 aneurysms in our series, turbulent flow could be seen through the thin portion of the neck. Rupture of the neck is rare (about 2%) (7), but when it occurs, it probably results from the thin portion described above. During surgery, these changes demand careful attention in dissecting around the neck and placing a clip. Wrap-clipping will be necessary if the clip is unacceptable. Clinically, few aneurysms less than 4 mm rupture, possibly because no local weak point exists, and the aneurysm appears to be stable. Our experience shows the wall of the small aneurysm to be smooth on the surface.

At the stage of type 3, the aneurysmal wall was thicker and it had the same consistency as the parent artery. However, 7 of the 12 type 3 aneurysms had one or more red portions. Handa *et al.* (12) found hemosiderin deposits in and around the aneurysmal wall in their experimental aneurysm study and stated that intramural hemorrhage played a role in aneurysmal growth. Artmann *et al.* (16) also found a small patent lumen filled with fresh blood cells in a large aneurysmal sac in his autopsy case. Although, as of yet, there are no reports which clearly describes the histologic aspects of the red portion seen in the aneurysmal wall, these changes may indicate intramural hemorrhage or cellular infiltration within the aneurysmal wall. When such a situation occurs, the wall undergoes secondary degeneration such as coarsening or necrosis (7, 17), resulting in the formation of local weak points. These weak points protrude either suddenly or gradually in reaction to hemodynamic forces and increased turbulent flow. Consequently, when the aneurysm reaches 4 mm or more, its wall shows various morphologic and qualitative changes (7, 8). Most of these

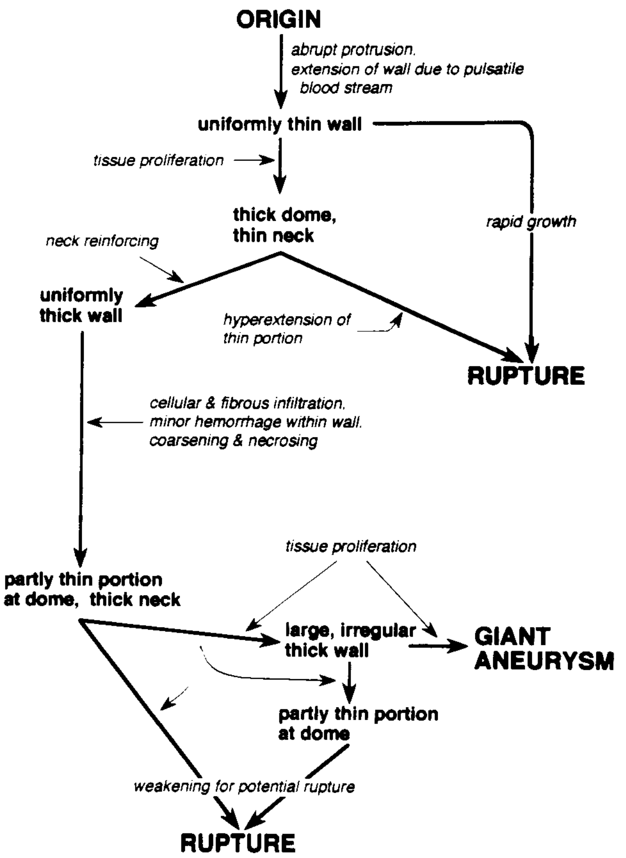

Fig. 3 The hypothesis of growth and rupture of unruptured cerebral aneurysms.

changes were seen at the dome, particularly near the apex, and were typically manifested in type 4 aneurysms. Thus, type 3 appears to be a transition from type 2 to type 4, and may be called a transitional stage in the growth of an aneurysm.

Bubbles or loculi formation at the dome is characteristic change in type 4 aneurysms. Further, small red and/or transparent portions were observed in these bubbles or loculi in nine aneurysms. In the histologic investigations, Stehbens (9) and Hassler (18) each found eosinophilic clumps resembling fibrin or fibrinoid materials in the thin portions of cerebral aneurysms. Stehbens (9) stated that this histologic change indicated that rupture was imminent. Crompton's autopsy study (7) revealed that, before an aneurysm grew, cellular or fibrin infiltration which resulted from intimal injury due to pulsation or turbulence was found in the aneurysmal wall, especially at the apex of the dome. He reported that cellular or fibrin infiltration in the aneurysmal wall tends to occur at a high frequency when the aneurysm grows to 4 mm or more, and emphasized that these were important changes associated with the growth and rupture of an aneurysm. The configurations of aneurysms we observed intraoperatively in the type 4 aneurysms are important because they promote weakening and potential rupture of thin portions. Loculated or multiloculated aneurysms in particular showed the most severe changes in the thin portions, which might indicate imminent rupture, even if the patient's blood pressure is sufficiently controlled. The process of growth and rupture of cerebral aneurysms based on our intraoperative study is shown in Fig. 3.

Angiographically, the loculation or irregularity of an aneurysmal sac occurs as the aneurysm grows and the likelihood of rupture increases (19, 20). Kassell and Torner (21) asserted that 71 % of ruptured aneurysms were less than 10 mm in diameter and 13 % of those were less than 5 mm. Our study revealed that aneurysms reaching 4 mm already showed local morphologic changes in the wall and were likely in a critical stage. Therefore, when aneurysms of 4 mm or more are detected, surgery should be considered. Furthermore, to prevent catastrophic subarachnoid hemorrhage, noninvasive screening of patients with unruptured cerebral aneurysms is important.

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Received January 31, 1994; accepted May 28, 1994.