Symptomatic Recurrence of Intracranial Arterial Dissections
Follow-Up Study of 143 Consecutive Cases and Pathological Investigation

Hideaki Ono, MD*; Hirofumi Nakatomi, MD*; Kazuo Tsutsumi, MD; Tomohiro Inoue, MD; Akira Teraoka, MD; Yuhei Yoshimoto, MD; Takafumi Ide, MD; Chifumi Kitanaka, MD; Keisuke Ueki, MD; Hideaki Imai, MD; Nobuhito Saito, MD

Background and Purpose—The frequency and pattern of symptomatic recurrence of spontaneous intracranial arterial dissection (IAD) are unknown.

Methods—A follow-up study of 143 patients (85 men, 58 women; mean age, 50.7 [7–83] years) with spontaneous IADs at The University of Tokyo and affiliated hospitals from 1980 to 2000 was conducted. Tissue samples of IAD vessels obtained from 13 patients at various intervals from onset were also examined histologically.

Results—With a mean follow-up of 8.2 years, symptomatic recurrence occurred in 47 patients (33%). Of 37 cases initially presenting with hemorrhage, 35 developed hemorrhagic recurrence with a mean interval of 4.8 days, and 2 developed nonhemorrhagic recurrences after 21 and 85 months, respectively. Of 10 patients initially presenting with nonhemorrhagic symptoms, 1 developed hemorrhagic recurrence 4 days later, and 9 developed nonhemorrhagic recurrences with a mean interval of 8.6 months. Histopathologically, the affected vessels in the acute stage of hemorrhage (days 0–6) demonstrated insufficient granulation formation within the pseudolumen, followed by marked intimal thickening around the pseudolumen and recapillarization vessel formation in the late stage (>day 30). In the late stage of brain ischemia, subintimal and subadventitial hemorrhage accompanied with intimal thickening was observed.

Conclusions—These data indicate that IAD is a disease carrying a relatively high risk of symptomatic recurrence, apparently occurring in 3 phases and patterns: early hemorrhagic recurrence, late nonhemorrhagic recurrence, and chronic fusiform aneurysm transformation. Knowledge of this triphasic recurrence and corresponding histopathological characteristics help determine the treatment and follow-up strategy for IAD patients. (Stroke. 2013;44:000-000.)

Key Words: follow-up ■ histopathology ■ infarction ■ intracranial arterial dissection ■ recurrence ■ subarachnoid hemorrhage ■ transformation

Spontaneous intracranial cerebral arterial dissection (IAD) has been attracting increasing attention as a cause of stroke.1–10 This entity is mainly divided into 2 types based on clinical manifestations: hemorrhagic type causing subarachnoid hemorrhage (SAH) by rupture of IAD, and nonhemorrhagic type presenting with headaches or symptoms caused by hemodynamic or thromboembolic brain ischemia. For patients with SAH, most neurosurgeons recommend early repair of the affected vessels either by open surgery or by endovascular technique,1,2,4,6–8 whereas conservative treatment has been advocated for unruptured IAD based on the recognition that such cases follow a relatively benign course.3,5,9,11 However, the long-term clinical course of IAD, which should influence clinical decision-making, is poorly understood.12 A detailed analysis of a series of 143 patients with acute IAD, including 13 cases in which tissues of IAD vessels could be obtained at surgery or at autopsy, is presented. In addition to the long-term follow-up information, a comparative analysis of their clinical course and histological findings was performed to gain insight into the mechanisms of this disease along its time course.

Patients and Methods

From April 1980 to December 2000, 143 consecutive patients with acute IADs were seen at our institutions. Cerebral angiography and computed tomography scans were performed in all cases for the diagnosis, and MRI was obtained in some cases to detect intramural hemorrhage. All cases satisfied 1 of the 3 diagnostic criteria for acute IAD: (1) the typical pearl and string or double lumen sign at a nonbranching site of the intracranial cerebral arteries on angiography; (2) fusiform dilatation with retention of contrast medium or angiographic steno-occlusive lesions accompanied by intramural hemorrhage

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From the Department of Neurosurgery, Faculty of Medicine, The University of Tokyo, Tokyo, Japan (H.O., H.N., H.I., N.S.); Showa General Hospital, Tokyo, Japan (K.T.); Fuji Brain Institute, Shizuoka, Japan (T.I.); Teraoka Memorial Hospital, Hiroshima, Japan (A.T.); Gunma University Hospital, Gunma, Japan (Y.Y.); Bokutoh General Hospital, Tokyo, Japan (T.I.); Department of Molecular Cancer Science, Faculty of Medicine, Yamagata University, Yamagata, Japan (C.K.); and Dokkyo University School of Medicine, Tochigi, Japan (K.U.).

*Drs Ono and Nakatomi contributed equally to this work.

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Correspondence to Hirofumi Nakatomi, MD, Department of Neurosurgery, The University of Tokyo Hospital, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113–8655, Japan. E-mail hnakatomi.tky@umin.ac.jp

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detected on MRI at the same region; or (3) histopathologically confirmed IAD. No obvious atherosclerotic changes were found in other intracranial arteries in any of the patients.

We defined symptomatic recurrence as any neurological symptoms attributable to recurrent arterial dissections after initial stroke. Thus, this definition includes three different forms of recurrent IAD, which are rediscrion of the same IAD, de novo formation of IAD, and chronic transformation of previously diagnosed IAD.

Medical records including all available imaging studies were reviewed. All patients were first contacted by letters and then by interviews or phone calls to collect follow-up information. In some cases, information was obtained indirectly through local physicians, hospital records, autopsy records, or death certificates. When available, angiograms obtained during the follow-up period were also reviewed. Follow-up information was obtained for all 143 patients. The study was approved by the internal review board of each hospital.

IAD vessels were obtained at surgery in 6 cases and at autopsy in 7. For histological examination, the tissues were fixed in 10% buffered formalin and embedded in paraffin. Four-micrometer thick tissue sections were made and stained with hematoxylin and eosin, elastica van Gieson, and elastica Masson stains. Histopathological findings on axial slices at the site with the maximum arterial diameter were used as representative findings. The degree of subadventitial or subintimal hemorrhage was classified into 4 groups based on the ratio of the portion lacking in IEL: none (<15%), slight (15%–30%), moderate (30%–50%), and severe (>50%). The degree of internal elastic lamina (IEL) fragmentation was classified into 4 groups based on the ratio of the portion lacking IEL relative to the whole circumferential length: none (<15%), slight (15%–30%), moderate (30%–50%), and severe (>50%). The degree of disruption of the media by intramural hemorrhage or its replacement by granulation tissue was classified based on the ratio of the occupied area relative to the whole area of the pseudolumen: none (<15%), slight (15%–30%), moderate (30%–50%), and severe (>50%). The degree of intimal hyperplasia was assessed based on the ratio of the portion accompanied by intimal hyperplasia relative to the portion lacking in IEL: none (<15%), slight (15%–30%), moderate (30%–50%), and severe (>50%). The degree of subadventitial hemorrhage assessed based on the ratio of the portion lacking in IEL relative to the whole circumferential length: none (<15%), slight (15%–30%), moderate (30%–50%), and severe (>50%). The degree of intimal hyperplasia was assessed based on the ratio of the portion accompanied by intimal hyperplasia relative to the portion lacking in IEL: none (<15%), slight (15%–30%), moderate (30%–50%), and severe (>50%). The degree of disruption of the media by intramural hemorrhage or its replacement by granulation tissue was classified based on the ratio of the occupied area relative to the whole area of the pseudolumen: none (<15%), slight (15%–30%), moderate (30%–50%), and severe (>50%). The degree of intimal hyperplasia was assessed based on the ratio of the portion accompanied by intimal hyperplasia relative to the portion lacking in IEL: none (<15%), slight (15%–30%), moderate (30%–50%), and severe (>50%). The degree of disruption of the media by intramural hemorrhage or its replacement by granulation tissue was classified based on the ratio of the occupied area relative to the whole area of the pseudolumen: none (<15%), slight (15%–30%), moderate (30%–50%), and severe (>50%). The degree of intimal hyperplasia was assessed based on the ratio of the portion accompanied by intimal hyperplasia relative to the portion lacking in IEL: none (<15%), slight (15%–30%), moderate (30%–50%), and severe (>50%). The degree of disruption of the media by intramural hemorrhage or its replacement by granulation tissue was classified based on the ratio of the occupied area relative to the whole area of the pseudolumen: none (<15%), slight (15%–30%), moderate (30%–50%), and severe (>50%).

The relation between recurrent arterial dissection and several risk factors was assessed on univariate analysis with the χ² test or Fisher exact probability test. The threshold of significance was set at 0.05. All calculated P values were 2-tailed.

**Results**

The ages of the 143 patients ranged from 7 to 83 years (mean, 50.7 years). There were 85 men and 58 women (Table 1). IADs were located in the anterior circulation in 31 cases: internal carotid artery in 8; anterior cerebral artery in 11; middle cerebral artery in 11; and posterior communicating artery in 1. The posterior circulation was affected in 112 cases: basilar artery in 7; vertebral artery in 99; posterior cerebral artery in 1; and posterior inferior cerebellar artery in 5. Multiple vessel dissections, consisting of bilateral vertebral artery lesions or vertebral artery and basilar artery lesions, were present in 21 (Supplemental Table 1).

The patients were divided into 2 groups based on their initial presentation: the hemorrhagic group presenting with SAH (86 patients, 60%), and the nonhemorrhagic group presenting with headache or neurological symptoms caused by brain ischemia (57 patients, 40%). The more patients with nonhemorrhagic IADs were diagnosed later in this study, as more MRI examinations have been performed (Supplemental Figure 1). The mean ages of the hemorrhagic and nonhemorrhagic groups were 52.8 and 47.5 years, respectively. Male patients were predominant in both hemorrhagic and nonhemorrhagic groups, with male/female ratios of 50/36 and 35/22, respectively. The vertebral artery was preferentially affected: 74.4% in the hemorrhagic group, and 61.4% in the nonhemorrhagic group. Male dominance was observed among patients with posterior circulation IAD (male/female=68/44), but not in those with anterior circulation IAD (male/female=17/14).

Follow-up periods ranged from 1 day to 25 years (mean, 8.2 years). Of the 86 patients in the hemorrhagic group, 54 (63%) were treated surgically with proximal clipping of the parent artery in 26, trapping in 17, wrapping in 3, base clipping in 4, and transarterial embolization in 4. The remaining 32 patients were treated conservatively. Of the 86 hemorrhagic group patients, 47 (55%) recovered well, 14 recovered with severe disability, and 25 (29%) died. Of the 57 patients in the nonhemorrhagic group, 45 (79%) were managed conservatively, and 12 (21%) underwent surgical intervention. Overall, 51 of the 57 patients (89%) made a good recovery, 6 recovered with severe disability, and none died. Survival outcomes did not differ significantly between patients with anterior circulation lesions and those with posterior circulation lesions. The clinical characteristics of the 47 patients (32.9%) developing symptomatic recurrence are shown in Table 2. The occurrence of recurrent 0 day to 7 years after the initial dissection. Of 86 cases initially presenting with hemorrhage (SAH), 35 developed hemorrhagic recurrence with a mean interval of 4.8 days (range, 0–26 days), and 2 developed nonhemorrhagic recurrences after 21 and 85 months, respectively: one patient developed uncontrollable hemifacial spasm because...
of gradual progression of a large dolichoectatic aneurysm (Figure 1A and 1B), and the other had a minor embolic stroke because of recanalization of the occluded middle cerebral artery by dissection. Of 10 patients initially presenting with nonhemorrhagic symptoms, 1 developed SAH 4 days after the initial ischemic event (Supplemental Figure 2A–C), and 9 developed nonhemorrhagic recurrence with a mean interval of 8.6 months: 5 patients developed new major strokes (Figure 1C and 1D), and the other 4 had new minor strokes caused by occlusion of perforating arteries.

In the hemorrhagic group, patients >50 years of age were more likely to have recurrent dissections (P=0.0100). Furthermore, patients with World Federation of Neurologic Surgeon’s clinical grade >3 also tended to recur (P=0.0093). In the nonhemorrhagic group, patients with internal carotid artery lesions were more likely to have a recurrent dissection (P=0.0158), and those with National Institute of Health Stroke Scale scores >6 tended to have recurrence (P=0.0383; Table 3). Pathological specimens were obtained from 9 untreated patients with hemorrhagic onset, 3 untreated patients with nonhemorrhagic onset, and 2 patients with hemorrhagic onset who were treated by proximal clipping or by trapping. There were no patients with past medical history of systemic connective tissue disease, vasculitis, and other vasculopathies. The time to histological examination from the initial onset varied from 0 days to 8 months (Table 4). In the pathological specimens, there was no evidence of an underlying vasculopathy predisposing to IAD and recurrence. Complete investigation of systemic blood vessels in them did not show any underlying vasculopathy predisposing to IAD and recurrence. Four characteristic features were identified: (1) IEL disruption and intramural hemorrhage (IMH) causing additional medial disruption; (2) replacement of IMH within the pseudolumen by granulation tissue; (3) reactive intimal thickening around the pseudolumen; and (4) recanalizing vessel formation in the thickened intima. Disruption of the IEL and media were found in all cases (Figure 2A–D, Supplemental Figure 3A–D). Replacement of IMH within the pseudolumen by granulation tissue was observed in all 6 samples obtained >14 days after onset (Figure 2A, Supplemental Figure 3C). In addition, intimal thickening was observed in 4 samples obtained 26 days from onset (Figure 2A–D, Supplemental Figure 3C and 3D). Recanalizing vessel formation within the thickened intima was observed in the 2 samples obtained >30 days after onset (Figure 2B, Supplemental Figure 3D). Three IADs presenting with cerebral ischemia but showing aneurysmal enlargement demonstrated subintimal hemorrhage (Figure 2C), medial disruption, and subadventitial hemorrhage (Figure 2D).

**Discussion**

The present study demonstrated that IAD is a disease carrying a relatively high risk of symptomatic recurrence (33%), which occurs in 3 phases: early recurrence within 1 month, mainly causing hemorrhagic events; late recurrence mainly presenting with nonhemorrhagic symptoms; and...
chronic fusiform aneurysm transformation. Late recurrence did occur, even long after the first year from the initial dissection, reflecting the slow process of this disease. Having lacked sufficient long-term follow-up studies, late recurrence of IAD has not been well recognized to date, and the prognosis of patients with IAD surviving the first month after the initial event has been presumed to be good. The results of the present study, however, indicate that closer follow-up for such patients would be necessary to monitor possible recurrences.

The type of recurrences followed the pattern of the initial event in the vast majority: 35 of 37 (95%) of recurrences in initially hemorrhagic cases developed hemorrhagic recurrences, and 9 of 10 (90%) recurrences in initially nonhemorrhagic cases had nonhemorrhagic recurrences. However, a transition from one type to another did occur in a small number of cases (6.4%). There was 1 case in the present series that initially presented with nonhemorrhagic symptoms and later developed SAH, and there were also 2 cases that initially presented with hemorrhage and later developed nonhemorrhagic symptoms. There have been sporadic case reports describing similar cases, and the present study of a large consecutive series confirmed that such a phenomenon can be observed in a small portion of patients with IAD. In one of the present cases, a transition from hemorrhagic to nonhemorrhagic led to the formation of chronic fusiform/dolichoectatic aneurysms 7 years after the initial event. Although such a possibility seems to be even less frequent, this case suggested that the underlying mechanisms are similar between arterial dissections and dolichoectatic aneurysms. Similar cases were reported by Dohi et al with vertebral artery dissection and by Tomasello et al with dissection at a distal branch of the middle cerebral artery.13,14

### Table 3. Significant Risk Factors of Patients With Recurrent Intracranial Arterial Dissections

| Risk Factor                              | Recurrence (+) (n=37) | Recurrence (−) (n=49) | P Value 
|------------------------------------------|-----------------------|-----------------------|--------
| **Hemorrhagic group**                   |                       |                       |        |
| Initial clinical grade: WFNS>3          | 27                    | 22                    | 0.0081* |
| GOS (>6 mo): independent                | 9                     | 38                    | <0.0001* |
| Age >50                                  | 26                    | 21                    | 0.0100* |

| **Nonhemorrhagic group**                |                       |                       |        |
| Lesion location: ICA                    | 3                     | 2                     | 0.0334* |
| NIHSS >6                                | 4                     | 6                     | 0.0383* |

WFNS indicates World Federation of Neurological Surgeon’s clinical grade; GOS, Glasgow outcome scale; ICA, internal carotid artery; NIHSS, National Institute of Health Stroke Scale.
*Statistically significant on either the χ2 test or Fisher’s exact probability test.

### Table 4. Pathological Findings of IAD Vessel Tissues at Various Times From the Initial Onset

<table>
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<tr>
<th>Days after onset</th>
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<tr>
<td>Lesion location</td>
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<td>Disruption of media by intramural hemorrhage</td>
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<td>Subintimal hemorrhage</td>
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<td>Granulation formation within pseudolumen</td>
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<td>Intimal thickening around pseudolumen</td>
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<td>Recanalizing vessel formation in thickened intima</td>
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ACA, indicates anterior cerebral artery; BA, basilar artery; H, hemorrhagic onset; IAD, intracranial arterial dissection; ICA, internal carotid artery; IEL, internal elastic lamina; Lt, left; N, nonhemorrhagic onset; NA, autopsied specimens were not available; PICA, posterior inferior cerebellar artery; Rt, right; VA, vertebral artery; (−), none; (+/−); slight; (+), moderate; (++), severe.
*These patients did have early hemorrhagic recurrence.
†These patients showed aneurysmal growth. Note that all the 3 IAD vessel tissues with nonhemorrhagic onset contained both subintimal and subadventitial hemorrhages.
Histological examination demonstrated several changes that apparently occurred after a specific time course. The universal histological observations of the IAD vessels were IEL disruption and medial disruption by IMH. Therefore, these changes probably were among the earliest processes of acute IAD formation. The next most common finding was replacement of IMH within the pseudolumen by granulation tissue. Notably, this pathological finding was not usually found in IAD vessels obtained at an acute stage, but it was observed in samples obtained >14 days after onset. The third most common finding was replacement of subintimal hemorrhage by the granulation tissue (asterisk) and marked intimal hyperplasia (small arrow) in the media (large arrow). Another segment of the IAD vessel tissue reveals recent subadventitial hemorrhage and disruption of the intima (arrowheads). Recanalized vessel formation within the thickened intima is also demonstrated in the other segment (arrowheads). Elastica Masson, original magnification ×50.

Figure 2. Pathological photomicrographs of representative cases with recurrent IAD along their time course. Tissues of IAD vessels were obtained from hemorrhagic IAD (A) or ischemic IAD (B–D). A. Histology of the IAD vessel 26 days after onset (van Gieson) shows that the IMH is almost all replaced by granulation tissue (asterisk), and reactive intimal thickening has started (small arrow) (Original magnification ×100). B–D, Histology of IAD vessel presenting with brain ischemia initially, then showing progressive aneurysm growth, obtained 30 days after onset at surgery, shows both replacement of subintimal hemorrhage by the granulation tissue (asterisk) and marked intimal hyperplasia (small arrow) (C). Another segment of the IAD vessel tissue reveals recent subadventitial hemorrhage and disruption of the media (large arrow) (D). Recanalized vessel formation within the thickened intima is also demonstrated in the other segment (arrowheads) (B). C: van Gieson, original magnification ×25; B, D, elastica Masson, original magnification ×50.)

Based on the findings presented here, we propose the following hypothesis for the mechanism of cerebral arterial dissection and its recurrence to explain the observed clinical course. The first change in IAD seems to be IEL and medial disruption. Some of the nonhemorrhagic dissections at this stage carry the risk of evolving into hemorrhagic dissection before initiation of the repair process. The earliest repair process seems to be replacement of intramural hemorrhage within the pseudolumen by granulation tissue, which is rapidly followed by intimal hyperplasia possibly occurring as a compensatory reaction to the damage. This process might start around 14 days after onset, but probably does not restore sufficient strength to the vessel wall. Therefore, the risk of rebleeding remains even after 21 days and would lead to hemorrhagic recurrence within a month. When intimal thickening reaches a sufficient level to prevent further medial dissection, neovascularization within the thickened intima seems to start, which can be as early as 30 days after onset. The new vessels within the intima seem to be fragile and cause repetitive intramural hemorrhage, which leads to the formation of chronic fusiform and dolichoectatic aneurysms as demonstrated in our previous study.15

Although further studies are needed to confirm this hypothesis, knowledge of this possible mechanism of formation, repair, and recurrence of IAD and their possible clinical manifestations would help understand the clinical features of IAD at different stages and would also help determine the appropriate treatment strategy.

One limitation of this study needs to be acknowledged. The study included only Japanese population which limits the generalizability of the results. The risk of symptomatic recurrence could be affected by the incidence of IAD. In fact, majority of the reported case series of IAD were from Asia.12,16,17 Therefore, caution must be applied in extrapolating the symptomatic recurrence in our cohort to other populations.

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Disclosures
None.

References
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Symptomatic recurrence of intracranial arterial dissections: follow-up study of 143 consecutive cases and pathological investigation
Supplemental Table S1.
Distribution of arterial involvement in 143 patients with intracranial arterial dissections

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<th>Arterial System</th>
<th>Hemorrhagic group: 86</th>
<th>Non-hemorrhagic group: 57</th>
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<td>VA unilateral: 78</td>
<td>52 (60%)</td>
<td>26 (46%)</td>
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<td>VA bilateral: 16</td>
<td>9 (10%)</td>
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<td>VA and BA: 5</td>
<td>3 (3.5%)</td>
<td>2 (3.5%)</td>
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<td>Carotid system: 31</td>
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<td>ICA extending into MCA: 5</td>
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<td>MCA: 11</td>
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<tr>
<td>Pcom: 1</td>
<td>1 (1.2%)</td>
<td>0</td>
</tr>
</tbody>
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VA, vertebral artery; BA, basilar artery; PICA, posterior inferior cerebellar artery; PCA, posterior cerebral artery; ICA, internal carotid artery; MCA, middle cerebral artery; ACA, anterior cerebral artery; Pcom, posterior communicating artery
Supplemental Figure S1.
Graph showing the number of cases of hemorrhagic and non-hemorrhagic IAD, and magnetic resonance imaging (MRI) in chronological order.

H, hemorrhagic IAD; N, non-hemorrhagic IAD
Supplemental Figure S2.
Neuroradiological imaging findings of representative case with initially ischemic intracranial arterial dissection (IAD) followed by recurrent hemorrhagic IAD

Initial CT scan (A) shows no obvious subarachnoid hemorrhage (SAH), but a small infarction in the right cerebellar watershed area between the superior cerebellar artery and anterior inferior cerebellar artery is seen. The second CT (B) show thick SAH at the right cerebellopontine cistern 4 days after admission. The cerebral angiogram (C) shows a right vertebral artery (VA) dissecting aneurysm involving the posterior inferior cerebellar artery (right anterior oblique view). The contralateral VA is hypoplastic. Arrowheads indicate the pearl and string sign.
Supplemental Figure S3.
Pathological photomicrographs of representative cases with recurrent IAD along their time course. Tissues of IAD vessels were obtained from hemorrhagic IAD (A-C) or ischemic IAD (D).

(A, B), Histology of the IAD vessel 2 days (A) and 6 days (B) after onset (van Gieson) shows disruption of the internal elastic lamina (IEL), medial disruption, intramural hemorrhage (IMH), and formation of the pseudolumen (PL). There is only slight granulation tissue in the PL (asterisk) (Original magnification x40).

(C), Histology of the IAD vessel 39 days after onset (van Gieson) shows complete replacement of the PL by granulation tissue (asterisk) and severe intimal thickening (small arrow) (Original magnification x10).

(D), Histology of IAD vessel presenting with cerebellar infarction obtained 39 days after onset at autopsy shows complete replacement of the PL by granulation tissue (asterisk), severe intimal thickening (small arrow), and formation of vasa vasorum within the adventitia (arrowheads) (van Gieson) (Original magnification x20).
頭蓋内動脈解離の症候性再発
連続 143 例の経過観察と病理学的検査

Symptomatic Recurrence of Intracranial Arterial Dissections
Follow-Up Study of 143 Consecutive Cases and Pathological Investigation

Hideaki Ono, MD1; Hirofumi Nakatomi, MD1; Kazuo Tsutsumi, MD2; Tomohiro Inoue, MD3; Akira Teraoka, MD4; Yuhei Yoshimoto5, MD; Takafumi Ide, MD6; Chifumi Kitanaka, MD7; Keisuke Ueki, MD8; Hideaki Imai, MD1; Nobuhito Saito, MD1

1 Department of Neurosurgery, Faculty of Medicine, The University of Tokyo, Tokyo, Japan ; 2 Showa General Hospital, Tokyo, Japan ; 3 Fuji Brain Institute, Shizuoka, Japan ; 4 Teraoka Memorial Hospital, Hiroshima, Japan ; 5 Gunma University Hospital, Gunma, Japan ; 6 Bokutoh General Hospital, Tokyo, Japan ; 7 Department of Molecular Cancer Science, Faculty of Medicine, Yamagata University, Yamagata, Japan ; 8 Dokkyo University School of Medicine, Tochigi, Japan

Abstract

背景および目的：自然発症の頭蓋内動脈解離（IAD）の症候性再発の頻度およびパターンは未知である。

方法：1980年から2000年までに東京大学病院およびその関連病院で自然発症のIAD 143例（男性85例、女性58例、平均年齢50.7歳（7〜83歳））の経過観察を行った。発症から様々な間隔で採取した13例のIAD血管の組織標本につき組織学検査を行った。

結果：平均経過観察期間は8.2年、症候性再発を生じたのは47例（33%）であった。初期に出血が認められた37例（35例に平均4.8日以内に出血を伴う再発が認められ、残り2例はそれぞれ21か月後と85か月後に非出血性の再発を認めた。初期に出血が認められなかった10例中1例は4日後に出血を伴う再発を生じ、残り9例では、平均8.6カ月で非出血性の再発を認めた。組織病理学的には、出血急性期（0〜6日目の血管）では、血管偽腔内の肉芽形成は不十分で、その後（31日目以降）、偽腔周囲に顕著な内膜肥厚と血管再開通が認められた。脳虚血の後期には、内膜肥厚を伴う内膜下出血と血管外膜下の出血が認められた。

結論：上記データにより、IADは症候性再発のリスクが比較的高い疾患で、早期の出血性再発、後期の非出血性再発、および慢性化した結節状動脈瘤の3相とパターンがあることが示された。IAD患者の治療と経過観察の戦略決定には、この3相の再発とそれぞれの病理解剖学的特徴の知見は、治療と経過観察の計画策定に役立つ。

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図2
classical IAD再発症例の時系列病理学的観察細微写真。IAD血管の組織は出血性IAD(A)および虚血性IAD(B〜D)から得た。A、発症後26日目のIAD血管の組織像（van Gieson染色）。偽内血腫がほとんどすべて肉芽組織に代わっており（*）、反応性の内膜肥厚が始まっており（原寸×100）。B〜D、最初に脳虚血を呈し、その後、動脈瘤が進行性に増大し、手術時発症後30日目のIAD血管の組織像。内膜下出血は、肉芽組織（*）および顕著な内膜肥厚（小さな矢印）に代わっている（C）。IAD血管の他の部位では、最近生じた内膜下出血と中膜の断面を呈している（大きな矢印）（D）。その他の部位では、肥厚した内膜内で再開通した血管の形成も見られる（矢頭）（B）。C、van Gieson染色、原寸×25；B、D、elastica Masson染色、原寸×50。