

# Cerebral dissecting aneurysm and intimal fibroelastic thickening of cerebral arteries

## Case report

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✓ A 19-year-old white man developed aphasia and right hemiplegia after several falls while waterskiing. Cerebral angiography displayed a ripple appearance and a "string of beads" sign along the left middle cerebral artery, with occlusion or stenosis of most of its branches. The patient died after 6 days, of transtentorial herniation due to massive left cerebral infarction. At necropsy, the infarct was found to be due to a subintimal dissecting aneurysm of the left middle cerebral artery. Multifocal areas of intimal fibroelastic thickening (IFT) were found not only at the site of dissection, but also in the other cerebral arteries, most prominent at the bifurcations of the vessels.

A systematic study of cerebral arteries performed in six control cases revealed that IFT was present in a similar distribution to that seen in the patient described. However, the degree of IFT in this patient was greater than in the controls. Some individuals with excessive IFT may be more susceptible to cerebral dissecting aneurysm under a variety of stresses, especially trauma.

**KEY WORDS** • cerebral dissecting aneurysm • ripple appearance • intimal fibroelastic thickening • intimal pad • fibromuscular dysplasia

**C**EREBRAL dissecting aneurysm (CDA) is much less common than dissecting aneurysm of the aorta or other peripheral vessels,<sup>17,24,25,35,38</sup> although this entity has been reported more frequently in recent years.<sup>39</sup> It is an infrequent cause of cerebral infarction.<sup>4,5,26</sup> Some authors have emphasized that when cerebral infarction occurs in young, previously healthy individuals, CDA should be considered in the differential diagnosis.<sup>5,8,17,24,25,38</sup> The exact mechanism of CDA, however, is obscure in the majority of the cases.

This case involves a 19-year-old student who sustained a massive cerebral infarct due to an extensive subintimal dissecting aneurysm of the left middle cerebral artery (MCA). Pathological studies disclosed a moderate to marked degree of intimal fibroelastic thickening (IFT) in the cerebral arteries, which was more prominent than in six cases studied as controls.

## Case Report

This 19-year-old previously healthy youth was transferred to the Hospital of the University of Pennsylvania from a local hospital because of aphasia and right hemiplegia. On the previous day, while waterskiing, he had taken several hard falls and suddenly signaled to his friends that he wanted to stop. He appeared ill on climbing into the boat, had difficulty in expressing himself, and was noted by his friends to have weakness of his right side. He was said to have consumed beer and may have ingested lysergic acid diethylamide (LSD). He became progressively unresponsive and comatose. Past medical history and family history were noncontributory.

**Examination.** Physical examination on admission revealed a well developed, well nourished young man in a semicomatose state. Blood pressure was 160/80

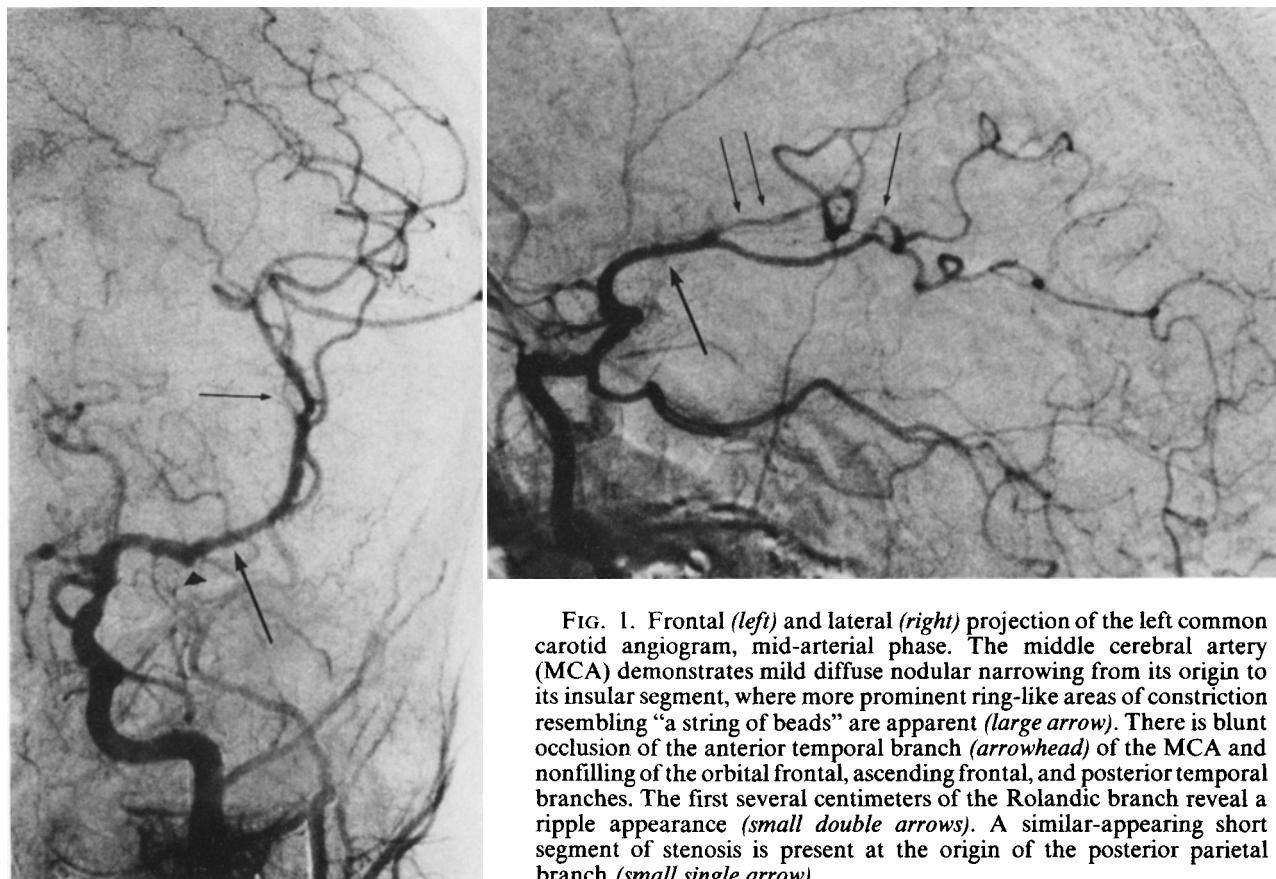


FIG. 1. Frontal (left) and lateral (right) projection of the left common carotid angiogram, mid-arterial phase. The middle cerebral artery (MCA) demonstrates mild diffuse nodular narrowing from its origin to its insular segment, where more prominent ring-like areas of constriction resembling "a string of beads" are apparent (large arrow). There is blunt occlusion of the anterior temporal branch (arrowhead) of the MCA and nonfilling of the orbital frontal, ascending frontal, and posterior temporal branches. The first several centimeters of the Rolandic branch reveal a ripple appearance (small double arrows). A similar-appearing short segment of stenosis is present at the origin of the posterior parietal branch (small single arrow).

mm Hg in both arms, respiration was 18/min, and pulse 54/min. There was no evidence of trauma. The carotid pulses were equal bilaterally, and there were no bruits. He had a right hemiparesis and hemihypesthesia. There was no papilledema. The rest of the general physical examination was unremarkable.

Laboratory data on admission revealed normal blood examination, platelet counts, and coagulation studies. The electrocardiogram showed sinus tachycardia with nonspecific ST-T wave abnormalities. The cerebrospinal fluid was of normal pressure and without cells.

Cranial computerized tomography on admission showed an ill-defined large low-density area in the left cerebral hemisphere in the distribution of the MCA, with a moderate shift of the midline structures to the right. Bilateral carotid angiography was performed via percutaneous transfemoral catheterization on the same day. The left carotid angiogram revealed no abnormality in the extracranial arteries. There was a slightly tapered and nodular narrowing of the supraclinoid segment of the left internal carotid artery (ICA) which was most marked just beyond the origin of the posterior communicating artery (Fig. 1). The left MCA was narrowed in a nodular fashion, beginning at its origin and extending into the insular

branches, where multiple constricting ring-like ridges caused a "string of beads" appearance (Fig. 1). There was blunt occlusion of the anterior temporal branch and no filling of the orbital frontal, ascending frontal, and posterior temporal branches. The Rolandic branch had a wavy ribbon-like segment of narrowing for several centimeters from its origin (Fig. 1). This ripple appearance was suggestive of an intraluminal filling defect. A similar appearance was noted at the origin of the posterior parietal branch (Fig. 1). The right carotid angiogram showed no evidence of extra-cranial or intracranial vascular disease, and both anterior cerebral arteries filled.

**Course.** The patient was intubated, and a bolt was placed in the subdural space to record intracranial pressure (ICP) continuously. The ICP was elevated from 30 to 50 mm Hg and was difficult to control despite high doses of dexamethasone, hyperventilation, hypertonic mannitol, and, ultimately, pentobarbital coma. Four days later, the patient developed signs of transtentorial herniation due to the massive left cerebral infarction with brain swelling, and died on the 5th hospital day.

**Postmortem Examination.** The pertinent findings of the visceral autopsy consisted of hemorrhagic gas-

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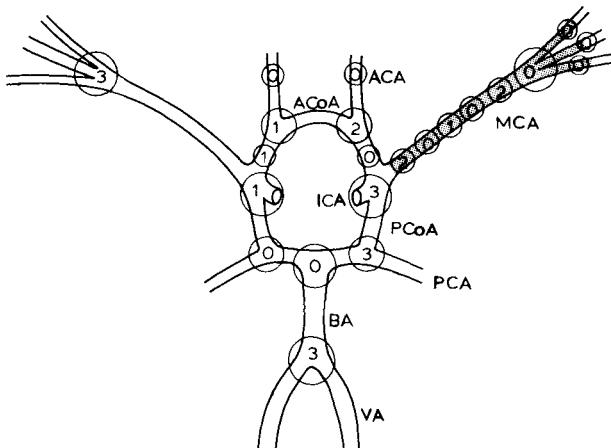


FIG. 2. Distribution of intimal fibroelastic thickening (IFT) in the present case. *Shaded area*: site of the subintimal dissecting aneurysm of the left middle cerebral artery (MCA). Degree of IFT: 0 = normal artery; 1 = mild IFT; 3 = marked IFT. Abbreviations: ACA = anterior cerebral artery; BA = basilar artery; VA = vertebral artery; ACoA = anterior communicating artery; PCoA = posterior communicating artery; PCA = posterior cerebral artery.

tritis without ulcers and hemorrhagic pneumonia. No evidence of atherosclerosis was noted. Focal IFT (composed of fraying, duplication, interruption, and hyperplasia of the internal elastic lamina) was seen in the coronary, renal, and splenic arteries, and was particularly common in the pulmonary arteries.

The ICA's were patent when perfused with water. Examination of the brain before and after fixation in formalin revealed complete occlusion of the left MCA from just distal to its origin to beyond the trifurcation. There was an acute cerebral infarction of the entire territory of the left MCA. There were herniations of the left cingulate gyrus, left uncus, and both parahippocampal gyri.

Microscopic examination confirmed the presence of acute cerebral infarction. Multiple sections were taken from the occluded left MCA and other cerebral arteries (Fig. 2). A subintimal dissecting aneurysm began at the origin of the left MCA, the true arterial lumen being markedly compressed by the hematoma in the dissection (Fig. 3). The dissecting aneurysm extended to the branches of the left MCA beyond its trifurcation. A tear was noted at the beginning of the aneurysm in a region of IFT, which consisted of fraying, duplication, and hyperplasia of the internal elastic lamina (Fig. 3). The media and adventitia appeared normal. Similar areas of IFT were found in more distal segments of the left MCA and in all the nondissected cerebral arteries examined (Fig. 2). These fibroelastic prominences were more common and more prominent at or near bifurcations of the cerebral arteries (Fig. 3 *lower*).

## Studies on Control Cerebral Arteries

Cerebral and visceral arteries were studied in cadavers from the following six control cases: 1) a 27-year-old man with cerebral astrocytoma; 2) a 26-year-old man, whose sudden death was probably due to abnormalities in the cardiac conducting system; 3) a 22-year-old woman with sudden death and a history of myocarditis; 4) a 31-year-old woman with juvenile diabetes mellitus and arteriosclerosis without atherosclerosis of the large vessels; 5) a 52-year-old man with idiopathic interstitial fibrosis of the lungs and alcoholic liver cirrhosis; and 6) a 9-year-old boy with leukemia.

All major cerebral arteries were dissected, fixed in formalin, and examined systematically. Serial longitudinal and transverse sections were embedded in paraffin, and sections were stained with hematoxylin and eosin and elastica-van Gieson methods. Many arterial segments contained areas of IFT, but they were more common at or near bifurcations, as noted in our patient. However, comparison of IFT between our case and the controls showed that IFT of our case was more prominent.

Representative sections from visceral organs also revealed areas of IFT which were primarily situated at or near branching sites of the coronary, renal, and splenic arteries, but were most prominent in the pulmonary arteries. Comparison between our patient and the controls did not demonstrate any consistent differences in the degree of visceral arterial IFT.

## Discussion

Cerebral dissecting aneurysms have been reviewed by Stehbens,<sup>35</sup> Kunze and Schiefer,<sup>17</sup> Sato, *et al.*,<sup>24</sup> and Yonas, *et al.*<sup>39</sup> Many of the reviews and case reports indicate common clinical and pathological features of this entity: 1) CDA primarily occurs in the second to the fourth decade of life, with the age peak between 20 and 30 years.<sup>17,35</sup> 2) Most patients are previously healthy without any predisposing factors of stroke.<sup>5,8,25,35,39</sup> 3) The plane of dissection is usually subintimal,<sup>8,17,22,24,26,30,35,39</sup> while that of the aorta and other extracranial arteries is medial or between the media and adventitia.<sup>19,35,37</sup> 4) Clinically, CDA usually takes the form of an acute cerebral infarct<sup>8,17,24,35,39</sup> and the MCA's are the most commonly involved territory, followed by the basilar artery.<sup>17,35</sup>

Various angiographic findings of CDA have been reported,<sup>1,8,17,22,25,30,39</sup> among which two patterns have been suggested as characteristic of CDA. The first is a wavy ribbon-like (ripple) appearance in the vessel wall,<sup>30</sup> which was noted in our case (Fig. 1) and probably represents an infolding and buckling of the intima following the dissection (Fig. 3 *upper right*). A more specific angiographic appearance of CDA, as described by Kunze and Schiefer,<sup>17</sup> is visualization of flow in true and false lumens, which was not seen in the current case.

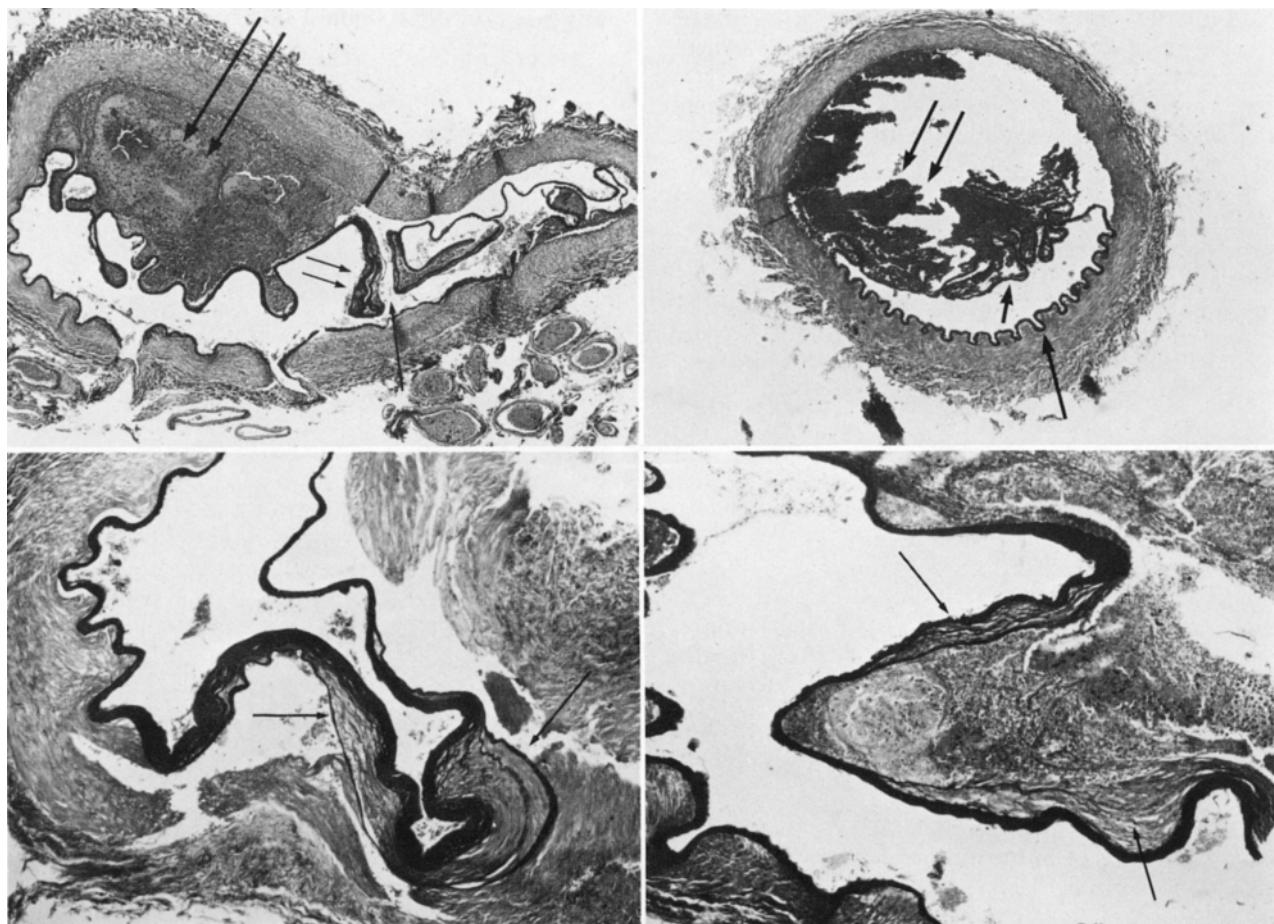


FIG. 3. Photomicrographs of sections of the cerebral arteries. *Upper Left*: The beginning of the subintimal dissecting aneurysm at the origin of the left middle cerebral artery (MCA). A small single arrow indicates a tear of the internal elastic lamina which exhibits fraying, duplication, and hyperplasia (small double arrows). Double large arrows: subintimal hematoma. Elastica-van Gieson,  $\times 18.5$ . *Upper Right*: Cerebral dissecting aneurysm of the left MCA proximal to its trifurcation (in the region of the "string of beads" seen in Fig. 1). Single arrows show the internal elastic lamina, double arrows subintimal hematoma. Elastica-van Gieson,  $\times 18.5$ . *Lower Left*: A marked degree of intimal fibroelastic thickening (arrows) of the internal elastic lamina at the termination of the left internal carotid artery just proximal to the section shown (*upper left*). Elastica-van Gieson,  $\times 74$ . *Lower Right*: Intimal fibroelastic thickening (arrows) of the internal elastic lamina at the trifurcation of the nondissected MCA on the right. Elastica-van Gieson,  $\times 74$ .

Whereas atherosclerosis is considered a major factor in the subintimal dissection of extracranial arteries,<sup>6</sup> several hypotheses concerning the pathogenesis of CDA have been discussed in the literature.<sup>17,24,35,39</sup> Trauma and congenital defects in the cerebral arterial wall are most commonly mentioned. A few cases of dissection have been attributed to luetic arteritis, medial degeneration, migraine, and atherosclerosis.<sup>1</sup> However, congenital defects in the cerebral arterial wall may be of doubtful significance.<sup>35</sup> Trauma, which may be minimal, is associated with many cases of CDA.<sup>5,15,17,24,35,39</sup> In this patient, CDA may have been associated with several hard falls while waterskiing. Interestingly, an almost identical case to ours has been reported previously, diagnosed as posttraumatic MCA

occlusion.<sup>5</sup> Nevertheless, the mechanism by which trauma causes disruption of the vessel wall is unknown.<sup>5,35</sup>

Histologically, the majority of reported cases with CDA display little or no alteration in the arterial wall, apart from lesions of the internal elastic lamina.<sup>4,5,8,22,25,26,35,38</sup> However, systematic study of all cerebral arteries has rarely been carried out. Chang, et al.,<sup>4</sup> described intimal lesions in an 8-year-old boy with bilateral CDA of the MCA's. Intimal lesions were noted in all the major vessels of the intracranial carotid system, whereas the vertebral and posterior cerebral arteries were spared. The intimal lesions were more common at the bifurcations and were more prominent than in the MCA's of two age-matched

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controls. Pilz and Hartjes<sup>20</sup> also described diffused intimal changes in the intracranial arteries in a patient with multiple CDA's. A systematic study of the cerebral arteries of our patient and six controls revealed that IFT was more prominent in the cerebral arteries of our patient (Figs. 2 and 3 *lower*). This suggests that some individuals may have excessive development of IFT and, as a result, may be more susceptible to CDA under a variety of stresses, particularly trauma. It is unknown to what extent these intimal changes are developmental and/or acquired. The study of visceral arteries did not demonstrate consistent differences of IFT between our patient and the controls. However, no definite conclusions could be made about the difference, because more numerous and serial sections of the arteries in and outside the visceral organs would be required for precise comparison.

We prefer the term "intimal fibroelastic thickening" to "intimal pad," because "intimal pad" indicates an area of intimal proliferation at the bifurcations,<sup>3,11,16,31-34,36</sup> and the intimal changes here were seen not only at the bifurcations, but also in the intervening segments of the cerebral arteries. Virtually all cerebral artery bifurcations in all age groups have intimal pads or intimal cushions.<sup>16</sup> "Pads" are also noted at points of bifurcation of peripheral vessels such as splenic, coronary, and renal arteries.<sup>28</sup>

The significance of "intimal pads" has been debated.<sup>3,11,31,33,34</sup> "Pads" are related to hemodynamic factors at points of bifurcation.<sup>3,34,36</sup> They are considered to be a physiological structure that may play a role in the regulation of blood flow and may represent compensatory contractile anatomic structures that respond to hemodynamic stress. Such stresses could lead to degeneration of the elastica, which could be a pathological precursor to atherosclerosis.<sup>32</sup> A transition from intimal pad to atherosclerosis has been noted.<sup>34</sup> Similar intimal changes of lesser severity have also been noted in nonbifurcating segments of cerebral arteries.<sup>3,4</sup>

A disorder that may well be confused with CDA is fibromuscular dysplasia (FMD). Several case reports of intracranial FMD have been published, with the diagnosis based solely on the "string of beads" sign in the affected cerebral arteries seen on angiography.<sup>7,13,18,27,29,40</sup> This sign has been claimed to be pathognomonic of FMD;<sup>7,13,18,27,29,40</sup> however, similar angiographic findings were noted in the present case, and have been seen in other cases of CDA.<sup>8,17,20,39</sup> Therefore, it may not be possible to differentiate between these two conditions with cerebral angiography. In fact, a case identical to that of our patient has been reported as FMD, based on cerebral angiography.<sup>14</sup> Typically, FMD involves the extracranial portion of the ICA, and spares intracranial arteries.<sup>2,12,23</sup> Relatively few of the cases of intracranial FMD include pathological studies;<sup>10,18,20,21</sup> some of them are histologically not convincing and show IFT similar to that noted in our case.<sup>18,20</sup> It is unlikely that

our case is of intracranial FMD because of the distribution of IFT and histological differences between IFT and FMD. Arterial lesions due to FMD involve the entire circumference of the arterial wall, resulting in significant constriction of the arterial vascular lumen.<sup>9,10,21</sup> This was not seen in the present case. Also, the visceral organs of our patient did not contain evidence of FMD. Pilz and Hartjes<sup>20</sup> described a case of FMD and multiple dissections of cerebral arteries associated with moyamoya syndrome. In their case, changes typical of FMD were noted in the extracranial portion of the ICA, and angiographic characteristics of FMD and "intimal dysplasia" as seen in our patient were present in their patient's intracranial arteries. They assumed that CDA was causally related to FMD, but the combination may be coincidental because of the ubiquitous prevalence of IFT in cerebral arteries. However, CDA may be one of the underlying causes of moyamoya syndrome.

No cases of CDA have been treated successfully by surgical intervention.<sup>17,39</sup> This is because of the relative rarity of the disease and/or failure to consider the possibility of CDA<sup>17,24,25,38,39</sup> in the differential diagnosis. However, operative possibilities, especially microvascular bypass procedures, may help in cases of partial or complete occlusion of the cerebral arteries.<sup>8,17,39</sup> In order to make surgical therapy possible, it is necessary to consider the possibility of CDA in cases of all young or relatively young patients with cerebral infarctions without any predisposing factors of stroke.<sup>5,8,17,24,25,38</sup> Prompt cerebral angiography is required to identify the characteristic angiographic patterns, because of the rapid occurrence of thrombosis.<sup>17,39</sup>

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