Intracranial aneurysms (IAs) that undergo rupture causing subarachnoid hemorrhage (SAH), are common in young patients with coarctation of the aorta (CoA), but rarer in middle-aged and elderly patients. The pathogenesis of IAs associated with CoA remains unclear. We report the case of a 50-year-old woman who presented with SAH. On evaluation, six IAs were distributed among the anterior communicating artery (ACoA) (ruptured), distal segments of both anterior cerebral arteries (ACA), the left internal carotid artery (ICA), the bifurcation of the left middle cerebral artery (MCA)/MCA early branch, and the inferior trunk of the left MCA. CoA was also diagnosed. The ruptured ACoA IA, and two other unruptured IAs, were successfully clipped during emergency surgery. Postoperative intensive care was instituted to avoid cerebral vasospasm and renal or spinal cord ischemia. During the same hospitalization, the remaining three IAs were clipped at a second surgery. She was discharged with slight cognitive impairment eighty days after admission. Subsequently, she underwent elective treatment for the CoA. According to the literature, IAs associated with CoA have a higher tendency to involve the ACoA than IAs without CoA. Moreover, adult CoA patients tend to have multiple IAs, considered to be due to hypertension associated with CoA, as well as genetic predisposition. In CoA patients, ruptured IAs should be treated as early as possible before correction of the CoA. Close postoperative observation with management of cerebral vasospasm, renal or spinal cord ischemia, and respiratory compromise in the perioperative period is vital. (J Nippon Med Sch 2017; 84: 186–192)

Key words: intracranial aneurysm, subarachnoid hemorrhage, coarctation of the aorta
distal segments of both anterior cerebral arteries (ACAs), a 2 mm IA in the communicating segment of the left internal carotid artery (ICA), a 4 mm IA at the bifurcation of the left middle cerebral artery (MCA)/MCA early branch, and a 2 mm IA involving the inferior trunk of the left MCA (Fig. 2). 3DCTA of the aorta demonstrated CoA located just distal to the origin of the left subclavian artery, with extensive collateral circulation, including internal thoracic artery-external iliac artery anastomoses and axillary artery-chest wall anastomoses (Fig. 3). Physical examination revealed a grade 3/6 systolic murmur at the left sternal border. Blood pressure was 146/69 mm Hg in the upper extremity and 75/58 mm Hg in the lower extremity. Based on these clinical and radiological findings, SAH due to the ruptured ACoA aneurysm was strongly suspected. Informed consent was obtained from a legal representative and emergency surgery was performed to treat the IAs.

First Operation
After bifrontal craniotomy, an anterior interhemispheric approach revealed the large IA arising from the ACoA. We confirmed the rupture point, and its neck was closed with one clip. The remnant of the IA was then obliterated with another clip. The unruptured IAs located in the distal segments of the ACAs were closed with one clip (right ACA) and two clips (left ACA), respectively.

First Postoperative Course
The patient regained consciousness on the first postop-
Fig. 3 (a) Three dimensional computed tomography angiography (3DCTA) of the aorta, left lateral view, showing coarctation of the aorta (CoA) localized just distal to the left subclavian artery (arrow). (b) 3DCTA of the aorta, anterior view, showing collateral circulation including internal thoracic artery-external iliac artery anastomoses and axillary artery-chest wall anastomoses (arrowheads).

operative day. Mainly using diuretics and low doses of nicardipine, we lowered the blood pressure to maintain an upper extremity systolic pressure of 140 to 160 mm Hg and a lower extremity systolic pressure of 70 to 90 mm Hg. Dyspnea developed; bilateral pleural effusions were found, and treated with bilateral chest tubes on the 11th postoperative day. Symptomatic cerebral vasospasm was not observed. Because of concern for intracranial hypertension potentially causing additional IA ruptures, she was scheduled for a second operation on the 34th postoperative day.

Second Operation
After left frontotemporal craniotomy via a pterional approach, the IAs involving the ICA, the bifurcation of the left MCA/MCA early branch, and the inferior trunk of the left MCA were identified, and their necks were each closed with one clip.

Second Postoperative Course
The postoperative course was uneventful and she was discharged 46 days after the second operation with slight cognitive impairment. She underwent left subclavian artery-distal descending aortic bypass grafting at another hospital three months after discharge, and her blood pressure normalized, with no difference between upper and lower extremities and no need for antihypertensive medication.

Discussion
The pathophysiologic basis of the association of IAs with CoA is still unknown. Two lines of thought suggest that there is either a common inherited predisposition for the two lesions\(^{19-22}\), or that both entities result from inadequately controlled hypertension\(^{23,24}\).

The myocardial and cervicocephalic arteries and the aortic arch all arise from embryonic neural ridge tissue, also called the neural crest. An error in neural crest development may be the common factor in the association between IA and CoA\(^{19-22}\). Table 1 shows the demographic and clinical features of previously reported SAH cases associated with CoA. In these series, there were 28 SAH patients with CoA and 41 IAs, with 11 (26.8%) involving the ACoA, nine (22.0%) involving the IC-posterior communicating artery (PCoA) junction, six each (14.6%) involving theACA and the MCA, four (9.8%) involving the ICA, three (7.3%) involving the basilar artery (BA), and one each (2.4%) involving the posterior cerebral artery.
SAH Associated with CoA

Table 1  Reported cases of subarachnoid aneurysmal hemorrhage associated with coarctation of the aorta

<table>
<thead>
<tr>
<th>Author (Year)</th>
<th>Age/Sex</th>
<th>Prior diagnosis of CoA</th>
<th>No. of IAs</th>
<th>Location of IAs</th>
<th>GOS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benyounes (2011)⁶</td>
<td>20/M</td>
<td>No</td>
<td>2</td>
<td>*MCA×2</td>
<td>GR or MD</td>
</tr>
<tr>
<td>Helbok (2011)⁷</td>
<td>28/M</td>
<td>No</td>
<td>3</td>
<td>*ACoA, ICA, MCA</td>
<td>GR</td>
</tr>
<tr>
<td>Martin (2010)¹⁰</td>
<td>N.D. (young)/F</td>
<td>No</td>
<td>1</td>
<td>*IC-PCoA</td>
<td>GR</td>
</tr>
<tr>
<td>Hudaoglu (2006)⁸</td>
<td>15/F</td>
<td>No</td>
<td>1</td>
<td>*IC-PCoA</td>
<td>D</td>
</tr>
<tr>
<td>Victor (2005)¹⁷</td>
<td>27/M</td>
<td>No</td>
<td>2</td>
<td>*IC-PCoA×2</td>
<td>GR or MD</td>
</tr>
<tr>
<td>Harikrishnan (2005)¹⁸</td>
<td>70/F</td>
<td>No</td>
<td>2</td>
<td>BA, VA</td>
<td>GR or MD</td>
</tr>
<tr>
<td>Mercado (2002)¹²</td>
<td>24/M</td>
<td>No</td>
<td>1</td>
<td>*ACA</td>
<td>GR</td>
</tr>
<tr>
<td></td>
<td>20/F</td>
<td>No</td>
<td>1</td>
<td>*IC-PCoA</td>
<td>MD</td>
</tr>
<tr>
<td></td>
<td>14/M</td>
<td>No</td>
<td>1</td>
<td>*IC-PCoA</td>
<td>MD</td>
</tr>
<tr>
<td>Serizawa (1992)¹⁶</td>
<td>33/F</td>
<td>Yes (at 31 y/o)</td>
<td>5</td>
<td>*MCA, ACA×3, IC-PCoA</td>
<td>MD</td>
</tr>
<tr>
<td></td>
<td>15/M</td>
<td>No</td>
<td>1</td>
<td>*ACoA</td>
<td>GR</td>
</tr>
<tr>
<td>Aris (1986)⁴</td>
<td>34/F</td>
<td>No</td>
<td>2</td>
<td>ACoA, MCA</td>
<td>MD</td>
</tr>
<tr>
<td></td>
<td>19/M</td>
<td>No</td>
<td>1</td>
<td>*IC-PCoA</td>
<td>D</td>
</tr>
<tr>
<td>Fukuda (1985)⁶</td>
<td>19/F</td>
<td>No</td>
<td>1</td>
<td>*ACoA</td>
<td>GR</td>
</tr>
<tr>
<td>Patel (1971)¹³</td>
<td>17/M</td>
<td>N.D.</td>
<td>1</td>
<td>*ACoA</td>
<td>GR</td>
</tr>
<tr>
<td></td>
<td>17/M</td>
<td>N.D.</td>
<td>1</td>
<td>*IC-PCoA</td>
<td>GR</td>
</tr>
<tr>
<td></td>
<td>15/M</td>
<td>N.D.</td>
<td>1</td>
<td>*ICA</td>
<td>GR</td>
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<tr>
<td></td>
<td>15/F</td>
<td>N.D.</td>
<td>1</td>
<td>*ACoA</td>
<td>D</td>
</tr>
<tr>
<td></td>
<td>13/F</td>
<td>N.D.</td>
<td>1</td>
<td>*ACoA</td>
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<tr>
<td></td>
<td>11/F</td>
<td>N.D.</td>
<td>1</td>
<td>*MCA</td>
<td>GR</td>
</tr>
<tr>
<td></td>
<td>8/M</td>
<td>N.D.</td>
<td>1</td>
<td>*BA</td>
<td>D</td>
</tr>
<tr>
<td>LeBlanc (1968)⁹</td>
<td>31/M</td>
<td>No</td>
<td>1</td>
<td>*ACoA</td>
<td>D</td>
</tr>
<tr>
<td></td>
<td>15/M</td>
<td>No</td>
<td>1</td>
<td>*ACA</td>
<td>GR</td>
</tr>
<tr>
<td>Robinson RG (1967)¹⁴</td>
<td>35/M</td>
<td>No</td>
<td>1</td>
<td>*ACoA</td>
<td>GR</td>
</tr>
<tr>
<td></td>
<td>19/M</td>
<td>No</td>
<td>3</td>
<td>ACoA, ACA, ICA</td>
<td>D</td>
</tr>
<tr>
<td>Matson (1965)¹¹</td>
<td>13/M</td>
<td>No</td>
<td>1</td>
<td>*ACoA</td>
<td>GR</td>
</tr>
<tr>
<td></td>
<td>11/N.D.</td>
<td>No</td>
<td>1</td>
<td>*BA</td>
<td>D</td>
</tr>
<tr>
<td>Schwartz (1960)¹⁵</td>
<td>14/M</td>
<td>Yes (at 8 y/o)</td>
<td>2</td>
<td>ICA, PCA</td>
<td>D</td>
</tr>
</tbody>
</table>

* indicates ruptured aneurysm.


(PCA) and vertebral artery (VA). As for the ruptured IAs, 11 of 24 patients (45.8%) had the ruptured IA arising from the ACoA. The report on the natural history of SAH and ruptured IAs demonstrated a different distribution of IAs, involving the ACoA (28.0%), the IC-PCoA (25.0%), the ICA (16.2%), and the MCA (12.1%)²⁻⁴. This confirms that, in CoA patients, IAs have a tendency to involve the ACoA in comparison to patients with IAs not associated with CoA. Padget considers that the embryonic development of the ACA begins as a secondary branch off the primitive olfactory artery at 5 weeks gestation. At 6 weeks, the ACA extends to join with its counterpart from the opposite side by way of plexiform anastomoses in the midline, which will develop into the ACoA². Errors in this process result in the various well-known anomalies of the ACoA and ACA²⁻⁴. We suggest that an error of embryological differentiation in the development of the neural crest and ACoA causes the formation of IAs in the ACoA.

In CoA patients, narrowing of the aortic lumen usually occurs distal to the origin of the left subclavian artery, leading to upper extremity and intracranial hypertension⁵. Hypertension is the main risk factor for the formation of single IAs²⁻⁵, multiple IAs²⁻⁴, and their rupture⁵⁴. Spikes in blood pressure can spur the IAs’ growth²⁻⁴. However, Curtis et al. showed that most IAs in adult patients with CoA were small and at low risk of rupture¹. In their study, mean IA diameter was
4.0 mm, close to the 3.5 mm found in the Mayo Clinic cohort. Interestingly, none of the patients in Curtis’ study had multiple IAs, in contrast to other studies in which multiple IAs were identified in 30% of CoA patients. We think that the absence of multiple IAs in Curtis’ study may be due to the relatively younger age of the patients (mean age, 29 years). In young CoA patients, genetic factors are thought to be the main etiology of the formation of single or small numbers of IAs, with the hypertension from CoA combining with the genetic predisposition, inducing the formation of additional IAs. Table 1 also shows that the age of patients with multiple IAs was significantly greater than that of patients with a single IA (P =0.01, the Mann-Whitney U-test), consistent with our case.

A relatively common cause of death in patients with untreated CoA is hemorrhagic stroke, including SAH, before the age of 40 years. In 30 years of follow-up, of 880 operated patients, Nieminen et al. showed that only one patient with surgically corrected CoA died of SAH, implying the salutary effect of operating on patients while young. Hashemzadeh et al. showed that in patients treated with surgical repair of CoA, a significant decrease in mean systolic blood pressure occurred after operation. This is consistent with our experience. The length of time and degree of hypertension experienced by a patient affects cerebrovascular anatomy, as well as cerebral blood flow autoregulatory mechanisms, and increases the risk of the formation and growth of IAs. Early detection and treatment of CoA can prevent secondary hypertension and IA rupture. Therefore, in CoA patients with unruptured IAs, including those both causally associated with the CoA or incidental to it, CoA should be treated as early as possible to increase the survival rate, while ruptured IAs should be treated as an emergency before correcting the CoA, as in our case. Ruptured IAs are at high risk of rebleeding, and surgical treatment enables hypertensive therapy to prevent vasospasm. Advances in anesthesia and perioperative management, as well as newer neurosurgical techniques, have enabled surgical treatment of ruptured IAs in the presence of untreated CoA with relative safety. We performed a second surgery to treat the additional unruptured IAs before the CoA itself was addressed, because it is well known that IAs in patients with a history of SAH are at greater risk for subsequent rupture.

It is rare for CoA to be asymptomatic into adulthood, especially as it is associated with aneurysmal rupture at a mean age of 25 years. The mean life expectancy of patients with untreated CoA is 35 years, and mortality rate at 50 years is 90%, due to sequelae such as left ventricular failure, bacterial endocarditis, or cerebrovascular accident. Furthermore, in CoA patients, the kidneys and the spinal cord receive their blood supply through the narrowed segment of the aorta and the collateral circulation, so it is well known that decreasing blood pressure can lead to renal and/or spinal cord ischemia. In the postoperative period of our case, antihypertensives were used to control excessive hypertension, while keeping the blood pressure high enough to prevent vasospasm. We selected diuretics in addition to low doses of nicardipine because decreasing blood pressure leads to reduced blood flow to the kidneys and decreased urine volume. In spite of this treatment, bilateral pleural effusions and dyspnea were recognized, and bilateral chest tubes had to be inserted. Intensive postoperative care is essential for the management of cerebral vasospasm and other complications during the perioperative period after surgery for a ruptured IA.

### Conclusion

This case highlights two points. First, there are fewer middle-aged and elderly cases of IA rupture associated with CoA, most likely due to the high early mortality in untreated cases. Second, ruptured IAs can be successfully treated with surgery. Ruptured IAs in CoA patients should be treated emergently, before surgical treatment of the CoA, in contrast to CoA patients with unruptured IAs, where the aorta can be repaired first. Intensive postoperative care, including management of cerebral vasospasm, renal or spinal cord ischemia, and respiratory compromise, is essential during the perioperative period.

### Conflict of Interest: No competing financial interests exist.

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