

# A De Novo Aneurysm of the Anterior Cerebral Azygos Artery Following a Middle Cerebral Arterial Aneurysm with Subarachnoid Hemorrhage

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## Abstract

A de novo aneurysm of a cerebral artery, defined as a newly growing aneurysm after aneurysmal clipping, but not close to a previously clipped one, is relatively rare. Five studies have reported that the annual incidence of de novo aneurysm formation ranged from 0.3% to 1.8%. A 56-year-old man presented with headache. Magnetic resonance angiography (MRA) and computed tomography (CT) showed an aneurysm with arachnoid hemorrhage located at the left middle cerebral artery (MCA) associated with an azygos anterior cerebral artery (ACA). Eight years later, the patient complained of dizziness, and MRA demonstrated no visualization of the MCA on the left due to metal artifact, but a new lesion, an azygos ACA aneurysm, 9 mm in diameter, was seen. Clipping was performed using multiple clips through the interhemispheric space. Late follow-up examination with MRA or three-dimensional CT to detect de novo aneurysms should be considered in a patient with this vascular anomaly after subarachnoid hemorrhage.

Keywords: de novo intracerebral aneurysm, azygos artery, arterial stress, arachnoid hemorrhage, middle cerebral arterial aneurysm

## Introduction

De novo aneurysm formation following previous aneurysmal clipping was first reported in 1964 by Graf and Hamby. The incidence of de novo aneurysms is 0.89–1.8% per year. Such aneurysms appear most commonly in the anterior circulation. The location of de novo aneurysms shows a more variable distribution, in which high-frequency sites are the anterior communicating artery (AcomA) and the internal carotid-posterior communicating artery (more than 20%). On the other hand, the azygos artery is consistent with Baptista type 1 when studying the anomalies of the pericallosal artery, in which the azygos artery is a single trunk not like the normal paired anterior cerebral artery (ACA; A2 portion from distal A1 to the genu of the corpus callosum).

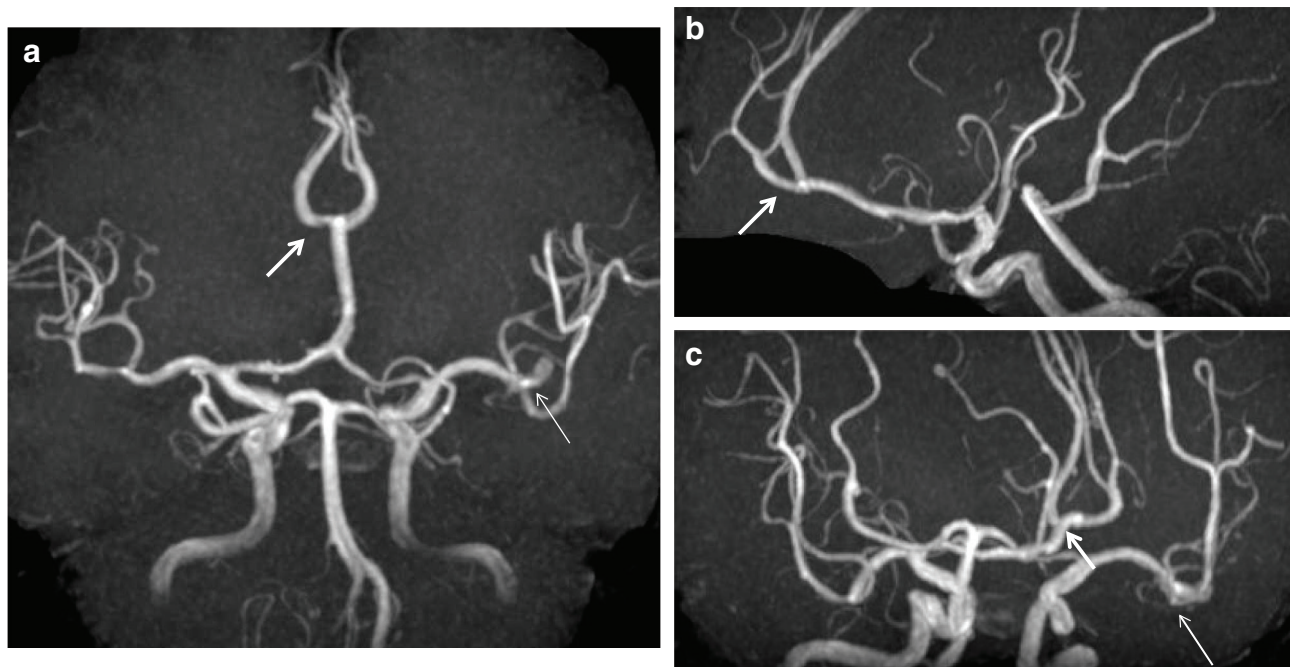
An azygos ACA aneurysm accounted for 0.5% of all treated lesions and 1.7% of all ACA and AcomA aneurysms. An ACA aneurysm is apt to be larger, but the annual incidence of ruptured ACA aneurysms has remained unknown because of their rarity.

## Case Report

A 56-year-old man with acute onset of severe occipital headache two days earlier presented to our hospital as a walk-in patient. There was no relevant past or family history. He did not have hypertension or diabetes mellitus and did not smoke. His consciousness was clear, and the neurological examination was normal except for mild nuchal stiffness. Computed tomography (CT) showed slight high density in the left Sylvian fissure. Magnetic resonance angiography (MRA) showed a saccular aneurysm, 5 mm in diameter, arising at the bifurcation of the left middle cerebral artery (MCA; M1) and an azygos ACA without an aneurysm, with no other anomalies on magnetic resonance imaging (MRI) (Fig. 1). He immediately underwent a left frontotemporal

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**Fig. 1** (a) MRA shows an aneurysm of the MCA at the left bifurcation (long arrow) and the anomalous azygos ACA (arrow). (b) Lateral view of MRA shows no definitive aneurysm at the azygos ACA bifurcation (arrow). (c) Oblique view of MRA shows overlapping vessels, with small vascular bulging at the azygos ACA bifurcation (arrow) and a part of the aneurysm at the MCA bifurcation. (long arrow). ACA: anterior cerebral artery, MCA: middle cerebral artery, MRA: magnetic resonance angiography.

craniotomy with aneurysmal neck clipping that same day. He was discharged without problems 2 weeks after the operation. Eight years later, he presented with initial dizziness and underwent MRI. MRA showed a relatively large aneurysm (about 9 mm in diameter) arising from the bifurcation of the azygos ACA as a *de novo* aneurysm (Fig. 2). Dizziness associated with shoulder stiffness due to stress disappeared within a couple days. Five days later, the aneurysm was identified and clipped with complete occlusion by multiple clips through an interhemispheric approach (Fig. 3). Complete occlusion of the azygos ACA aneurysm was confirmed by indocyanine green during microscopic surgery (Fig. 4). He was discharged without problems 10 days after the operation.

## Discussion

The case of a patient who presented with a *de novo* ACA aneurysm after treatment of a previous aneurysm was described. There has been only one other report of a similar case. Differences between the two cases were the site of the initial aneurysm (MCA and proximal ACA) treated and rupture or non-rupture of a *de novo* ACA aneurysm. The time from first aneurysmal treatment to discovered

non-ruptured and ruptured aneurysm in both cases was 7–8 years.<sup>1)</sup>

Baptista<sup>2)</sup> classified the anatomical variations of the distal ACA (A2 segment) into three types (Type 1, azygos ACA; Type 2, bihemispheric ACA resembling an azygos ACA; and Type 3, accessory ACA). An azygos ACA may develop from abnormal fusion of the paired A2 segment from the medial branch of the primitive olfactory artery at the 18-mm stage of the embryo. Based on angiographic and autopsy studies, the incidence of azygos ACA aneurysm is 0.3–4.0%.<sup>3–6)</sup> Five studies reported that the annual incidence of *de novo* aneurysm formation ranged from 0.3 to 1.8%.<sup>7–11)</sup> In general, the location with the highest aneurysm incidence is the ACA area including the AcomA. The rate of *de novo* aneurysm formation after carotid artery occlusion for cerebral giant aneurysms and dissected carotid arteries deemed to be impossible to clip was 4.3% (7/163 cases).<sup>12)</sup> In 36 cases of a *de novo* aneurysm with the same above situation, many aneurysms were located at the AcomA. For this reason, Stehbens<sup>6)</sup> explained that, where there is a sizeable shunt from one ACA to a contralateral vessel, aneurysm formation has been attributed to augmented hemodynamic stress. Huber et al.<sup>13)</sup> reported that 7 (41%) of 17 cases with azygos and bihemispheric ACAs had

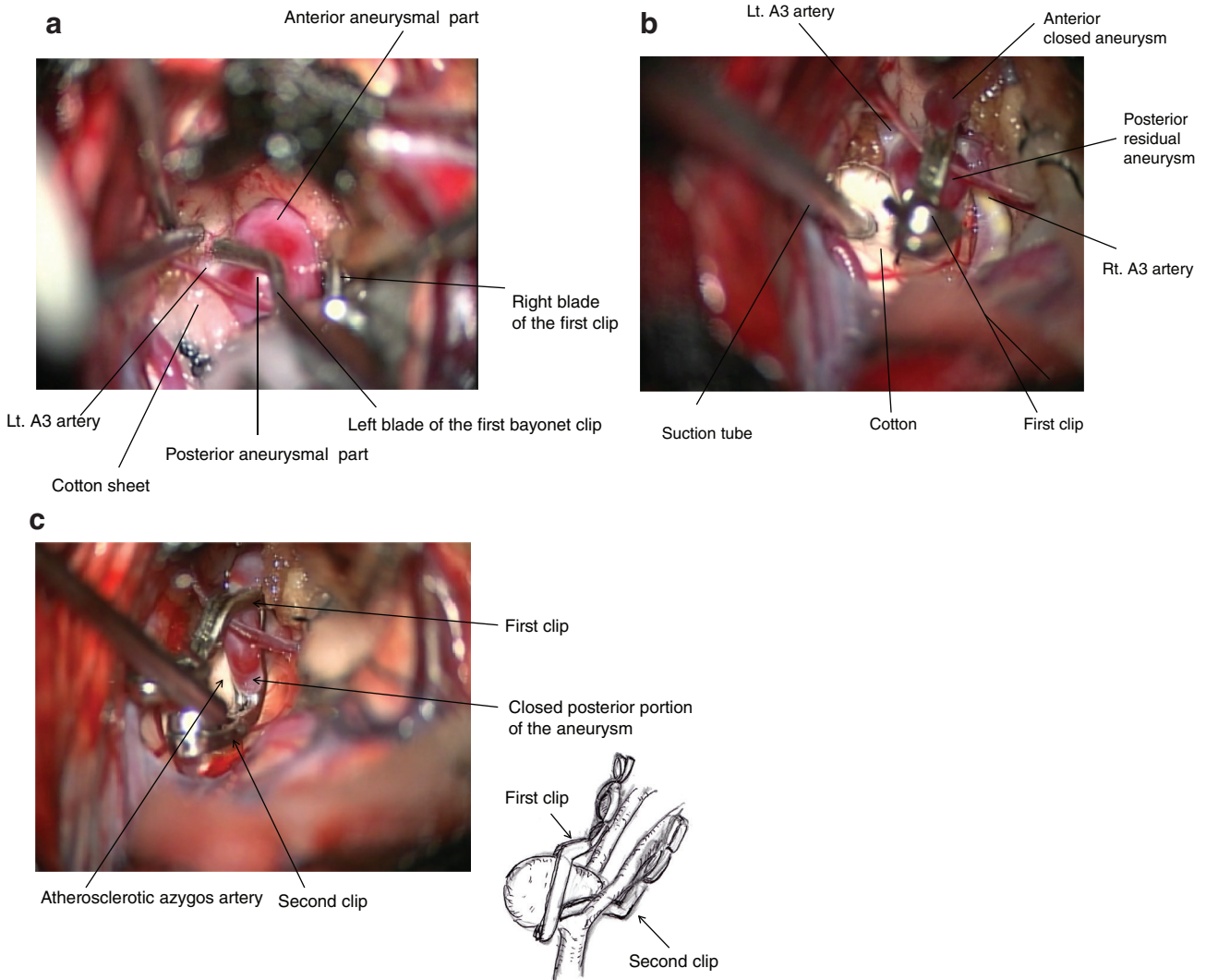


**Fig. 2** Eight years later, follow-up MRA shows a large new aneurysm of the azygos ACA. ACA: anterior cerebral artery, MRA: magnetic resonance angiography.

aneurysms. As a reason, an azygos ACA formed by fusion of the usual paired ACA (A2) may receive twice the blood flow velocity, and, furthermore, the pathological vascular wall structure may also be integrated in the embryo stage. However, Kaspera<sup>14)</sup> reported that the mean blood velocity in the azygos ACA compared to the ACA (A2 segment) of the control group using transcranial sonography was not significantly different. He concluded that hemodynamic stress was related to the azygos ACA bifurcation geometry together with the aberrant course of this artery around the genu of the corpus callosum, where the pericallosal artery arches sharply posteriorly, predisposing to aneurysm formation developing to the anterior superior direction due to vascular wall stress caused by the centrifugal force of blood flow.<sup>15,16)</sup> On the other hand, an azygos artery aneurysm at the proximal location is rare, and it tends to develop to the posterior direction, because of the azygos artery trunk running to superior-anterior around the infracallosal portion.<sup>17)</sup> We consider that the vascular geometry and the direction of the aneurysmal dome due to hemodynamic stress are related. In general, hypertension, female sex, young age, previous subarachnoid hemorrhage (SAH), smoking, hereditary connective tissue disease (e.g., Ehlers-Danlos,<sup>4)</sup> Marfan's syndrome), multiple renal cysts and family history of cerebrovascular

disease<sup>18–22)</sup> may serve as risk factors for de novo cerebral aneurysm formation. The present case did not have the above risk factors or an embryonal anomaly (agenesis of the corpus callosum, lipoma, prosencephaly, arterio-venous malformation and fenestration<sup>17,23)</sup>, except for the azygos ACA. In Dietrich's case,<sup>1)</sup> an initially ruptured aneurysm arising from a branch of A1 was related to an anomaly of the ACA plexus linked with an azygos ACA. Formation of a secondary de novo aneurysm of the azygos ACA seven years later is reasonably logical. However, the present case presented with the initial aneurysm located at the left MCA, which is subject to a different hemodynamic stress and a different arterial course than an azygos ACA. The reason for the second aneurysm is unknown. In a review of 32 cases with an azygos artery aneurysm from 1998 to 2020, 12 cases had another cerebral artery aneurysm.<sup>24)</sup> Most of these aneurysms involved the MCA (7/12), which is consistent with the review reported by Topsakal<sup>25)</sup> before 2000.<sup>3,4,26–28)</sup> There has been no previous report similar to the present case except for Dietrich's case.<sup>1)</sup> The average time interval between the initial SAH and diagnosis of de novo aneurysm formation was 9.2 years, with 75% of patients presenting by 12.5 years.<sup>10)</sup>

A de novo azygos artery aneurysm such as the present case and Dietrich's<sup>1)</sup> ruptured case were

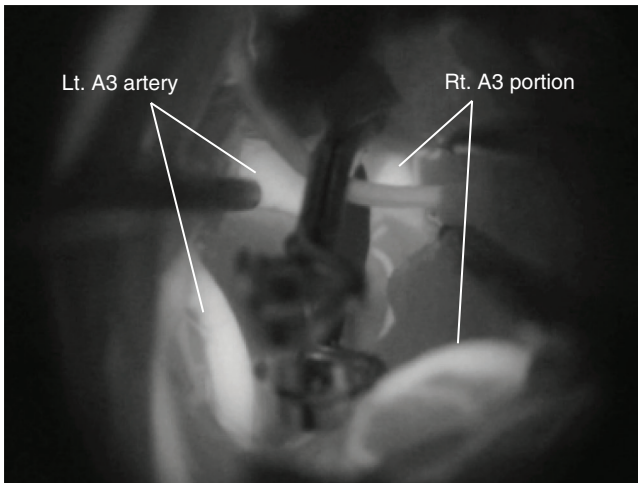


**Fig. 3** (a) The interhemispheric operative field is very narrow. First, the right blade of the clip is inserted between the anterior aneurysmal neck and the origin of the pericallosal artery on the right. The left one is put between the aneurysmal neck and the left pericallosal artery. (b) Operative view shows bilateral pericallosal arteries, the posterior aneurysm, and the anterior aneurysm closed by the first clip. (c) Operative view shows the second clip in L formation applied to the posteriorly residual aneurysm. Thus, multiple clips are required to close the aneurysm. The schema presents the final clips applied to the azygos ACA. ACA: anterior cerebral artery.

discovered 8 and 7 years, respectively, after initial aneurysm clipping. The interval between de novo aneurysm formation at an azygos ACA and other arteries after initial aneurysm clipping is not significantly different.

There is a consensus that aneurysmal size >5 mm is an indication for surgery. Most of the aneurysms at the distal end of the azygos ACA are single, saccular, and small in size,<sup>24,25,29</sup> and they tend to rupture early and present with SAH because of the lack of resistant arachnoid membranes at the part covered by the bilateral cingulate gyri.<sup>30</sup> Even if the de novo azygos ACA aneurysmal size

is >3 mm and <5 mm, it requires surgical intervention.<sup>1,6</sup> A de novo aneurysm may have a risk for SAH that is relatively higher than the risk of a similarly sized, initially discovered, non-ruptured saccular aneurysm.<sup>31</sup> Furthermore, patients with a distal ACA aneurysm associated with multiple aneurysms developed bleeding in 30%–50% of cases.<sup>25</sup> Regarding aneurysmal size at an azygos ACA, Auguste<sup>3</sup> reported that aneurysms of an azygos ACA tend to be large (>10 mm) and be irregular-saccular type involving adjacent or parent arteries, needing multiple clipping for closure, similar to the present case.



**Fig. 4** Indocyanine green (ICG) image demonstrates the disappearance of the aneurysm using multiple clips.

## Conclusion

Although an azygos ACA is relatively rare, the incidence of ruptured aneurysms arising from an azygos ACA is high compared with aneurysms at other common sites. Therefore, the development of a de novo azygos ACA aneurysm after treating an initial aneurysm at another site is even rarer, with only two cases including the present case reported so far. The azygos artery has a predisposition to form an aneurysm due to an embryonal vascular anomaly and the complex geometry at the bifurcation of the azygos ACA along with the bend at the genu of the corpus callosum, as seen in the present case, and a history of SAH is an important factor. It is important to keep in mind that patients with an azygos ACA and a history of SAH should undergo careful follow-up by MRI and three-dimensional CT every year.

## Informed Consent

Consent for publication was obtained from the patient.

## Conflicts of Interest Disclosure

All authors have no conflicts of interest.

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