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ORIGINAL ARTICLE

Radiological classification of azygos anterior cerebral artery and evaluation of the accompanying vascular anomalies

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Abstract

Purpose There is not a classification of azygos anterior cerebral artery (ACA) based on anatomical branching levels in the literature. In the present study, a classification of azygos ACA was made based on radiological imaging for a common terminology, and frequency, accompanying vascular anomalies and malformations were investigated.

Methods A total of 4913 cases who had brain CTA, MRA, contrast-enhanced MRI and DSA in January 2010–January 2020 period were screened for the study. Based on anatomical branching level, azygos ACAs were classified into four groups. Aneurysms, anomalies and malformations accompanying azygos ACA were identified. The associations of azygos ACA types with the presence of aneurysm or ACA A1 segment anomalies were investigated.

Results Azygos ACA was observed in 57 cases (29 male and 28 female) and frequency of azygos ACA was 1.16%. Average age of the cases with ACA was 56.19 ± 19.65 years. Forty-eight of the cases had type C azygos ACA, four cases type B, four cases type D and one case type A azygos ACA. A total of nine intracranial aneurysms were identified in seven of the cases (12.28%). Five of the aneurysms were located in MCA and four in distal ACA. Most common vascular anomalies accompanying azygos ACA were unilateral vertebral artery hypoplasia and ACA A1 segment hypoplasia. Azygos types did not have significant correlations with the presence of aneurysms or ACA A1 segmental anomalies ($p = 0.683$ and $p = 0.949$, respectively).

Conclusion Azygos ACA is a rare variation, but it could be accompanied by aneurysms or other vascular anomalies.

Keywords Aneurysm · Azygos anterior cerebral artery · Computerized tomography angiography · Magnetic resonance angiography · Unpaired pericallosal artery

Introduction

Azygos anterior cerebral artery (ACA) is a vascular anomaly characterized by the formation of a single A2 segment in the midline as a result of the persistence of the embryonic median artery of the corpus callosum. It produces branches supplying the two ACA territories [5]. Frequency of azygos ACA variation was reported to be in a wide range of 0–10% [8, 13]. It was reported that about 9–71% azygos ACA cases had distal ACA aneurysms [4, 8, 14]. It has been known that azygos ACA is associated with predisposition to holoprosencephaly, various neuronal migration anomalies and aneurysm development [5]. There is no classification about anatomical branching levels of azygos ACA in the literature. Identifying the type of azygos ACA is crucial in directing the treatment before the surgical or endovascular interventions and in preventing the possible complications. Previously, digital subtraction angiography (DSA) was the gold standard for the azygos ACA and aneurysm imaging. However, due to its non-invasive nature, safety and speed, computerized tomography angiography (CTA) have become the primary imaging method [11]. In the present study, a classification of azygos ACA types based on radiological

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imaging was proposed, and accompanying vascular anomalies and malformations were evaluated.

Materials and methods

A total of 4913 cases were surveyed retrospectively for the present study among the all consecutive patients who had one or more of brain CTA (1567 patients), magnetic resonance angiography (MRA) (924 patients), contrast-enhanced magnetic resonance imaging (MRI) (2296 patients) and DSA (126 patients) for indications and findings such as headache, vertigo, cerebrovascular disease, seizures, etc. in Radiology Departments of Tokat Gaziosmanpasa University Faculty of Medicine Hospital and Sivas Numune Hospital in January 2010–January 2020 period. The cases who only had noncontrast-enhanced MRI were excluded. All radiological examinations were evaluated by two experienced radiologists (E.G. with more than 10 years of experience and M.B. with more than 5 years of experience). Azygos ACA was divided into four types: branching at root of A2 segment was referred Type A (Figs. 1, 2), branching at corpus callosum genu was referred Type B (Figs. 1, 3), branching between corpus callosum genu and body middle level was referred Type C (Figs. 1, 4), and branching after body middle level of the corpus callosum was referred Type D (Figs. 1, 5). Anomalies and malformations accompanying azygos ACA were also investigated. Descriptive statistics were expressed as mean ± SD. Associations of azygos ACA types with the presence of aneurysms were examined. In addition, relations between azygos ACA types and anomalies in ACA A1 segments (hypoplasia, agenesis and fenestration) were searched. Pearson's Chi-Square test was used to evaluate the associations of azygos ACA types with the presence of aneurysms or with the anomalies in ACA A1 segments. Statistical analyses were performed using SPSS Statistics 22 software (SPSS Inc., an IBM Co., Armonk, NY, USA). Local ethics committee approved the study procedures (15-KAEK-149).

Results

Azygos ACA was found in a total of 57 cases. Twenty-nine of them were male (50.88%) and 28 were female (49.12%). The frequency of azygos ACA was 1.16%. Age of the patients ranged from 2 to 86 years (mean 56.19 ± 19.65). The most common azygos ACA type was type C (84.21%), while the least common one was type A (1.75%). Frequencies of azygos ACA types are given in Table 1.

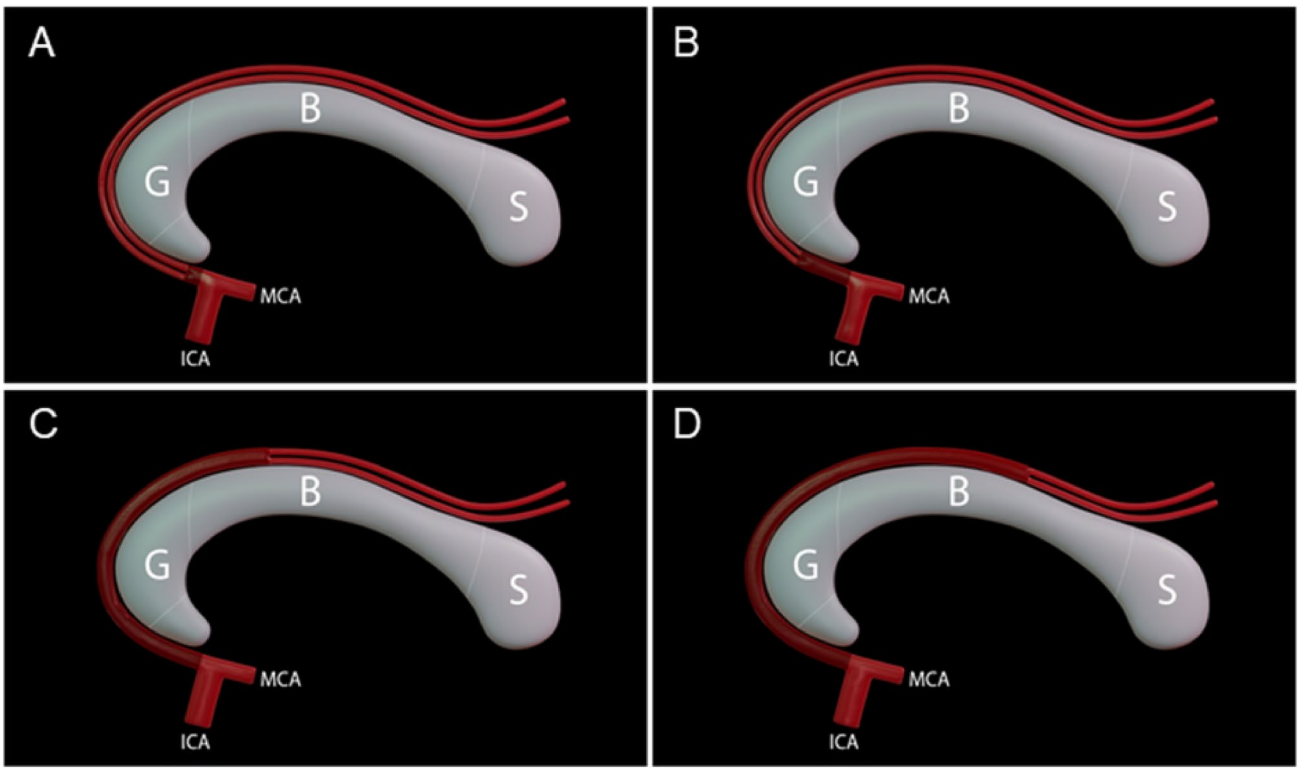


Fig. 1 Schematic drawings of azygos anterior cerebral artery types. **a** Type A. **b** Type B. **c** Type C. **d** Type D. *G* genu of corpus callosum, *B* body of corpus callosum, *S* splenium of corpus callosum

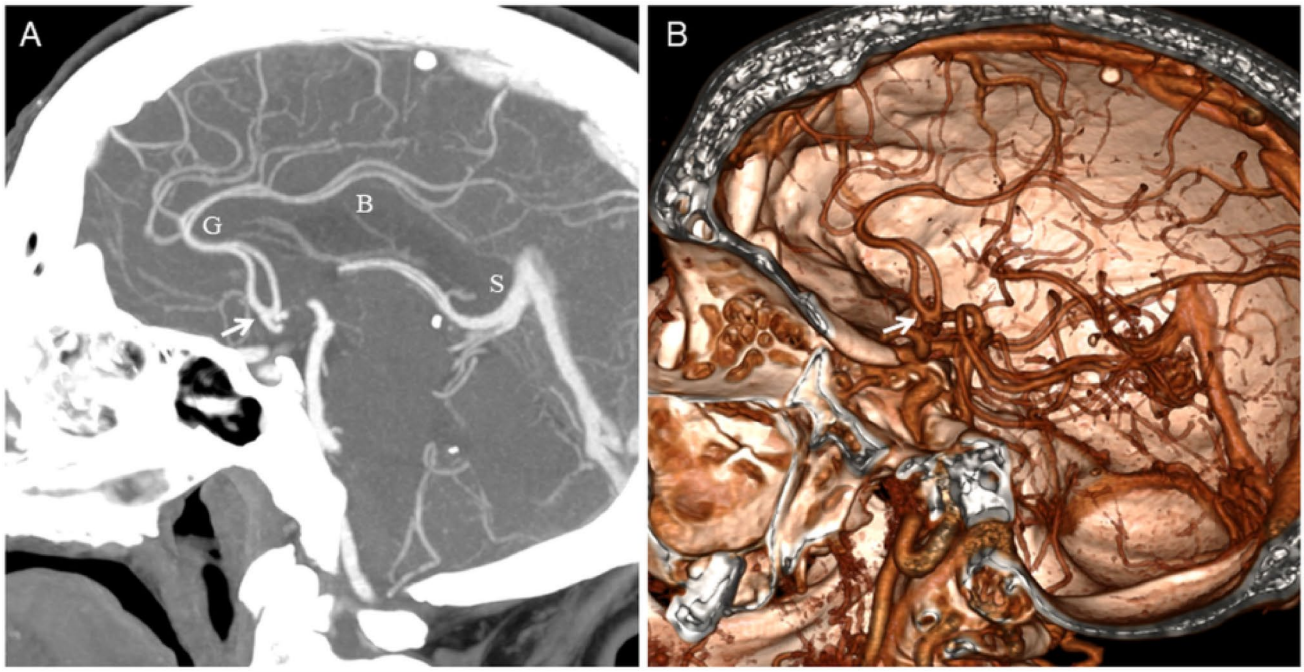


Fig. 2 Type A azygos anterior cerebral artery (arrows) on computerized tomography angiography images of a 76-year-old female patient. **a** Sagittal maximum intensity projection image. **b** Volume-rendering image. *G* genu of the corpus callosum, *B* body of corpus callosum, *S* splenium of the corpus callosum

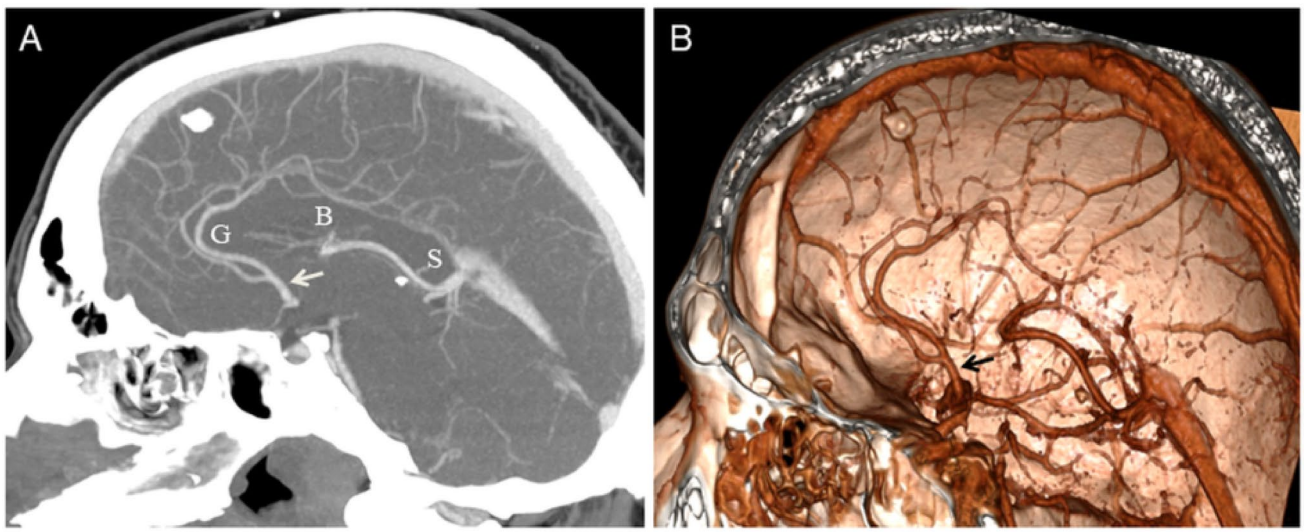


Fig. 3 Type B azygos anterior cerebral artery (arrows) on computerized tomography angiography images of a 56-year-old male patient. **a** Sagittal maximum intensity projection image. **b** Volume-rendering image. *G* genu of the corpus callosum, *B* body of corpus callosum, *S* splenium of the corpus callosum

Seven of the 57 patients (12.28%) had a total of nine intracranial aneurysms. Seven of them were saccular and two were fusiform aneurysms (Figs. 6, 7). Five of the aneurysms were located in the middle cerebral artery (MCA), while four were in distal ACA (Fig. 8). Locations and sizes of the aneurysms identified in azygos ACA cases are given in Table 2. Azygos ACA types were not significantly associated with the presence of aneurysms or ACA A1 segment anomalies ($p = 0.683$ and $p = 0.949$, respectively). Upon detecting subarachnoid hemorrhage (SAH) in two cases with aneurysms, surgery was performed for one case (Case 4), and endovascular stent-assisted coil embolization was applied

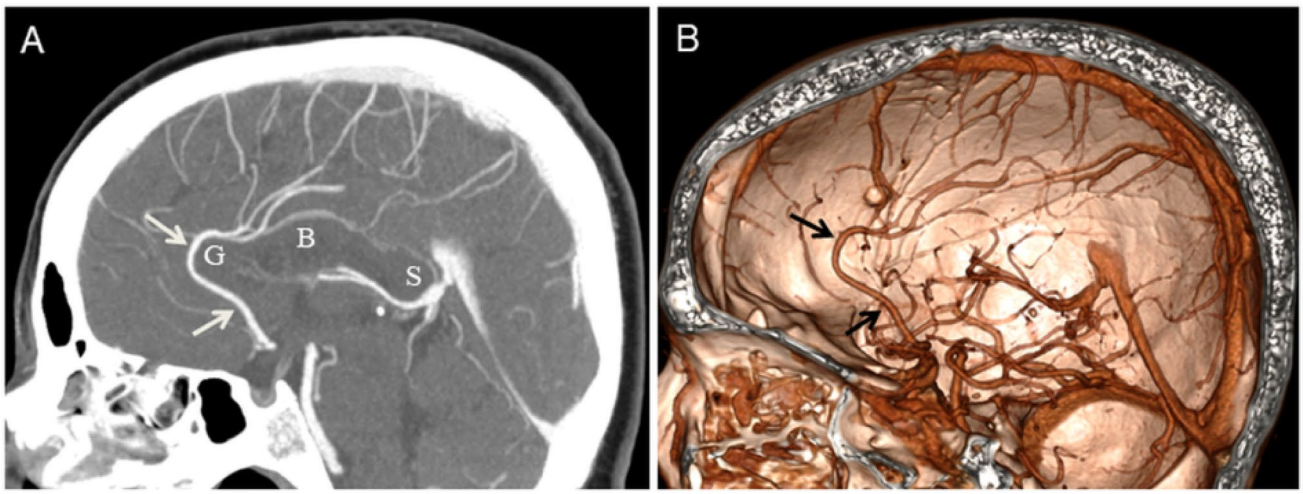


Fig. 4 Type C azygos anterior cerebral artery (arrows) on computerized tomography angiography images of a 60-year-old male patient. **a** Sagittal maximum intensity projection image. **b** Volume-rendering image. *G* genu of corpus callosum, *B* body of corpus callosum, *S* splenium of corpus callosum

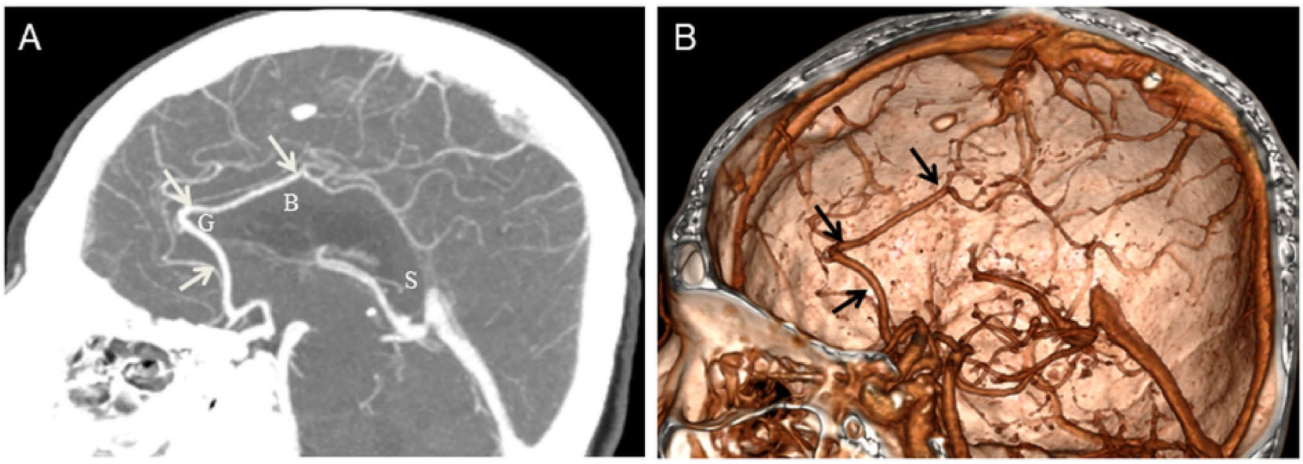


Fig. 5 Type D azygos anterior cerebral artery (arrows) on computerized tomography angiography images of an 86-year-old male patient. **a** Sagittal maximum intensity projection image. **b** Volume-rendering image. *G* genu of the corpus callosum, *B* body of corpus callosum, *S* splenium of the corpus callosum

Table 1 Azygos anterior cerebral artery types and their frequencies

	n	%
Type A	1	1.75
Type B	4	7.02
Type C	48	84.21
Type D	4	7.02
Total	57	100

to the another (Case 19). Acute ischemias were observed in cerebellum of the patient with basilar artery occlusion (Case 3) and in pons of the patient with unilateral vertebral artery hypoplasia (Case 28). Bilateral ACA A1 segments of 38 cases were of normal caliber, while 18 cases had unilateral normal ACA A1 segment. ACA A1 segment was agenesic in six cases and hypoplastic in 13 cases, one of which had fenestration in A1–A2 segmental junction. Bilateral posterior communicating artery (PComA) could not be visualized in 20 cases, and unilateral PComA could not be visualized in seven cases, while bilateral PComA could be visualized in 30 patients. The most common vascular anomaly accompanying azygos ACA was unilateral artery hypoplasia. All vascular anomalies accompanying azygos ACA and their frequencies are given in Table 3. Total agenesis of the corpus callosum was observed in two cases, while corpus callosum rostrum and splenium hypoplasia, polymicrogyria in cingulate gyrus anterior, mega cisterna magna, microcephaly, cavum vergae, arachnoid cyst, pineal cyst and developmental

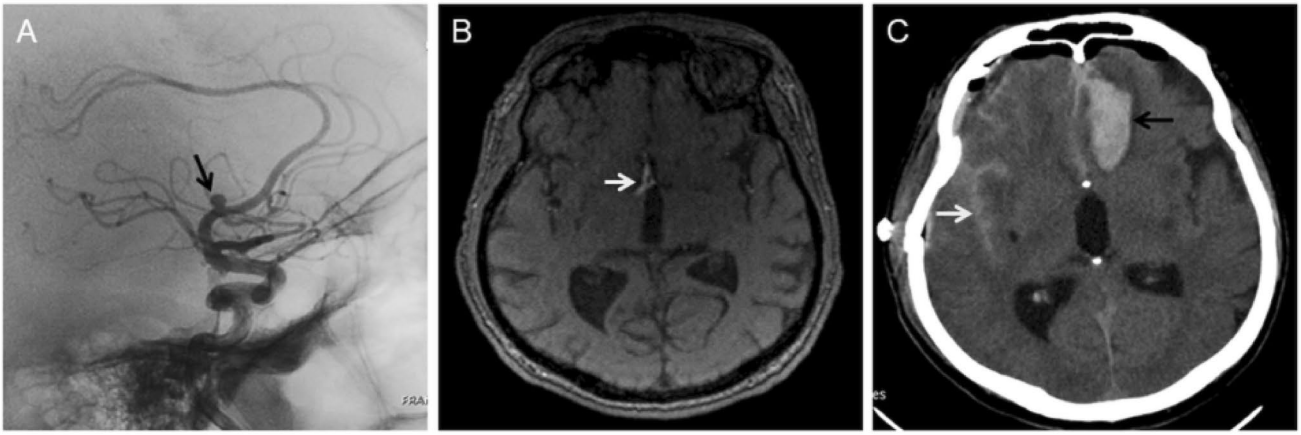


Fig. 6 Type D azygos anterior cerebral artery of a 58-year-old male patient. **a** Saccular aneurysm distal to azygos anterior cerebral artery on digital subtraction angiography image (black arrow). **b** Fenestration at the junction of right anterior cerebral artery A1–A2 segments on axial magnetic resonance imaging (white arrow). **c** Subarachnoid hemorrhage (white arrow) and hematoma (black arrow) on axial plane computerized tomography image taken six months later

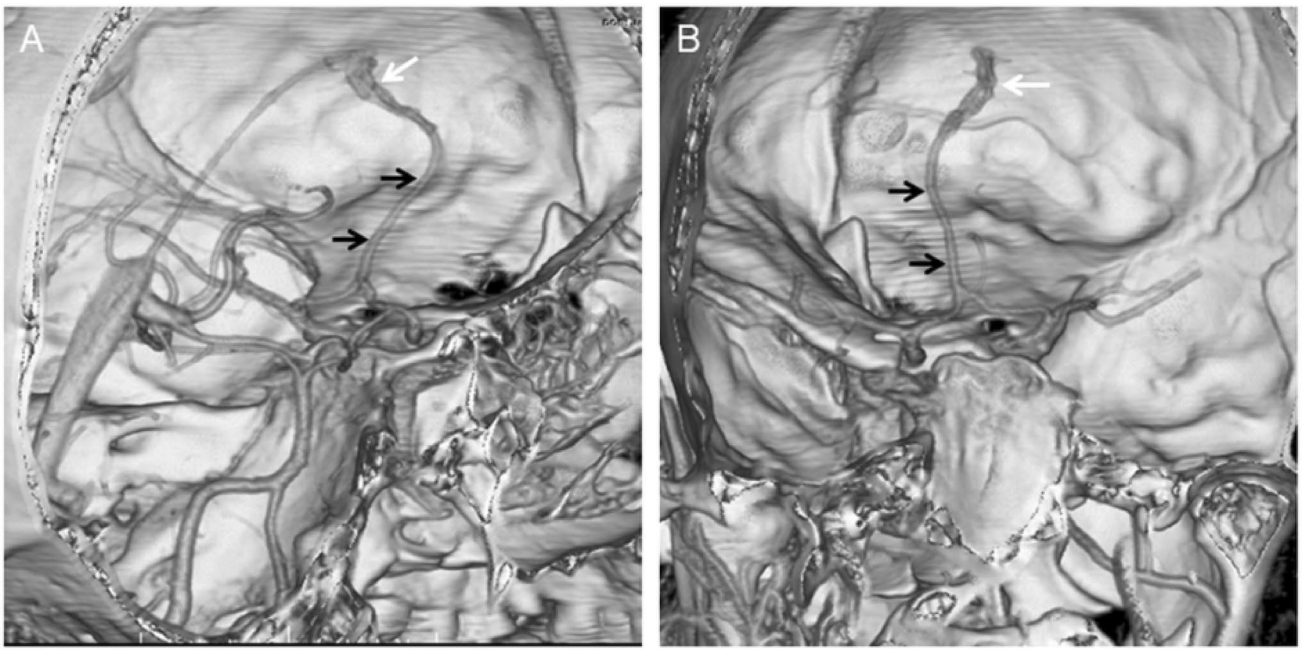


Fig. 7 Fusiform aneurysm distal to azygos anterior cerebral artery (white arrows). **a**, **b** Volume-rendering computerized tomography angiography images of 21 years old male patient with Type C azygos anterior cerebral artery (black arrows)

venous anomaly (DVA) were observed in one patient each (Fig. 9).

Discussion

Wilder [21] described the artery which is not separated into two on the surface of both cerebral hemispheres as azygos pericallosal artery in 1885. Azygos ACA has different names in the literature such as arteria termatica, azygos pericallosal artery, unpaired pericallosal artery, unpaired cerebral artery and common arterial cerebral trunk [12]. The primitive olfactory artery originating from the internal carotid artery extends towards medial to form ACA [16]. Anomalous fusion of two ACA segments after communicant segments arises from a medial branch of an olfactory artery in the first 18 mm long embryo or from the persistence of median artery in the corpus callosum in 20–24 mm long

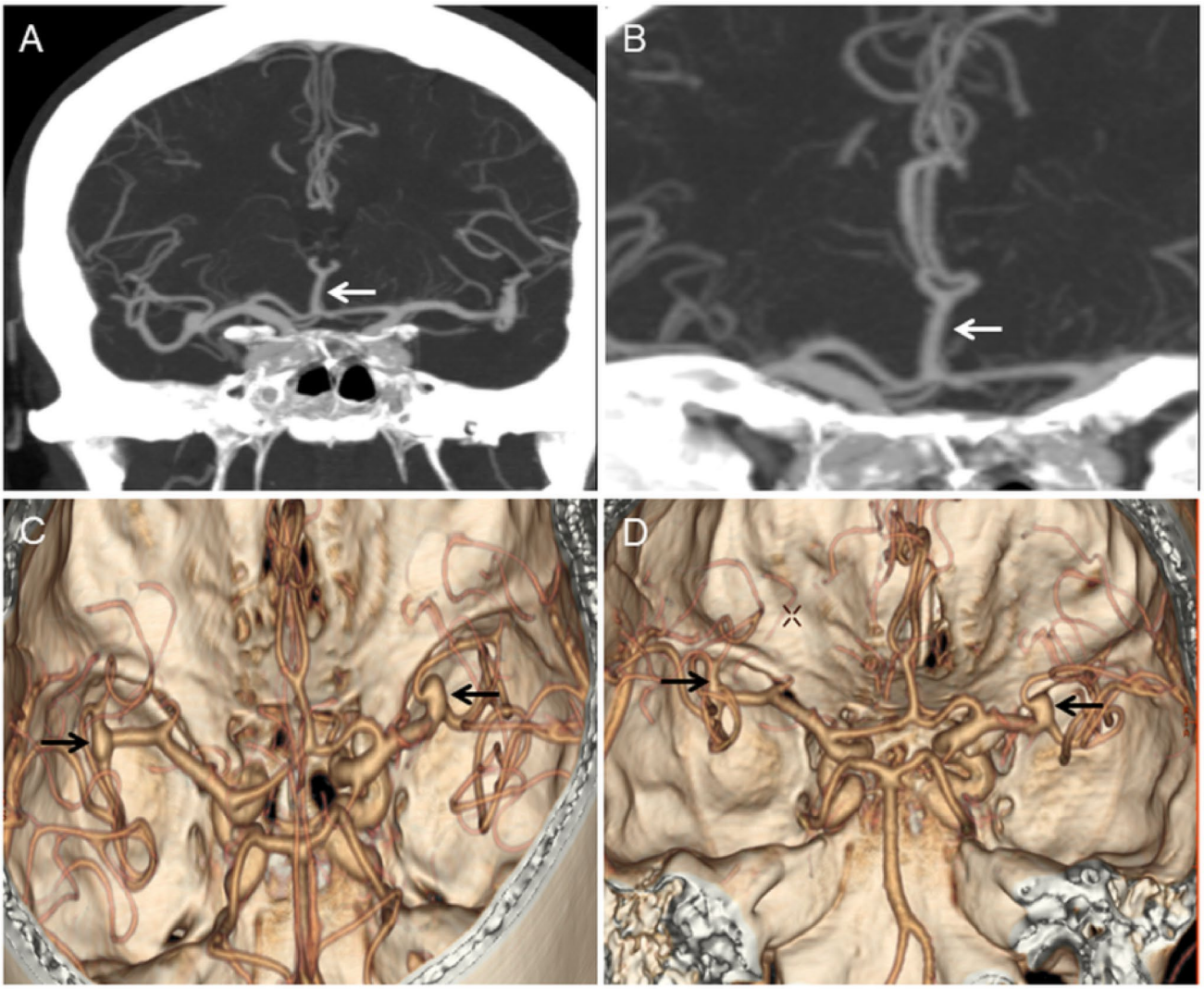


Fig. 8 **a**, **b** Coronal reformatted computerized tomography angiography images of a 76-year-old female patient with Type C azygos anterior cerebral artery (white arrows). **c**, **d** Right saccular-left saccular aneurysms at bilateral middle cerebral artery bifurcation on volume-rendering computerized tomography angiography images (black arrows)

Table 2 Locations and sizes of aneurysms detected in azygos anterior cerebral artery cases

Case no.	Gender	Age	Location and size of aneurysm
1	F	76	Right MCA bifurcation, saccular aneurysm (5.5×4 mm)
1	F	76	Left MCA bifurcation, saccular aneurysm (4.5×4 mm)
1	F	76	Left M1-anterior temporal junction, saccular aneurysm (2.5×2.5 mm)
4	M	58	Saccular aneurysm distal to azygos ACA (4×3.5 mm) (SAH in follow-ups)
5	M	21	Fusiform aneurysm distal to azygos ACA
19	F	29	Right MCA trifurcation aneurysm (12×5 mm) (SAH in follow-ups)
34	F	66	Saccular aneurysm distal to azygos ACA (5.5×4.5 mm)
35	F	75	Saccular aneurysm in left MCA M1-M2 junction (7.5×7 mm)
49	M	70	Fusiform aneurysm with calcific wall distal to azygos ACA

F female, *M* male, *MCA* middle cerebral artery, *ACA* anterior cerebral artery, *SAH* subarachnoid hemorrhage, *mm* millimeter

Table 3 Accompanying vascular anomalies in azygos anterior cerebral artery cases and their frequencies

Vessels	Normal/abnormal	*n*	%
Right ACA A1 segment	Normal	43	75.44
	Hypoplasia	7	12.28
	Agenesis	6	10.53
	Fenestration	1	1.75
Left ACA A1 segment	Normal	51	89.47
	Hypoplasia	6	10.53
Right PComA	Visualized	35	61.40
	Non-visualized	22	38.60
Left PComA	Visualized	32	56.14
	Non-visualized	25	43.86
Right vertebral artery	Normal	41	71.93
	Hypoplasia	13	22.81
	Occlusion	3	5.26
Left vertebral artery	Normal	49	85.96
	Hypoplasia	3	5.26
	Dolichoectasia	2	3.51
	Occlusion	2	3.51
	Stenosis	1	1.75
Basilar artery	Occlusion	1	1.75
	Hypoplasia	1	1.75
PCA	Fetal PCA	2	3.51
	P1 segment agenesis	2	3.51

ACA anterior cerebral artery, *PComA* posterior communicating artery, *PCA* posterior cerebral artery

embryo stage [4, 8]. Baptista [3] grouped ACA variations in distal to anterior communicating artery: type 1 azygos ACA, type 2 bihemispheric ACA and type 3 median callosal artery or accessory ACA. On the other hand, Gunnal et al. [6] categorized azygos ACA into five subtypes where Type I was mentioned to be classical or true azygos ACA. Azygos ACA with a short median trunk was referred Type II. ACA with two A2 segments where one terminates early was designated as Type III. Type IV also have two A2 segments but one terminates as callosomarginal artery. In Type V, on the other hand, a third median A2 artery exists [6]. Incomplete fusion of ACA arterial segments in which the trunk is first divided above the genu of the corpus callosum was termed single ACA trunk, which is observed more frequently than classical azygos ACA [13]. Singh et al. [18] suggested that the azygos distal ACA could be divided into three subtypes based on division pattern: Type 1A manifests bifurcation pattern of branching, while Type 1B shows trifurcation and Type 1C quadrifurcation pattern. Although Gunnal et al. [6] mentioned that they classified azygos ACA, they in fact classified ACA variations, since Types I and II in their classification are in parallel with that of Baptista [3] azygos ACA definition, Types III and IV corresponds to bihemispheric ACA, and Type V represents accessory ACA or triple ACA. Besides, Type II in Gunnal et al. [6] classification corresponds to single ACA trunk. Therefore, since there is no classification of azygos ACA based on branching levels, we established a classification system in which we classified azygos ACA based on relevant anatomic branching levels (Types A, B, C and D). We observed that azygos ACA form which dissociated with corpus callosum genu at the middle body level (Type C) was the most frequently observed type (84.21%) across our cases.

Osborn [15] reported the frequency of azygos ACA as 10%. Up to 10% of azygos ACAs were reported in case series who underwent vascular surgery [9]. Yasargil [22] found frequency rates of 2% in cadaveric dissections and 2.1% in surgery case series. The author also reported azygos ACA in 17 of 7782 DSA series [22]. Frequency of azygos ACA in the present study was 1.16%, which was around the lower limits reported in the literature.

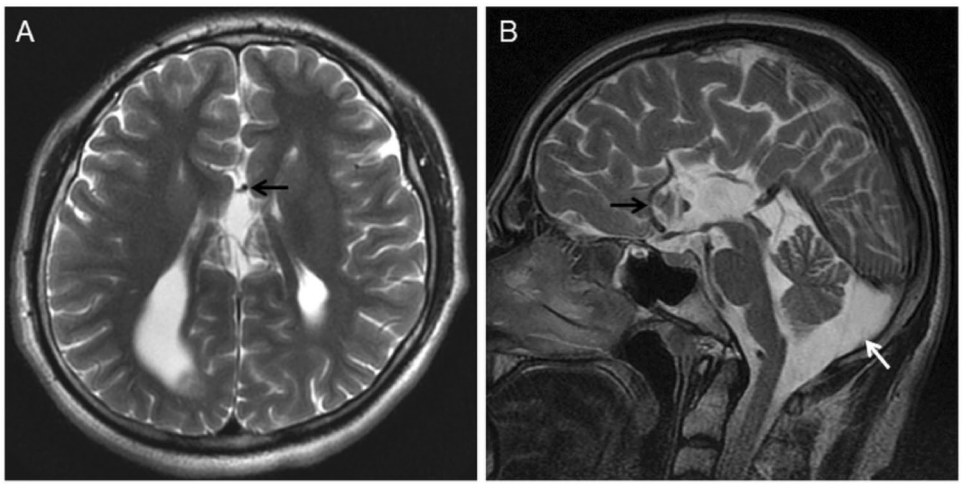


Fig. 9 Corpus callosum total agenesis in 19 years old male patient. **a** Azygos anterior cerebral artery on axial T2-weighted magnetic resonance imaging (black arrow). **b** Azygos anterior cerebral artery (black arrow) and mega cisterna magna (white arrow) on sagittal T2-weighted magnetic resonance imaging

Intracranial aneurysm frequency in the general population is 1–2% and is responsible for 80–85% of all SAHs. Adult autopsy examinations, on the other hand, showed frequency rates of 1–5% for aneurysms [1]. Clinical importance of azygos ACA lies in the fact that it has only A2 and, therefore, it could lead to bilateral ischemic changes, thereby resulting in higher ACA aneurysm frequency as a result of hemodynamic changes [7]. It was suggested that aneurysms involve a congenital defect in tunica media of the artery, and hemodynamic stress leads to development and growth of aneurysms [4]. Distal ACA (pericallosal) aneurysms are rare and accounts for only 2–6.7% of all intracranial aneurysms [20]. Lehecka et al. [11] studied 101 distal ACA aneurysms and found azygos ACA in four cases. In all cases, aneurysms were in azygos bifurcation. Aneurysms not involving azygos ACA generally arises at corpus callosum genu level. Distal aneurysms associated with azygos ACA are generally located at the distal end of the azygos ACA, in callosomarginal bifurcation or trifurcation [20]. Most of the reported azygos ACA aneurysms are saccular; however, unusual nonsaccular anatomy could also be observed (e.g. fusiform shape, large base, complex branching and/or thrombus in lumen) [2]. Our results showed that azygos ACA cases had higher frequency rates for aneurysms in intracranial arteries (12.28%) compared to the normal population. Frequency of distal ACA aneurysm was 7.02% in azygous ACA cases in the present study, which was lower than 9–71% reported in the previous studies [4, 8, 14]. Low rates in the present study could be related to the ethnic characteristic of our study population. Besides, no significant association was found between azygos ACA types and the presence of aneurysms. Two of the distal ACA aneurysms in the present study were saccular and two were fusiform. Nine of the 15 cases with giant distal ACA aneurysms reported in the literature were accompanied by azygos ACA variation [23]. On the other hand, no giant distal ACA aneurysms were observed in any of our cases.

Besides aneurysms, holoprosencephaly, corpus callosum agenesis, arteriovenous malformation, hydranencephaly and porencephalic cyst also could be frequently encountered in cases with azygos ACA variation [8, 20]. Corpus callosum agenesis was observed in two of our cases, while corpus callosum rostrum and splenium hypoplasia were observed in one case each. Therefore, when azygos ACA or cerebral developmental anomalies are observed in cranial MRI, it should be kept in mind that these two entities could coexist, and vascular traces and cerebral structures should be examined.

In autopsy studies, ACA A1 segment was found to have hypoplasia in 10% while this segment was agenesis in 1–2% [5]. These two variants are often associated with anterior communicating artery aneurysms [13]. In thromboembolic events, collateral supply is diminished in these variants, increasing ischemia risk. Fenestration of ACA A1 segment varied from 0 to 4% in anatomic imaging studies, which was reported to be 0.058% in angiography examinations [5]. Since fenestration is often accompanied by aneurysms or other anomalies, it could lead to difficulties in surgical treatment [15]. Krzyżewski et al. [10] studied the anatomical variations of the anterior communicating artery complex and found a frequency of 7.25% for A1 segment hypoplasia, 4.59% for agenesis of the A1 segment and 0.48% for the fenestration of A1. Frequencies of ACA A1 segment anomalies (hypoplasia, agenesis and fenestration) in the present study were higher than those reported rates. Frequency of vertebral artery hypoplasia was reported to have a wide range of 1.9–26.5% [19]. The frequency of vertebral artery hypoplasia 28.07% in the present study was also somewhat higher than this reported range. It was mentioned that the patients with posterior inferior cerebellar artery infarction or lateral medullary infarction had higher tendency to have ipsilateral vertebral artery hypoplasia, which suggests that vertebral artery hypoplasia increases ischemic stroke risk [10]. In previous studies, bilateral fetal posterior cerebral artery (PCA) was reported to be in the range of 2–4% [17]. The frequency of bilateral fetal PCA in the present study was 3.51%, and this rate was in accordance with the literature. To our best knowledge, there have been no studies in the literature dealing with the vascular anomalies accompanying azygos ACA. Unilateral vertebral artery hypoplasia and ACA A1 segment hypoplasia were the vascular anomalies accompanying azygos ACA in the present study. ACA A1 segments were hypoplastic in two of the four cases who were found to have aneurysm distal to the azygos ACA (Cases 4 and 34). Unilateral vertebral artery hypoplasia and ACA A1 segment hypoplasia were observed in our case (Case 28) who was found to have ischemia in pons.

Radiological examinations before the surgeries are crucial for the success of the operations. Not only the internal shape of the angiographies but also the outer shape of the aneurysms should be determined using MRI since large aneurysms could have partial thrombosis inside. A suitable preoperative evaluation along with the use of microsurgery approaches which allow minimal tissue loss and preservation of the bridging veins reduce postoperative mortality and morbidity risks [20]. Treatment of azygos ACA aneurysms has higher risks and is more difficult compared to paired distal ACA [4, 9]. Narrowing or curling of unpaired arteries can cause ischemia in both frontal lobes [4]. Nonsaccular morphology of aneurysms could make them unsuitable for endovascular coil treatment, making the microsurgery more difficult [2]. Distal ACA aneurysms are most commonly handled with the unilateral frontal interhemispheric approach. On the other hand, the subfrontal approach is preferred for more proximal aneurysms. Inci et al. [9] proposed that a good knowledge

of surgical anatomy and experience in microsurgery techniques could minimize the difficulties pertaining to distal ACA aneurysms.

Different radiological examinations must be evaluated together to distinguish between azygos ACA and its mimics. During our evaluation of radiological images, we determined that three cases were, in fact, azygos ACA mimics. In two of the cases, bilateral ACA A1 segments were of normal caliber, while ACA segments distal to A2 were of normal caliber in one side, but of thin caliber in the other (Fig. 10). In the third case, left ACA A1 originated as two roots, one extending to the anterior communicating artery and the other directly to ACA A2 segment. The first radiological examination of the third case using noncontrast-enhanced MRA was concluded to be azygos ACA. However, subsequent CTA evaluation revealed that it was an azygos ACA mimic (Fig. 11).

Our study has some limitations. First, because of the retrospective nature of the study, radiological examinations were not fully standardized in all cases. Some cases had only CTA, MRA or DSA while some others had a combination of these examinations. Second, additional cerebral pathologies could not be adequately evaluated since cerebral MRI was not performed for all cases.

Conclusion

Azygos ACA is a rare variation, but it could be accompanied with aneurysms or other vascular anomalies. With developing radiological examinations, azygos ACA could be more easily detected and categorized. Identifying the type of azygos ACA before the invasive procedures could be useful in the prevention of possible complications.

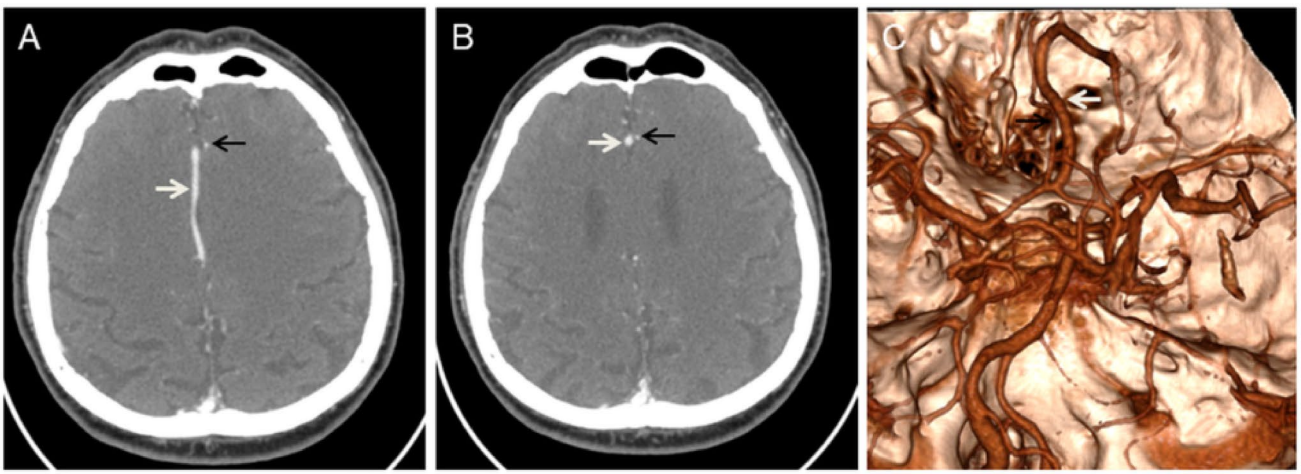


Fig. 10 **a**, **b** Axial computerized tomography angiography images; **c** volume-rendering computerized tomography angiography image of a 67-year-old male patient with azygos anterior cerebral artery mimic. Anterior cerebral artery segments distal to right A2 (white arrows) was of normal caliber in one side, while segments distal to A2 in the left side (black arrows) was of thin caliber

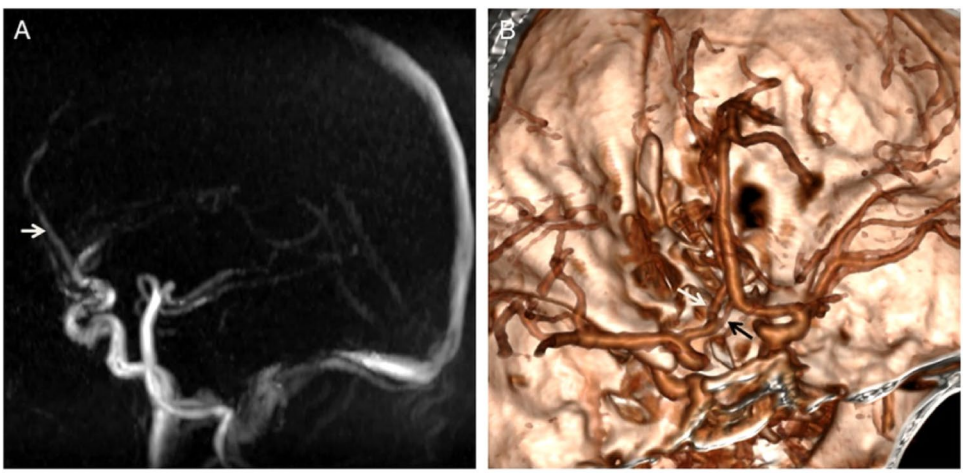


Fig. 11 **a** Magnetic resonance angiography maximum intensity projection image of a 38-year-old female patient with azygos anterior cerebral artery mimic was first considered to be azygos anterior cerebral artery (white arrow). **b** Left anterior cerebral artery A1 segment originated as two roots, one extending to anterior communicating artery (black arrow), and the other directly to anterior cerebral artery A2 segment (white arrow) on volume-rendering computerized tomography angiography image

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Author contributions MB: data collection, analysis, writing. EG: data collection, analysis, writing and final editing. KK: data collection and revision.

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Availability of data and material All data generated or analysed during this study are included in this published article.

Compliance with ethical standards

Conflict of interest The authors declare that they have no financial/personal conflicts of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of our research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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