CASE REPORT

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Multiple congenital anomalies of carotid and vertebral arteries in a patient with an ischemic stroke in the vertebrobasilar territory. Case report and review of the literature

DRAGOŞ CĂTĂLIN JIANU[1,2], SILVIANA NINA JIANU[3], GRAŢIAN DRAGOSLAV MICLĂUŞ[4], GEORGIANA MUNTEANU[2], TRAIAN FLAVIUS DAN[2], CLAUDIA BÂRSAN[2], MIHNEA MUNTEANU[5], HORIA TUDOR STANCA[6], ANDREI GHEORGHE MARIUS MOTOC[7], OCTAVIAN MARIUS CREŢU[8]

[1] *Department of Neurology, "Victor Babeş" University of Medicine and Pharmacy, Timişoara, Romania*

[2] *Department of Neurology, "Pius Brînzeu" Emergency County Hospital, Timişoara, Romania*

[3] *Department of Ophthalmology, "Dr. Victor Popescu" Emergency Military Hospital, Timişoara, Romania*

[4] *Department of Multidetector Computed Tomography and Magnetic Resonance Imaging, Neuromed Diagnostic Imaging Centre, Timişoara, Romania*

[5] *Department of Ophthalmology, "Victor Babeş" University of Medicine and Pharmacy, Timişoara, Romania*

[6] *Department of Ophthalmology, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania*

[7] *Department of Anatomy and Embryology, "Victor Babeş" University of Medicine and Pharmacy, Timişoara, Romania*

[8] *Department of Surgery, "Victor Babeş" University of Medicine and Pharmacy, Timişoara, Romania; Department of Surgery, Clinical Emergency Municipal Hospital, Timişoara, Romania*

Abstract

The congenital anomalies of the supra-aortic arteries and their branches as potential risk factors for cerebrovascular insufficiency are not yet fully investigated and clarified. This report describes the case of a 68-year-old man who was admitted in our Clinic for an acute ischemic stroke in the vertebrobasilar territory. Extracranial color-coded duplex sonography (CCDS) and computed tomography angiography revealed a combination of congenital anomalies of the neck arteries: left internal carotid artery hypoplasia, left common carotid artery hypoplasia, right vertebral artery hypoplasia and the emergence of the left vertebral artery directly from the aortic arch. The aim of this article is to emphasize the value of CCDS as an accurate, non-invasive method of assessing the neck arteries and, also, the importance of the morphological anomalies of the carotid and vertebral arteries in the cerebral hemodynamics.

Keywords: hypoplasia, color-coded duplex sonography (CCDS), computed tomography angiography (CTA).

Introduction

The congenital anomalies of the supra-aortic arteries and their branches as potential risk factors for cerebrovascular insufficiency are not yet fully investigated and understood.

The internal carotid artery (ICA) is one of the most stable arteries and its congenital anomalies (agenesis, aplasia, or hypoplasia) are an infrequent occurrence [1–4]. Hypoplasia is characterized by ICA narrowing along its entire course because of incomplete development. The anomaly has a prevalence of 0.079% and may be unilateral or, more rarely, bilateral [5]. Despite the significantly altered vascular anomaly, the majority of patients are asymptomatic due to the extensive collateral flow on the affected side [5–7]. However, ICA dysgenesis is associated with a higher prevalence of cerebral aneurysms and has important implications during carotid endarterectomy or trans-sphenoidal pituitary surgery [8, 9].

The vertebral artery (VA) usually originates as the first branch of the subclavian artery being its largest and most constant stem [10, 11]. However, it was shown that the anatomical features of VAs are quite diverse [12, 13]. In 6% of the population (usually asymptomatic patients), the left VA arises directly from the aortic arch, while VA hypoplasia has frequently been recognized among healthy individuals [10, 12, 14]. Nevertheless, it has been suggested that VA hypoplasia involves an increased probability of ischemic stroke in the vertebrobasilar circulation territory [12, 15].

The diagnosis of ICA and VA hypoplasia is usually incidental [8]. Extracranial and transcranial color-coded duplex sonography (CCDS) followed by angiography – including computed tomography angiography (CTA), magnetic resonance angiography (MRA), or digital subtraction angiography (DSA) – are the most important methods of assessing these vascular anatomic abnormalities [7, 16]. Also, a hypoplastic carotid canal observed on CT of the skull base and sometimes, a decrease in ipsilateral common carotid artery (CCA) lumen diameter are considered hallmarks of congenital ICA hypoplasia [1, 8].

We present here the case of an old man diagnosed in our clinic with an acute ischemic stroke in the vertebrobasilar territory (unilateral pontine infarct) and a rare combination of morphological abnormalities of the neck

arteries: left ICA hypoplasia, left CCA hypoplasia, right VA hypoplasia and the emergence of the left VA from the aortic arch. These findings were demonstrated by brain CT, brain magnetic resonance imaging (MRI), CCDS, and CTA.

In this article, we want to emphasize the value of CCDS as a valuable diagnostic tool for assessing the neck arteries and the practical neurological importance of recognizing the anatomical variants and anomalies of the carotid and vertebral arteries [16].

Case presentation

We describe the case of a 68-year-old man (S.V.) examined in the Emergency Room (ER) Department of "Pius Brînzeu" Emergency County Hospital, Timişoara, Romania, in 23.02.2018, for vertigo, gait disturbances, and right lateropulsion. The symptoms described had a sudden onset on the day of presentation. Therefore, the patient was admitted in the First Department of Neurology (File No. 9367), with the presumptive diagnosis of stroke in the vertebrobasilar territory. From the patient past medical history, we knew that he was hypertensive under antihypertensive and antiplatelet therapy; the latter one was stopped seven days before the symptoms onset.

At the time of admission, the patient was clinically stable – afebrile, with normal blood pressure (BP) 120/80 mmHg and oxygen saturation of the arterial blood (SpO_2 96%). His heart was regular [heart rate (HR) 72 beats/min], with normal heart sounds and no audible murmur, rubs, or gallops. His lungs were clear to auscultation, without wheezes or rhonchi. His abdomen was benign with normoactive bowel sounds. His peripheral pulses were full and there were no edema or rash on the skin.

On the neurological examination, we observed gait disturbances with right lateropulsion and a wider base, evidence of right dysmetria; tendon reflexes were 2+ and symmetrical throughout, while the plantar responses where flexors on both sides; there were no meningeal signs nor evidence for intracranial hypertension; the patient had a normal tone in all four extremities and no motor deficits; the sensation was found to be intact to light touch, pinprick, proprioception, vibration and temperature throughout; cranial nerves tests were normal and the speech was fluent, with no errors in comprehension or repetition.

During the admission, several investigations were performed including: non-enhanced brain CT (with no pathological findings concerning the brain, but the CT axial image at the level of the left petrous ICA showed a small left carotid canal to the skull base), brain MRI (Figure 1), CTA neck/carotids (Figure 2) and brain (circle of Willis), and extracranial (Figure 3) and transcranial CCDS. These tests had led to discovery of an acute (over 12 hours after onset of symptoms) ischemic lesion localized in the pons (unilateral, and paramedian), and of several vascular abnormalities: left ICA hypoplasia, left CCA hypoplasia, right VA hypoplasia and the emergence of the left VA from the aortic arch. Other paraclinical tests were performed: laboratory blood tests [complete blood count (CBC), renal and liver function tests, electrolyte assessment, erythrocyte sedimentation rate (ESR), coagulation tests], electrocardiogram (ECG), abdominal echography and chest X-ray – none of them showing relevant pathological changes.

Other causes (vasculopathies, such as arteritis or tubular fibromuscular dysplasia) able to determine the symptoms accused by our patient were excluded by the imaging tests listed above.

Under antiplatelet (Clopidogrel), lipid control with statins and antihypertensive therapies [angiotensin-converting enzyme (ACE) inhibitor in combination with a diuretic: Perindopril and Indapamide], the patient's clinical evolution was good and the neurological symptoms completely resolved in the next three days. No surgical interventions were considered necessary in order to resolve the vascular abnormalities.

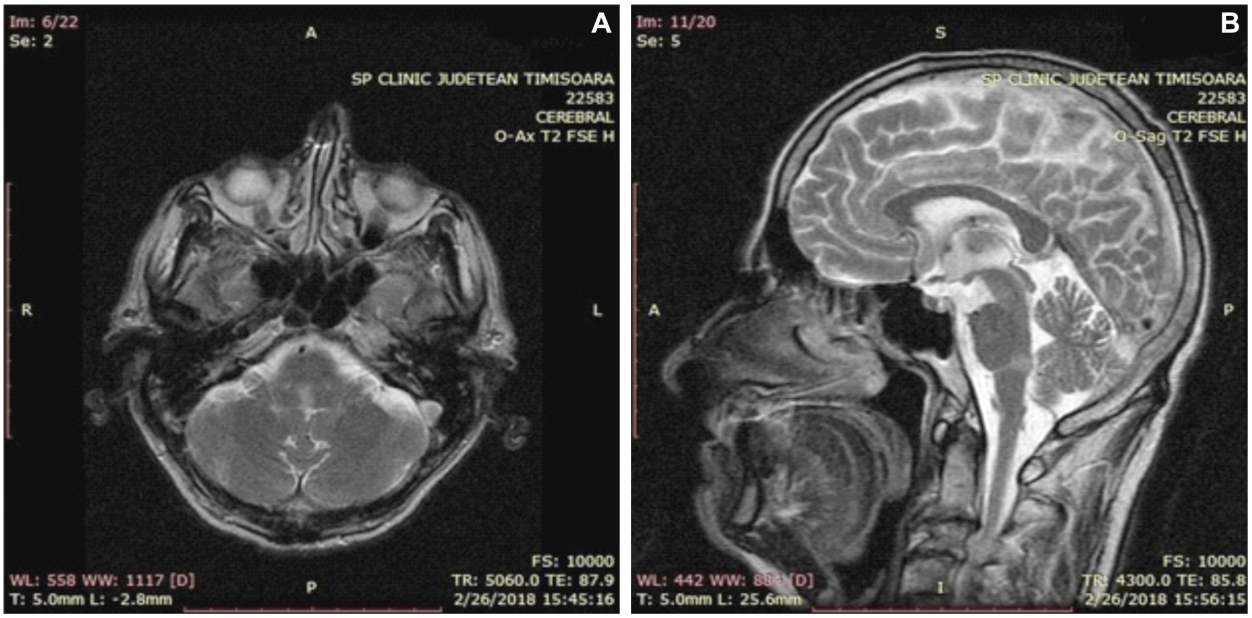

Figure 1 – ***Brain magnetic resonance imaging (MRI). The FSE T2-weighted axial (A) and sagittal (B) scans show high signal intensity, representing vasogenic edema – unilateral paramedian acute (over 12 hours after onset of symptoms) pontine infarct. FSE: Fast spin echo.***

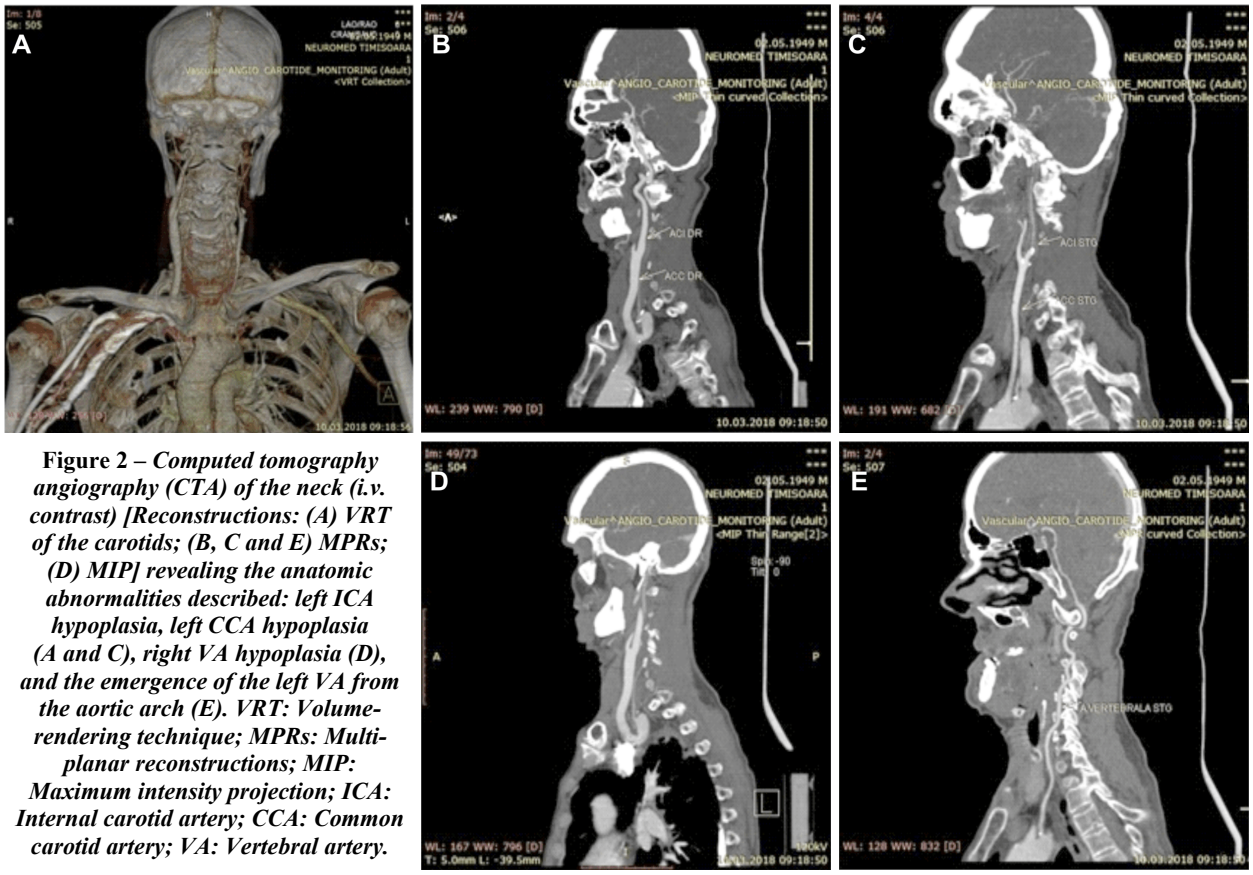

Figure 2 – ***Computed tomography angiography (CTA) of the neck (i.v. contrast) [Reconstructions: (A) VRT of the carotids; (B, C and E) MPRs; (D) MIP] revealing the anatomic abnormalities described: left ICA hypoplasia, left CCA hypoplasia (A and C), right VA hypoplasia (D), and the emergence of the left VA from the aortic arch (E). VRT: Volume-rendering technique; MPRs: Multi-planar reconstructions; MIP: Maximum intensity projection; ICA: Internal carotid artery; CCA: Common carotid artery; VA: Vertebral artery.***

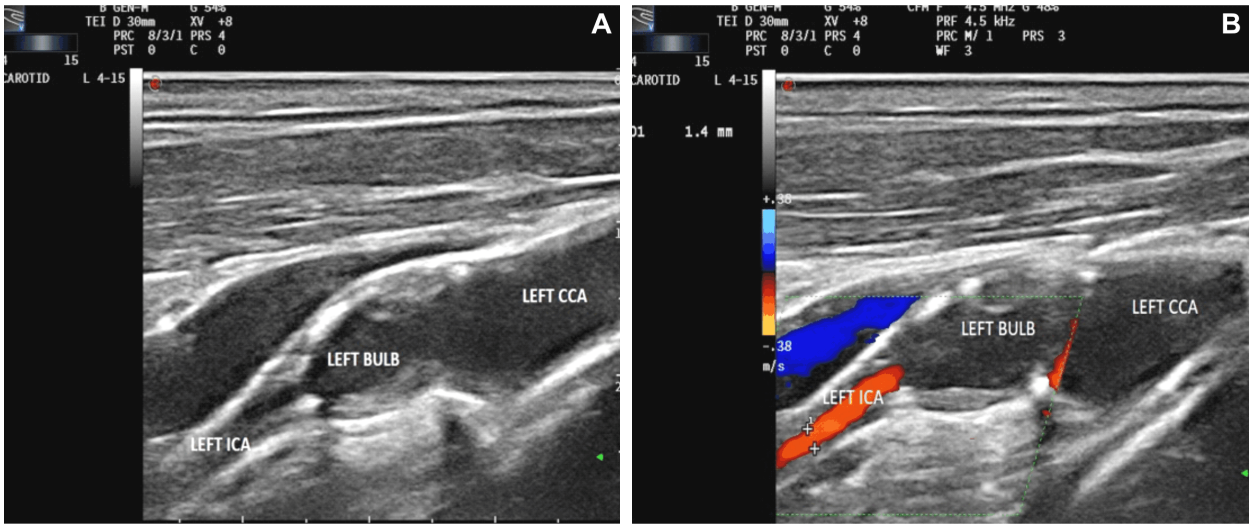

Figure 3 – ***Extracranial color-coded duplex sonography (CCDS) indicating the anatomic abnormalities described: (A) B-mode imaging (left ICA hypoplasia); (B) Color Doppler flow imaging (left ICA hypoplasia). ICA: Internal carotid artery; CCA: Common carotid artery.***

Discussions

Internal carotid artery (ICA) hypoplasia

ICA is a terminal branch of CCA. It arises at the level of the hyoid bone, (between the C4 and C6 vertebral bodies) where CCA divides into ICA and external carotid artery (ECA) [17].

Morphological variations of ICA are exceptionally rare, while carotid anomalies related to developmental defects are an infrequent occurrence [1, 18]. They have been categorized by Lie into three groups: agenesis (absence of the entire artery and its bony canal), aplasia (a vestige of ICA is present, as well as the carotid canal) and hypoplasia (both the artery and the carotid canal are small but with a normal structure) [18, 19]. The left ICA dysgenesis cases are three times more frequent that those concerning the right one (as in our case) [7].

ICA hypoplasia – the carotid anomaly identified in our case – is a very rare anomaly occurring in 0.079% of individuals [7, 18, 20].

The formation of the ICA occurs in the 3- to 5-mm embryonic stage, and it is completed by the 6th week of gestation [21]; the formation of the skull base is first seen in the 5th or 6th embryonal week [22, 23]. Therefore, the

development of ICA is mandatory for the formation of the carotid canal in the skull base [8, 22]. The structures that give rise to ICA are the dorsal aorta, the ventral aorta, and the third aortic arch [21, 24]. The embryological developmental defect that causes ICA hypoplasia is still unclear: it has been suggested as possible mechanisms a secondary involution of the ICA ensuing a phase of proper development or an arrest of the artery development at a given moment in time [1, 7].

The lack of blood flow caused by unilateral ICA hypoplasia is mostly compensated by the intact collateral circulation developed from the contralateral ICA and vertebrobasilar system [3, 8, 20]. Thus, the condition is usually asymptomatic and incidentally discovered. Also, even when the vascular anatomy is markedly altered, MRI or single-photon emission computed tomography (SPECT) rarely found evidence of brain lesions or perfusion defects [1, 6, 25]. Although most of the cases of ICA hypoplasia remain asymptomatic, some patients present ischemic or hemorrhagic cerebral events secondary to cerebral hypoperfusion or bleeding from aneurysms or dilated collaterals. The clinical presentations of this condition may include seizure, transient ischemic attack (TIA), ischemic or hemorrhagic stroke, migraine-like headache and spasmodic torticollis [7]. In our case, the ICA hypoplasia was an incidental diagnosis – none of the symptoms accused, as neither the imaging lesion found being consistent with the vascular territory of this artery.

The diameter of the ICA ranges between 4 mm and 5 mm [26]. The diagnosis of ICA hypoplasia is based on neuroimaging and includes: color-coded carotid duplex sonography followed by angiography – CT/MRA or DSA [7, 8]. The CT of the skull base will help to differentiate the congenital from the acquired narrowing of the ICA [1]. The presence of a small bony carotid canal on CT imaging at the level of the left petrous ICA, demonstrated, in our patient case, the diagnosis of ICA hypoplasia, excluding the hypothesis of ICA acquired stenosis and respectively of ICA agenesis.

CCDS is usually the first study performed by physicians to rule out carotid disease. It is non-invasive and accurate in analyzing both parietal anomalies (hypoechoic plaques, clotting and parietal hematoma) and the external diameter of the artery; it can rule out both stenosis and occlusion in the carotid bulb. Also, the use of a color-coded Doppler flow imaging technique improves the accuracy of flow measurement and provides information on smaller arteries with low flow. Among the limitations of CCDS, the most important one is represented by the fact that, using this technique, it is impossible to exam the ICA in its high cervical, intrapetrous and intracranial segments and also, it is especially difficult to describe a deep cervical variant of this artery [1, 7]. There have been several reports concerning the CCDS findings in ICA hypoplasia, but, until now, there is no consistent evidence on the reliability of CCDS as an assessment tool of the diameter and flow volume in hypoplastic ICA [27].

According to Chen *et al.*, there are direct and indirect CCDS signs suggesting ICA hypoplasia [7]. Direct findings are a long segmental small-caliber (about 50% smaller than the size of the unaffected contralateral artery) lumen accompanied by a significant reduced flow volume (13% of the normal side) in the affected vessel, but without important atherosclerosis, a false lumen, or notable wall thickening (as in our case). Indirect signs encompass a significantly augmented total flow volume in the bilateral VAs (augmented by over 130% of the normal value), anterogade ipsilateral ophthalmic arterial flow, a diminishing artery diameter, and higher flow resistance in the ipsilateral CCA (as in our case) [1, 7].

However, MR/CTA is the best noninvasive method to assess narrowed ICA, collateral circulation and possible associated intracranial aneurysms. As we stated above, congenital ICA hypoplasia is always accompanied by a small carotid canal given that the carotid canal formation is a direct consequence of its respective embryonic artery presence. Thus, demonstration of a small carotid canal (on CT of the skull base) (as in our case), along with a well-developed collateral circulation (on CT/MRA) are essential arguments in favor of the congenital nature of the condition [1, 7, 8].

ICA hypoplasia should be differentiated from a variety of other vasculopathies including atherosclerosis, arteritis, tubular fibromuscular dysplasia, intimal dissection, transient perivascular inflammation of the carotid artery (TIPIC) syndrome and Moyamoya syndrome. Also, a hypoplastic ICA may be confused with a "functional narrowing" of the arterial lumen (*e.g.*, vasospasm, increased intracranial pressure) or with a dilated ascending pharyngeal artery [1, 7, 28]. The ICA hypoplasia prognosis depends on the eventual concomitant presence of intracranial aneurysms given that this anatomic anomaly induces a hemodynamic pressure increase in collateral arteries [1, 8]. Lhermitte *et al.* described three vascular conditions associated with ICA hypoplasia; anomalies and variants of the circle of Willis, aneurysms, and intense collateralization [7, 29]. It is important to emphasize that the reported prevalence of intracranial aneurysms in affected patients is 24–34% – about 10 times higher compared to the normal population (2–4%) [8, 30]. No aneurysms have been found in our case. Also, discovering an ICA hypoplasia has important implications in the assessment of cerebral embolic events considering that emboli in one cerebral hemisphere may originate from an atherosclerotic contralateral ICA [8, 9]. Also, this condition, alongside other carotid dysgenesis, should be taken into account, when interventions including carotid endarterectomy or trans-sphenoidal pituitary surgery are considered [8, 31].

Due to the rarity of this condition, no optimal treatment has been yet established for the symptomatic stenosed hypoplastic ICA [3].

Common carotid artery (CCA) hypoplasia

The ICA hypoplasia is often associated with a smaller diameter of the ipsilateral CCA (also found in our patient). The presence of concomitant CCA hypoplasia suggests the congenital character of the process [7].

It is important to know that patients with distal ICA dissection may show a similar CCDS pattern, but the reductions in the ICA and CCA calibers and augmentation in collateral flow from the VA are usually less pronounced than those found in the cases of congenital hypoplasia [7].

Vertebral artery (VA) anomalies

The VA is a part of the vertebrobasilar cerebral circulation being the largest and most constant stem of

the ipsilateral subclavian artery (SCA) [11, 13, 15]. However, the VA origin can be variable in a minority of cases – VA can arise from the aortic arch (in 6% of the population, mostly on the left) (as in our case), brachiocephalic artery (on the right) or from the ECA [10, 13, 32]. From its origin, VA takes a postero-vertical course to enter into the sixth cervical transverse foramen (90–95% of the cases), then bends medially, behind atlas, and goes into the cranium through the *foramen magnum* [14, 33–36]. After giving rise to the posterior inferior cerebellar artery, the VAs join at the lower pontine border to form the basilar artery (BA) [10, 36]. We have to mention that when the origin of the VA is from the aortic arch, then the artery usually enters the *foramen transversarium* at a higher level than normal (C5 instead of C6) [32]. This artery is typically divided into four sections: the first segment (V1 – preforaminal) starts from its origin (V0 – ostium) on the SCA to the C6 transverse process; the second (V2 – foraminal) from C6 to C2 transverse process; the third (V3 – atlantic): from C2 to the *foramen magnum*; and the fourth (V4 – intracranial) from the *foramen magnum* to the vertebrobasilar junction [15, 32, 36].

The VA has a normal diameter of 3–5 mm. It has important anatomical relationships with the ipsilateral ICA and hypoglossal nerve (CN XII) and represents the primary blood supply for the infratentorial brain structures [12, 32].

Aortic arch origin of VA

The VA is subject to numerous anatomical variations, most of them incidentally discovered during angiographic or anatomic postmortem studies [14, 37, 38]. Among these variants, the most frequently reported form is represented by a VA arising from the aortic arch, situation that occurs in about 6% of the population. In other rare cases, left VA arises from the left CCA or the root of the left SCA [13, 14, 39]. The abnormal arising of VA from the aortic arch (also described in our patient) is the consequence of an error that occurs during the human embryonic development [37].

It was reported that the left VAs originating from the aortic arch are frequently hypoplastic and go into the *foramen transversarium* at a different level (C5 instead of C6) [16, 32, 37]. However, in our case, the left VA had a normal caliber, while the right VA is hypoplastic; also, the CTA revealed that, in our patient, the left VA entered into the C6 transverse foramen.

In most cases, these anomalies are asymptomatic or incidental, however, we should be able to recognize them for several reasons [13, 38, 39]:

- the aortic arch and VA anomalies may interfere with endovascular, neurosurgical or ear-nose-throat (ENT) interventions [38–40];
- variants of the aortic arch can be taken as occluded vessels, when the artery is not found at its conventional site during angiography or surgical interventions [39];
- it has been suggested that, possibly due to the resulting altered hemodynamics, these variants can be associated with the presence of intracerebral aneurysms [39, 41].

VA hypoplasia

The normal diameter of VAs varies from 1.5 to 5 mm. Congenital anatomical variations of both VAs are common among healthy individuals without symptoms of vertebrobasilar insufficiency; left VA dominance presents in 65% of the population, identical width of VAs occurs with a 25% prevalence, whereas in only 10%, the right VA is larger than the left one [12, 15, 42–44].

There is a lack of consensus on the definition of VA hypoplasia because the majority of studies were not conducted on healthy subjects or the sample size was small [45]. Thus, operational definitions of VA hypoplasia varies between diameters of less than 2 mm to less than 3 mm (measured in the entire course of the artery), associated with an asymmetry ratio threshold >1:1.7 (also, observed in up to 10% of normal individuals) [12, 15, 46]. Additional suggestive sonographic criteria include reduced blood flow velocity and volume, increased resistance index (RI) values, and a compensatory increase in the vessel diameter of the contralateral VA. According to recent data, a cut-off point of 2.2 mm was fixed as a defining criterion for VA hypoplasia [15, 45, 47].

VA hypoplasia is a common vascular variant; however, its reported frequency is dependent on the definition used for this abnormality [20, 45]. Thus, the VA hypoplasia prevalence found in the literature is highly inconsistent ranging from 1.9 to 26.5% [12]. In terms of side difference, the right hypoplastic VA occurring more frequent than the left one, may be explained by the fact that the left SCA (the VA's origin), being a direct branch of the aortic arch, is exposed to an increased shear stress during development. Thus, the blood supply, usually, end-up being dominated by the left VA [12, 15].

Visualization of VA and its eventual pathological modifications is possible by using Doppler ultrasonography or some sort of angiography techniques, such as DSA, CT/MRA [33, 38].

Nowadays, CCDS is the first test used in the assessment of extracranial segment of VA, being non-invasive, cost-effective and reproducible [16, 33]. With CCDS, it can be obtained significant information especially about the proximal brachiocephalic vessels, while the intervertebral segment of the artery is usually more difficult to assess. The Doppler waveform, which corresponds to VAs, is monophasic with prominent diastolic flow and spectral broadening [10]. The CCDS assessment of the VA includes the measurement of the arterial diameter (4.6 mm in average), the peak systolic velocity (PSV) (56 cm/s in average) and end diastolic velocity (EDV) (17 cm/s in average), the RI (0.69 in average) and the net vertebral flow volume (200 mL/min in average) [10, 47, 48].

The hemodynamic consequences of VA hypoplasia revealed by CCDS include:

- a narrower vessel lumen [diameter of ≤2.5 mm (5), ≤2.2 mm (9), or ≤2 mm (7), according to different definitions of VA hypoplasia] [12, 15].
- an increase of ipsilateral RI (>0.75) [47];
- a PSV usually <40 cm/s [15];
- a decreased ispilateral net vertebral flow volume <100 mL/min [8] and a slightly increased one in the contralateral VA [42, 47];
- a significantly lower mean net flow volume (the sum of the net flow volume of bilateral VA) [42].

We have to mention that this method is not useful in the assessment of the exact trajectory of this artery and

it may not be enough in order to differentiate VA hypoplasia from aplasia, occlusion or dissection. CT/MRA usually confirms the diagnosis [16, 42].

In our case, the CCDS assessment of the VAs revealed a right VA hypoplasia, diagnosis which was then confirmed by CTA.

The clinical relevance of VA hypoplasia is still debatable; however, it was reported that VA hypoplasia is more common in patients with migraine with aura or those suffering from vestibular neuronitis rather than in those without these diseases, suggesting that this anomaly may be an additional factor involved in the pathogenesis of these conditions [12, 46, 47, 49].

In the past years, it was suggested that an ipsilateral hypoplastic VA represents a risk factor for ischemic stroke in the vertebrobasilar territory – particularly for ischemic events in the posterior inferior cerebellar artery (PICA) and lateral medullary territories [12, 20]. Recent evidence has revealed that the diminished blood flow detected on the same side with the hypoplastic VA might augment the risk for thrombosis and deficient clearance of thrombi leading to stenosis of the distal artery [12, 33, 42]. Supporting these statements, we mention a study that showed that the VA hypoplasia leads to regional hypoperfusion in the respective PICA territory in 42% of individuals tested [47].

According to Palmer, the presence of this anomaly may increase the hemodynamic significance of the atheromatous disease affecting the proximal CCA, possibly by limiting the potentialities of compensatory blood circulation [49–51]. Related to this, it is also the fact that the patients with both carotid and VA diseases seems to have a higher incidence of vertebrobasilar TIAs (71%) in comparison with those diagnosed with isolated carotid artery disease (8%) [42].

At the moment, the hypoplastic VA is not seen as an independent risk factor for stroke, however it is important to know that, if associated with other risk factors, it may induce ischemic stroke in the posterior circulation territories [38, 42]. Therefore, we can assume that the presence of the right hypoplastic VA (associated to other vascular anomalies in a hypertensive patient) may have played an important role in the cerebral ischemic event presented in our case.

VA hypoplasia can be associated with other coexisting pathologies, such as aneurysms, BA hypoplasia, arachnoid cyst and hereditary connective tissue disorder (*e.g.*, Ehlers–Danlos syndrome) [38, 49].

The structural anomalies of VA are important to be identified in those cases when spinal, laryngeal or thyroid gland surgery is needed and also, if the patient has to undergo an endovascular intervention or an endarterectomy of extracranial arteries [16].

Accurate assessment of anatomic variations of VAs is mandatory when planning surgical treatment in order to avoid an eventual injury of the artery during surgery [14, 16].

Ischemic stroke in the vertebrobasilar territory

Penetrating arteries (thalamoperforators) from the BA supply the pons. Frequently, infarcts in the pons are unilateral, and paramedian (as in our case). The differential diagnosis of a unilateral pontine lesion always should include multiple sclerosis – which, in our patient, was excluded based on clinical and imagistic findings [52, 53].

Conclusions

Our diagnosis – multiple congenital anomalies of carotid and vertebral arteries – was based on CCDS and CTA, knowing that the combined use of these methods allows a non-invasive and precise assessment of the neck vessels and their pathology. It was shown that the ICA and VA dysgenesis, in coexistence with other risk factors for stroke may be involved in cerebral ischemic events and respectively in the vertebrobasilar ischemic stroke pathogenesis.

Conflict of interests

The authors declare that they have no conflict of interests.

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Corresponding authors

Andrei Gheorghe Marius Motoc, MD, PhD, Professor of Anatomy, Department of Anatomy and Embryology, "Victor Babeş" University of Medicine and Pharmacy, 2 Eftimie Murgu Square, 300041 Timişoara, Romania; Phone/Fax +40256–220 482, Mobile +40722–277 806, e-mail: amotoc@umft.ro

Claudia Bârsan, MD, Senior Neurologist, First Department of Neurology, "Pius Brînzeu" Emergency County Hospital, IX Floor, 156 Liviu Rebreanu Street, 300723 Timişoara, Romania; Mobile +40746–983 358, e-mail: barsan.clau@yahoo.com

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