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Anatomical Anomalies of Carotid-Vertebral Arteries in Patients with Dizziness and Impaired Hearing

Jurek Olszewski and Piotr Niewiadomski

Abstract

Currently, Doppler ultrasound examinations are of particular importance, including continuous wave Doppler and color-coded pulsed wave Doppler. Excellent images are obtained using contrast computed tomography angiography (CTA) and magnetic resonance angiography (MRA), which give greater understanding of blood flow in the cranial and intracranial vessels under normal conditions and in pathological situations caused by both anatomical anomalies and acquired abnormalities. Our previous studies, concerning the analysis of the frequency and types of anatomical anomalies of the cranial arteries, i.e. vertebral and carotid arteries, in patients with dizziness and impaired hearing, demonstrated that hypoplasia of the right vertebral artery was the most common anatomical anomaly occurring in 58.7% of cases, of which 51.7% were women and 6.9% men; hypoplasia of the left vertebral artery, occurring in 24.7% of the study group, of which 13.8% were women and 10.3% men; hypoplasia of the right internal carotid artery found in 3.4% of women and of the left internal carotid artery in 6.8% of cases, 3.4% in women and 3.4% in men; and hypoplasia of the right common carotid artery was reported in 3.4% of men, whereas critical stenosis of the left subclavian artery with subclavian steal syndrome was observed in 3.4% of women. Although tinnitus was the most frequent symptom occurring in those patients, in this study dizziness was most common in patients admitted to the Department for the diagnosis, possibly because they found it more disturbing.

Keywords: anomaly, carotid, vertebral arteries, dizziness, impaired hearing

1. Introduction

The complex anatomy of cranial and intracranial arteries and the formation of collateral circulation have been studied for many years. Currently, Doppler ultrasound examinations are of particular importance, including continuous wave Doppler and color-coded pulsed...
wave Doppler. Excellent images are obtained using contrast computed tomography angiography (CTA) and magnetic resonance angiography (MRA) [1–3], which give greater understanding of blood flow in the cranial and intracranial vessels under normal conditions and in pathological situations caused by both anatomical anomalies and acquired abnormalities [4–8].

Anomalies of the vertebral arteries include: underdevelopment of one vertebral artery, coexisting with compensatory dilatation of the contralateral artery, total absence of one of the vertebral arteries, variations in vertebral artery origin from the aorta or from the common carotid artery, double origin of one vertebral artery forming a common vascular trunk, and duplication of the vertebral artery on one side [9].

The reduction of blood flow caused by a hemodynamically significant factor triggers numerous compensatory mechanisms. These include local regulation of the cerebral circulation, increase in systemic blood pressure and, in the case of permanent reduction of blood supply, the formation of collateral circulation [1].

Anatomical anomalies do not produce specific symptoms that could suggest early diagnostic tests aiming at their identification, and they often coexist with other disorders that can cause similar symptoms in the ENT organs (post-traumatic or degenerative changes in the cervical spine, hypertension, hormonal or metabolic disorders). Therefore, many authors are inclined to the view that in adults, anatomical anomalies are diagnosed only when other factors that impair the vascularization of the central nervous system are present in these patients. A possible example of this involves reports that indicate that hypoplasia of the vertebral artery is more common in menopausal women, who often suffer from symptoms of vertebrobasilar insufficiency [5, 6].

1.1. Anatomical anomalies of the intracranial vessels

The sense of balance and spatial orientation is conditioned by efficient functioning of individual elements of the system of balance and proper communication between them. Proper blood supply to each of its elements is one of the basic and necessary conditions of efficient functioning of this system [10–12].

It originates from intracranial vessels that, among other things, include vertebral arteries, merging and creating the vertebrobasilar system that supplies blood to a part of the brain, the inner ear, pons, cerebellum, and spinal cord. For proper functioning of the peripheral organ of balance, the most important is the labyrinthine artery that, in accordance with the declining frequency of anatomical variations, branches off from the anterior inferior cerebellar artery, basilar artery or vertebral artery and then, usually already in the inner auditory canal, divides into three branches: the vestibular artery, the vestibular-cochlear artery and the cochlear artery.

Regardless of the anatomical variation, blood supply to the inner ear directly or indirectly arises from the vertebral artery identical on each side of the body.

The vertebral artery branches off from the ipsilateral subclavian artery with four possible anatomical varieties, with a prevalence of 0.1–90%, and for the branch-off from the vessel in relation to the thyroid-cervical trunk [13]. Its further course is divided into four segments:
• V1 – arises from the subclavian artery and enters the transverse foramen of C6,
• V2 – a segment of the vessel running from the transverse foramen of C6 to the transverse foramen of C2,
• V3 – a suboccipital segment, emerges from the transverse process of C2 to pierce the dura at the height of the foramen magnum,
• V4 – an intracranial segment, from the foramen magnum joins its contralateral counterpart at the lower border of the pons to form the basilar artery of the brain.

Some authors also distinguish the V0 segment, which is the site of branching off the vessel [16]. After branching off from the subclavian artery, the vertebral artery is directed upwards and enters the canal formed by the transverse processes of the cervical vertebrae, in 90% of cases at the C6 level, although possible are also entry variants at the level of the C5 (in 5%), C4 (2%), C7 (2%), C3 (1%). In the case of entry other than the C6 level, the vessel runs ventrally in relation to the transverse processes of the vertebrae located below, between the pre-vertebral muscles and the bone forming the spinal process. Next, it runs upwards vertically, surrounded by the spinal venous plexus and closed in the periosteal envelope derived from the periosteum of the transverse processes of the vertebrae, which forms two fibrous rings: proximal, in the place of entry to the channel, and distal, at the site where the vessel penetrates the dura mater. The fibrous rings are the only sites to integrate the vessel with the surroundings. The vertical course of the vessel changes above the height of the C3. This is due to the different construction of the spinal process of the C2 which, in contrast to the others, is set diagonally down in relation to the vertebral body, and, in addition, it is longer than the others. This makes the vertebral artery take the lateral and almost horizontal directions to reach the C2 transverse hole. Then it returns to its vertical course in a short section, from the C2 to the C1, to take its near-horizontal direction again, running in the sulcus of the C1 rear arch, and then it heads obliquely, vertically and medially, pierces the dura mater to continue in the intracranial segment. On the surface of the occipital bone, both vertebral arteries merge to form the basilar artery. The entire length of the artery is accompanied by the spinal nerve from the stellate ganglion which, together with the branches of the middle and upper cervical ganglia and branches of the cervical spinal nerves, forms the spinal plexus.

The spinal arteries in their course give off:
• muscular branches,
• spinal branches,
• meningeal branch,
• anterior spinal artery,
• posterior spinal artery,
• posterior inferior cerebellar artery.

Muscular branches seem to be particularly noteworthy. In addition to supplying the structures corresponding to the name of the branch with blood, like other branches of the vertebral arteries, muscular branches have connections with the relevant branches of the ascending
muscular carotid artery, deep carotid artery and external carotid artery. Due to these connections, a vascular network is formed, that in the event of the closure of the proximal segment of the vertebral artery could allow it to refill with blood above the site of closure or narrowing and thus ensuring the proper functioning of the vertebrobasilar system. The vascular networks mentioned above do not need to be visible in the standard angiographic studies, which does not preclude their existence. Visualization of these anastomoses may require the use of special imaging techniques.

Basing on the data obtained at the Department of Otolaryngology, Laryngological Oncology, Audiology and Phoniatrics at the Medical University of Lodz, Poland, collected in the years 2007–2012 and comprising 2167 patients diagnosed as having dizziness and hearing disorders, anomalies of intracranial vessels were confirmed in 29 patients (1.3%) [9]. It could be expected that the incidence of such anomalies is greater than that shown above, as indicated by other authors who estimated the incidence of anomalies of the vertebral arteries in the population at a level of 31% in the case of isolated changes and 15% of the population in the case of two-sided changes, or a few changes within one vessel in its different segments [14]. The anomalies more frequently concern the left vertebral artery and can be isolated and coexist with other vascular anomalies related to the aortic arch or subclavian artery [4, 15]. Figure 1 shows an example of complex anomalies.

The overview of the anomalies should start from the most prevalent ones, and such is the degree of asymmetry of their diameter, though it is generally considered an anatomical variant. Differences in the diameter of these vessels range from small, virtually imperceptible in imaging studies, to substantial hypoplasia of one of the arteries with proper or increased width of the artery on the opposite side (Figure 2). Depending on the source, it is said that vertebral arteries vary in diameter in 40–75% of the population [6, 10, 11]. The study results unanimously indicate a higher incidence of domination in terms of the width of the left vertebral artery (50–65%), whereas the right spinal artery is wider only in 10–25% of the study population [11, 12]. The limit value of the diameter of the vertebral artery above which it is no longer asymmetry but hypoplasia is not explicitly specified. As a criterion for hypoplasia the diameter of the vessel amounts to ≤2 mm along its entire length [13], though some authors give a limit value of ≤3 mm, possibly extending the criteria for diagnosis of, disclosed in the ultrasound with Doppler, high resistance and reduced blood flow [14]. Other criteria are also used for eligibility of the vertebral arteries as hypoplastic, these are the degree of asymmetry between the vessels that, depending on the author, fluctuates between 1:1.7 [15] and 1:2, and a functional criterion defined as the proportion of narrower arteries at ≤10% of the total volume of the vertebral flow. Speaking of the vertebral artery hypoplasia, it should be remembered that we refer to it only if it meets the above-mentioned criteria while maintaining the condition that it eventually connects to the spinal artery of the opposite side by forming the basilar artery. Otherwise, when, for example, one of the arteries, inclusive of an artery that initially has its normal course, leaves the canal of the transverse processes at the site different from the typical one and, finishing its course, connects to a vessel other than the contralateral vertebral artery, this is considered an aplastic artery (Figure 3). Most often, such a connection occurs with the posterior inferior cerebellar artery of the cerebellum, yet a merger of the occipital artery or spinal arteries is also possible.
Figure 1. Angio-CT of the vertebrobasilar system vascular anomaly in the female patient. Branch-off of the right common carotid artery directly from the aortic arch with the concomitant hypoplastic right vertebral artery.

Figure 2. Angio-CT of the vertebrobasilar system vascular anomaly in the male patient. Asymmetry of the diameter of the vertebral arteries with the dominant left spinal artery.
Abnormal site of the vertebral artery branch-off is found among the typical anatomical anomalies. It can be the aortic arch—it mostly concerns the left vertebral artery (2.4–5.8% of the population), very rarely the right vertebral artery, while the simultaneous branch-off of both vertebral arteries from the aortic arch has been described in the world literature less than 10 times. Less commonly, the spinal arteries take their origin from the external or internal carotid artery whereas the left vertebral artery isolated branch-off from the common left carotid artery has been described in the literature only twice. Other anomalies of the vertebral arteries include the total lack of one of them or the double branch-off of the vertebral artery, two independent trunks of which, each originating from different vessel, then meeting in one common trunk and penetrating into the holes of the transverse processes, to complete their course in a typical manner—this type of anomaly can occur on one or both sides [16, 17].

Improper course of vertebral arteries is their another anomaly. It can be curved along the entire length of the vessel as well as in its short segment, both within the canal of the transverse processes of the cervical vertebrae and before and after leaving the canal. A staple duplication of a blood vessel can also be met which, after branching off properly splits into two trunks that run separately to merge again and complete the course by connecting to the spinal artery on the opposite side [18, 19]. Anomalies can also affect other intracranial vessels, among them the hypoplasia of the right internal carotid artery, hypoplasia of the left internal carotid artery, hypoplasia of the right common carotid artery, hypoplasia of the left subclavian artery and aplasia of the left common carotid artery. We can also meet with adult-preserved vessels of angiogenesis of the embryonic period. An analysis of the literature reveals that the above is observed especially in cases when there is abnormal flow in the vertebral, intracranial or cervical arteries due to their innate or acquired obstruction. This takes place probably because...
these persistent vessels constitute a connection between the system of the carotid arteries and the system of the vertebrobasilar arteries. Thus, according to their decreasing occurrence, the persistent tricuspid artery, sublingual artery, auricular artery and peri-levatorial artery can be distinguished, all taking their names from the cranial nerves along which they run [20].

The symptomatology of the presence of anomalies in intracranial vessels is very diverse and it seems to be associated with the type of existing anomalousness. The anomalies may be clinically silent and detected accidentally when performing imaging tests involving the vascular system; it may cause isolated symptoms or complex assemblies of subjective complaints in the affected person. The nature of reported complaints depends on, as mentioned above, the type of anomaly where the point is whether the given anomaly affects the capacity of the vessel in fulfilling its basic function, what the provision is of appropriate structures with blood, or it causes changes in anatomic relations resulting from the improper course or construction of the vessel which may cause adverse effects in the neighboring structures, in normal conditions not contacting with the vessel affected by the anomaly. Since the vast majority of information about the anomalies of the intracranial vessels comes from descriptions of individual cases, the search for symptoms, the occurrence of which could indicate, with a high degree of sensitivity and specificity, the existence of such a condition, is limited. Among the ailments most commonly reported in the medical literature, the paroxysmal dizziness of systemic and non-systemic nature is in the foreground. Other complaints, which may coexist or occur as isolated ailments or in groups include gait instability, nausea, double vision, presyncope/syncope, bilateral tinnitus, hearing loss, cervical radiculopathy and headaches [18, 21, 22]. Vanrietvelde et al. also described the case of a patient complaining of chronic neck pain radiating to both upper limbs for 2 months, in whom vertebral artery loop formation was revealed at the level of C4, coexisting with degenerative changes of the neighboring cervical vertebrae without imaging evidence of the spinal nerve root compression. The second case, described by the same authors, concerns the same anomaly with accompanying widening of the intervertebral foramen at the level of C4-C5, and severe torticollis with loss of sensation on the right side of the face and impaired consciousness [23].

A large and heterogeneous range of symptoms induced by the presence of the anomalies of the intracranial vessels and their not always well explained pathogenesis along with coexisting systemic diseases that may be the cause of the reported ailments, make the diagnosis of these lesions a big challenge. Therefore, it seems justified to look for more and more efficient algorithms of management, allowing at least to select a group of patients in whom diagnostic procedures will be properly targeted and more complex which finally will be the most accurate way to achieve the proper diagnosis.

1.2. Doppler ultrasound of the system of the vertebrobasilar arteries

The Doppler ultrasound is a non-invasive research modality that allows to assess the speed of blood flow in the blood vessels, which was first described by Satomura in 1959. However, the basis for its creation, that is, the discovery and definition of the Doppler phenomenon, is the merit of two physicists who had worked independently over a century before Satomura: Ch. Doppler, who in 1842 observed the effect of changing the color of light under the effect of
motion in the double star system and A. Fizeau, who in 1848 described a similar phenomenon related to electromagnetic waves.

The study of Miyzaki and Kato on the measurement of the blood flow velocity in the arteries supplying the brain and in extracranial arteries was published for the first time in 1965. In 1982 Aaslid was the author of the first report about assessing the test speed of blood flow in the cerebral and intracranial vessels as well as the constructor the first measuring device. This method uses ultrasound, that is acoustic waves of frequencies exceeding the hearing range of the human ear (over 20 kHz), generated by a piezoelectric transducer. Piezoelectrics are crystals which generate an electric charge in response to applied mechanical stress and electrical fields can deform piezoelectric materials (“inverse piezoelectric effect”). The second component used in the study is the Doppler effect consisting in the change of the frequency of the wave reflected from the moving object in relation to the frequency of the wave being transmitted. Frequencies of 1–10 MHz are most commonly used for diagnostic purposes [24–26].

In the Doppler ultrasound of the blood vessels, the sound waves sent by the camera head bounce off from the blood cells flowing in the vessels, changing their frequency which is read by the ultrasound device. The change in the frequency is called the Doppler frequency and it is proportional to the speed of blood flow. In the Doppler apparatus this frequency is processed for the acoustic signal which allows to distinguish the nature and position of the vessel. Introduction of colored Doppler ultrasound has improved the identification of blood vessels and determination of the direction of blood flow. In this modality, different colors are assigned to different frequencies, depending on the direction of the moving blood cells and their speed. Red and blue colors are usually used to determine the direction of blood flow whereas shades of these colors serve to demonstrate different flow velocities. Power Doppler introduced in 1993 is an improved color Doppler ultrasonography. The difference lies in imaging of the flow by analyzing the total energy of the Doppler signal and not, as in the case of the color Doppler, the mean Doppler shift. The most important advantage of this diagnostic modality is its ability to evaluate blood vessels of smaller caliber and with low blood flow and longer segments and greater number. When evaluating the vertebral arteries, this method more precisely assesses the vessel lumen and possible atherosclerotic plaques found there.

Availability, relatively low cost, non-invasiveness and, in some cases, the possibility to supplement the information obtained from more advanced vascular imaging techniques are the advantages of Doppler ultrasonography in the diagnostics of vascular diseases. No specific preparations are needed for its implementation and the procedure itself is performed in supine position with the head slightly tilted backward and rotated in the opposite direction to the tested vessel or the head in straight position. In special cases, for example, in strong dizziness, the test may be carried out in a sitting position with the same head positioning. However, this modification should be reserved for the evaluation of the carotid but not the vertebral arteries.

In studies of the extracranial segments of the carotid and vertebral arteries vascular probes are used designed for this purpose of the footprint length not exceeding 45 mm. Their frequency should range from 5–7 to 8–12 MHz. An exception to the rule may be the use of a convex-type probe with a lower frequency of 3–5 MHz in cases of the soft tissue thickness above the average and in difficult test conditions. However, it should be remembered that, due to its lower frequency, there is no possibility of a detailed assessment of atherosclerotic lesions.
Nevertheless, when using color presentation, it is possible to evaluate the vessel course, its diameter and blood flow velocity.

According to the standards of the Polish Ultrasound Society, the examination starts with an overall assessment of the topography of blood vessels, imaging in the transverse plane, from the top of the supraclavicular area to the angles of the mandible. The main part of the procedure is carried out in long-axis view relative to the course the vessel. The following are assessed: the intima-media complex, possible atherosclerotic plaques and stenoses, both morphologically and hemodynamically. Another important part of the test is the measurement of the blood flow velocity performed in the blood stream axis inside the vessels in pre-defined locations. For the common carotid artery, it is its middle section at least 2 cm from the carotid sinus. The assessment of the internal carotid artery is carried about 1 cm above the bulb and in the external carotid artery about 1 cm above its branch-off. Measurements of the blood flow velocity in the vertebral arteries are performed in the V1 and/or V2 sections. Normal values of the blood flow velocity in individual vessels are shown in Table 1. When interpreting the study results the physiological decrease of the speed of the blood flow in the intracranial vessels which appears with age should be considered. These changes affect at most the common carotid arteries and subclavian arteries and, to a lesser extent, the vertebral arteries.

The cerebral arteries are examined using a 2-MHz frequency ultrasound probe applied to the so-called “acoustic windows”. The acoustic windows are natural holes or thinner regions of the skull, in general there are four acoustic windows described: the transtemporal window, the transorbital window, submandibular window and suboccipital window. The basilar and the vertebral arteries in the intracranial section are assessed through the suboccipital window. The identification is made on the basis of the depth of the vessel position and the direction of the blood flow in its lumen. The basilar artery is evaluated at the depth of 80–120 mm and the direction of the blood flow is opposite to the position of the probe and the mean peak flow is 0.39 m/s. The intracranial segments of the vertebral arteries (VA) are assessed at a depth of 60–70 mm, and the mean peak flow is 0.36 m/s [26].

Numerous studies justify the use of the transcranial and classic Doppler in the assessment of the vertebrobasilar function [27–29]. In cases of a high degree of carotid stenosis (> 90%), the Power Doppler modality is a good supplementation of magnetic resonance imaging with contrast, which may in these cases yield false positive results [30]. AbuRahma et al. report the superiority of the Duplex Doppler over arteriography in the evaluation of heterogeneous atherosclerotic plaque with the average degree of carotid artery stenosis. It is also an effective tool in the diagnostics and monitoring of the treatment efficacy of the vertebral artery dissection. The Doppler ultrasound supplemented by angio-MR and angio-CT examinations is a

<table>
<thead>
<tr>
<th>Vessel tested</th>
<th>Peak systolic velocity (m/s)</th>
<th>End-diastolic velocity (m/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common carotid artery</td>
<td>0.8–1.2</td>
<td>0.1–0.3</td>
</tr>
<tr>
<td>Internal carotid artery</td>
<td>0.8–1.2</td>
<td>≤ 0.3</td>
</tr>
<tr>
<td>External carotid artery</td>
<td>0.8–1.2</td>
<td>≤ 0.25</td>
</tr>
<tr>
<td>Vertebral artery</td>
<td>&lt;0.6</td>
<td>0.05–0.2</td>
</tr>
</tbody>
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Table 1. The normal range of the blood flow velocity in the intracranial vessels in Doppler ultrasonography (m/s).
reliable tool in detecting flow disturbances in the middle cerebral artery and the vertebral arteries, which cause tinnitus [31]. It is also used in traumatology and is comparable with arteriography in detecting traumatic changes in cervical vessels.

The more and more perfect ultrasound technique allows to limit the number of invasive tests required for performing vascular examinations, thus reducing the patient’s exposure to complications associated with them.

2. Overview

Our previous studies [9] concerning the analysis of the frequency and types of anatomical anomalies of the cranial arteries, i.e. vertebral and carotid arteries, in patients with dizziness and impaired hearing, demonstrated that the most common anatomical anomaly of cranial arteries was hypoplasia of the right vertebral artery, occurring in 58.7% of cases, of which 51.7% were women and 6.9% men; hypoplasia of the left vertebral artery, occurring in 24.7% of the study group, of which 13.8% were women and 10.3% men; hypoplasia of the right internal carotid artery found in 3.4% of women, and of the left internal carotid artery in 6.8% of cases, 3.4% in women and 3.4% in men; and hypoplasia of the right common carotid artery was reported in 3.4% of men, while critical stenosis of the left subclavian artery with subclavian steal syndrome was observed in 3.4% of women. Although the most common symptom occurring in these patients was tinnitus, the most frequent cause found in patients admitted to the Department for diagnosis was dizziness, possibly because the patients found it more disturbing.

In the case of anatomical anomalies it is difficult to make any suggestions as to the nature of abnormalities without carrying out imaging tests.

The diagnostic procedure to detect anatomical abnormalities in the cranial arteries generally starts with vascular ultrasound. Blood flow disorders observed on the ultrasound should be further verified by contrast CTA or MRA to evaluate the morphology of the artery [2].

However, the diagnostics of vertigo does not always involve contrast CT angiography of the cranial arteries. In our study, the ultrasound of the vertebrobasilar system showed no abnormalities in the blood flow velocity, a vascular anomaly being only suggested by pathological blood flow velocity on ultrasound after applying the neck torsion test.

Normally, the unpaired basilar artery is formed by both vertebral arteries merging on the clivus of the occipital bone. In turn, the labyrinthine artery is a paired thin vessel originating from the middle section of the basilar artery or from the anterior inferior cerebellar artery which runs laterally along with the atrio-cochlear nerve and enters the internal auditory canal to vascularize the inner ear structures. The anterior inferior cerebellar artery is a paired vessel originating from the lower part of the basilar artery, finally merging with the posterior inferior cerebellar artery.

In the presented case, the basilar artery was an extension of the right vertebral artery, and the left atrophic vertebral artery extended into the posterior inferior cerebellar artery whereas the labyrinthine artery originated bilaterally from the basilar artery.
The described vascular anomaly, osteochondrosis of the C4/C5 and hyperlipidemia present in the patient resulted in mixed-type vertigo with decreased excitability of the labyrinth on the affected side (anomaly) due to insufficient blood supply to the inner ear and the lack of vascular compensation of the vertebral artery on the other side.

The treatment of diagnosed anatomical anomalies in adults is usually conservative and depends on coexisting disorders. Surgical treatment in the case of disorders of blood supply to the central nervous system caused by anomalous cranial vessels includes implantation of stents, arterial anastomosis and vascular bypass.

Conservative treatment and implementation of motor rehabilitation resulted in a very good therapeutic effect in the patient.

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References


