Review paper

Anatomical and clinical aspects of aberrant right subclavian artery

Anatomiczne i kliniczne aspekty błądzącej tętnicy podobojczykowej prawej

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Słowa kluczowe: *arteria lusoria*, uchyłek Kommerella, wady płodu, *dysfagia lusoria*.

Abstract

Atrophy of the fourth right aortic arch during embryogenesis can lead to arteria lusoria. This occurs with a frequency of 0.5–2%. This artery originates directly from the aortic arch as a fourth branch or from the proximal part of the descending aorta. Then it follows an upward and rightward direction crossing the trachea and esophagus in its course. This abnormal artery is accompanied in 20–60% of cases by dilatation of its proximal part, called Kommerell's diverticulum. A correlation has been noted between the presence of arteria lusoria and chromosomal aberrations, mainly Down syndrome. Arteria lusoria in fetuses is diagnosed using ultrasound, and in adults, the gold diagnostic standard is computed tomography or magnetic resonance angiography. Consequences of arteria lusoria may include dysphagia (dysphagia lusoria), chronic cough, arterio-oesophageal fistula, retrosternal pain, respiratory problems, and numbness of the right upper limb. Respiratory disorders accompanying arteria lusoria occur mainly in children because their trachea is less rigid than in adults and more prone to deformation. Arteria lusoria is a clinically significant marker of fetal congenital malformations. It also may be a cause of non-specific symptoms in children and adults that should be considered during differential diagnosis.

Streszczenie

Zanik czwartego prawego łuku aorty podczas embriogenezy może prowadzić do powstania *arteria lusoria*. Występuje ona z częstością 0,5–2%. Tętnica ta odchodzi bezpośrednio z łuku aorty jako czwarte odgałęzienie lub z proksymalnej części aorty zstępującej. Podąża następnie w kierunku górnym i prawym, krzyżując w swym przebiegu tchawicę i przełyk. Tej nieprawidłowej tętnicy w 20–60% przypadków towarzyszy poszerzenie jej proksymalnej części, zwane uchyłkiem Kommerella. Stwierdzono zależność między występowaniem *arteria lusoria* a aberracjami chromosomowymi, głównie zespołu Downa. *Arteria lusoria* u płodów rozpoznaje się z wykorzystaniem badania ultrasonograficznego, a u osób dorosłych złotym standardem jest angiografia CT lub rezonans magnetyczny. Konsekwencją *arteria lusoria* mogą być: dysfagia (*dysfagia lusoria*), przewlekły kaszel, przetoka tętniczo-przełykowa, ból zamostkowy, trudności w oddychaniu, drętwienie prawej kończyny górnej. Zaburzenia oddychania towarzyszące *arteria lusoria* występują głównie u dzieci, ponieważ ich tchawica jest mniej sztywna niż u dorosłych i bardziej podatna na odkształcenia. *Arteria lusoria* stanowi istotny klinicznie marker wad wrodzonych płodu. Może być przyczyną niespecyficznych objawów u dzieci i dorosłych, którą należy uwzględniać podczas diagnostyki różnicowej.

Embryology

The heart of the fetus in the 4th–5th week of life delivers blood into the circulation through a single vessel. This is the aortic sac, which in its further course divides into two abdominal aortas: the right and left. These connect via six vessels – the aortic arch – to the right and left dorsal aorta. The first three segments form the carotid system. The first segment develops into the external carotid arteries and the maxillary arteries. The second segment develops into the stapedial arteries. The distal part of the third segment gives origin to the internal carotid arteries, while the proximal part gives rise to the common carotid arteries [1].

The brachiocephalic trunk and right subclavian artery arise from the fourth right aortic arch (proximal part), the right sixth inter-segmental artery, and a fragment of the ventral and dorsal aorta. The distal part of the fourth right aortic arch vanishes [1]. The fourth aortic arches are formed around the 31st day of fetal life, when the fetal length is about 4 mm [2]. The left subclavian artery arises from the left fourth aortic arch and from the seventh dorsal intersegmental artery. From the left fourth aortic arch,

the right fetal aortic arch also develops. The fifth aortic arches atrophy, while the pulmonary arteries and the aortic sac develop from the sixth aortic arches, which transform into the arterial ligament of Botall after birth [1]. In further organogenesis, the left dorsal aorta atrophies [2–6].

Sometimes, as a result of abnormal embryogenesis, the fourth right aortic arch is atrophied or disrupted, and the right subclavian artery forms from the seventh intersegmental artery, which departs from the descending aorta. This leads to the formation of an aberrant right subclavian artery (ARSA), also known as the *arteria lusoria* [1]. This abnormal artery is accompanied in 20–60% of cases by dilatation of its proximal portion, called Kommerell's diverticulum, which is a remnant of the original right aortic arch that normally regresses during embryogenesis [7]. The role of the intercostal arteries in the embryo body is to supply blood to the peripheral parts of the body. In further organogenesis, they develop into the intercostal and lumbar arteries [5, 6, 8].

Due to the separate differentiation of the right and left aortic arches, the course of the recurrent laryngeal nerves is also different. During embryonic development, the recurrent laryngeal nerves pass under the sixth aortic arch. On the right side, due to the transformation of the sixth aortic arch and the involution of the fifth aortic arch, the recurrent laryngeal nerve passes under the fourth aortic arch. As a result, after embryogenesis, this nerve runs under the right subclavian artery, while the left recurrent laryngeal nerve runs under the aortic arch medial to the arterial trunk, developing into the arterial ligament of Botall. The terminal branches of the left and right recurrent laryngeal nerve are the left and right inferior laryngeal nerves, respectively [2].

During embryonic development, the recurrent laryngeal nerves pass under the sixth aortic arch. On the right side, due to the transformation of the sixth aortic arch and the involution of the fifth aortic arch, the recurrent laryngeal nerve passes under the fourth aortic arch. Consequently, as mentioned earlier after embryogenesis, this nerve runs under the right subclavian artery.

Anatomy

The aortic arch gives off three large arteries in adults. The brachiocephalic trunk is the first branch, followed by the left common carotid artery and the left subclavian artery. The brachiocephalic trunk divides into the right subclavian artery and the right common carotid artery. A common anatomical abnormality of the heart and great vessels is the ARSA. Another anatomical abnormality is an aberrant left subclavian artery (ALSA).

An ARSA should be referred to when this artery branches directly from the aortic arch as the fourth branch or from the proximal part of the descending aorta [9]. It is preceded by the left subclavian artery. The ARSA departs from the aortic arch about 2.2 cm distal to the left subclavian artery and about 5 mm dorsal to it [10]. In about 30–60% of cases, the origin of this artery takes the form of arterial dilatation in the form of Kommerell's diverticulum [7, 9, 11–13]. In a study conducted by Jeannon *et al*. it was found in 66% of cases [2], but in a study by Elumala *et al*. of 141 cases, it was found in only 14.9% of cases [1]. It should be noted that this diverticulum is a location of increased risk of aneurysm formation [11]. The ARSA later follows the upper and right direction, crossing the trachea and esophagus in its course. In about 82% of cases, it runs behind the esophagus, in 13% between the esophagus and trachea, and in 4.2–5% in front of the trachea [9, 14].

Wang *et al*. performed a retrospective analysis of 7169 patients undergoing thyroidectomy or parathyroidectomy. Five patients, all female, were visualized with an ARSA along with a recurrent laryngeal nerve as a right recurrent laryngeal nerve (NRLN) anomaly. Recurrent laryngeal nerve (RLN) palsy is one of the most common complications after thyroid surgery. RLN abnormalities can increase the risk of iatrogenic damage to this nerve, which can lead to vocal cord paralysis and reduced quality of life for the patient. The NRLN accompanying the ARSA has been divided into different types depending on where the nerve originates. On this basis, a distinction is made between type I which arises directly from the vagus nerve and running along with the superior thyroid vessels; type IIA which originates from the vagus on the level of the trunk of the inferior thyroid artery; and type IIB that originates from the vagus and travels under the level of the trunk of the inferior thyroid artery or between the branches [15].

Aberrations of the right subclavian artery are often associated with anatomical abnormalities of the carotid arteries. Normally, the proximal origins of the right and left common carotid artery parts are 4 cm apart. Klinkhamer found in a sample of 295 cases that in 29% the right and left carotid arteries had a common origin, while in 10% the two carotid arteries were separated by an extremely small distance. In 60%, the carotid arteries had a normal course [14]. In a study by Elumala *et al*. of 141 cases with ARSA, truncus bicaroticus was found in 19.2% of cases [1], while Krupiński *et al*. observed it in 9 out of 32 cases (28%) [16].

Jeannon *et al*. measured the diameter of the ARSA in 150 patients at different distances from its onset. Their study showed that it had a diameter of 16.4 mm at its origin, and 13.1 mm at a distance of 1 cm from its origin [2]. Alghamdi *et al*., on the other hand, described a case in which the diameter of the ARSA was 16 mm. The study involved the cadaver of a woman of unknown age, and the measurement was made at a distance of 1 cm from the origin of the ARSA [17].

Ostrowski *et al.* made a detailed description of ARSA branches and diameter measurements using the cadaver of a 63-year-old man as an example. The ARSA crossed the esophagus and trachea at the level of the Th2/Th3 vertebrae. The rib-chest trunk arose from the ARSA at the level of the first intercostal space, while the thyrocervical trunk arose above the first rib. In the case described, the right vertebral artery was not a branch of the right subclavian artery, but arose as a branch of the right common carotid artery. The ARSA left the thoracic cage through the upper thoracic orifice [18]. This departure of the right vertebral artery is not the rule, when ARSA is present, however, as Ito *et al.* describing two cases of ARSA on cadavers found vertebral arteries departing from the subclavian arteries in both cases [19]. Similarly, Kurt *et al.* described the departure of the right vertebral artery from the ARSA at a distance of 6.3 cm from the aorta [20]. Ostrowski *et al.* also measured the diameter and area of the artery in their study. At its origin, the diameter of the ARSA was 12.9 cm, at the intersection of the esophagus and trachea it was 9.9 cm, and after the costocervical trunk it was 8.4 cm. The left subclavian artery in its origin had a diameter of 8.3 cm [18].

Krupiński *et al.* measured the median diameter and area of the ARSA at different levels of its course and depending on the presence or absence of associated dysphagia in 32 patients. At the onset, the ARSA had an area of 180 mm^2 in patients without dysphagia and 268 mm^2 in patients with dysphagia. The median distance of ARSA from the trachea was 5.5 mm and the median lumen area of the ARSA at the esophageal level was 128 mm^2. However, the values of ARSA distance from the trachea were smaller in patients with dysphagia, at 3.5–5.5 mm, than in patients without dysphagia, at 4.5–9.0 mm. In contrast, the median area of the ARSA at the level of the esophagus was larger in patients with dysphagia at 208 mm^2 than in patients without dysphagia, where the value was 108 mm^2 [16].

An extremely unusual course of the ARSA was described by Epstein *et al.* In a 33-year-old man, the ARSA departed from the aortic arch with a common trunk with the right and left common carotid arteries. In its further course, it was located behind the esophagus [21].

Szpinda described a new variant of the retroesophageal aberrant left brachiocephalic trunk. It outlines the triple anomaly observed in the left aortic arch, including the presence of a hypoplastic left brachiocephalic trunk behind the esophagus, the absence of a brachiocephalic trunk on the right side, and separate origins of the arteries on the right side, with the right common artery preceding the right subclavian artery [22].

Epidemiology

Establishing the incidence of this anatomical anomaly is difficult to determine, as such a condition usually does not cause clinical symptoms [2]. However, it is estimated that ARSA occurs in 0.5–2% of healthy people [8, 11, 12].

Of particular value is the study by Krupiński *et al.* during which a retrospective screening for right subclavian artery abnormalities was performed in 6833 patients. ARSA was detected in 32 (0.47%) patients, including 13 men and 19 women. Among them, truncus bicaroticus was further detected in 9 (28%) cases, Kommerell's diverticulum in 9 (28%) cases, aneurysm of the right subclavian artery in 4 (12%) cases and aortic origin of the right vertebral artery in 1 (3%) case [16].

Fisher *et al.* analyzed 2418 aortic angiography results during a retrospective study. The mean age of the subjects was 41 years. Twenty-two cases of aberrant subclavian artery (0.9%) were diagnosed. Of these, 19 (86%) cases had ARSA as the disorder and 3 (14%) cases had ALSA. In addition, 4 patients with an ARSA (21%) were diagnosed with associated aneurysms [12].

A study by Zapata *et al.* on 11,000 cadavers showed that 91% of patients with an ARSA also had heart abnormalities [23]. On the other hand, Ramaswamy *et al.*, after evaluating echocardiographic studies on 15,871 patients, reported a value of 68% [24]. Ventricular septal defects were the most common [9].

ARSA has also been shown to have a genetic basis with Down syndrome, a 22q11.2 microdeletion, and abnormal right thoracic duct and heart defects [9, 11].

Carles *et al.* analyzed 11,479 fetal autopsies. ARSA was found in 382 (3.2%) cases. Of these cases, as many as 126 (33%) cases had trisomy 21 of the chromosome. During the same period, 712 cases of trisomy 21 were found in the center whose databases they used. This means that, according to this study, ARSA occurs in about 18% of trisomy 21 cases. Moreover, among ARSA cases, in addition to trisomy 21, 29 cases of trisomy 18, 21 cases of triploidy, 12 cases of monosomy X and 9 cases of trisomy 13 were found. In addition, ARSA was found in 17% of DiGeorge syndrome cases [25]. It should be kept in mind, however, that the studied fetal cadavers are not the general population, as they were pathological fetuses.

Chaoui *et al.* examining by ultrasound 14 fetuses with Down syndrome at 18–33 weeks of pregnancy found ARSA in 5 cases, representing 35.7% [26]. Fehmi Yazıcıoğlu *et al.* using ultrasonography examined 2081 live fetuses. ARSA was found in 23 (1.1%) cases. Among the 20 fetuses diagnosed with trisomy 21, an ARSA was found in 7 (35%) [27].

Rembouskos *et al.* examined 6617 fetuses using ultrasound. An ARSA was found in 89 (1.42%) fetuses. Among them, 12 cases were found to have an abnormal karyotype: six trisomy 21, three trisomy 18, one mosaic of chromosome 2, one microdeletion of 15q11.2 and one microdeletion of 22q11.2. For euploid fetuses, the incidence of ARSA was higher in women by a ratio of 2 : 1 compared to men [28].

Zalel *et al.* conducted a study of routine ultrasonography in 924 fetuses between 13 and 26 weeks of pregnancy. ARSA was detected in 13 (1.4%) cases and no karyotype abnormalities were detected [29]. Paladini *et al.* tested 106 fetuses with Down syndrome for ARSA among them. A positive result was obtained in 27 (25%) fetuses [30]. Ranzini *et al.* conducted genetic testing in 76 fetuses with ARSA. A 22q11.2 deletion was identified in 38 (50%) cases, 7 (9%) cases were diagnosed with trisomy 21, and 1 case each of Wolf-Hirschhorn syndrome, deletion 8p23.1, 5p1 5.2p15.1(14,444,119-16,375,547)x1 *de novo*, and Mosaic Turner syndrome were found [31]. De Leon-Luis *et al.* examined 8781 fetuses, among which ARSA was detected in 60 (0.7%) cases. In 17/60 cases, a karyotype study was performed, which revealed 6 cases of trisomy 21. In addition, one more trisomy 21 in a child with ARSA was diagnosed after birth [32]. Borenstein *et al.* performed an ultrasound examination of the right subclavian artery in 2,670 fetuses. ARSA was diagnosed in 43 (1.61%) fetuses, among which 12 cases had simultaneous chromosomal abnormalities in the karyotype. Eight cases of trisomy 21, two cases of trisomy 18, one case with monosomy X and one case with partial monosomy X were detected [33].

It should be noted that ARSA is more common in women than in men, while ALSA is more common in men [6]. In a study by Zschoch, of 104 cases of AL (Arteria Lusoria), 68 (65%) cases were women and 36 (35%) cases were men [34]. Elumala *et al.* studied 141 cases of ARSA, of which 55.3% were women and 44.7% were men [1]. ALSA, on the other hand, is twice as common in men [6].

Clinical aspects

An ARSA was first reported by Hunauld in 1735. In 1794 Bayford described a case of ARSA in a deceased 62-year-old female patient and linked it to associated dysphagia. It was Bayford who introduced the term *"arteria lusoria"* (after lusus naturae, freak of nature). More than 200 years later, in 1936, Kommerell described a diverticulum representing the origin of the aberrant right subclavian artery, later named after him [9, 12, 14, 35]. Kommerell also performed the first X-ray imaging of the ARSA in 1936 in a living patient. In contrast, the first angiography showing the disorder was presented by Apley in 1949, and the first surgical correction of ARSA was performed in 1945 by Gross [6].

Diagnostics

ARSA is diagnosed in fetuses using ultrasound. This examination can visualize the right subclavian artery in the second trimester of pregnancy in about 95–98% of cases. During the examination, attention should be paid to the course of the azygos vein, the hemi-azygos vein and sometimes the aberrant vertebral artery, which may resemble the ARSA on imaging [11].

It should be mentioned that ARSA can be diagnosed using a number of methods such as contrast examination of the esophagus showing visible stenosis at the Th3/Th4 level in the case of ARSA, angiography, CT/MR angiography, or endoscopic ultrasonography. However, the gold standard for the diagnosis of ARSA is CT or MR angiography [36].

In adults, distinguishing Kommerell's diverticulum from an acquired aneurysm is difficult due to progressive morphological changes in the vessels [4].

Symptoms of ARSA

The consequences of ARSA can include dysphagia (dysphagia lusoria), chronic cough, atrioesophageal fistula, chest pain, breathing disorder, and numbness of the right upper limb [1, 6, 8, 11, 13, 16, 37, 38]. Respiratory disorders accompanying ARSA mainly occur in children because their trachea is less rigid than in adults and more prone to deformation. They may also develop cyanosis and recurrent respiratory infections [2, 14, 37]. However, the condition for the occurrence of dysphagia as a consequence of ARSA seems to be accompanying anatomical abnormalities of the left and right common carotid arteries. The presence of the ARSA is not a direct cause of dysphagia, since the esophagus and trachea bend abdominally under compression. However, if along with the ARSA, the distance between the right and left common carotid arteries is too short or they share a common trunk and are located ventral to the trachea, the possibility of ventral bending of the trachea and esophagus is reduced, which can lead to dysphagia [14]. Compression of the ARSA on the esophagus mostly occurs at Th4 [35]. The common trunk of the common carotid arteries in patients with ARSA is found in 51% of cases [2]. Dysphagia lusoria can lead to retarded child growth, weight loss and malnutrition in adults [1, 2].

Treatment of ARSA

Asymptomatic ARSA occurs in 60–80% of cases and does not require treatment [37]. Classical or endovascular surgical treatment is generally performed only in cases of persistent dysphagia, upper limb ischemia or the presence of an aneurysm [2]. Such a procedure is performed by a supraclavicular incision, ligating the proximal part of the ARSA, and then anastomosing this artery to the right common carotid artery. During the operation, it is particularly important to accurately identify the structures of the right brachial plexus and the right recurrent laryngeal nerve, in order to avoid injuring them [37]. The endovascular method makes it possible to treat ARSA aneurysms. The most common treatments include stent-graft implantation with surgical revascularization (bypass, vessel debranching or transposition). Coil embolization raises the concern of persistent com-

pression of the esophagus as the regression of the aneurysm takes time [38].

Conclusions

Knowledge of ARSA helps with the interpretation of different radiological versions of the vessels, as well as special monitoring for additional markers of fetal abnormalities during prenatal testing. In both children and adults, ARSA can generate vague symptoms which should be included in the spectrum of possible diagnoses.

Conflict of interest

The authors declare no conflict of interest.

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