Clarifying the anatomy of the fifth arch artery

Saurabh Kumar Gupta, Gurpreet Singh Gulati[1], Robert H Anderson[2]

Departments of Cardiology and [1]Cardiac Radiology, All India Institute of Medical Sciences, New Delhi, India, [2]Institute of Genetic Medicine, Newcastle University, Newcastle-upon-Tyne, UK

ABSTRACT

The artery allegedly forming in the fifth pharyngeal arch has increasingly been implicated as responsible for various vascular malformations in patients with congenitally malformed hearts. Observations from studies on developing embryos, however, have failed to provide support to substantiate several of these inferences such that the very existence of the fifth arch artery remains debatable. To the best of our knowledge, in only a solitary human embryo has a vascular channel been found that truly resembled the artery of the fifth arch. Despite the meager evidence to support its existence, the fifth arch artery has been invoked to explain the morphogenesis of double-barreled aorta, some unusual forms of aortopulmonary communications, and abnormalities of the brachiocephalic arteries. In most of these instances, the interpretations have proved fallible when examined in the light of existing knowledge of cardiac development. In our opinion, there are more plausible alternative explanations for the majority of these descriptions. Double-barreled aorta is more likely to result from retention of the recently identified dorsal collateral channels while abnormalities of brachiocephalic arteries are better explained on the basis of extensive remodeling of aortic arches during fetal development. Some examples of aortopulmonary communications, nonetheless, may well represent persistence of the developing artery of the fifth pharyngeal arch. We here present one such case — a patient with tetralogy of Fallot and pulmonary atresia, in whom the fifth arch artery provided a necessary communication between the ascending aorta and the pulmonary arteries. In this light, we discuss the features we consider to be essential before attaching the tag of "fifth arch artery" to a candidate vascular channel.

Keywords: Bovine arch, cardiac development, double-barreled aorta, fifth arch artery

INTRODUCTION

It is conventional wisdom that during embryonic development, mammals have six pharyngeal arches, with the fifth arch being evident only for a short duration. As discussed by Congdon, an artery developing in the alleged fifth pharyngeal arch was first described more than a century ago.[1] As Congdon also discussed,[1] nonetheless, its very existence has remained controversial. The interpretation of double-barreled aorta by Van Praagh *et al.*,[2] on the basis of persistence of the alleged artery, nonetheless caught the fancy of the pediatric cardiologists worldwide. Since that initial report, nearly 100 cases have been reported in the literature in which the fifth arch artery has been implicated in the morphogenesis of various vascular malformations.[3] Despite the ever increasing number of reported cases, convincing supportive developmental evidence remains elusive. To the best of our knowledge, a channel that resembles a true artery of the fifth pharyngeal arch artery has been visualized only on one occasion.[4] In the light of the burgeoning number of clinical observations

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Address for correspondence: Dr. Saurabh Kumar Gupta, Room No. 23, 7th Floor CT Centre, All India Institute of Medical Sciences, New Delhi - 110 029, India. E-mail: drsaurabhmd@gmail.com

invoking persistence of the fifth arch artery, this is surprising. In the era of evidence-based medicine, this contradiction is little more than astounding. Because of the ongoing confusion, we recently provided a critical review of the existing literature.[3]

Our review showed that persistence of the alleged artery of the fifth pharyngeal arch had been implicated in the morphogenesis of double-barreled aorta and aortopulmonary communications. In some instances, it has also been used to explain the abnormal origin of brachiocephalic arteries. In our opinion, neither the cases of so-called double-barreled aorta nor those involving abnormalities of the pattern of brachiocephalic arteries could convincingly be interpreted on the basis of persistence of a true fifth arch artery. We suggested that alternative explanations such as the persistence of dorsal collateral channels or extensive remodeling of the remaining pharyngeal arch arteries provided more realistic explanations.[3] In the case of certain forms of aortopulmonary communication, nonetheless, we acknowledged that persistence of the fifth arch artery did offer a logical explanation. In this light, we here present the findings in a patient with an aortopulmonary communication best explained, in our opinion, on the basis of persistence of the fifth arch artery. Based on the conclusions drawn during our ongoing review of the existing literature, which has produced further examples of the alleged structure since our initial assessment,[3] we propose criteria for determining whether or not a vascular channel deserves the label of "fifth arch artery."

CASE REPORT

A 10-day-old male neonate presented to the emergency department with cyanosis, which had worsened since birth. Pulse oximetry revealed severe hypoxia, with oxygen saturation measured at 62%. He was immediately started on an infusion of prostaglandin E1 following which, the oxygen saturation improved to 80%. Subsequent clinical evaluation confirmed the presence of persistent cyanosis, with no heart failure. On auscultation, the first heart sound was normal while the second sound was single. A grade 3/6 systolic murmur was heard at the left upper sternal border. There was no respiratory distress, cardiomegaly, or hepatomegaly.

The chest radiograph revealed a left-sided heart of normal size, with pulmonary oligemia while the electrocardiogram revealed normal sinus rhythm, right axis deviation, and right ventricular hypertrophy. The echocardiogram showed usual arrangement of the abdominal vessels and atrial appendages. The systemic and pulmonary venoatrial connections were normal. The atrioventricular connections were concordant. The aortic root was seen to be overriding the crest of a deficient ventricular septum, with half supported by each ventricle in the presence of discontinuity between the leaflets of the aortic and mitral valves. There was continuity between the leaflets of the tricuspid and mitral valves posteroinferiorly, making the septal defect perimembranous, and the right ventricular outflow was atretic. The great arterial trunks spiraled as they extended into the mediastinum, with the pulmonary trunk lying to the left and anterior of the aorta. The pulmonary arteries themselves were confluent and good-sized, with the right and left arteries measuring 5 mm and 4.5 mm in diameter, respectively. A vascular channel arising from the ascending aorta could be traced to a termination at the confluence of the pulmonary arteries [Figure 1 and online video 1]. The channel was constricted at its pulmonary end, resulting in a gradient of 30 mmHg on Doppler interrogation. Considering its unusually proximal location, we deemed the channel to represent persistence of the artery of the fifth pharyngeal arch. Computed tomography was performed for better demonstration of the anatomy, confirming the origin of the vascular channel from the posteromedial aspect of the ascending aorta proximal to the origin of the brachiocephalic artery, and demonstrating its tortuous course to its termination at the confluence of the pulmonary arteries [Figure 2]. Because of persistent systemic desaturation, we proceeded to construct a modified Blalock-Taussig shunt of 4 mm diameter through a right lateral thoracotomy. The vascular channel supplying the pulmonary arteries was left untouched. Postoperatively, the child showed improvement in the saturation of oxygen, and

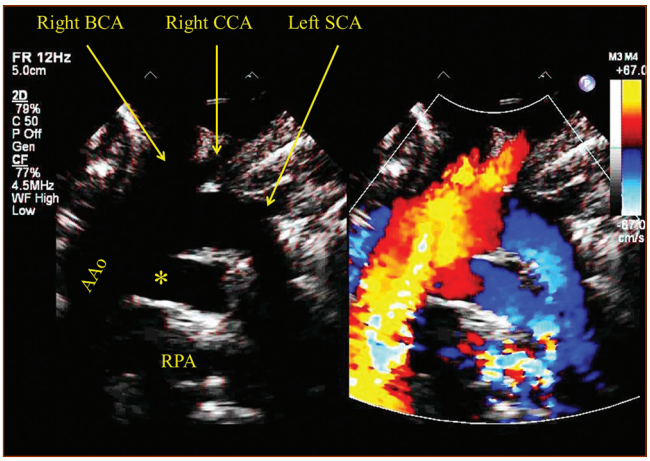

Figure 1: Transthoracic echocardiogram in suprasternal long axis view shows left-sided aortic arch with normal branching pattern of neck vessels. A vascular channel (*) originates unequivocally proximal to the origin of the right brachiocephalic artery and terminates at the pulmonary artery confluence. The pulmonary end of this vascular channel is constricted with turbulence seen on color Doppler interrogation (right panel). AAo = Ascending aorta, BCA = Brachiocephalic artery, CCA = Common carotid artery, RPA = Right pulmonary artery, SCA = Subclavian artery

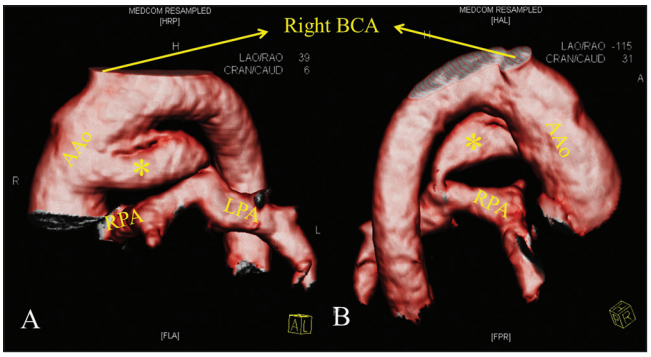

Figure 2: CT angiographic images reconstructed using volume rendering technique (VRT) in right anterior oblique view (panel A) and left posterior oblique view (panel B). The vascular channel (*) supplying the pulmonary arteries originates from the ascending aorta. The origin is unequivocally proximal to the origin of the brachiocephalic artery and it terminates into the pulmonary artery confluence at the usual sight of patent arterial duct making it very likely to represent the fifth arch artery. The narrowing at the pulmonary end is visualized in panel B. AAo = Ascending aorta, LPA = Left pulmonary artery, RPA = Right pulmonary artery, BCA = Brachiocephalic artery

is currently doing well on follow-up prior to future definitive surgical correction.

DISCUSSION

Arteries extending through the fifth pharyngeal arch, if they exist, are exceedingly rare. It is our opinion that very few of the proposed candidates justify this label.[3] Despite claims made by many earlier researchers, the very existence of this elusive structure during normal development remains debatable.[4] To the best of our knowledge, despite studies on large numbers of developing mice, vascular structures have yet to be demonstrated in this experimental animal that satisfy the requirements to justify description as arteries of the fifth pharyngeal arch. A solitary human embryo, nonetheless, has been found in which a vascular structure extends through the larger part of a discrete segment of pharyngeal mesoderm.[4] Other researchers have certainly shown the presence of transient dorsal collateral channels in the developing mouse but these channels do not extend through the parietal components of the pharyngeal mesoderm.[5,6] Similar collateral channels are also to be found in the developing human but they do not resemble the solitary structure observed running in parallel to the fourth and sixth arch arteries.[4]

What, then, is a true fifth arch artery?

The arteries of the pharyngeal arches develop extrapericardially within the parietal components of the pharyngeal mesoderm, and undergo extensive remodeling before attaining their final shape. This process is complex. Researchers are yet to reveal, during normal development, the bilaterally symmetrical channels as often depicted in standard textbooks of cardiac embryology. The pharyngeal arches themselves in such standard depictions, are numbered one through six, with the alleged artery of the fifth arch shown to lie between the fourth and sixth arch arteries. If persisting on the left side, such an artery would extend between the aortic arch derived from the left fourth arch artery and the arterial duct formed from the left sixth arch artery. As we have indicated, studies exploring large numbers of mouse embryos have failed to demonstrate any such artery.[6] The solitary human embryo,[4] nonetheless, did show the presence of such a channel, albeit partially obliterated proximally that terminated in the descending aorta via the artery of the sixth arch, comparable to the arrangement anticipated by Congdon[1] for the true fifth arch artery. Using the illustrations provided by Congdon[1] as our yardstick, and combining this with our current understanding of the development of the pharyngeal mesenchyme,[4] it seems to us that persistence of an artery of the fifth pharyngeal arch is extremely rare. We suggest that, to be considered a true artery of the fifth arch, the channel must be confined to the extrapericardial space, must arise from the ascending aorta proximal to the origin of brachiocephalic arteries, and must terminate either in the dorsal aorta or in the pulmonary arteries via the persistently patent arterial duct.

How frequent is the fifth arch artery?

The discrepancies between the claims made by clinicians and the evidence provided from normal development are striking. Arteries of the fifth arch, if they exist, must be exceedingly rare. Most of the vascular malformations attributed to persistence of the fifth arch artery, in our opinion, can be the result of alternative developmental aberrations instead. We discuss briefly, therefore, our own analysis of various candidates for fifth arch arteries so far described in the literature.

Double-barreled aorta or double lumen aortic arch

This was the first vascular malformation interpreted on the basis of persistence of the artery of the fifth pharyngeal arch. Van Praagh *et al.*[2] must be credited for their astute observation of proximal origin of dual channels extending from the ascending aorta to the descending aorta. Their description caught the fancy of the pediatric cardiologists worldwide and so several cases were soon encountered and interpreted in a comparable fashion. Although most investigators presumed the origin of the second channel proximal to the origin of the brachiocephalic arteries, unequivocal demonstration of this feature is lacking in the majority of cases. It soon became conventional wisdom, therefore, that all patients with double-barreled aortas had persistent fifth arch arteries. Such interpretations are now frequent based solely on echocardiographic diagnosis.

How easy is to determine the site of proximal connection to aorta?

During development, there is differential growth of the medial and lateral surfaces of aorta, making it possible for the brachiocephalic arteries to originate from the transverse arch in a position seemingly distal to the channel presumed to represent the artery of the fifth arch. Assessment of the relationships of the channel in such a position is the more difficult if based solely on echocardiography. Accuracy is much improved with the use of techniques such as computed tomography or magnetic resonance imaging. To justify interpretation as a fifth arch artery, therefore, we suggest that the channel in question must arise from ascending aorta and should be unequivocally proximal to the origin of the brachiocephalic arteries.

How then to explain double-barreled aorta?

In the absence, at the time, of plausible alternative explanations it was justifiable to implicate the artery of the fifth arch to explain this interesting anomaly. Subsequent evidence shows that this simplified interpretation is questionable. The much more frequent presence of dorsal collateral channels during normal development provides a better explanation for the malformation.

Aortopulmonary communications

In the only demonstration of a true fifth arch artery encountered in a human embryo,[4] the vascular channel was found to terminate in the artery of the sixth pharyngeal arch, and hence satisfied the criteria established by Congdon nearly a century ago.[1] In addition to its proximal origin, therefore, any vascular channel satisfying these criteria must terminate in the pulmonary arteries via a derivative of the sixth arch artery or in other words the persistently patent arterial duct, and hence run a serpentine course.[3] Claims in favor of fifth arch origin are further strengthened in cases where the candidate channels arise from the lateral aspect of the ascending aorta. Such features are present in some of the instances where investigators have invoked the fifth arch artery but are wanting in the majority. It is the inclusion of the persistently patent arterial duct as part of the channel that explains response of some these channels to infusions of prostaglandin E1.

Channels extending from the ascending aorta to a pulmonary arterial confluence

This subset of cases accounts for the strongest candidates of true fifth arch artery. Vascular channels falling within in this category all arise unequivocally from the ascending aorta, and run a serpentine course before terminating at the confluence of the pulmonary arteries [Table 1].

Table 1: Reported examples in the literature that represent true fifth arch artery

Year	Author	No. of cases	Anatomy of the putative fifth arch	Ref.
1974	Macartney	1 of 8 cases	Ascending aorta to pulmonary artery confluence	7
1989	Gerlis	Case 3	Ascending aorta to pulmonary artery confluence	8
1993	Yoo	1 case	Ascending aorta to pulmonary artery confluence	9
1995	Wu	1 case	Ascending aorta to pulmonary artery confluence	10
1999	Lee	1 case	Ascending aorta to pulmonary artery confluence	11
2000	Chiu	Case 1	Ascending aorta to pulmonary artery confluence	12
2000	Chiu	Case 2	Ascending aorta to pulmonary artery confluence	12
2003	Hwang	1 case	Ascending aorta to pulmonary artery confluence	13
2006	Khan	Case 2	Ascending aorta to pulmonary artery confluence	14
2006	Khan	Case 3	Ascending aorta to pulmonary artery confluence	14
2007	Lee	1 case	Ascending aorta to pulmonary artery confluence	15
2010	Subramanyan	1 case	Ascending aorta to pulmonary artery confluence	16
2010	Holmes	1 case	Ascending aorta to distal main pulmonary artery	17
2012	Fatih	1 case	Ascending aorta to pulmonary artery confluence	18
2012	Jowett	Case 1	Ascending aorta to pulmonary artery confluence	19
2012	Jowett	Case 2	Ascending aorta to pulmonary artery confluence	19
2015	Bhatla	1 case	Ascending aorta to pulmonary artery confluence	20
2015	Gupta	Figure 11	Ascending aorta to pulmonary artery confluence	3
2015	Gupta	Figure 13	Ascending aorta to solitary left pulmonary artery	3
2015	Gupta	Index case	Ascending aorta to the pulmonary artery confluence	

Fifth arch artery versus distal aortopulmonary window

Distal aortopulmonary windows resemble potential fifth arch arteries with regard to their origin from the ascending aorta and their communication with the confluence of the pulmonary arteries but their course is typically not tortuous although on occasion they can have length. Most significantly, however, aortopulmonary windows must lie within the confines of the pericardial sac unlike fifth arch arteries and collateral channels, which are extrapericardial. Such a distinction is readily made in the operating room but can be extremely difficult to make on preoperative imaging.

Channels from the ascending aorta to the right or left pulmonary arteries

At times, a channel arising from the ascending aorta can take a tortuous course before terminating in either the

right or left pulmonary artery. Such a termination makes it unlikely that the channel represents a true fifth arch artery, which should terminate in the confluence of the pulmonary arteries via an arterial duct. It is, of course, possible that such a tortuous channel could terminate via the arterial duct should the pulmonary arteries themselves be discontinuous but then the entire channel is likely to represent the artery of the sixth arch. Thus, although such channels have described, on occasions, as fifth arch arteries, they are most likely the result of extensive remodeling of the arterial duct.

Anomalous origin of the right or left pulmonary artery from the ascending aorta

In some instances, investigators have attributed the anomalous origin of a pulmonary artery from the aorta to persistence of the fifth arch artery, albeit without convincing development support. Evidence from developing mouse embryos shows that the right and left pulmonary arteries develop within the pharyngeal mesenchyme, arising from the arteries of the sixth arch close to their exit from the aortic sac.[21] It is the unequal separation of the aortic sac itself that provides a better explanation for this variant of pulmonary arterial origin.

The situation is the more complicated, however, when seeking a logical explanation for some anatomic aberrations.[22,23] In both of these reported cases, the left pulmonary artery arose from the ascending aorta but in coexistence with double-barreled aortic arch, which was right-sided in one case[23] but left-sided in the other.[22] If the argument was accepted for the fifth arch artery underscoring the anomalous origin of the pulmonary artery from the ascending aorta, it would be necessary to invoke either dual left-sided fifth arch arteries or bilateral fifth arch arteries in these instances. Since the very existence of the fifth arch artery is debatable, these speculations seem unlikely.

Unusual forms of systemic-to-pulmonary connections

These examples are relatively sparse, being described in the setting of complex cardiac malformations, and representing either a variant of common arterial trunk with pulmonary arterial dominance or presence of an arterial duct providing pulmonary-to-systemic flow in the setting of aortic atresia. In these instances, on the basis of the principle of parsimony known as Occam's razor, the cases are unlikely to represent true fifth arch arteries.

Abnormalities of the origin of brachiocephalic arteries

In seeming ignorance of the extensive remodeling of the pharyngeal arches that takes place during the embryonic period, a large number of cases has been interpreted, incorrectly in our opinion,[3] on the basis of persistence of the arteries of the fifth arch. The majority of these anatomic aberrations are no more than common variations in the development of aortic arches, particularly the cases described as so-called "bovine aortic arches." In fact, the widespread use of the generic term "bovine arch" is unfortunate since the lesions bear scant resemblance to the pattern of the aortic arch in cattle. The arrangement is nothing more than the origin of all brachiocephalic arteries from a common trunk. It is more practical to explain such cases of the basis of remodeling than persistence of the enigmatic fifth arch artery. In Table 2, therefore, we have summarized our own conclusions in this regard, based on our recent review,[3] summarizing also the various morphologic characteristics that justify the label of "fifth arch artery."

Aortopulmonary connection in our index case — Is it the fifth arch?

The vascular channel in our index patient fulfills all our chosen criteria. It has a proximal origin, takes a tortuous course, and inserts at the pulmonary arterial confluence. In all probability, therefore, it represents a persisting artery of the fifth pharyngeal arch. The evidence of constriction at its pulmonary end in response to infusion of prostaglandin E1 supports further the involvement of ductal tissue at its termination, as was observed in the solitary human embryo so far encountered to exhibit such a persisting fifth arch artery.[4]

Table 2: Conclusions drawn from our review of published reports of the alleged fifth arch artery (adapted from Gupta *et al.*[3])

Bilateral fifth arch arteries have never been documented
Unilateral partial fifth arch artery has been seen only once in the developing human embryo
Dorsal collateral arteries connecting the fourth and sixth arches are much more common
To qualify as the fifth arch artery any channel must
Arise from the ascending aorta proximal to the brachiocephalic artery
Have a serpentine course
Terminate in the dorsal aorta or through the sixth arch into the pulmonary artery confluence
Alternative explanations are equally compelling for all the proposed malformations
Double-barreled aorta
None of the cases unequivocally represents the fifth arch artery
Can better be explained invoking the dorsal collateral arteries
Aortopulmonary connections
Majority of cases do not fit the description of putative fifth arch artery
Only few cases qualify for the label of fifth arch artery
Extensively remodeled arterial duct or aortopulmonary collateral channel provides a better explanation
Anomalous origin of pulmonary artery from ascending aorta does not represent fifth arch artery
Systemic-to-pulmonary connections
Too infrequent to draw conclusions
Better explained as variant of common arterial trunk with pulmonary dominance or as the persistence of arterial duct
Abnormalities of the brachiocephalic arteries
Better explained by extensive remodeling of the aortic arch and its branches

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Conflicts of interest

There are no conflicts of interest.

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