Angiocardiographic Study of Coarctation of the Aorta —Morphology and Morphogenesis—

KAZUO MOMMA, M.D., ATSUYOSHI TAKAO, M.D.
AND MASAHIKO ANDO, M.D.

Angiocardiographic morphology and associated cardiac anomalies of the coarctation of the aorta (COA) were analysed in the light of recently advanced theory of its morphogenesis. Analysis of 154 clinical cases of COA revealed the presence of associated cardiac anomalies which could obstruct fetal blood flow to the ascending aorta in many cases. Systolic left ventricular outflow tract was significantly narrow in cases of ventricular septal defect (VSD) associated with COA in comparison with the isolated VSD ($p < 0.01$).

Good quality aortograms obtained from 41 cases of COA were analysed. Ages ranged from one month to 20 years and major cardiac anomalies were associated in 25 cases. Age-matched 37 cases were studied as the controls. In COA, the isthmus was narrower than the controls in 88% of the cases, and in the remaining it was low in the normal range. Severely hypoplastic isthmus in early infancy became the adult type after 5 years in one of the 4 cases which had repeated aortography. Localized stenosis at the distal end of isthmus was present in 89%, and absent in 11% (4 cases). In these 4, isthmal narrowing was associated with major intracardiac anomalies, large patent ductus arteriosus (PDA) and pulmonary hypertension (PH). The anterior ostium to the descending aorta was obstructed by constricted ductus arteriosus in some infants with COA. These angiographic findings are compatible with the following working hypothesis: ischemic hypoplasia results from prenatal decrease of blood flow to the ascending aorta, and localized stenosis is related to abnormal distribution of the ductal tissue to the descending aorta and post-natal constriction of the ductus arteriosus.

In 3 infants COA was associated with persistent fifth aortic arch.

MORPHOLOGICALLY, coarctation of the aorta (COA) includes tubular narrowing or hypoplasia of the aortic isthmus and localized stenosis at the junction of the isthmus and the descending aorta.¹⁻³ Its morphogenesis has been studied experimentally,⁴ clinically⁵⁻⁸ and pathologically.⁸⁻¹² Experimental animal study re-

vealed that fetal blood flow through the isthmus was very small.⁴

Morphometric study of human aortic arch in fetus and neonates showed that the isthmus was physiologically hypoplastic at this age.^{8,13} In COA and interruption of the aortic arch, it is generally believed, based on the analysis of associated cardiac anomalies, that isthmic hypoplasia or interruption results from decreased blood flow to the ascending aorta in early fetal life.^{4,14,15} Morphogenesis of localized stenosis at the lower end of the isthmus was attributed by

Key Words:

Coarctation of aorta
Isthmus hypoplasia
Persistent fifth aortic arch
Angiocardiography

Department of Pediatric Cardiology, The Heart Institute, Tokyo Women's Medical College, Tokyo, Japan

Address for correspondence: Kazuo Momma, M.D., The Heart Institute, Tokyo Women's Medical College, 10 Kawada-cho, Shinjuku-ku, Tokyo 162, Japan

TABLE I ASSOCIATED CARDIAC ANOMALIES AND AGES IN THOSE PATIENTS WITH COA AND THE CONTROLS

	No	Age	0-2 mo	3-11 mo	1-20 yr
I. COA	41				
A. Minor or no cardiac anomalies	16				
No cardiac anomalies	7		4		3
Mitral stenosis or regurgitation	4			4	1
Aortic stenosis or bicuspid valve	2				2
Small VSD	3		1		2
B. Major cardiac anomalies	25				
VSD + PDA + PH	15		6	4	5
VSD + PH	5		3	1	1
TGA + VSD + PH	2		1	1	
A-V canal + PH	2		2		
A-P window + PH	1				1
II. CONTROL	37				
VSD	18		3		15
Aortic stenosis, mild	5				5
PDA, small	3		2	1	
ECD, incomplete	3		3		
TGA	2		2		
Cor triatriatum	2			1	1
Others	4		1	2	1

Abbreviations: A-P window = aorto-pulmonary window, A-V canal = persistent atrioventricular canal, mo = month-old, PDA = patent ductus arteriosus, PH = pulmonary hypertension, TGA = transposition of the great arteries, VSD = ventricular septal defect, yr = years-old.

Skoda to the extended distribution of ductal tissue into the descending aorta and its postnatal constriction.¹⁶ This Skoda's theory has been supported with some modification by several scholars,¹⁷⁻²⁰ but denied by others.^{1-3,12} Alternatively branch-point theory explains the localized stenosis at the distal end of the isthmus as an altered angle of the isthmus due to reversed fetal blood flow from the ductus arteriosus into the isthmus which occurs in compensation for the decreased blood flow to the ascending aorta through the aortic valve in fetal life.^{9,19}

Clinically good quality aortograms permit morphologic analysis of COA *in situ*, and morphogenetic hypothesis of COA can be tested.

Repeated aortograms performed both in early infancy and later in childhood can provide unique information concerning post-natal development of COA. This is a report of angiographic study of COA with discussion in the light of the current theories of its morphogenesis.

MATERIALS AND METHODS

The subjects were 154 patients with COA admitted to our hospital from 1966 to 1980. Their diagnosis was confirmed by either cardiac catheterization, cardiac operation or autopsy in all except one. Serial biplane angiocardiograms, 6 per sec, were analysed. Left ventricular outflow tract on lateral left ventriculogram was assessed in 14 VSD associated with COA and in 18 isolated VSD (control). The narrowest diameter of left ventricular outflow in systole was measured and the degree of narrowing was expressed as a ratio to the diameter of the middle ascending aorta.

Good quality aortograms in 41 cases of COA were assessed. Repeated aortograms at one or 2 months of age and 4 to 5 years later without surgical intervention were available in 4 cases. Age-matched control aortograms were obtained in 37 patients, whose cardiac anomalies are listed in Table I.

TABLE II ASSOCIATED CARDIAC ANOMALIES IN 154 CLINICAL CASES OF COA. POSSIBLE OBSTRUCTION TO THE ASCENDING AORTA IS IDENTIFIED

A. MAJOR ANOMALIES. (N = 100)			Obst.
VSD & PH	71		+, -
A-V Canal	5		+
TGA (+VSD, +DORV, +SV)	17		+
TAPVC	1		+
A-P Window	1		-
AS & PH	2		+
MS & PDA & PH	1		+
B. MINOR ANOMALIES. (N = 27)			Obst.
AS, mild or Bicuspid AV	7		+
AR	5		+, -
VSD, small	9		-
PDA, small	18		-
MR	7		-
Persistent 5th Ao. Arch	2		-
C. NO ANOMALY (N = 27)			-

Obst: Associated obstruction proximal to aorta, +': proximal to LV.

Fig.1. Systolic left-ventricular to ascending aorta diameter ratios in COA and VSD was compared with those of isolated VSD. Statistically significant subaortic narrowing was present in COA associated with VSD.

Morphology of COA in these cases was assessed as follows. The length of the isthmus was measured from branching point of the left subclavian artery to the confluence of the ductus

Fig.2. COA with very short isthmus in a 4 month-old boy with COA, VSD, PDA and PH. Lateral projection of retrograde aortogram.

arteriosus, and was expressed as a ratio to the length from the aortic arch to the diaphragm. The diameter of the isthmus was measured at the middle of the isthmus and was expressed as a ratio to the aortic diameter at the diaphragmatic level.

To test the branch-point theory, branching angles in the aortic arch and relative diameters of the middle arch compared to the isthmus were assessed.

Morphology of localized stenosis of COA was assessed according to the localized posterior shelf, obstruction of the anterior part of the ostium of the isthmus to the descending aorta by constricted ductus arteriosus, and narrowing of the upper end of the descending aorta adjacent to the ductus.

RESULTS

Associated cardiac anomalies in 154 cases of COA are listed in Table II. One hundred cases (65%) were associated with major cardiac anomalies, 27 cases had minor cardiac anomalies and in

Fig.3. COA with normal length isthmus in a 2 month-old girl with isolated COA. Lateral left ventriculography with a transvenous catheter through patent foramen ovale.

Fig.5. Abnormally long isthmus without localized stenosis in a 3 year-old boy with VSD, large PDA with bidirectional shunt, and PH. Lateral aortogram.

Fig.4. COA with abnormally long isthmus in a 5-year-old girl with COA, membranous septal aneurysm and patent foramen ovale. Lateral projection of left ventriculogram.

Fig.6. Isthmus to aortic arch-diaphragm length ratio in COA (closed marks) and the controls (open marks). Abnormally long isthmus was present in COA.

the remaining no cardiac anomalies were observed. The ratio of left ventricular outflow to ascending aorta was 0.94 ± 0.09 (mean $\pm$ SD) in isolated VSD and 0.71 ± 0.11 in VSD associated with COA. The difference was highly significant

($p < 0.01$) (Fig. 1). Length of the isthmus in COA was classified into 3 groups. Abnormally short isthmus was observed in 11% (Fig. 2). Left subclavian artery branched shortly above the localized stenosis. In this type of COA localized

Fig. 7. Isthmus to descending aorta diameter ratio in COA and the controls. COA had significantly narrow isthmus from infancy through childhood.

stenosis appeared accentuated, but the presence of isthmic narrowing was apparent by comparing it to the diameter of the descending aorta. Isthmus of normal length (0.07 to 0.15 in ratio) was present in 33% of COA (Fig. 3). Abnormally long isthmus with a more than 0.15 ratio of the isthmus length to the length from the ascending aorta to the diaphragm (Fig. 4) was present in 56% of COA. In any type, isthmus was narrowed homogeneously from the branching point of the

Fig. 8. Diameter ratio and length ratio of the isthmus of COA. Those isthmus with relatively long appearance (above the line $Y = 0.21 X$) were associated with major cardiac anomalies in higher percentage than those isthmus with relatively short appearance (below the line).

left subclavian artery to the junction to the ductus arteriosus. Localized stenosis was present at the distal end of the isthmus in 89% of COA,

Fig. 9. Aortic arch and its branching pattern that shows evidences of reversed flow in a 4 month-old girl with COA, mitral stenosis, PDA and PH. In addition, anterior portion of the lower end of the isthmus was obstructed by the constricted ductus arteriosus.

2 month-old: Ao.A. 120/50, Angle: -47° ,
D.Ao. 75/50 } 5 year-old: Ao.A. 150/80, Angle: -23° ,
D.Ao. 105/80

Fig.10 Obstruction of the anterior portion of the lower end of the isthmus by the constricted ductus arteriosus in a 2 month-old girl with COA, small PDA and membranous septal aneurysm (left). Posterior shelf became more prominent and PDA had closed at 5 years of age (right).

and in the remaining (4 cases, 11%) tubular narrow isthmus was connected to the descending aorta without localized stenosis, and widely patent ductus arteriosus and right to left shunt, pulmonary hypertension and major cardiac anomalies were associated with all these 4 cases (Fig. 5).

Isthmus length in COA and the control group is compared in Fig. 6. Isthmus length ratio in the control group ranged from 0.07 to 0.15. In COA isthmus length was variable and abnormally long

in 56%. No apparent correlation was found between the isthmus length and association of cardiac anomalies.

Isthmus diameter in COA is shown in Fig. 7. Diameter ratio of isthmus to descending aorta was 0.75 to 1.1 in the control infants and 1.0 to 1.3 in the control children. In COA isthmus was abnormally narrow in all except 5 infants, whose isthmus was low in the normal range.

The diameter and the length of the isthmus were plotted to check the correlation between

Fig.11 Conversion of hypoplastic isthmus (left, at 2 months of age) to adult type (right, at 5 years of age) in a boy with isolated COA.

the isthmal morphology and association of major cardiac anomalies (Fig. 8). In those with relatively long tubular isthmus which were above an arbitrary line of $Y = 0.21X$, major cardiac anomalies were associated in 85%. In contrast, in those with relatively short isthmus which were below this line, 47% were associated with major cardiac anomalies.

Branching pattern in the aortic arch in those without COA was uniform and all these branches of the aorta in the arch directed towards the ascending aorta, and aortic arch had larger diameter than the isthmus. In COA 21 out of 25 cases showed normal branching pattern of the aorta, 3 showed equivocal pattern, and only one showed reversed branching pattern (Fig. 9).

Morphology of localized stenosis at the distal end of the isthmus was more clearly observed on the lateral aortogram. Localized stenosis was produced usually by sharp indentation protruding from the posterior aortic wall. In 4 infants anterior lower end of the isthmus was obstructed by the constricted ductus arteriosus (Fig. 10). In these 4 cases, 2 were associated with major cardiac anomalies and 2 were not. In one of them repeated aortogram showed obscuring of the anterior obstruction by the ductus and more apparent posterior shelf (Fig. 10).

Morphology of the upper descending aorta was uniform in all cases of COA. It directed antero-superiorly towards the ductus or its cord, and it showed fusiform narrowing.

In one of 4 cases repeated aortogram revealed marked change of isthmic morphology. This occurred in a boy with isolated COA. In the first study at the age of 2 months when he was admitted with congestive heart failure, aortogram showed markedly hypoplastic narrow isthmus (Fig. 11). Intravascular pressure (mmHg) was 143/73 in the ascending aorta, and 75/65 in the descending aorta. Congestive heart failure was controlled with administration of digoxin for one year. His second aortogram at the age of 5 years revealed only mildly hypoplastic isthmus, and well developed collateral vessels. Intravascular pressure (mmHg) was 125/80 in the ascending aorta and 100/78 in the descending aorta.

In 3 infants with COA without major cardiac anomalies very peculiar branching pattern of the aortic arch was observed (one of them was studied in 1981 and not included in Table II). Innominate artery, left common carotid artery, and left subclavian artery branched from one common trunk, and another aortic arch, just caudal to the former trunk, continued to the descending aorta with localized stenosis (Fig. 12). All 3 were operated, and a white cord connecting left subclavian artery and descending aorta was noticed in one (Case 1) but not in the other 2.

DISCUSSION

The theory on pathogenesis of coarctation of the aorta was originated by Craigie²¹ and Skoda¹⁶ who proposed in the 19th century that

Fig.12 Frontal left ventriculograms of 3 cases of COA associated with persistent 5th aortic arch. In Case 1 operative procedure included division of 5th arch and side to end anastomosis between left subclavian artery and proximal descending aorta.

the localized stenosis of COA was caused by the post-natal constriction of the ductus arteriosus in the presence of ductal tissue in the upper descending aorta (Skoda's theory). In the early 20th century Bonnet¹⁸ classified COA into infantile and adult type, and attributed isthmal tubular hypoplasia of infantile COA to decreased blood flow to the ascending aorta in fetal circulation. Recent histologic study of the aorta around the coarcted segment revealed repeatedly the extended distribution of ductal tissue to the upper descending aorta, surrounding the ostium of the isthmus.^{7,11,17,22} This provides potent

support to Skoda's theory, but some controversies exist in this respect.^{1,3}

The present study provides evidence which supports Skoda's theory as follows: localized stenosis of COA located uniformly in the juxta-ductal area and localized stenosis of COA consisted of shelf-like protrusion of the dorsal wall of the aorta. These two points are compatible with both Skoda's theory and the branch-point theory. In some infants anterior distal end of the isthmus was obstructed by the constricted ductus arteriosus. Uniformly fusiform stenosis of the upper descending aorta was observed.

Fig.13 Current hypothesis of morphogenesis of COA and isthmic hypoplasia. Blood flow and morphology of aortic arch and ductus arteriosus, and distribution of the ductal tissue in fetus and neonate with COA are schematically shown.

These two points are compatible with the histologic finding of extension of ductal tissue into the descending aorta. Hypoplastic tubular isthmus without localized stenosis was always associated with large PDA, and absence of localized stenosis is explained to be due to absent constriction of the ductal tissue. In only one out of 25 cases aortic arch morphology was compatible with branch-point theory. It is concluded that Skoda's theory rather than the branch-point theory fits the angiographic morphology of COA better in most cases. Since Bonnet's classical article¹⁸ the association of isthmic hypoplasia with COA was noticed, at first in infantile type, but recently in adult type too.^{5,22} Our study confirmed it. Isthmus hypoplasia in COA associated with those cardiac anomalies which obstruct fetal blood flow to the ascending aorta is easily explained.

The association of isthmic hypoplasia in isolated COA was reported previously by Sinha⁵ and by Shinebourne²². In these cases it is not apparent why the isthmus was hypoplastic or why blood flow to the ascending aorta was decreased in fetal life. Careful pathologic study or serial clinical observation with UCG may elucidate this point.

This paper documents postnatal enlargement of hypoplastic isthmus. This was called conversion of isthmic hypoplasia into adult type by Lev²⁰ but this concept was criticized as not

documented fully.⁵ This phenomenon explains the observation that isolated COA in neonatal period is often associated with isthmic hypoplasia, and Shinebourne²² observed this association in 41% of their cases.

The association of isthmic hypoplasia with abnormal distribution of the ductal tissue extending into the descending aorta in COA was explained by Krediet¹⁹ as follows: In early development of the aorta, the left subclavian artery migrates upwards passing the junction of the ductus arteriosus from the thoracic aorta up to the arch. A portion of the aortic wall moves upwards associating with the migrating ostium of this artery. In the presence of isthmic hypoplasia ductal tissue is pulled into the descending aorta in compensation when the ostium of this artery passes by the junction of the isthmus and descending aorta, thus ductal tissue distributes in the descending aorta surrounding the ostium of the isthmus to the descending aorta.

From the present observation and supportive evidence COA is most reasonably presumed to be a sequential occurrence as schematically shown in Fig. 13. In early fetal circulation blood flow to the ascending aorta is decreased for some reason, resulting in isthmic hypoplasia. Upwards migration of the left subclavian artery pulls ductal tissue into the descending aorta. Post-natal ductal constriction causes fusiform narrowing of the upper descending aorta, and local-

ized narrowing of the lower end of the isthmus just like pulling the string of purse-string suture. In COA associated with major cardiac anomalies severe congestive heart failure develops in early infancy and clinical and pathological studies are done in this age. In COA without major cardiac anomalies congestive heart failure is generally milder and many survive to childhood or adulthood without early operation. In some of these survivors hypoplastic isthmus becomes wider, and this is the so-called conversion to the adult type of COA.

Persistent fifth aortic arch is a rare anomaly in man. It has been reported in association with tricuspid atresia^{23,24} VSD and pulmonary atresia²⁵ PDA²⁶ or COA²⁶. In these reported cases both 4th arch and 5th arch were present. Of 3 cases in this paper only one had a cord between the left subclavian artery and the descending aorta and this cord was presumed to be a portion of the left dorsal aorta between the 4th and 5th arch. In the other 2 cases, no such cord was found on operation. Aortic arch pattern of these 3 cases of COA is interpreted as persistent 5th aortic arch with involution of a portion of the dorsal aorta between the 4th and 5th arch.

Acknowledgement

Editorial help of Leonard M. Linde M.D., Clinical Professor of Pediatric Cardiology, UCLA, is highly appreciated.

REFERENCES

- EDWARDS JE, CHRISTENSEN NA, CLAGETT OT, MACDONALD JR: Pathologic considerations in coarctation of the aorta. *Proc Staff Meet Mayo Clin* 23: 324, 1948
- CLAGETT OT, KIRKLIN JW, EDWARDS JE: Anatomic variations and pathologic changes in coarctation of the aorta. *Surg Gynec Obst* 98: 103, 1954
- ROSENBERG HS: Coarctation of the aorta: Morphology and pathologic considerations. *Perspective in Pediatric Pathology* 1: 339, 1973
- RUDOLPH AM, HEYMANN MA, SPINAS U: Hemodynamic considerations in the development of narrowing of the aorta. *Am J Cardiol* 30: 514, 1972
- SINHA SN, KARDATZKE ML, COLE RB, MUSTER AJ, WESSEL HU, PAUL MH: Coarctation of the aorta in infancy. *Circulation* 40: 385, 1969
- BRUINS C: Competition between aortic isthmus and ductus arteriosus: Reciprocal influence of structure and flow. *Eur J Cardiol* 8: 87, 1978
- BROM AG: Narrowing of the aortic isthmus and enlargement of the mind. *J Thorac Cardiovasc Surg* 50: 166, 1965
- VAN MEURS-VAN WOEZIK H, KLEIN HW, KREDIET P: Normal internal calibers of ostia of great arteries and of aortic isthmus in infants and children. *Br Heart J* 39: 860, 1977
- HUTCHINS GM: Coarctation of the aorta explained as a branch-point of the ductus arteriosus. *Am J Pathol* 63: 203, 1971
- BREMER JL: Coarctation of the aorta and aortic isthmus. *Arch Pathol* 45: 425, 1948
- HO SY, ANDERSON RH: Coarctation, tubular hypoplasia, and the ductus arteriosus. *Br Heart J* 41: 268, 1979
- EDWARDS JE: Coarctation of the aorta. In *Pathology of the Heart*, 2nd edit ed by GOULD SE, CC Thomas, Springfield, 1960, p 449
- PATTEN BM: The development of the heart. In *Pathology of the Heart*, 2nd edit, ed by GOULD SE, CC Thomas, Springfield, 1960, p 85
- VAN PRAAGH R, BENHARD WF, ROSENTHAL A, PARISI LF, FYLER DC: Interrupted aortic arch: Surgical treatment. *Am J Cardiol* 27: 200, 1971
- FREEDOM RM, BAIN HH, ESPLUGAS E, DISCH R, ROWE RD: Ventricular septal defect in interruption of aortic arch. *Am J Cardiol* 39: 572, 1977
- SKODA J: Protokoll der Sektions-Sitzung fur Physiologie und Pathologie. *Wbl Ztsch Ges Aerzte Wien* 7: 720, 1855 (cited from 3)
- WIELENGA G, DANKMEIJER J: Coarctation of the aorta. *J Path Bact* 95: 265, 1968
- BONNET LM: Sur la lesion dite stenose congenitale de l'aorte dans la region de l'isthme. *Rev Med Paris* 23: 108, 335, 418, 481, 1903 (cited from 3)
- KREDIET P: A hypothesis of the development of coarctation in man. *Acta Morphol Neerlando-Scandinavica* 6: 207, 1965
- DE BOOR A, GRANA L, POTTS WJ, LEV M: Coarctation of the aorta. *Arch Surg* 82: 801, 1961
- CRAIGIE D: Instance of obliteration of the aorta beyond the arch, illustrated by similar cases and observations. *Edinburgh Med Surg J* 54: 427, 1841 (cited from 3)
- SHINEBOURNE EA, HART S, DE SWIET M: Management of symptomatic coarctation of the aorta in infancy. In *Pediatric Cardiology*, Vol 2, ed by GODMAN MJ, MARQUIS RM, Churchill Livingstone, Edinburgh, 1979, p 234
- VAN PRAAGH R, VAN PRAAGH S: Persistent fifth arterial arch in man. *Am J Cardiol* 24: 279, 1969
- YAMAZAKI N: A case of tricuspid atresia associated with persistent fifth aortic arch. *Shinzo* 13: 79, 1981 (in Japanese)
- MACARTNEY FJ, SCOTT O, DEVERALL PB: Hemodynamics and anatomical characteristics of pulmonary blood supply in pulmonary atresia with ventricular septal defect including a case of persistent fifth aortic arch. *Br Heart J* 36: 1046, 1974
- IZUKAWA T, SCOTT ME, DURRANT F, MOES CAF: Persistent fifth aortic arch in man: Report of two cases. *Br Heart J* 35: 1190, 1973