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Clinical–Pathologic Correlations 1

Jesse E. Edwards, M.D. | Guest Editor

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Editor's Commentary

The clinical-pathologic conference has long been recognized as the penultimate teaching exercise and learning experience. Such conferences provide for a precise correlation between the clinical and laboratory observations and the underlying abnormality. It is noteworthy that such correlations date back more than 400 years to the amphitheaters of the classic Italian school where the first coordinated attempts were made to relate the findings at the autopsy table to clinical observations. In subsequent years, such towering medical figures as Hunter, Hodgkin, Bright, Addison, Laennec, and others combined brilliantly their clinical and laboratory studies. As the science of medicine has expanded, so has the challenge of clinical-pathologic correlations. In the specialty of cardiovascular diseases, no one has provided more erudite or more important clinical-pathologic observations than has Jesse E. Edwards; and, therefore, I am enormously proud to have his stewardship as Guest Editor of the present issue. Both of us are grateful to the participants in this issue for their extraordinary contributions.

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Congenital Obstructive Malformations of the Aortic Arch

Anton E. Becker, M.D

From a *clinical* point of view, congenital obstructive aortic arch malformations can be divided into two main groups: Group I, those with the obstruction located proximal to the ductus arteriosus, the *preductal type*, and Group II, those with the obstruction located distal to the ductus arteriosus, the *postductal type*. In each group the ductus arteriosus can be patent or closed. A "patent" ductus is identified when the caliber of the ductus is such that it may allow a significant shunt, while a "closed" ductus indicates either a caliber that could allow only insignificant shunting or else a true anatomic closure, i.e., ligamentum arteriosum. The exceptional cases, where an obstructive aortic arch anomaly is located opposite the ductus, are not identified as a separate entity in this presentation since from a hemodynamic point of view these cases will belong either to the preductal or to the postductal type.[1]

From an *anatomic* point of view, the congenital obstructive anomalies of the aortic arch can be classified into three types: (1) *coarctation*, defined as a localized narrowing of the aortic lumen resulting from an eccentric ridge-like thickening of the aortic media,[2] (2) *tubular hypoplasia* of the aortic arch, defined as a uniform narrowing of a segment of the aortic arch,[3] and (3) *interruption* or atresia of the aortic arch, defined as complete interruption of luminal continuity. Usually there is a complete separation of the two parts, i.e., true interruption. Occasionally, however, the two portions may be connected by a strand of connective tissue. The latter situation is termed *atresia of the aortic arch*. From a functional point of view, however, the two conditions are identical. For that reason no further distinction will be made in this presentation between the two variants.

It is the purpose of this report to correlate the three types of anatomic obstructive malformations with pre- and postductal types of the clinical classification. Particular attention will be given to the occurrence of associated malformations and their possible functional implications. The atypical clinical findings that may result from unusual locations of the ostia of the subclavian arteries relative to the obstruction in the aortic arch will be dealt with separately.

Not included in this presentation are those conditions in which an obstructive aortic arch lesion forms part of a major cardiovascular disorder, such as the hypoplastic left heart syndrome, single ventricle, transpositional complexes and persistent atrioventricular canal, notwithstanding the fact that the obstructive anomaly may significantly alter the hemodynamic situation in those cases.

PREDUCTAL AORTIC ARCH OBSTRUCTION

Patent Ductus Arteriosus

Usually this type of obstruction leads to congestive heart failure and death in the neonatal period or shortly thereafter. The *clinical* picture in these circumstances varies, depending on the size of the accompanying ductus arteriosus and on the presence of associated malformations. Hemodynamically, the malformation is characterized by resistance to blood flow across the aortic arch, obstructive pulmonary hypertension, and shunting of blood from the pulmonary

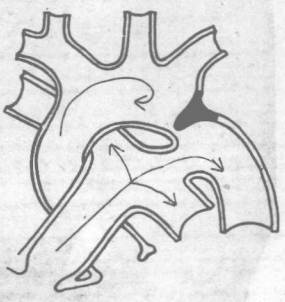

Figure 1. Diagram of the circulation in preductal aortic arch obstruction (portrayed as coarctation) with patent ductus arteriosus.

trunk into the descending aorta through the ductus arteriosus (Fig. 1). Among the salient clinical findings in the symptomatic child are: (1) cardiomegaly with definite right ventricular enlargement and often congestive heart failure, (2) slightly lower blood pressures in the legs than in the arms, even if the femoral and radial pulses are equally perceptible, (3) mild or moderate cyanosis, (4) a nonspecific systolic murmur in the midprecordium, and (5) accentuation of the pulmonic component of the second heart sound.

Each of the three *anatomic* conditions, i.e., coarctation, tubular hypoplasia and interrupted aortic arch, may be found under these circumstances.

Coarctation

Coarctation is characterized by a sharply defined zone of narrowing in the aortic arch, usually localized immediately proximal to that part of the descending aorta which is in continuity with the ductus arteriosus. The narrowing is caused by a localized thickening of the media, which in a curtain-like fashion projects into the lumen from the ventral, dorsal and cephalic sides (Fig. 2a). It leaves a stenotic, eccentrically located lumen. Histologic sections reveal that the intima overlying the coarctation is thickened by fibrous tissue (see Fig. 2b, c). The latter shows a peculiar lamellated arrangement with fibrinoid changes at the surface (see Fig. 2c, d). These changes, which are already present in infancy but become more pronounced with increasing age, are a response to the impact of blood at the site of the luminal narrowing.

The patent ductus arteriosus, which is present in the great majority of symptomatic infants with the preductal type of coarctation, tends to minimize the differences in blood pressure recordings from arms and legs.

The hemodynamic situation is significantly influenced, furthermore, by the presence or absence of associated malformations.

Associated Anomalies. Preductal obstructions have a high incidence of associated malformations. Clinical series [4–6] present an overall incidence of associated anomalies of approximately 70 per cent, among infants presenting with congestive heart failure. In a series of 100 consecutive necropsy specimens exhibiting coarctation of the aorta, associated malformations were present in 87 per cent.[7] These reports indicate a trend for a direct relationship between the presence of associated malformations and early onset of symptoms. The

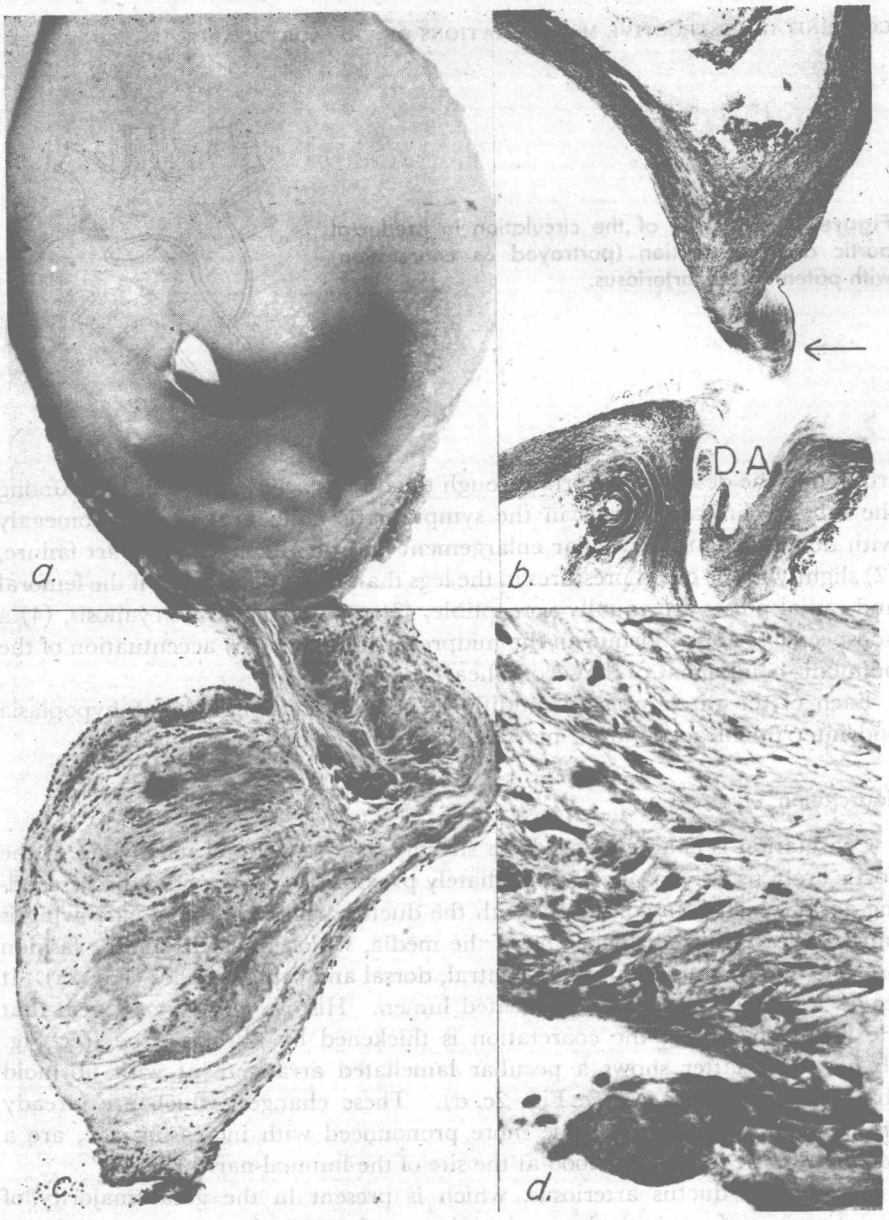

Figure 2. a, The distal end of a segment of aorta with coarctation. The lumen is narrowed and eccentrically situated. b, Photomicrograph of a segment of aorta with preductal coarctation and patent ductus arteriosus (D.A.), sectioned longitudinally. The aortic arch is to the left, the descending aorta is to the right. The coarctation is characterized by a medial infolding. The intima overlying the coarctation is markedly thickened (arrow), due to the jet effect of the blood shunted through the ductus arteriosus into the descending aorta. (elastic stain, reduced 10 % from × 7) c, Photomicrograph of intimal patch overlying cocarctation, showing the lamellated, edematous aspect of the fibrous tissue. (hematoxylin-eosin, reduced 10% from × 50) d, Same specimen as c. Higher magnification of surface area showing fibrinoid changes with fibroblastic activity. (hematoxylin-eosin, reduced 10% from × 350)

following associated malformations, in order of decreasing frequency, can be expected: (1) tubular hypoplasia of the aortic arch, (2) abnormal communications, mainly ventricular septal defects, (3) left ventricular outflow obstructions, and (4) left ventricular inflow obstructions. Not taken into account is the bicuspid aortic valve, which is present in approximately half of all patients with coarctation of the aorta. Only rarely, however, is the latter condition of importance in the young, although the high incidence of this anomaly should be kept in mind since late complications may arise from it.

Tubular Hypoplasia. This condition frequently occurs in association with coarctation (Fig. 3), in particular when symptoms occur early in life.[6,7]

Of further interest is the fact that when coarctation and tubular hypoplasia coexist, there is a distinct tendency for additional anomalies to be present. Among these, ventricular septal defect and the muscular type of left ventricular outflow obstruction are the most common.

The hemodynamic importance of tubular hypoplasia relates to the fact that it may add significantly to the systemic vascular resistance. The associated cardiac anomalies further contribute to the complexity of the hemodynamic and clinical features described earlier.

Intracardiac Septal Defects. Among the intracardiac defects, ventricular septal defect is the most common type.[7] In the majority of cases the defect is located inferior to the supraventricular crest, i.e., the predominant location for ventricular septal defects. The combination of ventricular septal defect with tubular hypoplasia is common.

The high systemic vascular resistance tends to increase the quantity of blood shunted through the ventricular septal defect and so contributes to the right ventricular load, the high pulmonary vascular resistance, and the magnitude of the shunt into the descending aorta through the ductus.[8]

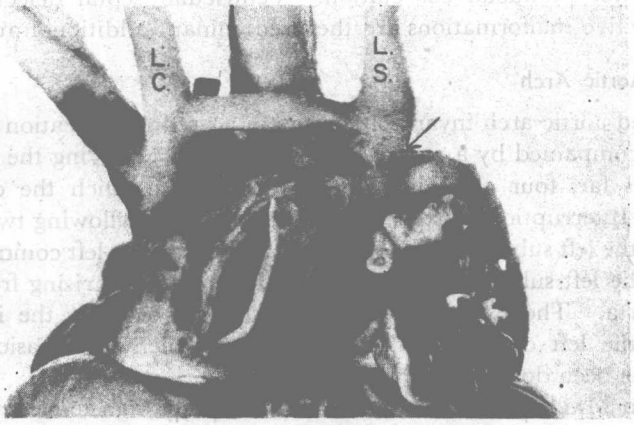

Figure 3. Coarctation of aorta (arrow), located immediately proximal to a patent ductus arteriosus (D.A.) and closely related to the origin of the left subclavian artery (L.S.). Tubular hypoplasia is present between the left common carotid artery (L.C.) and the left subclavian artery (L.S.).

Left Ventricular Outflow Obstruction. The most common anomaly in this group is subaortic stenosis, of which the muscular (hypertrophic) type is the predominant one. Occasionally, subaortic stenosis may be part of a syndrome characterized by coarctation, bicuspid aortic valve, subaortic stenosis, parachute mitral valve, and supravalvular ring of the left atrium.[9] Tubular hypoplasia or ventricular septal defect, or both, commonly coexist with subaortic stenosis. Congenital unicommissural aortic valvular stenosis may occur, though often associated with varying degrees of hypoplasia of the left ventricle and mitral valve.

Left Ventricular Inflow Obstruction. The most common condition in this group is hypoplasia of the mitral valve and left ventricle associated with fibroelastosis of the left ventricular endocardium. Parachute mitral valve may occasionally be encountered, either as an isolated condition or in combination with one or several other additional malformations.

Tubular Hypoplasia

The term *tubular hypoplasia* refers to an obstructive malformation of the aortic arch, characterized by a uniformly narrow segment of the aortic arch.[3] Despite the gross anomaly, the wall is normal histologically. Tubular hypoplasia may involve all of the aortic arch from a level just beyond the origin of the innominate artery to the origin of the ductus arteriosus, or it may involve only part of this segment of the aorta. The two most common forms are: (1) tubular hypoplasia between the origin of the left common carotid artery and the origin of the left subclavian artery (see Fig. 3), and (2) tubular hypoplasia between the origin of the left subclavian artery and the point of entrance of the ductus arteriosus.

Associated Anomalies. Tubular hypoplasia seldom occurs as an isolated lesion, but instead commonly coexists with preductal coarctation. For that reason, intracardiac anomalies can be expected with a similar high incidence as indicated for preductal coarctation. Ventricular septal defects and left-sided obstructive malformations are the predominant additional anomalies.

Interrupted Aortic Arch

Interrupted aortic arch invariably occurs in a preductal location and nearly always is accompanied by a patent ductus arteriosus supplying the descending aorta. Thus far, four cases have been reported in which the ductus was closed.[10–13] Interruption most commonly occurs at the following two sites[14,15]: (1) distal to the left subclavian artery, and (2) between the left common carotid artery and the left subclavian artery (Fig. 4a), the latter arising from the descending aorta. The existence of an interruption between the innominate artery and the left common carotid artery, of which an occasional report exists,[16,17] has been doubted by others.[15]

Associated Malformations. There is a strikingly high tendency for interrupted aortic arch to be associated with a ventricular septal defect. Among 105 reviewed cases, a ventricular septal defect was found in 98 instances.[15] In fact, the combination of interruption of the aortic arch, patent ductus arteriosus, and ventricular septal defect is so frequent that it has been considered