Localised coarctation of the aorta

An age dependent spectrum

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SUMMARY Localised coarctation of the aorta was studied histologically in 45 cases. The age range of the patients, from 2 weeks to 40 years, enabled us to make a comparison between early and late findings.

The basic histological architecture of all coarctations was identical. The ridge consisted mainly of thickening plus some infolding of the aortic wall. Ductal tissue formed the inner part of the ridge for more than half of its total circumference. In older cases masses of secondary intimal proliferation were present, which narrowed the residual lumen of the coarctation.

The coarctation was located preductally in most young patients and postductally in the majority of older patients.

It is concluded that ductal tissue is invariably present in the ridge and that all coarctations develop in a preductal position. Secondary changes include a gradual shift of the ridge from a preductal to a postductal position, and progressive narrowing of the residual lumen by intimal proliferation.

There is still controversy in the published reports concerning the aetiology of aortic coarctation, and the possible relation between coarctation and the ductus arteriosus. The fact that a coarctation of the aorta in its most typical form is located near the entrance of the ductus arteriosus into the aorta has led several investigators to study the possible relation between the two. Reports concerning the role of the ductus arteriosus in the aetiology of coarctation have been conflicting. Some authors have given pathophysiological explanations for the development of a coarctation, suggesting it resulted from fetal flow abnormalities through the ductus arteriosus. Another hypothesis explaining the development of a coarctation is based on the presence of ductal tissue in the aorta, leading to narrowing of the aorta during the closing process of the ductus. In histological studies ductal tissue was indeed found in the ridge of the coarctation by some investigators, but whether ductal tissue plays an active part in the narrowing process has been questioned, since a coarctation can be present in combination with a widely patent ductus. Some investigators denied the presence of ductal tissue in the coarctation because they could not trace it in their histological studies.

Bonnet introduced the terms infantile and adult type of aortic coarctation to describe a long narrow segment and a sharp localised constriction, respectively. This classification does not account for the frequent finding of an adult type of coarctation in a newborn baby. We have chosen to use the terminology of Edwards et al. and to refer to the long narrow segment as “tubular hypoplasia”, and reserve the term “coarctation” for a sharp localised constriction (ridge or shelf). In the present study, which is confined to localised coarctation, special attention was paid to the following.

(1) The histology of the coarctation and the ductus arteriosus, and their possible relation.

(2) The level of the coarctation in the aorta and the site of entrance of the ductus arteriosus.

In contrast to several previous investigations, we chose our material from a very wide age range, allowing comparison of young and old cases.

Subjects and methods

Forty-five specimens with aortic coarctation, most of them obtained at operation, were studied. The age range of the patients was from 2 weeks to 40 years (Table 1). Some of the specimens studied had been described earlier by Wielenga. None of the patients
had complex intracardiac lesions, though in some of them a ventricular septal defect or a bicuspid aortic valve was present. Ten normal aortic arches were used as control material. Three of these specimens were derived from patients with a grossly normal aortic arch but with an intracardiac lesion. The remaining specimens were from patients who died of non-cardiac diseases (Table 2).

All specimens were fixed in formaldehyde 4% solution immediately in the operating room. They were completely serially sectioned and mounted on glass slides. The slides were stained alternately with haematoxylin and eosin, azan, and an elastic tissue stain. Special attention was paid to the possibility of ductal tissue being present in the aortic arch, and to the spatial relation between ductus and coarctation. In order to clarify this relation, graphic reconstructions were made of some of the specimens using the technique described by Tinkelenberg.10

### Table 1 Coarctations

<table>
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<th>Case No.</th>
<th>Age</th>
<th>Site of coarctation in relation to ductus arteriosus</th>
<th>Patency of ductus arteriosus</th>
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Intimal proliferation: - not present, + minimal, ++ pronounced, +++ excessive.
* Normal ductal wall structure.
† Persistent type of ductal wall.
‡ Second stenosis in aortic arch, see text.

In order to clarify this relation, graphic reconstructions were made of some of the specimens using the technique described by Tinkelenberg.10

### Table 2 Normal subjects

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* Prematures, gestational age 32 to 36 wk.
VSD, ventricular septal defect.
Coarctation of the aorta

Results

NORMAL SUBJECTS: HISTOLOGY
In the first few months after birth the difference between the aortic and ductal wall was easily visualised, especially in the elastic tissue stains. In the aortic media ± 40 concentric elastic lamellae could be distinguished, with smooth muscle cells in between. The aortic intima was thin; only a few cellular layers were found underneath the endothelium. The ductus arteriosus was built as a muscular artery. Its media consisted principally of smooth muscle cells and was very poor in elastic tissue. The internal elastic lamina formed the borderline between media and intima. In the normal mature ductus arteriosus the intimal thickness varied from only a few cellular layers in some areas to distinct intimal cushions in other areas. These cushions contained more elastic material than the media. The elastic material was present as fine elastic fibres, very different from the elastic lamellae of the aorta.

In older specimens the aortic wall was thicker, with an increasing number of elastic lamellae in the media. There was a thickening of the subendothelial layer of the intima as well, which merged gradually with the media. Anatomical closure of the ductus arteriosus was complete and a ligamentum arteriosum formed, consisting principally of fibrous tissue, relatively poor in elastic tissue. This made the ligament easily discernible from aortic wall tissue.

In a transverse section of a normal aorta at the level of the ductus arteriosus or ligamentum arteriosum, ductal tissue was found to border a small part of the aortic lumen. At the site of the junction of ductal and aortic wall the inner third of the aortic lamellae merged into the internal elastic lamina of the ductus, whereas the outer two thirds merged into the adventitia of the ductus. This resulted in a typical fish tail appearance of the elastic tissue of the aorta bordering the ductus (Fig. 1, 2).

The percentage of aortic wall occupied by ductal tissue was limited. Up to 30% of the total circumference of the aorta could contain ductal tissue. In the specimens of the older patients relatively less ductal tissue was present (Fig. 1, 2).

PATIENTS WITH COARCTATION: HISTOLOGY
All 45 coarctations consisted mainly of a thickening, with some degree of infolding of the aortic media. At the site of the coarctation the number of elastic lamellae was the same as in the normal aortic wall. The thickening appeared to be related to an increase in the distance between the elastic lamellae. The infolding of aortic wall was very pronounced in some specimens and hardly visible in others.

The junction between aortic and ductal tissue did not resemble a fish tail, as it did in the normal subjects. Instead, all elastic lamellae of the aortic media formed the outer part of the coarctation and eventually merged into the adventitia of the ductus (Fig. 3).

Ductal tissue was invariably present in the ridge. In a transverse section of the aorta at the level of the coarctation, ductal tissue bordered the aortic lumen for more than half of the total aortic circumference in all cases. In some cases ductal tissue encircled the lumen completely (Fig. 3). Both medial and intimal tissue of the ductus were present in the coarctation, but an extension of intimal cushions into the ridge was found in only two very young specimens (Fig. 3).

In sagittal sections of coarctation specimens, ductal tissue was located predominantly at the side of the ridge which faced the descending aorta in all except one case (No. 2 in Table 1).

This case was a 2 week old infant who died in con-
gestive heart failure. Necropsy showed two muscular ventricular septal defects, a bicuspid aortic valve, and two sites of localised narrowing in the aorta. One narrowing was located in between the left carotid and left subclavian artery. At histological examination it was found to consist exclusively of an infolding of the aortic wall. The second narrowing was located just opposite the site of entrance of the ductus arteriosus. On histological examination this ridge consisted of an infolding and thickening of the aortic media with ductal tissue on top of the ridge, both at the distal and the proximal side. (This case has been reported by Bruins.)

The basic histological picture, as described above, was identical in all coarctation specimens. No difference was found between young and old cases. In older specimens though, on top of the original coarctation and directly distal to it large masses of intimal proliferation were present (Fig. 5). This intimal proliferation narrowed the residual lumen of the coarctation, and was present whether or not ductal tissue or aortic wall tissue bordered the original lumen. A distinct histological difference was noted between intimal proliferation and intimal cushions of the ductus (Fig. 3, 5). The intimal proliferation consisted principally of loose fibrous tissue, with some scattered smooth muscle cells. Elastic material was present only in the intimal proliferations of some of the older specimens, where it presented as thick, irregularly distributed elastic lamellae. The elastic material in the intimal cushions of the ductus, as mentioned before, was more abundant, with regularly distributed fine elastic fibres (Fig. 3 and 5).

In nine specimens with coarctation a persistent ductus arteriosus was present (Table 1). In eight of these cases an abnormal structure typical for a persistent ductus arteriosus (Fig. 4) was found. One, a 2 week old infant, had a normal ductal wall. There was no difference in histological architecture of the coarctation between specimens with a patent and those with a closed ductus arteriosus.

**PATIENTS WITH COARCTATIONS: SPATIAL AND TEMPORAL RELATION**

The level of the coarctation, compared with the site of entrance of the ductus arteriosus, varied considerably.
Coarctation of the aorta

Fig. 4  Sagittal section of the ridge of a preductal coarctation with persistent ductus arteriosus (case 16). The ridge (Coa) lies proximal to the entrance of the ductus into the descending aorta (d.Ao.). a.Ao., aortic arch. The structure of the ductus arteriosus is of a persistent type, showing aortification, with increase in elastic material. Ductal tissue is still distinguishable from aortic tissue, though it stains darker than a normal ductus. Ductal tissue extends into the ridge (top of white arrow). (Elastic tissue stain; original magnification x 10.)

Fig. 5  Sagittal section of the residual lumen of a post ductal coarctation (case 44). Ligamentous ductal tissue extends into the coarctation and encircles the aortic lumen in this specimen, as can be seen from its presence on the right side of the picture (white arrow). On the left side of the picture (*) the connection between ductal and aortic tissue is clearly visible. All elastic lamellae of the aorta merge into the adventitia of the ligamentum. Compare with Fig. 1 and 2. Intimal proliferation (i.p.) almost closes the residual lumen of the coarctation. Note the difference in structure between intimal proliferation and the intimal cushion of the ductus in Fig. 3. (Elastic tissue stain; original magnification x 7.)

Discussion

In our study coarctations were at different levels in the descending aorta compared with the site of entrance of the ductus, exactly opposite the ductal entrance, or below the ductus. We refer to the above mentioned positions as preductal, paraductal and postductal, respectively. Fig. 6 shows how the highest proportion of cases in these three positions moves smoothly with age, the highest proportion of the preductal being in infancy, of the paraductal in middle childhood, and of the post ductal in adult life.

The basic histological architecture, as already mentioned, was identical in all specimens and independent of the position of the ridge. Even in distant post ductal coarctations there was continuity between the ductal tissue in the ridge and the tissue of the ductus arteriosus.

Fig. 6  Age distribution of the three types of coarctation. Vertical axis: number of cases.
rence of the duc-
sus or the ligamentum
arteriosum. The ridge could be located preductally,
pathologic, or postductally. Preductal coarctations
were common in young patients and rare in older
patients, whereas postductal coarctations were not
found in patients under 5 years of age, with one
exception. This finding is not reflected in the distinc-
tion that has been made in earlier days between
"infantile" and "adult" coarctation. The term
"infantile coarctation" does not distinguish between
tubular hypoplasia of the isthmus, localised preductal
coarctation, and a combination of both.

Our histological studies of serial sections disclosed
that, irrespective of the site, all coarctations had a
basically identical histological architecture—infolding
and thickening of the aortic media whereby the inner
part of the ridge consisted of ductal tissue.

Wielenga studied specimens of aortic coarctation
and found ductal tissue in the ridges of all spec-
imens. He postulated that the coarctation was formed
by traction of fibrously degenerated ductal tissue. No
preductal coarctation and only a few paradoctal coar-
tations were included in his study, which consisted
mainly of specimens from older patients. Only one
patient of less than 1 year of age and only two under 4
years were described. His theory explained how the
coarctation could develop at the site where it was
located, at the time the specimen was obtained (that is
in most cases postductally).

Ho and Anderson reported cases with coarctations,
most of them in combination with tubular hypoplasia.
A sling of ductal tissue, encircling the aortic isthmus,
was present in all cases. The coarctations in their
material were all located preductually, most probably
because all their patients were under 10 months of age.
Their hypothesis that the coarctation is caused by an
abnormal connection of the embryological fourth and
sixth left branchial arches (that is the isthmus enters
sideways into the ductus) and therefore develops preductually, seems attract-
tive. Yet, as far as we could judge from their pictures,
continuity between the elastic tissue of the isthmus
and that of the descending aorta was present, just as in
our material.

From our study and from other reports it is evi-
dent that young infants with a localised coarctation
almost always present with the preductal type. Our
hypothesis is that the coarctation is formed preduct-
tally in all cases. With advancing age, and altered flow
patterns after birth, the ridge can move gradually
towards ductal level, and eventually pass the ductus,
to become a postductal coarctation. Some authors
have already postulated from clinical observations
that this movement took place, and our histological
studies strongly support this.

Implications for pathophysiological experiments,
studying the effects of coarctation during fetal life, are
clear. Prenatally, experimental coarctations should be
created preductally to mimic the normal position of a
coarctation during fetal life. The value of some
reports concerning the development of the pulmo-

nary vasculature in the presence of a postductal
coarctation during fetal life is doubtful.

Apart from the shifting of the ridge from a predu-
tal position downwards into the descending aorta
with advancing age, another change occurs at the site
of the coarctation. A thick layer of intimal prolifer-
ation is formed on and distal to the ridge, leading to
progressive narrowing of the residual lumen. This
proliferation probably is the result of flow distur-

bances at the place of narrowing. Its contribution to
the eventual obstruction can be much more impres-
sive than the original ridge. Yet in all our specimens,
in contrast to some studies, the primary lesion,
consisting of aortic media and ductal tissue, could be
traced underneath this intimal proliferation.

Newborn infants with coarctation usually show no
clinical signs of aortic obstruction. Directly after birth
femoral pulsations are usually present. After a few
days or weeks these pulsations become weaker, and
signs of congestive heart failure may develop. Ductal
tissue in the ridge of a preductal coarctation might
contribute to aortic obstruction at the time of ductal
closure, especially when ductal intimal cushions are
present in the aorta. Intimal cushions in the aorta
have been reported but in our study they were found
in only two cases. Talner et al. postulated that flow
from the aortic isthmus can easily bypass the coar-
tation as long as the aortic end of the ductus is patent.
At the time of closure of the ductus at its aortic end,
Talner et al. suggest that an acute aortic obstruction
is created. This theory only holds if the coarctation is
located paradoctally, which, in our experience is rare
in a newborn infant. It therefore seems necessary to
find another explanation for the role ductal closure
plays in aggravating the clinical symptoms of a coar-
tation. The following theory might hold for several
coarctations.

Most infants with aortic coarctation have pulmo-
nary hypertension, sometimes up to systemic levels.
As long as the ductus is patent, pulmonary, instead of
aortic, pulsations can be felt in the femoral arteries.
At the time of ductal closure these pulsations disap-
ppear. The obstruction to aortic flow, located predu-
tally, is present at birth and may lead to some degree
of left heart failure. The raised left atrial pressure
gives rise to a left to right shunt through the foramen
ovale, thus leading to right ventricular volume over-
load. As long as the ductus is patent large pulmo-
nary flow is well tolerated because part of it can escape
through the ductus into the descending aorta. After
closure of the ductus massive pulmonary vascular
engorgement and signs of right heart failure become apparent.

It has been reported that prostaglandin E\(_1\) can relieve heart failure and re-establish femoral pulsations in infants with coarctation, as long as the ductus is not anatomically closed and is able to reopen.\(^{17,18}\)

The explanation given in these reports for this beneficial effect of prostaglandin E\(_1\), which is based on a paradoxic position of the coarctation, is not in keeping with our findings, as has been argued before. From our present theory it is also evident that prostaglandin E\(_1\) infusion, which dilutes the ductus, will help infants with coarctation. The reason is the same as in infants with aortic arch interruption.\(^{17}\) To evaluate further the true effect of prostaglandin E\(_1\) in infants with coarctation, both differential pressures and differential oxygen saturations between the upper and lower part of the body will have to be measured before and after prostaglandin E\(_1\) infusion.

It is very tempting to speculate about the exact aetiology of coarctation of the aorta. Our study, thus far, suggests that the explanation for the development of the coarctation must be sought with the coarctation in a preductal position. Abnormal fetal flow patterns and abnormal ductal tissue in the aortic arch must both be taken into consideration. The latter may be the result of the former, though a primary abnormality of ductal tissue still remains a possibility. Further studies of very young and fetal material will be necessary to answer this question.

References