Atypical Tetralogy of Fallot: A Noncyanotic Form with Increased Lung Vascularity
Report of Four Cases

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Only recently has the association of pulmonic stenosis with increased pulmonary blood flow been recognized. Four symptomatic infant cases are described in which the clinical diagnosis was large interventricular septal defect. Hemodynamic study showed the presence of associated pulmonic stenosis. Features suggesting that there is an overriding aorta in these patients, and that they, therefore, form an atypical group within the tetralogy of Fallot, are presented. The diagnosis has been confirmed in one case at autopsy. Their differentiation from clinically similar malformations as well as the surgical problems they pose is discussed.

Accurate diagnosis of cardiac malformations frequently requires special studies in any age group, but particularly is this so in young subjects. Nowhere is the fact better demonstrated than in a group of infants presenting with cardiorespiratory symptoms, a harsh systolic murmur and thrill over the lower precordium and pulmonary plethora.

The picture of a large, isolated ventricular septal defect in infancy has been well described. The malformation is characterized by failure to thrive, frequent respiratory infections, a harsh systolic murmur and a thrill over the lower left precordium, accentuated or obscured second pulmonic sound, cardiac enlargement with increased lung vascularity, combined ventricular hypertrophy in the electrocardiogram and often congestive heart failure.

While the clinical features and results of accessory investigations in the tetralogy of Fallot are now universally known, variations of the malformation in infancy have not been widely discussed. Although central cyanosis and normal heart size with clear lung fields are the chief diagnostic points in any age group, there are not infrequent exceptions to these criteria in the young baby. Taussig established that cyanosis may be delayed in its appearance in the infant case, a fact she attributes to patency of the ductus arteriosus. In our experience at the Toronto Hospital for Sick Children, one-third of the patients with this malformation were cyanotic at birth and a further one-third by six months of age. The remainder developed cyanosis at variable periods up to several years of age, a very few cases being clinically always acyanotic at rest. The cardiac murmur is usually systolic in time and in 75 per cent is maximal over the left lower precordium. While it is more difficult to be certain about splitting of the second basal sound in infants, it is unusual to detect other than a single sound in this region. Right ventricular hypertrophy in the electrocardiogram is the rule. Such abnormality may be recognized in even the very young infant. Rarely, left ventricular hypertrophy or combined ventricular hypertrophy has been recorded. Radiological findings vary. Some hearts certainly appear normal in size and shape, some have a slight pulmonary bay, but many bizarre contours and even enlarged hearts may be seen, especially in the first year. The association of a right aortic arch is suggestive but by no means conclusive evidence of the tetralogy, as it occurs in infants.

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with other cyanotic defects such as truncus arteriosus and tricuspid atresia.\textsuperscript{15, 19} Whereas in the older child with tetralogy, the lung vascular markings are reduced, they more often appear normal in infants. Usually the only occasions where markedly increased vascular markings will be seen in this malformation are in some cases with increased collateral flow to the lungs via enlarged bronchial arteries\textsuperscript{20} or in cases of unilateral pulmonary artery atresia.\textsuperscript{21, 22}

In both these variants the patient is most often obviously cyanotic and the full development of the former type is uncommon in infancy. In infants, then, though a case of tetrad may be noncyanotic clinically and have a cardiac murmur suggestive of ventricular septal defect, marked increase in lung vascularity in association with obvious congenital heart disease has been regarded as sufficient to exclude this malformation.

Nevertheless, it has been recently recognized that pulmonary stenosis may be associated with increased pulmonary blood flow.\textsuperscript{23-31} This occurs when, for example, pulmonary stenosis with normal aortic root is complicated by ventricular septal defect.\textsuperscript{24, 26-28, 20, 31} From the latter reports emerges the clinical picture of a noncyanotic older child or adult, free of any cardiac or respiratory symptoms, with a harsh systolic murmur in the lower precordium accompanied by a thrill. The second basal heart sound may be single or split. X-ray films reveal slight, if any, cardiac enlargement, a pulmonary artery segment bulge and slight pulmonary plethora. The electrocardiogram, though sometimes normal, more often reveals moderate right ventricular hypertrophy or incomplete right bundle branch block. Physiologic studies show moderate pulmonic stenosis frequently, but not necessarily, systemic systolic pressure levels in the right ventricle, a moderate-volume left-to-right interventricular shunt and only rarely any venoarterial shunt with exercise.

Recently we have encountered four noncyanotic infants with the clinical features of a large ventricular septal defect in whom further studies suggested the diagnosis, of tetralogy of Fallot of an atypical type.

Case Reports

Case 1. J. M., a 6-month old white male, was found to have a heart murmur soon after a normal

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure1.png}
\caption{Case 1. Six foot film of chest showing cardiac enlargement, right aortic arch and increased lung vascularity.}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure2.png}
\caption{Case 1. Electrocardiogram. Normal electrical axis, left auricular hypertrophy and combined ventricular hypertrophy. The voltage of R in the left precordial leads suggest that the left ventricle is more hypertrophied than the right.}
\end{figure}
ATYPICAL TETRALOGY OF FALLOT

Table 1.—Results of Cardiac Catheterization

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>VC</th>
<th>RA</th>
<th>RV</th>
<th>PA</th>
<th>SA</th>
<th>RA</th>
<th>RV</th>
<th>PA</th>
<th>SA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 J. M.</td>
<td>6 mos.</td>
<td>60†</td>
<td>53</td>
<td>86</td>
<td>NK</td>
<td>93†</td>
<td>3</td>
<td>75/5</td>
<td>25/10</td>
<td>75/40†</td>
</tr>
<tr>
<td>2 A. S.</td>
<td>7 mos.</td>
<td>58*</td>
<td>70</td>
<td>88</td>
<td>77</td>
<td>93</td>
<td>7</td>
<td>100/5</td>
<td>10/-5</td>
<td>95/70</td>
</tr>
<tr>
<td>3 S. K.</td>
<td>4 mos.</td>
<td>42*</td>
<td>47</td>
<td>75</td>
<td>77</td>
<td>94.5†</td>
<td>5</td>
<td>95/5</td>
<td>20/5</td>
<td>90/75†</td>
</tr>
<tr>
<td>4 M. F.</td>
<td>30 mos.</td>
<td>68†</td>
<td>61</td>
<td>86</td>
<td>88</td>
<td>97.5†</td>
<td>5</td>
<td>75/10</td>
<td>35/15</td>
<td>75/50†</td>
</tr>
</tbody>
</table>

* Superior vena cava.
† Inferior vena cava.

Birth. He failed to gain well and suffered from frequent respiratory infections. Cyanosis had not been noted. The physical examination revealed a thin, noncyanotic infant weighing 131/2 pounds. There was no evidence of heart failure, although the respiratory rate was increased. A grade V tearing systolic murmur was heard maximally at the fourth left intercostal space and accompanied by a systolic thrill. The second pulmonic sound was accentuated and split. The blood pressure was 100/55.

The cardiothoracic ratio (CTR) by roentgenogram (fig. 1) was 0.60. Fluoroscopy showed a rather straight left border to the heart and a right aortic arch. The lung vasculature was markedly increased and slight intrinsic pulsations were visible. Enlargement of the left auricle was evident on examination with barium.

The electrocardiogram (fig. 2) had an axis of QRS of about +75 degrees. Left auricular and combined ventricular hypertrophy were present.

Cardiac catheterization was performed on Feb. 2, 1954 (table 1). The cardiac catheter was passed readily from the right ventricle into both the ascending aorta and the main and right pulmonary arteries. A tracing recorded during withdrawal from the pulmonary artery to the right ventricle showed valvular pulmonic stenosis. The arterial oxygen saturation estimated by ear oximetry was 98 per cent at rest with no change on crying.

A venous angiogram (fig. 3) showed normal size and position of the pulmonary artery. No clear cut evidence of pulmonic stenosis was shown by this examination. The aorta opacified normally from the left ventricle in the late films.

Case 2. A. S., a 7-month old white male, was found to have a heart murmur at birth. Frequent respiratory infections with dyspnea and stridor had been a problem. Cyanosis had not been noted. The physical examination revealed a thin, noncyanotic infant weighing 111/2 pounds. There was no evidence of heart failure but a rapid respiratory rate and moderate stridor were present. A grade V systolic murmur with thrill was located maximally at the fourth left intercostal space. The second pulmonic sound was reduced and single. The blood pressure was 100/70.

The cardiothoracic ratio by roentgenogram was 0.57. Fluoroscopy showed no distinct pulmonary artery bulge and a left aortic arch. The lung vasculature was increased and minimal intrinsic pulsations were visible in the right lung. Left auricular size was normal as judged by barium swallow.

The electrocardiogram had an axis of QRS of about +75 degrees. There was evidence of combined ventricular hypertrophy.

Cardiac catheterization was performed on May 7, 1954 (table 1). The cardiac catheter was passed into the right pulmonary artery and a withdrawal pressure from this vessel to the right ventricle showed a combined valvular and infundibular

![Fig. 3. Case 1. Venous angiogram. Anteroposterior film at 0.4 second following injection of contrast material. There is good filling of normal size pulmonary arteries, absence of clear cut evidence of pulmonic stenosis and no evidence of aortic filling. Later films showed a large left atrium and an aorta filling from the left heart.](http://circ.ahajournals.org/)}
stenosis to be present. The aorta was not entered from the right ventricle. The arterial oxygen saturation, estimated by ear oxymetry, was 93 per cent at rest and 95 per cent with crying.

Angiocardiography was not performed in this patient.

Case 3. S. K., a 4-month old white female, was said to have been cyanosed briefly at birth when a heart defect was recognized. Because of frequent respiratory tract infections and failure to thrive, she was referred for further investigation of her malformation. The physical examination revealed a markedly dystrophic, non-cyanotic infant weighing 8½ pounds. There was no evidence of heart failure but the respiratory rate was increased at rest. A coarse, to and fro murmur was audible in the pulmonic area. A systolic thrill was palpable in the third left intercostal space. The second pulmonic sound was accentuated and splitting was not detected. The blood pressure was 90/75.

The CTR by roentgenogram (fig. 4) was 0.56. Fluoroscopy showed an elevated apex and a full left middle arc. A small left sided aortic arch was visible on barium swallow. The lung vasculature consisted in the right hilus of a dense pulsating mass, but the left sided vascularity was obscured by the cardiac shadow. The left auricle was not notably enlarged on barium swallow.

The electrocardiogram (fig. 5) showed an axis of QRS of +120 degrees. In the right precordial leads marked right ventricular hypertrophy with added right auricular dilatation was evident from the QR pattern present. The presence of Q waves in the left chest leads in the presence of right ventricular hypertrophy was considered to be evidence of associated left sided hypertrophy.

Cardiac catheterization was performed on April 27, 1954 (table 1). The cardiac catheter was passed both medially into the ascending aorta and from the outflow tract of the right ventricle into the main

![Fig. 4. Case 3. Six foot film of chest showing slight cardiac enlargement with increased lung vascularity, particularly noticeable on the right.](image)

...
pulmonary artery. A withdrawal pressure tracing from the latter vessel demonstrated valvular pulmonic stenosis. A dye dilution curve from the right ventricle failed to show evidence of right-to-left shunt and was consistent with the large volume left to right shunt. The arterial oxygen saturation, estimated by ear oximetry, was 97 per cent at rest and on crying.

A venous angiogram (fig. 6) revealed valvular pulmonic stenosis, an aneurysmal trunk and right main branch of the pulmonary artery with an apparently hypoplastic left branch. A hypoplastic aorta opacified in the late films.

This infant suffered repeated pulmonary infections over the next nine months and died from bronchopneumonia at 13 months of age. At autopsy (fig. 7), the heart weighed 95 Gm. The systemic and pulmonary venous connections were normal. The aorta was dextroposed, arising approximately 50 per cent from each ventricle. The internal circumference of the ascending and descending aorta was 32 mm. and 19 mm., respectively. The aortic arch and descending aorta lay on the left side of the spine. The pulmonary artery arose normally from the right ventricle and externally there was an obvious constriction at the pulmonic ring. The internal circumference of this ring was 20 mm. The main trunk was a short, narrow vessel giving rise to the main branches. These were of aneurysmal dimensions, the internal circumference of the left branch being 50 mm. and the right 70 mm. These aneurysmal branches ended bluntly at the hilus. Very small vessels, approximately 4 mm. in diameter, entered the lungs as offshoots of the main branches. Two slightly prominent ridges, crescentic in shape, with the concavity directed upwards, marked the expected site of the pulmonary valve. There were no cusps as such, numerous irregular nodules being present in their place. These rudimentary structures left the valve ring unguarded. The aortic, mitral and tricuspid valves were normally formed. The ductus arteriosus and foramen ovale were closed. The left auricle was markedly dilated, being three times larger than the right. The right ventricle was thick walled (8 mm.) and there was no evidence of infundibular stenosis. On the contrary, the outflow tract of this chamber was very large. The left ventricle was capacious, being twice as large as the right but was not thick walled (5 mm.). The ventricular septal defect measured 13 by 7 mm.

Case 4. M. F., a 2½ year old white female, was discovered to have a cardiac defect at 6 months of age when examined during a respiratory infection.
She failed to thrive and became dyspneic after effort from the age of 14 months. Physical examination revealed a thin, non-cyanotic infant weighing 21 pounds. There was no evidence of heart failure and no dyspnea at rest. A harsh grade V systolic murmur, maximal over the fourth and fifth left intercostal spaces, was accompanied by a thrill in this position. The second pulmonic sound was accentuated and closely split. The blood pressure was 110/80.

The cardiothoracic ratio by roentgenogram was 0.65. Fluoroscopy showed a moderate pulmonary artery bulge and a left aortic arch. The lung vasculature was markedly increased and pulsating. Enlargement of the left auricle was detected on barium examination.

The electrocardiogram showed an axis of QRS of ±0 degrees. Combined ventricular hypertrophy was present.

Cardiac catheterization was performed on Sept. 8, 1954 (table 1). The cardiac catheter was passed from the right ventricle both medially into the ascending aorta and via the outflow tract to the right pulmonary artery. A withdrawal tracing from the latter vessel to the right ventricle showed an infundibular stenosis, the pressure in the infundibular chamber being 35/5. A selective ether test from the right ventricle was inconclusive with 0.2 cc and positive with 0.3 cc of ether. The arterial oxygen saturation, estimated by ear oximetry, was 95 per cent at rest and on crying.

A selective angiocardogram from the right ventricle revealed a distinct infundibular stenosis and large, well filled pulmonary arteries with a normal pulmonic valve. The left auricle was enlarged in the late plates, while the aorta filled normally from the left ventricle.

**Discussion**

These four cases are strikingly similar. All young, noncyanotic infants, they have been plagued with lower respiratory infections from birth; seemingly their major handicap. Failure to thrive is a feature, all being dystrophic at the time of the study. The systolic murmur is localized to the left lower sternal border in three cases, a thrill being palpable at this site in all four patients. Splitting of the second sound in the pulmonic area is present in two cases. There is no evidence of heart failure, although an increased respiratory rate suggested increased pulmonary blood flow. Roentgenographically there is slight to moderate cardiac enlargement, marked pulmonary plethora in all four and a right aortic arch in one case. The electrocardiograms showed a normal axis in two instances and combined ventricular hypertrophy in all. From a clinical viewpoint all four might well be accepted as cases of ventricular septal defect of generous size. The only suspicion that this would not be the sole abnormality was the presence in case 1 of a right aortic arch, Keith having found only one instance of this association in 400 cases of ventricular septal defect.

Cardiac catheterization showed pulmonic stenosis, systemic systolic pressure levels in the right ventricle and a large left-to-right interventricular shunt. Although the aorta was entered from the right ventricle in three instances, the arterial oxygen saturation was normal in all cases and in only one case, where a positive selective ether test was obtained from the right ventricle, was there any evidence of right-to-left shunt. Outputs and flows were not determined, but it is almost certain that pulmonary blood flow is much increased in all patients. The systolic pressure gradient between the right ventricle and pulmonary artery ranges from 40 to 90 mm Hg in these cases. This is a distinctly greater difference than in the so-called "relative" stenosis sometimes present in isolated septal defects. It also exceeds the difference encountered by Rudolph and coworkers2 in a case of atrioventricular communis exhibiting a pressure gradient during life but with no organic pulmonic stenosis at autopsy. We therefore feel that our cases may fairly be classed as organic stenoses and that the presence of isolated interventricular communication is excluded.

Angiocardiograms in three instances showed normal sized or enlarged pulmonary arteries, considerable dilution of the contrast medium in the right ventricle in one case, and aortic filling in all at least a full second after pulmonary artery opacification. In only two cases (3 and 4) was the site of pulmonary stenosis well demonstrated by this method. Moreover, by angiocardiography nongenotic forms of basically cyanotic malformations such as a single ventricle with large pulmonary arteries or even complete transposition of great vessels were excluded.

A ventricular septal defect with pulmonic stenosis is not in doubt. The question remaining
is whether the aortic root is normally placed or overrides the septum. Moffitt,37 Campbell38 and Selz39 have raised this problem in the discussion of several of their cases of pulmonary stenosis with ventricular septal defect. Selzer's studies32-33 into the size of isolated ventricular septal defects and their relationship to anatomical aortic overriding have shown how difficult it may be pathologically as well as clinically to differentiate this very point.

The equality of systolic pressures in the right ventricle and systemic circuit favors aortic override although there are admitted fallacies to this interpretation. Probing of the aorta from the left ventricle after passage of the catheter tip through a simple ventricular septal defect is possible, but in infants at least it is much more common to enter the aorta from the right ventricle through an anatomical override. One older case where the aorta was thought to have been probed via the left ventricle41 eventually was proven to have the tetrad at autopsy. The site of pulmonary stenosis is, in our opinion, of no real assistance in separating the two malformations. In one of our cases,* the association of right aortic arch favors tetralogy of Fallot. It is generally agreed that the combination occurs in about 25 per cent of all cases of the tetrad, whereas in simple pulmonary stenosis with normal aortic root, right aortic arch is extremely rare. Campbell38 detected only one instance in his 75 cases. We have not found a right aortic arch in 100 cases and, to our knowledge, there has been no report of an autopsy-proven case.

Bouchard and Cornu42 have recently demonstrated in cases of pulmonary stenosis a characteristic appearance of the right ventricular pressure pulse similar to that previously noted under experimental conditions by Fineberg and Wiggers.33 In simple pulmonary stenosis of all grades of severity there is a delayed ascent during the period of isometric contraction, an absence of the ejection phase plateau and a delayed fall in pressure giving a symmetrical pointed tracing which differs strikingly from a left ventricular curve in the same patient. On the other hand, in tetralogy of Fallot the form of the right ventricular pressure curve is normal and identical with that obtained from the left ventricle. In two of our patients (cases 1 and 4), where the undamped right ventricular pressure curve recorded at fast chart, speed can be studied in detail, the form taken is normal. This suggests that an anatomical override is present in these cases. Records of the right ventricular pressure in two other personal cases of pulmonary stenosis with ventricular septal defect show that the addition of ventricular septal defect to pulmonary stenosis with normal aortic root need not affect the characteristic ventricular pressure curve found in the isolated condition.

In one patient (case 3) the diagnosis of tetralogy of Fallot made after cardiac catheterization was proven correct at a subsequent autopsy. The degree of aortic override was considerable and little different from the classical case of the malformation. The atypical anatomical features confined to the pulmonary artery were the aneurysmal size of its main branches, the constricted pulmonary root and the rudimentary pulmonic valve. The latter obviously permitted pulmonary regurgitation (suspected in life by the diastolic murmur in the pulmonary area), in addition to the obstructive element resulting from the narrow pulmonic ring. From the clinical findings it seems unlikely that pulmonary insufficiency is present in the other three patients.

If the remainder are in fact variants of the tetralogy of Fallot, they probably have only moderate pulmonic stenosis and this likely constitutes the significant deviation from the more usual form of the malformation. While in one the diagnosis has been established, the remainder await pathological confirmation.

* Two further cases not included in this analysis have been encountered with the same clinical picture in whom investigations are incomplete. These are both dystrophic, noncyanotic infants under 1 year of age with harsh systolic murmurs in the fourth left intercostal space accompanied by a thrill, slightly split second basal sound, absence of congestive failure, moderate cardiac enlargement, increased lung vascularity, right aortic arch, combined ventricular hypertrophy in the electrocardiogram and normal arterial oxygen saturation by oximetry at rest and crying. One has been denied further study. The other had cardiac catheterization which shows the same hemodynamic features as the four cases in table 1. The aorta was probed from the right ventricle but the pulmonary artery could not be entered. A venous angiogram is suggestive but not conclusive of valvular pulmonic stenosis.
Apart from academic distinctions, they present a practical problem in several ways. It seems unlikely that these infants will follow the benign course described in pulmonic stenosis with normal aortic root and ventricular septal defect. Follow-up is limited to between 6 and 14 months in our cases. Case 3 died of bronchopneumonia at 13 months, weighing 10½ pounds, after prolonged hospitalization from almost continual lower respiratory infections. Cases 1 and 2 have continued to have frequent attacks of pneumonia requiring hospitalization, despite attempts at prophylactic chemotherapy in one instance. Only case 4 has remained well in the interval. Whatever the true anatomy, these infants at the moment behave more like cases with large isolated ventricular septal defect than pulmonary stenosis. Accordingly the main medical problem is one of treating the recurrent episodes of pulmonary infection and endeavouring to support the infants through the obviously critical first years in the hope that ultimately surgery may relieve them. Sell and coworkers36 have described a similar clinical picture resulting after surgical correction of pulmonic stenosis in very mild cases of tetralogy of Fallot. Anastomotic procedures would therefore seem contraindicated and valvotomy or infundibulectomy at this stage unwise because of the removal of a relative safeguard to pulmonary vasculature. More hopeful might be the closure of the ventricular defect under direct vision combined with valvotomy or infundibulectomy.57

SUMMARY

Four infants apparently suffering from large isolated ventricular septal defects are presented in detail.

Accessory investigations showed that these infants have moderate pulmonic stenosis, a large ventricular left-to-right shunt, right ventricular hypertension equaling systemic systolic level and normal arterial oxygen saturation both at rest and with exercise.

It is suggested that these infants may be variants of the tetralogy of Fallot on the basis of the above findings, catheter entry into the aorta from the right ventricle, the contour of the right ventricular pressure pulse in two cases, and the association in one patient of a right aortic arch. In one infant the diagnosis was confirmed at necropsy, nine months after hemodynamic study.

The clinical resemblance in infancy of these cases, large isolated ventricular septal defects and pulmonic stenosis with normal aortic root plus ventricular septal defect is emphasized.

The available surgical procedures for the relief of the tetralogy of Fallot are not indicated in these cases. In the development of therapy for these children primary emphasis should be placed on the correction of the ventricular septal defect.

SUMMARIO IN INTERLINGUA

Es presentate un deliaile reporto del casos de 4 infantes qui apparentemente suffre de large isolate defectos septal ventricular.

Investigationes accessori demonstrava que iste infantes ha moderate grades de stenosis pulmonar, un large derivation ventricular ab le sinistra verso le dextera, hypertension dexteroventricular equal al nivello systolic in le circulation major, e normal saturation oxygenic in le arterias tanto in reposo como etiam post exercitio.

Super le base del supra-mentionate constatazione nos concludeva che il se tracta hic de variantes del tetralogia de Fallot. Iste interpretation se trovava supportate per catheterisation del aorta via le ventriculo dextere, per le contorno specific del pulso pressional ventricular que esseva observate in 2 casos, e per le co-presentia in un caso de un arco dextero-aortic. Confirmation necropsie del diagnose esseva obtenite in un caso, 9 menses post le studio hemodynamic.

Nos sublinea le similaritate clinic de iste casos in le stadio infantil con le manifestaciones de large isolate defectos septal ventricular e de stenosis pulmonar con normal radice aortic plus defecto septal ventricular.

Le application del methodos chirurgie que es normalmente disponibile pro le allevamento de tetralogia de Fallot non es indicate in casos del genere hic descriti. In le elaboration del terapia pro tal pacientes infantil on debe preoccupar se de corriger le defecto septal ventricular.

REFERENCES

Atypical Tetralogy of Fallot: A Noncyanotic Form with Increased Lung Vascularity: Report of Four Cases
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