Late Sudden Death After Repair of Tetralogy of Fallot: A Clinicopathologic Study


SUMMARY  Retrospective analysis was performed to determine the likely cause of death in six patients who died suddenly 1-9 years after repair of tetralogy of Fallot. The integrity of the atrioventricular conduction system and myocardium was examined in three hearts at necropsy. Two of three patients who complained of palpitation or syncope had frequent premature ventricular complexes on routine ECGs. All the patients had complete right bundle branch block and one had left-axis deviation after repair. Postoperative cardiac catheterization (four patients) showed no residual ventricular septal defects, but right ventricular pressure was elevated in all.

At necropsy, the atrioventricular conduction tissue was related to the margin of perimembranous ventricular septal defect in two patients, but was well posterior in one patient with an infundibular muscular defect. Histologic examination showed that in all cases the atrioventricular node, atrioventricular bundle and left bundle branch were undamaged. There was, however, extensive fibrosis of the right ventricular myocardium in the ventriculotomy site (three patients), septum (one patient) and outflow tract (one patient).

These clinical and necropsy findings suggest that ventricular arrhythmia rather than atrioventricular block was responsible for sudden death in these patients after repair of tetralogy of Fallot.

SUDDEN DEATH is a recognized late event after repair of tetralogy of Fallot, with a reported incidence of as high as 4.6%. These deaths are assumed to be due to cardiac arrhythmia, but the precise mechanism is controversial. Attention was focused initially on the possibility of late complete atrioventricular block from progressive damage to the proximal conduction system. This concept arose when the electrocardiographic pattern of right bundle branch block and left-axis deviation was found in a proportion of patients after intracardiac repair. A poor prognosis was reported for patients with these conduction defects, but has not been confirmed by others. Recently, a high incidence of ventricular arrhythmia has been demonstrated after radical correction, and has been associated with sudden death in retrospective series. Despite this controversy regarding the mechanism for sudden death, there have been no pathologic studies of the conduction system in patients who died suddenly after repair of tetralogy of Fallot. We therefore examined the integrity of the conduction system and myocardium in necropsy specimens from such patients to ascertain the anatomic correlates related to sudden death.
Materials and Methods

Patients

We studied six patients who died suddenly and unexpectedly during follow-up at the Hammersmith Hospital after intracardiac repair of tetralogy of Fallot between 1961 and 1973. These deaths occurred 1–9 years (median 5 years) after corrective surgery, when the patients were 13–25 years of age. Three other patients in our previously reported series3 of 196 consecutive patients who underwent repair during this period died suddenly, an overall incidence of 4.5% (nine patients), but adequate documentation of the precise circumstances of their death is not available.

Intracardiac repair was performed between 1961 and 1973. The ventricular septal defect was closed through a transverse right ventriculotomy with a “Teflon felt” patch faced with pericardium on the left ventricular aspect. The defect was of the typical outlet malalignment type in all. In five patients, it extended to become perimembranous, whereas in the other a muscular inferior rim was interposed between the edge of the defect and the central fibrous body. Direct infundibular resection was performed in all six patients and was augmented in one case by a gusset. Five patients had an additional pulmonary valvotomy. The clinical and follow-up electrocardiographic details of the patients are summarized in table 1.

Clinical Status

None of the patients had limitation of exercise tolerance and three were asymptomatic. Patient 6 complained of syncope, patient 5 of rapid palpitation and patient 2 of palpitation and syncope. The circumstances of death were known in all cases. Only in patient 3 could death be linked to strenuous physical exercise; he died after refereeing a soccer match. The other patients died at rest or during mild exertion (walking at normal pace).

ECG

After operation, all patients had complete right bundle branch block (QRS duration greater than 120 msec in the right precordial leads) and one developed additional left-axis deviation (mean frontal QRS axis of −30°). Neither serious ventricular arrhythmia nor transient atrioventricular block was documented in the immediate postoperative period.

During follow-up, both patients who complained of syncope had multif orm premature ventricular complexes on routine 12-lead ECGs. Neither patient developed arrhythmia during maximal treadmill exercise testing. Ambulatory electrocardiographic monitoring was not performed. No other serious arrhythmias were detected, and no patient had evidence of atrioventricular block.

Hemodynamic State

Cardiac catheterization was performed in four patients 1–8 years after repair (table 2). All four patients had a residual right ventricular outflow gradient and right ventricular systolic pressures of 50–100 mm Hg. Right ventricular end-diastolic pressures were not elevated. In none of the cases was there pulmonary hypertension or a detectable ventricular septal defect.

Necropsy specimens were available from three of the six patients and form the basis of the pathologic study. The gross morphology, the disposition and integrity of the conduction tissue and myocardial histology from the right and left ventricles were studied in the three hearts. We have used the terminology of Anderson and colleagues12 to describe the ventricular septal defect.

Conduction Tissue

Histologic examination of the atrioventricular conduction tissue was performed by removing the tissue block surrounding the central fibrous body, including the thickness of the ventricular septum. This block was processed using a prolonged paraffin wax method and sectioned at 10-μ intervals at right angles to the septum and to the plane of attachment of the tricuspid valve, as previously described.13 One section in 25 was mounted and examined; intervening sections in areas of interest were also studied. Particular attention was paid to the margin of the ventricular septal defect and to the position of the surgical sutures. Additional tissue blocks were removed from the distal interventricular septum and sectioned for examination of the distal ramifications of the bundle branches.

TABLE 1. Clinical and Electrocardiographic Findings

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age at repair (years)</th>
<th>Age at death (years)</th>
<th>Postoperative ECG</th>
<th>Arrhythmia</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1*</td>
<td>11</td>
<td>13</td>
<td>RBBB</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2*</td>
<td>8</td>
<td>17</td>
<td>RBBB</td>
<td>VPCs</td>
<td>Palpitation, syncope</td>
</tr>
<tr>
<td>3*</td>
<td>16</td>
<td>25</td>
<td>RBBB</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>11</td>
<td>12</td>
<td>RBBB</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>13</td>
<td>20</td>
<td>RBBB</td>
<td>0</td>
<td>Palpitation</td>
</tr>
<tr>
<td>6</td>
<td>14</td>
<td>19</td>
<td>RBBB + LAD</td>
<td>VPCs</td>
<td>Syncope</td>
</tr>
</tbody>
</table>

*Hearts studied at necropsy.

Abbreviations: RBBB = right bundle branch block; LAD = left-axis deviation; VPC = ventricular premature complex.

TABLE 2. Cardiac Catheterization Findings during Follow-up

<table>
<thead>
<tr>
<th>Pt</th>
<th>Interval after repair (years)</th>
<th>PA pressure (mm Hg)</th>
<th>RV pressure (mm Hg)</th>
<th>SA pressure (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>6</td>
<td>NE*</td>
<td>50/4</td>
<td>120/80</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>24/14</td>
<td>75/5</td>
<td>130/80</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>27/12</td>
<td>60/8</td>
<td>100/65</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
<td>17/8</td>
<td>100/6</td>
<td>135/75</td>
</tr>
</tbody>
</table>

*Ventricular tachycardia developed with catheter in the right ventricle and, after resuscitation, the procedure was abandoned without entering the pulmonary artery.

Abbreviations: NE = not entered; PA = pulmonary artery; RV = right ventricle; SA = systemic artery.
Myocardium

Tissue blocks were removed from the right ventricular free wall at the apex, the ventriculotomy site, the parietal wall of the subpulmonary infundibulum and the left ventricular wall. Sections from these sites were stained to demonstrate fibrous tissue and collagen.

Results

Morphology

In the hearts of cases 1 and 2, there was a perimembranous ventricular septal defect. In the heart of case 3, the defect had a muscular inferior rim (infundibular muscular defect) and the membranous septum itself was intact. In all three, the septal defect was closed and the patch well endothelialized. In cases 2 and 3, the right ventricular outflow tract was not severely narrowed and the areas of surgical resection were no longer evident. In case 1, however, there was an extensive stenotic area between the inlet and outlet components of the right ventricle, which was a consequence of gross hypertrophy of the body of the trabecula septomarginalis (fig. 1). In all three hearts, the area of the ventriculotomy was replaced by obvious fibrous tissue. Otherwise, the ventricular myocardium was not abnormal as judged by macroscopic examination. In none of the hearts was there any major anomaly of the coronary arteries.

Conduction Tissue

In all three hearts, the atrioventricular node was identified, as expected, as the apex of the triangle of Koch. No abnormalities were observed within the node. The penetrating bundle passed through the central fibrous body at the apex of the triangle. In one heart with a perimembranous defect (case 1), the non-branched bundle then descended the left ventricular aspect of the septum, well posterior to the margin of the defect. The bundle branched below the crest of the defect and was free of sutures placed on the right ventricular aspect of the septum. The right bundle branch penetrated the septum and then disappeared into an area of fibrosis on the right side of the septum. In the other heart with a perimembranous defect (case 2), the branching atrioventricular bundle was astride the free edge of the interventricular septum (fig. 2). However, both the nonbranching and branching bundles were well clear of the sutures and were histologically normal. The right bundle branch was directly subendocardial and descended into the fibrous tissue produced by stitches securing the patch. In the heart (case 3) with a complete muscular inferior rim to the septal defect, the conduction tissue was distal (i.e., markedly posterior) to the edge of the defect. The right bundle branch could not be traced beyond its proximal part in this heart. In all three hearts, the left bundle branch was identified and was histologically intact (fig. 3).

Myocardium

Fibrosis was present, to a varying degree, in the different right ventricular sites examined in all three hearts (table 3). In each case, the right ventriculotomy site was extensively replaced by fibrous tissue (fig. 4). In case 1, the entire right side of the ventricular septal
FIGURE 3. The normal left bundle branch fibers (arrows) from cases 2 and 3.

crest, in the area of attachment of the patch, was replaced by fibrous tissue. As described, the right bundle branch passed through this area. In case 2, the entire infundibulum was thinned and largely replaced by fibrous tissue (fig. 5). In none of the hearts was the left ventricular myocardium markedly fibrotic.

Discussion

Two mechanisms have been suggested for sudden death, which may occur years after repair of tetralogy of Fallot: late-onset complete atrioventricular block4 5 14 15 and ventricular fibrillation.1"3

Conduction defects are extremely common after operation. Right bundle branch block occurs in the majority of patients and may occur in combination with left-axis deviation.4 Wolff et al.5 reported a high incidence of late atrioventricular block and sudden death in patients with this “bifascicular block pattern,” thought to represent central damage to the conduction system.5 Subsequent studies, however, have failed to confirm a worse prognosis for patients with these conduction defects.3 6-8 Others have suggested that transient perioperative complete atrioventricular block may be an ominous sign, predicting patients at risk from late sudden death.14,15 In our experience, late sudden death was not associated more frequently with either postoperative left-axis deviation or transient perioperative atrioventricular block.3

Although the disposition of the conduction system

| TABLE 3. Distribution of Myocardial Fibrosis |
|-------------------|-------------------|-------------------|-------------------|
| Right ventricle   | Left ventricle    |
| Pt                | Ventriculotomy    | Septum           | Outflow          | Free wall | Free wall |
| Pt  | site          |         |                 |         |         |
| 1   | + + +         | + + +    | +               | + +       | 0         |
| 2   | + + +         | +        | + + +           | +        | 0         |
| 3   | + + +         | +        | +               | + +       | 0         |

Abbreviations: + = mild fibrosis; ++ = moderate fibrosis; +++ = severe fibrosis; 0 = normal.

FIGURE 4. Replacement of the myocardium by fibrous tissue at the site of ventriculotomy in case 3.

FIGURE 5. Fibrosis of infundibular musculature in case 2.
in tetralogy of Fallot has been well described, the state of the conduction system in patients who have died suddenly after intracardiac repair has not previously been studied. Pathologic examination revealed that the proximal conduction tissue was intact, even in the two hearts with perimembranous ventricular septal defects in which the conduction system was theoretically vulnerable to surgical damage (fig. 6A). In the third heart, the conduction tissue was distant from the margin of the infundibular muscular defect and therefore not at risk (fig. 6B). We cannot locate the precise anatomic lesion or lesions responsible for the right bundle branch block in all three cases. In patients 1 and 3, damage probably occurred as the right bundle branch ran down the right side of the septum through an area of fibrosis. We can, however, exclude a surgical lesion of the more proximal conduction tissue and thus have good evidence that atrioventricular block was not the cause of death in any of these three patients.

It is much more likely that sudden death results from ventricular arrhythmia. Two of our six patients complained of rapid palpitation, and frequent multiformal ventricular extrasystoles were noted on routine follow-up ECGs in two. Such ventricular extrasystoles have been linked with sudden death in several retrospective studies. Myocardial fibrosis, as found in this study, has been observed in patients who died suddenly after intracardiac repair. It is easy to envisage how ventricular arrhythmia might originate in the presence of fibrosis of the right ventricular myocardium, with localized slowing of conduction favoring the development of reentry circuits. This concept is supported by observations of sustained ventricular tachycardia originating from reentry circuits in the right ventricular outflow tract in four postoperative patients.

There has been much recent work aimed at the identification of predisposing factors for these ventricular arrhythmias. Exercise may aggravate ventricular arrhythmia, but in our series only one death followed physical exertion. Garson et al. suggested that a poor surgical result with residual elevation of right ventricular pressure and poor postoperative right ventricular function are associated with ventricular arrhythmia and sudden death. We can only speculate how much the myocardial fibrosis, demonstrated in this study, is part of the natural history of the uncorrected heart with tetralogy of Fallot and how much is related to the operation and postoperative hemodynamic status. Three of the four patients in our series who underwent postoperative cardiac catheterization had elevated right ventricular systolic pressures greater than 60 mm Hg. However, serious ventricular arrhythmia, including ventricular tachycardia, is not invariably associated with a poor hemodynamic result.

This study provides necropsy evidence that sudden death in our patients after correction of tetralogy of Fallot was not due to atrioventricular block. The clinical findings and the presence of severe right ventricular fibrosis favor the hypothesis that death resulted from ventricular arrhythmia. Studies to define the predisposing factors for such arrhythmias and to determine whether treatment can prevent late sudden death are needed.

References
Late sudden death after repair of tetralogy of Fallot: a clinicopathologic study.
J E Deanfield, S Y Ho, R H Anderson, W J McKenna, S P Allwork and K A Hallidie-Smith

Circulation. 1983;67:626-631
doi: 10.1161/01.CIR.67.3.626

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1983 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/67/3/626