Aortic regurgitation from infective endocarditis in Fallot’s tetralogy and pulmonary atresia

Richard Emanuel, Jane Somerville, S. Prusty, and Donald N. Ross
From the National Heart Hospital, and Institute of Cardiology, London

Three cases of aortic regurgitation acquired as the result of bacterial endocarditis complicating Fallot’s tetralogy and pulmonary atresia have been described. One also had mitral regurgitation from a ‘jet lesion’ of the anterior cusp of the mitral valve. Surgical treatment of all abnormalities with aortic valve repair or replacement was undertaken in each patient and was successful in two. Difficulties in diagnosis and surgical treatment are discussed.

The association of serious acquired valve disease from infective endocarditis in Fallot’s tetralogy and pulmonary atresia may cause difficulties in diagnosis and treatment. It appears to be an uncommon problem for only two patients with this combination have been reported (Peters, 1971; Maramba et al., 1971). The following account is concerned with 3 patients, 2 with Fallot’s tetralogy and 1 with complex pulmonary atresia. All had infective endocarditis which caused severe aortic regurgitation requiring surgical treatment. In one there was a secondary ‘jet lesion’ (Gonzalez-Lavin, Lise, and Ross, 1970) of the mitral valve which also needed correction.

Case reports

Case 1
A 38-year-old man, known to have been cyanosed since infancy with a history of effort dyspnoea and squatting in childhood, was admitted for investigation to the National Heart Hospital in 1962. He had been relatively well, with mild cyanosis, until age 29 (1953) when he was treated for infective endocarditis at the Royal Cornwall Infirmary.

In 1962 he was cyanosed and clubbed (Hb 19.9 g/dl), with a long systolic ejection murmur, a single second sound, a continuous murmur in the left subclavicular area, and a loud separate immediate diastolic murmur at the left sternal edge, blood pressure 150/65 mmHg (20.0/8.6 kPa). Angiocardioigraphy confirmed Fallot’s tetralogy with infundibular and pulmonary valve stenosis. Mitral regurgitation, which was unsuspected clinically, was demonstrated. Later retrograde aortography confirmed aortic regurgitation and a persistent duct. As symptoms were mild and the lesion was complex, surgery was not advised at this time.

In 1969 he had a second attack of infective endocarditis, on this occasion shown to be caused by Strep. viridans. He was again treated at the Royal Cornwall Infirmary. Atrial fibrillation occurred during the illness, causing congestive failure, but he improved after conversion to sinus rhythm with direct current shock. Following this infection he deteriorated slowly, and in June 1972 he again developed atrial fibrillation and congestive failure. At this time the chest radiograph showed pulmonary venous congestion and cardiomegaly, but there had been no increase in the heart size since he was first seen 10 years previously (Fig. 1). Comparing the electrocardiograms of 9 December 1963 and 23 January 1973 there was nothing to suggest progressive left ventricular enlargement (Fig. 2).

He was admitted to the National Heart Hospital in cardiac failure, for surgery. At operation on 29 January 1973 (D.N.R.) the pericardium was found to be obliterated. Digital exploration of the right atrium confirmed a normal tricuspid valve and intact atrial septum. A fibrous ligament only was present at the duct site. After incising the right ventricular outflow transversely a severe infundibular stenosis 1 cm across was excised and both parietal and septal bands of the crista were mobilized to reveal a large ventricular septal defect which was closed with a 'dacron' patch. The enlarged serra was then opened showing an incompetent aortic valve with a hole in the non-coronary cusp and a calcified retracted right coronary cusp. Using bilateral coronary perfusion the valve was excised and replaced with a Starr-Edwards prosthesis. Exploration of the left atrium confirmed a central hole in the anterior cusp of the mitral valve and elongated chordae. The valve was excised and replaced with a Björk prosthesis. The slightly stenosed pulmonary valve was opened fully.

The patient made an uneventful recovery, became acyanotic, and his effort tolerance increased during his convalescence, but one morning four months after the operation he was found dead in bed. There was no necropsy.
Case 2
A 23-year-old man with Fallot's tetralogy known to have been blue since childhood, was admitted to the National Heart Hospital in 1966 with severe central cyanosis and syncope.

At the age of 9 he had an attack of infective endocarditis caused by Staphylococcus aureus and was treated successfully with penicillin and aureomycin. Aortic regurgitation was noted after this but he remained well until aged 12 when a further attack occurred but no organism was isolated. Investigation, at the age of 15, at The Middlesex Hospital confirmed the diagnosis of Fallot's tetralogy, with severe pulmonary stenosis and some narrowing of the infundibulum. In addition, there was important aortic regurgitation (Fig. 3) with a blood pressure of 105/20 mmHg (14.0/2.7 kPa). His progress was satisfactory until the age of 23 when he developed progressive dyspnoea and syncope. At this time his haemoglobin was 20.8 g/dl.

The chest radiograph of 23 October 1959 was typical of Fallot's tetralogy, with slight cardiac enlargement (cardiothoracic ratio 51%), and there was little change during the next 7 years (30 November 1966 cardio-

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**Fig. 1** Case 1: Chest radiograph of June 1972. Enlarged heart with pulmonary venous congestion.

**Fig. 2** Case 1: Electrocardiograms: A) 9.12.63 - sinus rhythm; B) 23.1.73 - atrial fibrillation, digitalis effect, but no evidence of left ventricular enlargement.
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7 years after operation the heart size had returned to normal (Fig. 4) (16 April 1973 cardiothoracic ratio 45%). The electrocardiogram of 10 September 1962 showed a small P pulmonale and right ventricular enlargement. By 31 November 1966 there was an increase in the P pulmonale and evidence of biventricular enlargement; these changes regressed after operation (Fig. 5).

On 8 December 1966 an operation was performed by Sir Thomas Holmes Sellors. In addition to the classic appearances of Fallot's tetralogy, the left ventricle was large and when the aorta was opened a ragged perforation was obvious in the right coronary cusp which was closed with six fine sutures. The ventricular septal defect was closed by direct suture from the aortic root and the right ventricle was opened through an oblique incision, displaying an infundibular stenosis. The tissues of the right ventricular outflow tract were granular with fine vegetations extending some way into the infundibular chamber. A wide resection of the obstruction was made and a satisfactory outflow to the right ventricle achieved. In spite of the angiographic findings 8 years previously, there was no pulmonary valve stenosis.

The patient made an uninterrupted recovery and 7 years after operation is symptom free and acyanotic, with a normal electrocardiogram (Fig. 5). A pansystolic murmur persists, but it is not known if this arises from a residual ventricular septal defect or a jet lesion of the mitral valve which was not examined at operation.

**Case 3**

A 21-year-old woman was admitted to the National Heart Hospital on 15 November 1971 with complex pulmonary atresia. Heart disease had been diagnosed at the age of 2. She had two attacks of infective endocarditis due to *Streptococcus viridans*, at the age of 14 and 20 years. Symptoms were minimal until after the second attack when she developed heart failure, progressive dyspnoea, and angina at rest. A pregnancy was terminated 4 months after the second attack of infective endocarditis.

She had severe right heart failure, a collapsing pulse with a blood pressure of 110/40 mmHg (14.6/5.3 kPa), an immediate diastolic murmur, and loud aortic ejection click but no systolic murmur. Over the back there was a continuous murmur from large systemic arteries supplying the lungs. The haemoglobin was 12.0 g/dl and the blood urea 13.6 mmol/l (82 mg/dl). She deteriorated rapidly and had prolonged attacks of angina at rest. The

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**FIG. 3** Case 2: Phonocardiogram 29.10.59, showing aortic systolic and diastolic murmurs. ECG, electrocardiogram; AA, aortic area; HF, high frequency; MA, mitral area; MF, medium frequency; SM, systolic murmur; A2, aortic closure sound; DM, diastolic murmur.

**FIG. 4** Case 2: Chest radiograph A) 30.11.66, cardiothoracic ratio 53 per cent. B) 16.4.73, 7 years after surgery, cardiothoracic ratio 45 per cent.
FIG. 5 Case 2: Electrocardiograms: A) 10.9.62 – P pulmonale and right ventricular hypertrophy; B) 30.11.66 – increased P pulmonale with biventricular hypertrophy; C) 16.4.73 – regression of P pulmonale and biventricular hypertrophy, 7 years after surgery.
diagnosis of severe aortic regurgitation was not made immediately as it was thought that the wide pulse pressure was related to the arteriovenous shunt from the large collateral arteries supplying the lungs, but with the dominance of angina and right ventricular failure it was eventually considered that severe aortic regurgitation into the right ventricle must be present to explain the symptoms and signs.

Emergency surgical treatment (D.N.R.) was advised on 24 November 1971 knowing that this would require homograft correction of the pulmonary atresia as well as replacement of the aortic valve. The operative findings included typical pulmonary atresia (Type 1) with well-developed, normally sited, right and left pulmonary arteries. In addition, there was a pronounced diastolic thrill at the root of the aorta. The right coronary artery arose from the main pulmonary artery. Cardiac arrest occurred during cannulation and the patient was cooled to 19°C in order to use ischaemic arrest as there was a massive return of blood through the systemic collaterals arising from the descending aorta. The aortic valve was regurgitant, with perforations in all 3 cusps. The ventricular septal defect was of the classical Fallot type and closed with a ‘dacron’ patch through the aortic root. The aortic pulmonary outflow was then reconstructed using a fresh homograft and tubular ‘dacron’ graft. The anomalous right coronary artery which had a large retrograde flow was ligated. The aortic valve was replaced with a Starr-Edwards prosthesis. The right lung hilum was explored, and two large anomalous arteries from the descending aorta were clamped but there was still torrential bronchial return. The operation was completed. The heart came off bypass with adrenalin support, but there was torrential bleeding which could not be controlled in spite of re-exploration and the patient eventually died.

Discussion

In Fallot’s tetralogy and its variants, which involve abnormalities of the right ventricular outflow tract and a ventricular septal defect, infective endocarditis is not uncommon. The site of infection is usually the right ventricular outflow tract or the septal defect unless there has been an anastomotic operation, in which case the channel connecting systemic and pulmonary circulations may be involved. Gelfman and Levine (1942) reported a 6.6 per cent incidence of infective endocarditis in the necropsies of 453 cases of congenital heart disease and noted the infection was present in 29 per cent of all cases of Fallot’s tetralogy over the age of 2 years, but it is doubtful whether this high figure reflects the true incidence seen clinically. Later, Blumenthal, Griffiths, and Morgan (1960) reported that in postoperative cases of Fallot’s tetralogy in which an anastomosis had been created between the systemic and pulmonary circulations infective endocarditis was commoner than in any other type of congenital heart disease. Whatever the frequency of infective endocarditis, no one except Peters (1971) has reported severe aortic valve damage requiring surgery. Our experience, however, suggests this isolated report may not reflect the true state of affairs, for this complication, even when severe, may be overlooked. All our cases were adults, which may have been fortuitous or related to the increasing frequency of infective endocarditis with age. Multiple attacks of infective endocarditis may also be a factor, for in each of our 3 cases there had been a second attack. The interval between the two attacks was 16, 3, and 6 years, respectively. There was nothing remarkable about the organisms which were isolated. In 3 of the attacks, it was a Streptococcus viridans, in 1 a Staphylococcus aureus, and in another positive blood cultures were obtained, but details of the organism have been lost. In the remaining case blood cultures were negative. In all 3 cases the aortic valves were tricuspid and there was nothing in the history or surgical findings to suggest they had been abnormal before infection though we have not got angiographic confirmation.

Bacterial infection of normal endocardium and normal heart valves is rare. It is, therefore, difficult to postulate why the aortic valve should at times be affected, but in both Fallot’s tetralogy and pulmonary atresia the aortic root and ascending aorta are larger than usual (Pattinson and Emanuel, 1957), though the aortic cusps are normal and the valves competent. It may be that this allows turbulent flow of infected blood in the dilated aortic root sufficient to cause trauma to the normal endocardium and so make it susceptible to infection. A similar mechanism has been postulated in infective endocarditis to explain the ‘jet lesion’ of an otherwise normal mitral valve (Gonzalez-Lavin et al., 1970) which was also present in one of these patients.

Diagnostic difficulties are obvious, for even without aortic regurgitation a large volume or collapsing pulse is frequent in Fallot’s tetralogy and pulmonary atresia, with or without a persistent duct. A previous history of infective endocarditis and an immediate diastolic murmur at the left sternal edge may suggest the correct diagnosis. Furthermore, the effect of aortic regurgitation may be manifest by right heart failure (Case 3) and thus considered to be pulmonary regurgitation, for the anatomy of the ventricular septal defect in Fallot’s tetralogy and pulmonary atresia makes it easy for the regurgitant jet, particularly if coming from the right or non-coronary cusp, to go directly into the right ventricle. Once again, a previous history of infective endocarditis can be an important diagnostic clue. Left ventricular enlargement probably depends on the degree and duration of the aortic regurgitation,
always assuming the jet is entering the left rather than the right ventricle. In Case 1 the well-maintained diastolic pressure suggested only moderate reflux which, though present for at least 11 years, possibly 20 years, was insufficient to cause progressive left ventricular enlargement (Fig. 2). In Case 2 the regurgitation, which had been present for 14 years, was more serious and in keeping with the progressive left ventricular enlargement seen on the electrocardiogram (Fig. 5). The possibility of aortic regurgitation in Fallot's tetralogy and pulmonary atresia, particularly if the patient has had an infective endocarditis, adds a further reason for a routine aortogram (Rees and Somerville, 1969). Aortography should be performed by passing the catheter into the ascending aorta from the femoral route and not via the ventricular septal defect, for this may cause spurious aortic regurgitation. In the preoperative assessment of Fallot's tetralogy and pulmonary atresia an apical pansystolic murmur, increasing size of the left atrium or atrial fibrillation, either paroxysmal or permanent, may indicate a destructive lesion (jet lesion) of the mitral valve. Left ventricular angiography should be included, for without this investigation the mitral valve cannot be accepted as normal.

In our cases the problem of treating the infection and correcting the underlying anatomy has not been concurrent. Infective endocarditis in Fallot's tetralogy and pulmonary atresia should be treated in the usual way with the appropriate antibiotic, but if the infection cannot be controlled or valve damage is progressive, causing cardiac failure, then surgery may be required during the active phase. Indications for this have been described by English and Ross (1972).

Surgical management poses no specific problems related to Fallot's tetralogy itself. In the first case the patient, though an adult, withstood the somewhat prolonged bypass of 2 hours 21 minutes required for total correction, plus aortic and mitral valve replacement. His sudden and unexpected death 4 months later without fever or premonitory symptoms suggested a coronary embolus or mechanical dysfunction of the prosthesis. The use of homograft valves may well have obviated this but it would have added appreciably to the bypass time. Furthermore, if homografts are to be used in this type of case they will probably have to be frame mounted because of the size of the aortic root. In the last case with pulmonary atresia cardiac arrest occurred while opening the chest. Massive bleeding from systemic collateral vessels and the problem of residual right ventricular hypertension proved insurmountable.

Addendum

Since submitting this paper a case has been seen at the National Heart Hospital which provides further evidence on the development of aortic regurgitation and possibly infective endocarditis in Fallot's tetralogy.

A man aged 22 was admitted for total repair of Fallot's tetralogy. At the age of 3 a left Blalock anastomosis had been performed. After operation there was no clinical improvement and no continuous murmur was heard. At the age of 17 a Waterston-Cooley anastomosis was attempted; this too was unsuccessful. On two occasions after angiography comment had been made on the very large size of the aortic root. There was no history of infective endocarditis but before surgery on 31 July 1974 an aortic diastolic murmur was noted. The operative findings (D.N.R.) were typical of Fallot's tetralogy but in addition there was a triangular wedge of granulation-like material measuring 9.0 × 7.0 × 8.0 mm between the non-coronary and coronary cusps of the aortic valve. This was densely adherent to the under surface of the valve, which was otherwise normal. On histological examination the vegetation was found to consist almost entirely of fibrin, with some organization at the periphery. Special stains were used to demonstrate bacteria but none was found.

We consider this case lends further support to the thesis that long-standing turbulence in an unusually large aortic root may cause damage to the endothelium, allowing fibrin thrombi to form. The thrombi themselves may cause aortic regurgitation, as shown in this case. It also seems reasonable to postulate that if a bacteraemia develops these thrombi may become infected, causing progressive destruction of the valve and severe aortic regurgitation.

References


Requests for reprints to Dr. Richard Emanuel, National Heart Hospital, Westmoreland Street, London W1M 8BA.
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R Emanuel, J Somerville, S Prusty and D N Ross

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