CASE REPORTS

Double valve replacement after staphylococcal endocarditis

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THE incidence of bacterial endocarditis and its attendant mortality have undoubtedly been reduced since the introduction of antibiotics (Williams, Viroslav and Knight, 1970). The proportion of more virulent organisms is, however, increasing. The staphylococcus aureus is the most common of these and often causes ulcerative endocarditis of previously healthy valves (Quinn, Cox and Drake, 1966; *British Medical Journal*, 1969; Somers *et al.*, 1972).

Acute bacterial endocarditis of the aortic and mitral valves may produce cardiac failure that is not amenable to medical management. The sudden development of aortic incompetence is poorly tolerated and carries a particularly high mortality (Wise *et al.*, 1971). Urgent repair or replacement of one or both valves may become necessary and is often life saving.

There have been several reports of valve replacement for acute aortic incompetence after bacterial endocarditis (Wallace, Young and Osterhout, 1965; Windsor and Shanahan, 1967; Wise *et al.*, 1971) but few after acute mitral incompetence (Robicsek *et al.*, 1967; Yacoub *et al.*, 1972; English, Honey and Clelland, 1972). Urgent double valve replacement after acute bacterial endocarditis is, however, rare (Windsor and Shanahan, 1967; Kretschmer and Lawrence, 1969; Gonzalez-Lavin, Wise and Ross, 1971). It is thus thought worthwhile reporting the following case.

Case report

A previously healthy 35-year-old man was admitted to hospital on December 26 1971. He gave a 12-day history of malaise and pyrexia and an 8-day history of headache and rigors with measured fevers of 105°F (40.6°C). For 2 days he had had persistent vomiting with jaundice. Severe pain had developed in the left elbow 1 day before admission.

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On examination he was pyrexial at 102°F (38.9°C), dehydrated and mildly icteric. His liver was tender and palpably enlarged 4 cm below the costal margin. The left elbow was hot and swollen with painful restricted movements. There was a sinus tachycardia of 110/min and a B.P. of 150/70 without murmurs or cardiac failure. No neurological deficit was discernible.

His haemoglobin was 10.3 g/100 ml, MCHC 32, WBC 13,600/mm³ (90% neutrophils, 5% lymphocytes, 3% monocytes and 2% myelocytes). The platelet count was 250,000/mm³. His blood urea was 21 mg/100 ml, serum sodium 127 mEq/l, potassium 4.0 mEq/l, chloride 94 mEq/l, bicarbonate 23 mEq/l. The serum bilirubin was 1.6 mg/100 ml. SGPT 45 units/ml and alkaline phosphatase 17 KA units/100 ml. Radiography of the left elbow was normal as were his initial chest X-ray and ECG. Three MSUs were sterile on culture and showed no abnormality on microscopy. Throat swabs were sterile on bacterial culture but Influenza A virus was isolated. The Australia (hepatitis associated) antigen was negative. A coagulase positive staphylococcus aureus was isolated from blood cultures taken on admission and on December 27 1971, December 28 1971 and December 31 1971. The patient continued to be pyrexial and unwell for 36 hr after admission, with a swinging pyrexia of up to 105°F (39.4°C). On the morning of December 28 1971, a soft systolic murmur was heard at the left sternal edge, other physical signs remaining as on admission. Later that day the blood culture report was received and therapy was immediately commenced with intramuscular cephalothin 1 g 6-hourly.

The following day he developed severe pain in the first and second toes of his right foot and in the little toe of his left foot with discomfiture and tenderness over the first metatarsal of the left foot, the tip of the right index finger and the right hip. Several splinter haemorrhages were now evident under his finger and toe nails but there were no conjunctival or retinal

haemorrhages and no microscopic haematuria. Therapy was commenced with heparin by drip infusion, the cephalothin thereafter being given intravenously. The following day the systolic murmur was more marked and vigorous carotid pulses were noted together with a systolic flare at the root of the neck. The B.P. was 130/80 without cardiac failure and there were still no retinal or conjunctival haemorrhages. Repeated searches for microscopic haematuria were unrewarding.

An early aortic diastolic murmur was first heard on December 30 1971. Later that day the patient developed involuntary movements of his limbs, and particularly the right hand. No objective neurological abnormality was discernible and there was no finger clubbing or evidence of recent emboli. The swinging pyrexia of up to 104°F (40°C) continued. The following day, the patient developed pain over his left lower chest and upper abdomen, chest X-ray revealing evidence of bilateral pulmonary infarction. The ECG showed a sinus tachycardia with non-specific ST changes over the left ventricle (RV5+SV1 totalling 22 mm). His haemoglobin was 9.2 g/100 ml, MCHC 30, WBC 29,600/mm³ (77% neutrophils, 12% lymphocytes, 5% monocytes and 6% myelocytes). The neutrophils showed toxic granulation. His blood urea, electrolytes and liver function tests were now normal. The intravenous cephalothin dosage was increased to 2 g 6-hourly, and further increased to 4 g 6-hourly 24 hr later.

By January 5 1972, the signs of aortic stenosis and incompetence were more marked and a right pleural effusion had developed. The patient was, however, feeling subjectively much improved and the fever was settling. A moderate number of red cells and casts were then present on microscopy of freshly passed urine. A streptococcus viridans now appeared in one of the daily blood cultures. The parenteral cephalothin therapy was accordingly stopped, a total of 13 days having been given, and replaced with oral clindamycin 600 mg 6-hourly. The fever subsided only to reappear 48 hr later, levels of 101°F (38.3°C) being recorded. The patient was now experiencing severe pain from his toes, two of which were gangrenous. Therapy was changed to Phenoxymethyl-penicillin 500 mg 6-hourly, the patient thereafter becoming afebrile and improving subjectively although the signs of aortic incompetence persisted. The B.P. was 120/60 without cardiac failure although the systolic flare at the root of the neck was becoming more marked.

On January 21 1972, the murmurs suddenly changed. A grade 4/6 pansystolic murmur was now audible over the precordium, maximal in the mitral area and associated with a systolic thrill and clinical evidence of left ventricular hypertrophy. The B.P. was unaltered at 120/60 and there was no clinical or

radiographic evidence of cardiac failure, although it was noted that the right pleural effusion had cleared. The ECG showed upward coving of the ST segments in the antero-lateral leads, consistent with pericarditis; RV5 and SV1 now totalled 47 mm. It was considered probable on clinical grounds that the acute mitral incompetence was the result of rupture or perforation of a mitral valve cusp, possibly secondary to necrosis and rupture of chordae tendineae. The haemoglobin at this juncture was 9.2 g/100 ml, MCHC 32, WBC 9400/mm³ (80% neutrophils, 15% lymphocytes, 5% monocytes and 3% eosinophils). Repeated blood cultures were sterile.

On February 7 1972 the patient was seen by a cardiologist (Dr D.G. Julian) and a thoracic surgeon (Mr R.J.M. McCormack) both of whom had previously seen the patient. The decision was made to undertake aortic and mitral valve replacement, but whilst awaiting this procedure the patient developed breathlessness with a desire to sleep propped up at night. Over the following week he became increasingly breathless with a persistent cough and frothy sputum. A PA chest radiograph now revealed increasing cardiomegaly predominantly involving the left ventricle with pulmonary oedema and bilateral pleural effusions (Fig. 1). In view of the clear cardiac deterioration, it was decided to undertake urgent double valve replacement. The patient was

FIG. 1.

FIG. 2.

accordingly transferred to the Regional Cardio-Thoracic Unit where double valve replacement was performed on March 1 1972, under cardio-pulmonary bypass.

At operation the aortic valve was found to be bicuspid, with irregularity of the cusp edges, but without evidence of active vegetations. The septal cusp of the mitral valve was flail and several of the chordae were detached from it and were hanging from the tip of a necrotic papillary muscle. Near the attachment of the mural cusp the ventricular wall was necrotic. Both valves were excised and replaced by Starr-Edward's prostheses. The immediate post-operative period was uneventful.

During the convalescent period the gangrenous tips of two of his toes were amputated under local anaesthesia. The wounds healed well and the patient was finally discharged from hospital on May 17 1972, receiving Digoxin and long-term Warfarin. He was subjectively and clinically well, in sinus rhythm with a B.P. of 140/80 with normal valve clicks unassociated with murmurs. His chest radiograph was normal save for pleural thickening at the right costophrenic angle (Fig. 2a, b) while the ECG showed asymmetrical T wave inversion over the left ventricle, attributable to cardiomyopathy. RV5 and SV1 now totalled 20 mm. His effort tolerance is now excellent and he is asymptomatic save that he and his wife hear the valve clicks at night. He recom-

menced work on July 1 1972, and remains well to the present.

Discussion

Valve perforation or rupture leading to sudden aortic and less often mitral incompetence, with subsequent intractable cardiac failure, is now the most common cause of death in patients with bacterial endocarditis (Wise *et al.*, 1971). The mortality in recognized and treated cases of bacterial endocarditis is still considerable and in those who develop aortic incompetence may exceed 50% (Cohen and Freedman, 1961; Uwaydah and Weinberg, 1965).

Despite the availability of a spectrum of powerful antibiotics, with improved bacteriological control of the endocarditis, cardiac failure not infrequently develops during treatment as a sequel to valvular perforation or rupture. The myocardium is usually healthy in these patients, although coronary embolization or myocarditis may occur. Aortic incompetence is the commonest lesion and carries a mortality of 40–60%, a figure virtually twice that observed in patients with involvement of other valves (Kaiser *et al.*, 1967; Wise *et al.*, 1971). An aggressive therapeutic approach becomes especially necessary when aortic incompetence is followed by cardiac failure.

The first report of valvular surgery in bacterial

endocarditis appeared in 1959 (Morgan and Bland, 1959), a Hufnagel valve being inserted into the aorta in five patients who had developed aortic incompetence while receiving antibiotic therapy. Yeh, Hall and Ellison (1964) first reported repair or Starr-Edwards valve replacement of aortic valves damaged by endocarditis. The following year Wallace, Young and Osterhout (1965) excised and replaced an aortic valve during the phase of active endocarditis because of rapidly increasing and uncontrollable cardiac failure. Others have since reported similar experiences (Wilcox *et al.*, 1967; Kretschmer and Lawrence, 1969; Wise *et al.*, 1971). Few have, however, undertaken double valve surgery (Windsor and Shanahan, 1967; Gonzalez-Lavin and Ross, 1971).

In this patient the aortic incompetence appeared to be well compensated until acute mitral incompetence occurred. As isolated lesions, acute mitral incompetence is better tolerated than acute aortic incompetence (Braunwald, 1969). Acute mitral incompetence in this context is usually a sequel to valve perforation or rupture of chordae tendineae, and is often amenable to plication or repair although valve replacement may be necessary (Windsor and Shanahan, 1967; Robicsek *et al.*, 1967; Yacoub *et al.*, 1972). Double valve replacement became urgently necessary in this patient with the development of left ventricular failure.

It is tempting to postulate that the streptococcus viridans infection was superimposed upon valves already damaged by staphylococcal bacterial endocarditis. Structural damage and haemodynamic deterioration occurred, however, despite apparent bacteriological control and clinical improvement. Secondary involvement of the mitral valve is a recognized complication in those patients who develop aortic incompetence after bacterial endocarditis. It has been postulated that this might have primary haemodynamic implications, although an infective jet diverted against the mitral valve may produce infective lesions leading to sudden valve rupture, as occurred in this case (Gonzalez-Lavin and Ross, 1970; Gonzalez-Lavin *et al.*, 1971; English *et al.*, 1972). The source of infection was never discovered in this patient, although it is probable that the septicaemia was a sequel to his influenza illness. The suggestion that he might have had a suppurative arthritis of the left elbow was never substantiated.

The degree of ulcerative endocarditis might well have been less had blind antibacterial therapy been instituted on admission, before the blood culture results were available. Aortic incompetence may also have existed before it was detected, for the syndrome of acute aortic regurgitation differs clinically and haemodynamically from that of chronic aortic

incompetence and may be difficult to diagnose (Wise *et al.*, 1971). Clinical, radiographic and electrocardiographic evidence of left ventricular hypertrophy is often absent. In our patient, however, there was unequivocal evidence of increasing left ventricular hypertrophy which returned to normal following his double valve replacement. It is indeed doubtful whether he would have survived had surgical intervention been delayed.

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Primary acquired hypogammaglobulinaemia and auto-immune thyroiditis

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Summary

A patient with primary acquired hypogammaglobulinaemia and auto-immune thyroiditis is presented, an association which has not been described previously. The role of disturbances of cell-mediated immunity in the pathogenesis of the thyroid lesion is discussed.

PRIMARY acquired hypogammaglobulinaemia, characterized by frequent bacterial infections (particularly of the sinuses and respiratory tract), a very low serum level of γ globulin and failure to produce antibody in response to antigenic stimulation has been associated with a variety of other disorders. These include diseases of the reticulo-endothelial system such as lymphosarcoma, Hodgkin's disease, leukaemia and multiple myeloma (Douglas, Goldberg and Fudenberg, 1970; Fudenberg, 1971) and auto-immune disorders including acquired haemolytic anaemia, rheumatoid arthritis (Fudenberg, 1971) and pernicious anaemia (Lee *et al.*, 1964; Conn *et al.*, 1968; Twomey *et al.*, 1969).

An association between primary acquired hypogammaglobulinaemia and auto-immune thyroiditis has not been recorded previously and therefore the following case report is presented.

Case report

A 44-year-old man first presented in 1963 with a 10-year history of recurrent, frequent, febrile respiratory tract infections. Clinical examination and

his chest X-ray suggested the presence of bilateral bronchiectasis. At that time he was found to have hypogammaglobulinaemia with a serum γ globulin level of 10 mg/100 ml. He has received weekly injections of γ globulin (supplied by the MRC) and had fewer and less severe chest infections since this diagnosis was made.

In January 1969, he was found to have the clinical features of myxoedema. For the preceding 6 months he had noticed increasing loss of energy, decreased tolerance of cold, dry skin, constipation and marked loss of hair and eyebrows. There was no family history of auto-immune disease or hypogammaglobulinaemia. Examination revealed marked alopecia, complete loss of eyebrows, dry skin, pale, puffy face, deep voice, mental slowing, a bradycardia and delayed supinator and ankle reflexes. It is of interest that the alopecia became total and has persisted ever since.

Investigations confirmed the clinical diagnosis of hypothyroidism with a PBI 0.5 μ g/100 ml and I^{131} uptake 2% at 71 hr (normal 10–20%). Other investigations including thyroid auto-antibodies, SCAT, ANF and Coombs test were all negative.

At the time of the original investigations of his hypogammaglobulinaemia (1963), it was decided to carry out a lymph node biopsy from the right side of the neck. Fortunately, a small piece of accessory thyroid tissue was removed. Histological examination of this revealed pathological features consistent with a diagnosis of Hashimoto's or auto-immune thyroiditis. There was extensive infiltration of thyroid tissue by lymphocytes, but no plasma cells, and a small amount of fibrosis.

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