Aortic regurgitation in systemic lupus erythematosus requiring aortic valve replacement

W. M. C. Oh, R. T. Taylor,¹ and E. G. J. Olsen

From the National Heart Hospital and Westminster Hospital, London

A woman with proven systemic lupus erythematosus is described, in whom the aortic valve was also involved. She was treated with corticosteroids. The effect of the aortic valve involvement progressed and necessitated replacement by Starr-Edwards prosthesis. Pathological features of the operation specimen are detailed.

Endocarditis is well recognized in systemic lupus erythematosus since the original description by Libman and Sacks in 1924. In the series reported by Brigden *et al.* (1960) it was present in half the cases coming to necropsy, the mitral valve being more frequently affected than the aortic valve. It was clinically apparent in only 20 per cent of all their cases, as it was in the series of Dubois and Tuffanelli (1964). But severe valvar dysfunction is exceedingly rare. Shulman and Christian (1969) first reported a case of Starr valve replacement for severe aortic regurgitation due to systemic lupus erythematosus endocarditis. We describe here a further case.

¹ Present address: Kidderminster General Hospital, Kidderminster, Worcestershire.

Case report

A 38-year-old business woman first presented in 1965 with joint pains in her hands and wrists of 4 years' duration. She was normotensive. Her ESR was 30 mm/hr (Westergren) and tests for rheumatoid factor were negative. In 1968 a soft early diastolic murmur was first heard; electrocardiogram and chest x-ray were normal. There was no history of rheumatic fever and the Wassermann reaction was negative. In 1969 she had an episode of left-sided pleurisy. In February 1971 she was admitted to Westminster Hospital because of a low grade fever, night sweats, and dyspnoea. Her blood pressure was 240/130 mmHg; the heart murmur was louder. Chest x-ray showed some cardiac enlargement and there was electrocardiographic evidence of pericarditis. The ESR was 83 mm/hr (Westergren), blood cultures were negative,

FIG. 1 Surgical specimen of aortic valve. Note the vegetations arranged in bead-like chains over the closure margin and the free edge of the valve leaflets. (Reconstructed after tissue for histological investigation had been selected.)

blood urea 54 mg/100 ml, urine protein 200 mg/24 hr, and the total haemolytic complement level was low. The diagnosis of systemic lupus erythematosus was confirmed by positive tests for LE cells and antinuclear

FIG. 2 Section of a valve leaflet showing slight thickening of part of the cusp due to an increase in predominantly elastic tissue, while the top part shows destruction of normal architecture. Demarcation of valve cusp and fibrous core of the vegetation is indistinct. (Weigert's elastic van Gieson. $\times 8$.)

factor. Treatment was started with prednisone 40 mg/day and bethanidine, and her general condition improved. In June 1971 she developed cerebellar ataxia and was noted to be severely cushingoid in appearance. A gradual reduction in corticosteroid dosage was begun. Purpura associated with a low platelet count ($44,000/\text{mm}^3$) appeared in July 1971 and the cerebellar signs were worse. Azathioprine 125 mg/day was started. Then she was readmitted to hospital with acute left ventricular failure. There was pronounced cardiac enlargement with severe left ventricular hypertrophy. She improved with diuretic therapy but remained restricted by general weakness and some exertional dyspnoea. Six months later, in February 1972, she was readmitted in severe left ventricular failure. The cerebellar signs were less obvious, platelets $84,000/\text{mm}^3$, urea 76 mg/100 ml, urine protein 1.2g/24 hr. Though the antinuclear factor test was still positive, no LE cells were found: complement (C_3) was normal and DN binding not increased.

She was transferred to the National Heart Hospital where physical examination revealed blood pressure 190/95 mmHg, collapsing pulse, pronounced left ventricular hypertrophy, a loud long diastolic murmur, and an Austin Flint murmur. Electrocardiogram showed severe left ventricular hypertrophy and strain. An aortogram indicated severe aortic regurgitation with slight aortic dilatation and a left ventricular angiogram showed an enlarged left ventricular cavity with normal contractility and no mitral regurgitation. There was no gradient across the mitral or aortic valve. The left ventricular end-diastolic pressure was 20 mmHg and the mean indirect left atrial pressure was 22 mmHg.

In March 1972 her diseased aortic valve was replaced by a Starr-Edwards prosthesis. Dense pericardial adhesions were noted at operation. Her postoperative course was uneventful. Her heart diminished in size and the radiographic signs of pulmonary venous congestion disappeared. There has been no demonstrable deterioration in any of the other clinical or laboratory features of her disease since the operation.

Pathology

Macroscopical appearances

The aortic valve had been opened and measured 90 mm in length (upper limit of normal 80 mm). The valve leaflets were slightly thickened, particularly along the free margin and the line of closure. On the ventricular surface (deformed face) in line with the corpora arantii and along the line of closure, there were a few small discrete vegetations about 3 mm in diameter. More conspicuous, however, were confluent vegetations, reddish-yellow in colour, arranged in bead-like chains (Fig. 1).

Histological appearances

The valve cusps were slightly thickened throughout the entire length. The thickening was predominantly due to an increase in the elastic tissue, but the other major component (collagen tissue) of normal valve structure could be recognized. Along the line of closure and the free margin there was a moderately severe increase in collagen tissue, with destruction of normal architecture.

FIG. 3 Photomicrograph of the vegetation showing a fibrous core with superimposition of recent fibrin. The cellular infiltrate is sparse. (Haematoxylin and eosin. $\times 85$.)

The vegetations consisted of a core of cellular fibrous tissue but demarcations between valve component and those of the vegetation were impossible to define (Fig. 2). Superimposed on this fibrous core was recent fibrin (Fig. 3).

Using Lendrum *et al.* (1962) stain, recent 'fibrinoid' could be seen in a few small areas within the fibrous core. Cellular elements were scanty and consisted of some mononuclear cells. A very occasional Anitschkow cell was also found. Haematoxyphil bodies and LE cells were not found. Vascularity of the valve cusps was not increased.

Comment

In this patient it was felt that her prognosis as a result of severe aortic valve disease was extremely poor. Because of the improvement in cerebellar signs and platelet count, the normal DNA binding and serum complement, and the absence of LE cells, the systemic lupus erythematosus was thought to be under control.

Recent studies indicate a 10-year survival rate in systemic lupus erythematosus of nearly 60 per cent (Estes and Christian, 1971; Siegel *et al.*, 1969). The clinical features consistently associated with a poor prognosis are severe renal and neurological disease. In our patient renal biopsy was unsuccessful but judging from the clinical features it was unlikely that diffuse proliferative or membranous glomerulonephritis was present. Severe renal involvement in systemic lupus erythematosus is associated particularly with a poor prognosis (Baldwin *et al.*, 1970; Estes and Christian, 1971; Pollak and Pirani, 1969). Cerebellar ataxia is recognized as an uncommon feature of the disease (Johnson and Richardson, 1968). As this was improving it was felt that operation should be

undertaken, though its effect on our patient's ultimate prognosis is unknown.

The pathology was detailed, among others, by Gross in 1940, and Klemperer, Pollack, and Baehr in 1941. Both sides of the heart were equally affected in the series published by Baggenstoss (1952). This author found 'non-bacterial verrucous endocarditis' in 40 per cent of cases. Brigden *et al.* in 1960 reported predominantly left-sided heart involvement. The aortic valve is usually spared but these authors found aortic valve involvement in 4 of their cases.

Most of the pathological descriptions were detailed in the published reports before the advent of steroid therapy. Though the patient described here did not show all the classical features (haematoxyphil bodies and LE cells), the appearances are those of 'non-bacterial verrucous endocarditis'. The absence of these features can be explained as being due to the steroid therapy this patient had previously received.

We wish to thank Dr. F. Dudley Hart, Dr. Aubrey Leatham, and Mr. Donald Ross for their permission to report this case, and Dr. E. J. Holborow in whose laboratory at Taplow the measurements of DNA binding were made.

References

- Baggenstoss, A. H. (1952). Visceral lesions in disseminated lupus erythematosus. *Proceedings of the Staff Meetings of the Mayo Clinic*, 27, 412.
- Baldwin, D. S., Lowenstein, J., Rothfield, N. F., Gallo, G., and McCluskey, R. T. (1970). The clinical course of the proliferative and membranous forms of lupus nephritis. *Annals of Internal Medicine*, 73, 929.
- Brigden, W., Bywaters, E. G. L., Lessof, M. H., and Ross, I. P. (1960). The heart in systemic lupus erythematosus. *British Heart Journal*, 22, 1.

- Dubois, E. L., and Tuffanelli, D. L. (1964). Clinical manifestations of systemic lupus erythematosus; computer analysis of 520 cases. *Journal of the American Medical Association*, **190**, 104.
- Estes, D., and Christian, C. L. (1971). Natural history of systemic lupus erythematosus by prospective analysis. *Medicine*, **50**, 85.
- Gross, L. (1940). The cardiac lesions in Libman-Sacks disease. *American Journal of Pathology*, **16**, 375.
- Johnson, R. T., and Richardson, E. P. (1968). Neurological manifestations of systemic lupus erythematosus - Clinical pathological study of 24 cases and review of the literature. *Medicine*, **47**, 337.
- Klemperer, P., Pollack, A. D., and Bachr, G. (1941). Pathology of disseminated lupus erythematosus. *Archives of Pathology*, **32**, 569.
- Lendrum, A. C., Fraser, D. S., Slidders, W., and Henderson, R. (1962). Studies on the character and staining of fibrin. *Journal of Clinical Pathology*, **15**, 401.
- Libman, E., and Sacks, B. (1924). Hitherto undescribed form of valvular and mural endocarditis. *Archives of Internal Medicine*, **33**, 701.
- Pollak, V. E., and Pirani, C. L. (1969). Renal histologic findings in systemic lupus erythematosus. *Mayo Clinic Proceedings* **44**, 630.
- Shulman, H. J., and Christian, C. L. (1969). Aortic insufficiency in systemic lupus erythematosus. *Arthritis and Rheumatism*, **12**, 138.
- Siegel, M., Gwon, N., Lee, S. L., Rivero, I., and Wong, W. (1969). Survivorship in systemic lupus erythematosus: relationship to race and pregnancy. *Arthritis and Rheumatism*, **12**, 117.

Requests for reprints to Dr. E. G. J. Olsen, Department of Histopathology, National Heart Hospital, Westmoreland Street, London W1M 8BA.