Pathology of infective endocarditis

A postmortem evaluation

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A review of 28 necropsy cases of infective endocarditis seen over the 12-month period of 1969 is presented. The infection involved a previously apparently normal valve in 16 cases (57%). Isolated aortic valve endocarditis was the commonest lesion and was found in 15 cases. Infective endocarditis of the aortic valve characteristically occurred on a normal valve in middle-aged men. In the 10 cases of isolated mitral endocarditis evidence of previous abnormality, rheumatic disease or endomyocardial fibrosis, was usually present. Blood cultures in life had been positive in only 3 of the total series and were repeatedly negative in 8. Postmortem bacteriology of the vegetations was positive in 13 out of 19 cases so studied. Death had occurred within 2 weeks of the onset of illness in 14 cases (50%). The histopathology frequently showed focal myocardial scars and smaller coronary artery changes in the absence of evidence of coronary embolism.

Though infective endocarditis is frequently recognized in Uganda, there have been no detailed studies of its pathological features. Davies (1948) observed a 2.5 per cent prevalence of acute bacterial endocarditis in a general necropsy survey. The majority of cases arose from a primary septicaemia and the commonest organisms were pneumococci or neisseria. He noted that the affected valves usually showed no evidence of previous damage and that the aortic valve was most commonly affected. In a further necropsy study infective endocarditis was noted as a complication in 26 per cent of cases dying with rheumatic heart disease, and in 5.7 per cent of cases with endomyocardial fibrosis (Shaper, Hutt, and Coles, 1968).

A diagnosis of bacterial endocarditis was recorded in 2.2 per cent of all cardiac admissions to Mulago Hospital in 1966 (D'Arbela, Kanyerezi, and Tulloch). Present clinical experience of infective endocarditis in Uganda is described elsewhere (Somers *et al.*, 1972b).

In this study we have analysed 28 consecutive cases of infective endocarditis coming to necropsy in Mulago Hospital in 1969.

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Materials and methods

The majority of the necropsies were done by one of us (I.S.) and in every case the macroscopical and microscopical findings are derived from personal observations. A minimum of 8 sections was obtained from each of 24 of the 28 hearts. These were fixed in 10 per cent formol saline and processed in a standard manner. All sections were stained with haematoxylin and eosin and selected sections by Gram's method, periodic acid-Schiff, iron haematoxylin and van Gieson, phosphotungstic acid haematoxylin, and by Movat's pentachrome technique. For bacteriological studies a piece of the vegetation was removed with scissors and washed in several changes of broth to remove surface contamination. It was then crushed and the contents inoculated onto a variety of media. Such cultures were made in 19 cases.

Results

Incidence

The 28 cases of infective endocarditis (21 male and 7 female) were found in 875 necropsies, giving an incidence of 3.2 per cent. The average age at the time of death was 36.6 years in the male (range 14-75) and 25.1 years in the female cases (range 13 to 42). Seven cases came from the local Ganda tribe, 6 were migrant Rwanda, and the remainder came from other tribes in Uganda.

Clinical data

The apparent duration of the illness was less than 2 weeks in 14 cases, between 2 weeks and 2 months in

7, and more than 2 months in another 7. The longest history was 9 months. The diagnosis of infective endocarditis had been made in life in only 5 of the 28 cases; blood cultures had been taken in 11 and were positive for *Staph. aureus* in 2 and for *Strep. viridans* in one. In the other 8 cases blood cultures taken on at least 3 occasions were negative. Twelve patients had evidence of congestive cardiac failure.

Necropsy findings

The heart weights ranged from 200 g to 570 g with a mean weight of 363 g. The majority of cases had isolated aortic or mitral endocarditis. The aortic valve was involved alone in 15 cases, the aortic and tricuspid in one case, the aortic, mitral and pulmonary in one case, the mitral alone in 10 cases, and the tricuspid alone in one case. The vegetations were described as large in 7 cases, of medium size in 4 cases, and small in 17. Ulceration, destruction, or perforation of the infected valve was commonly found, involving the aortic valve in 15 (Fig. 1) and the mitral valve in 2 cases. Rupture of chordae tendineae was noted in a further 4 cases. In 3 cases of aortic endocarditis the regurgitant jet had resulted

in the formation of small ulcers and vegetations on the ventricular aspect of the anterior mitral cusp as described by Gonzalez-Lavin, Somerville, and Ross (1972). In each case aortic cusp perforation was present. All the 28 cases showed active lesions of infective endocarditis (see Table).

The macroscopical appearance of the affected valves was assessed as previously normal in 16 cases (57%), the majority being aortic. Seven cases of isolated mitral endocarditis showed major previous damage: chronic rheumatic heart disease in 3 and endomyocardial fibrosis affecting the posterior cusp of the mitral valve in 4. In the remaining cases the valves showed minor changes, probably rheumatic in origin, such as slight fusion of commissures or otherwise thin aortic valves and mild marginal thickening of the mitral valve.

The probable source of infection was identified in only 3 cases. These were *Esch. coli* aortic endocarditis in a case of urethral stricture with acute pyelonephritis, *Staph. albus* aortic endocarditis in a case of an infected hip fracture, and *Strep. viridans* tricuspid endocarditis in a case of bronchiectasis and bronchopneumonia.

FIG. 1 Aortic endocarditis in a 36-year-old man. The aortic left coronary cusp is almost entirely destroyed, with only strips of tissue preserved near the commissures. The sinus of Valsalva is aneurysmally dilated. There are small inconspicuous vegetations above the valve defect. The remaining aortic cusps are normal. Jet lesions are seen on the septum below the valve defect.

TABLE Pathological lesions in 28 cases of infective endocarditis

Valve affected	No. of cases	Average age (yr)	No. with previously normal valves	No. with perforation or rupture of chordae tendineae
Aortic	15	40.1	13	14
Mitral	10	25.5	0	6
Tricuspid	1		1	0
Aortic tricuspid	1		1	0
Aortic	1		1	1
Mitral	—		—	—
Pulmonary	28		16	21

Embolization

This was noted in 21 cases. In 9 the emboli involved multiple organs, usually the spleen, kidney, and brain. In one of these there was a saddle embolus of the aorta. The remaining cases had one or more emboli in a single organ, the spleen in 4, kidney in 3, brain in 3, and the nail beds in one. The case with

alone tricuspid involvement had several septic emboli in the lungs.

Other disease

Three cases had chronic glomerulonephritis, 3 had chronic pyelonephritis, 2 had idiopathic dilatation of the ascending aorta, one nonspecific aortitis, and

FIG. 2 Focus of myocytolysis in the myocardium of a 40-year-old man with *Esch. coli* mitral endocarditis. (Haematoxylin and eosin. $\times 210$.)

one tropical splenomegaly syndrome. There were no cases related to cardiac operation. No patients had malignant disease.

Bacteriology

Postmortem cultures of the vegetations were obtained in 19 cases. The following organisms were grown from the aortic lesions: *Esch. coli*, 3 cases; *Strep. viridans*, 1 case; *Strep. faecalis*, 2 cases; *Staph. aureus*, 1 case; *Staph. albus*, 1 case. The case with combined aortic and tricuspid endocarditis yielded a mixed growth of *Str. viridans* and *Esch. coli* from both valves. Cultures from the mitral lesions grew *Esch. coli* (2 cases), *Staph. aureus* (1 case), negative (1 case), and from the lone tricuspid lesion *Strep. viridans*. In 2 cases there was probable contamination and 3 were grossly contaminated.

Histopathological findings

In all 16 of the apparently previously normal valves the spared cusps or parts of cusps of the affected valve were also histologically of normal appearance.

The cusps from the remaining cases showed some vascularization or fibrosis or both. In 7 of the 13 cases in which there was a positive bacterial culture from a vegetation at necropsy an organism of similar type was seen in the vegetation. The involved cusps in all cases showed acute inflammatory changes typical of an infective aetiology.

Several microscopical defects were found. Of 24 hearts examined in detail, 21 showed focal scars and focal areas of myocytolysis (Fig. 2). Another frequent finding was the presence of intimal fibrous proliferation and mucoid oedema of the wall of the small coronary arteries (Fig. 3). The latter changes were found in 14 cases, all of which also showed focal myocardial scars. A conspicuous increase of a basophilic cystic substance, with the staining properties of acid mucopolysaccharides, was observed in many cases in the heart and in the great vessels (Fig. 4). It was to be found in one or more of the affected valves, the interstitial tissue of the myocardium, the walls of the main coronary arteries, the left ventricular endocardium, the media of the ascending aorta, and in the pulmonary artery trunk.

FIG. 3 Intimal proliferation and mucoid oedema in the media in a small coronary artery from a 42-year-old woman with mitral endocarditis. (Elastic and van Gieson. $\times 125$.)

FIG. 4 Muroid swelling of the intima of a small myocardial artery from a 32-year-old man with *Esch. coli* aortic endocarditis. (Haematoxylin and eosin. $\times 210$.)

In 17 of the 24 hearts examined in detail it was present in at least one of these sites.

Microabscesses were found in the myocardium in only 4 cases. No case showed coronary micro-emboli, myocardial infarction, or diffuse interstitial chronic inflammation. Aschoff bodies were not seen.

Comparison of aortic and mitral endocarditis

Isolated aortic and isolated mitral endocarditis together comprised 25 of the total 28 cases (see Table). While the picture of the mitral group was similar in many ways to classical infective endocarditis as seen in temperate climates, the aortic cases showed several special features and form a distinct group.

The 15 patients with isolated aortic endocarditis were all men, mostly in their third or fourth decades. The disease usually ran a rapid course, with death due to heart failure within 2 weeks from the onset of symptoms in about half the patients. Blood cultures taken in life from 6 cases had been negative. The characteristic aortic lesions consisted of small, pale vegetations lining the valve leaflet. Valve de-

struction was usually more impressive than the vegetations. Valve perforation, resulting in fatal massive aortic incompetence, was found in 14 cases. Apart from a varying degree of left ventricular hypertrophy, these hearts showed no other macroscopical abnormalities. In 13 cases there was no convincing evidence of previous valve abnormality.

Discussion

There has been considerable change over the past 20 years in Western countries in the clinical, bacteriological, and histopathological features presented by infective endocarditis (Lerner and Weinstein, 1966; Steiner, 1970). These changes have resulted mainly from an alteration of predisposing causes, especially rheumatic heart disease, from the widespread use of antibiotics, and from the development of new techniques in cardiac surgery, e.g. valve prosthetic replacement. The incidence of *Strep. viridans* as the infective agent has decreased, *Staph. aureus* has increased, and other organisms such as rickettsiae and fungi are more frequently recognized.

There has also been a real increase in the incidence of infective endocarditis among older male patients with no clear antecedent heart disease (Hughes and Gauld, 1966). While the classification into acute and subacute bacterial endocarditis lingers in the published reports, clinical and pathological experience show the difficulty in distinguishing the acute from the subacute, especially in the older patient. Despite the altered clinical picture, there does not appear to be a great change in the total number of cases admitted to hospital in most parts of the world. These general remarks apply in similar measure in developing countries (Somers, Patel, and D'Arbela, 1972a; Brockington and Edington, 1972).

An analysis of the clinical presentation of infective endocarditis seen in the Mulago Hospital (Somers *et al.*, 1972b) has shown that the classical forms of subacute bacterial endocarditis occurring on aortic and mitral valves previously damaged by rheumatism are usually diagnosed without much difficulty. In about a third of the cases in the present necropsy series, the valve lesions, mostly mitral, were compatible with previous damage, either rheumatic or from endomyocardial fibrosis.

A striking finding is the incidence of infective endocarditis affecting apparently normal aortic valves. These cases characteristically occurred acutely in middle-aged men. Death resulted rapidly from the development of massive aortic regurgitation. The lesions did not usually appear to be the terminal event in a septicaemia from an obvious focus of infection elsewhere. Necropsy cultures yielded *Esch. coli*, *Strep. faecalis*, and *Staph. aureus*, suggesting that the initial site of infection may have been the lower genitourinary tract. Unlike the experience of 2 decades ago there were no cases of neisserial or pneumococcal infection.

Among the unexpected histological features were the frequency of myocardial scars in the absence of occlusive main coronary artery disease. Various myocardial lesions may be encountered in infective endocarditis and presumably the focal myocardial lesions found in this study represent healed myocardial involvement (Morgan and Bland, 1959). The changes in the smaller coronary vessels were of a nonatheromatous nature. Similar changes have sometimes been seen in other types of heart disease

in Uganda such as rheumatic heart disease, endomyocardial fibrosis, and 'congestive cardiomyopathy' (Farrer-Brown *et al.*, 1972). They did not resemble the embolic or inflammatory lesions which are often found in infective endocarditis (Brunson, 1953), and we presume that they preceded the bacterial infection. The conspicuous lack of myocardial abscesses is a notable feature in the present series.

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