Eur J Vasc Endovasc Surg **19**, 288–293 (2000)
doi:10.1053/ejvs.1999.0982, available online at http://www.idealibrary.com on IDEAL®

Ten Years' Experience of Aortic Aneurysm Associated with Systemic Lupus Erythematosus

N. Ohara*[1], T. Miyata[1], A. Kurata[2], H. Oshiro, O. Sato†[1] and H. Shigematsu[1]

[1]*Division of Vascular Surgery, Department of Surgery, and* [2]*Department of Pathology, Faculty of Medicine, The University of Tokyo, Japan*

Background: *aortic aneurysm is a rare but life-threatening cardiovascular complication in patients with systemic lupus erythematosus (SLE). The purpose of this study was to clarify the characteristic clinical features and the pathological mechanism of aneurysmal formation in these patients.*
Methods: *among 429 patients operated on for abdominal aortic aneurysm (AAA) during the past 10 years, five cases with SLE were treated surgically. Their clinical data were reviewed, and the resected aneurysmal wall of the five patients was also examined histologically.*
Results: *the mean age of the patients with SLE was 55 years, which was statistically younger than that of the other patients (mean 77 years, S.D. 7.9, $p<0.05$). They had received long-term corticosteroid therapy for the treatment of SLE for a mean of 23 years. Histologically, destruction of the medial elastic lamina was characteristic. Four patients had no complications in the postoperative follow-up period (mean 4 years), while the remaining patient died of rupture of a dissecting aneurysm two years after operation.*
Conclusion: *prolonged steroid therapy may play a major role in accelerating atherosclerosis, which can result in aortic aneurysmal enlargement, possibly together with primary aortic wall involvement and/or vasculitic damage in patients with SLE.*

Key Words: Aortic aneurysm; Systemic lupus erythematosus; Corticosteroid.

Introduction

SLE is a chronic systemic inflammatory disease associated with the production of various autoantibodies and involvement of multiple organs. This autoimmune condition has also been known to affect the cardiovascular system; mainly as a pancarditis involving the pericardium, myocardium,[1–3] endocardium[4] and coronary arteries.[4–6] Because of the prolonged survival due to corticosteroid treatment and advances in diagnostic modalities, the cardiovascular manifestations of SLE have become more apparent, and several recent reports have indicated increasing cardiovascular morbidity and mortality in patients with SLE.[1–6]

Aortic aneurysm (AA) is one of the life-threatening cardiovascular complications in patients with SLE. Although the number of cases has been increasing recently, only a total of 16 cases of AA in patients with SLE have been reported hitherto, and little is known about this complication. This report deals with five cases of AAA in patients with SLE treated surgically at our institution during a 10-year period. Based on our experience and a review of the reported cases, we investigated the characteristic clinical features and the mechanism of aneurysmal formation in these patients.

Patients and Methods

Between January 1989 and December 1998, 429 patients with AAA were operated on in our institution. Among them, five cases were associated with SLE (1.2%: 5/429).

Case 1

A 52-year-old woman was admitted because of dysphasia. She had developed a butterfly-rash and fever at the age of 32 and had taken corticosteroid for 16 years (average 3.5 mg/day) after SLE had been

* Please address all correspondence to: N. Ohara, Division of Vascular Surgery, Department of Surgery, Faculty of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan.
† Present address: Division of Vascular Surgery, Department of Surgery, Saitama Medical School, Japan.

1078–5884/00/030288+06 $35.00/0

diagnosed. She had reduced complement levels and proteinuria. Anti-double-strand DNA antibody and anti-nuclear antibody were both positive. The angiogram demonstrated a descending AA and another infrarenal AAA, which were operated on in two stages. The postoperative course was uneventful, but 2 years later she died suddenly during admission for the treatment of a urinary tract infection. Autopsy revealed dissection of the ascending aorta with pericardial tamponade, which was the cause of death. The whole length of the aorta showed striking atherosclerotic change for her age.

Case 2

A 73-year-old man presented with a pulsating mass in his abdomen. He had developed proteinuria, optic hyperaesthesia and arthritis of both shoulders at the age of 72 and had been treated with steroid therapy for one year after the diagnosis of SLE (average 2.5 mg/day). Anti-nuclear antibody was positive. He underwent uneventful replacement of the infrarenal AAA.

Case 3

A 75-year-old woman was admitted for right inguinal herniorrhaphy. She had developed proteinuria, butterfly-rash, intraoral ulcer and endocarditis at the age of 39 and had been on corticosteroids for 32 years after a diagnosis of SLE had been made (average 3.2 mg/day). Physical examination disclosed a pulsating abdominal mass and computed tomography showed a pseudoaneurysm of the infrarenal aorta. At operation, a haematoma was noted to be protruding from the disrupted aneurysmal wall. She recovered uneventfully.

Case 4

A 43-year-old woman presented with a pulsating mass in her abdomen. She experienced Raynaud's phenomenon at the age of 18, endocarditis at 19 and proteinuria at 21. Anti-double-strand DNA antibody and anti-nuclear antibody were both positive. She had taken corticosteroid for 22 years (average 2.8 mg/day). Renal biopsy had proved the diagnosis of lupus nephritis. She underwent an uneventful replacement of the infrarenal AAA.

Case 5

A 34-year-old man was admitted because of bacterial pneumonia. He had been diagnosed with SLE at the age of 13 because of butterfly-rash, fever and proteinuria with positive anti-double-strand DNA antibody and anti-nuclear antibody, and had taken corticosteroid for 21 years (average 4.1 mg/day). The angiogram demonstrated a low thoracoabdominal and an infrarenal abdominal aortic aneurysm (Fig. 1). These were repaired in one stage with reconstruction of the coeliac artery and superior mesenteric artery. He recovered uneventfully.

All of the five patients fulfilled the diagnostic criteria for SLE, and the disease activity was in remission owing to the corticosteroid therapy at the time of surgical procedures for aortic aneurysms. None of them had previously taken any other therapy, e.g. immunosuppressive agents. The medical records were reviewed retrospectively to determine the following factors: age at initial operation, sex, location and type of aneurysm, duration of steroid therapy for SLE, survival and periods of follow-up after operation. The location and type of aneurysms were determined by preoperative angiography or computed tomography. The resected aortic aneurysmal wall of the five patients with SLE was examined histologically. Comparison of the clinical records was performed by Mann–Whitney *U*-test using Statistical Application System software (SAS Institute, Cary, NC, U.S.A.). A p-value less than 0.05 was considered significant.

Results

Four of the five patients had received long-term corticosteroid administration for the treatment of SLE (mean 23, range 1–32 years). The average age of the patients with SLE was younger than that of the other patients without SLE (mean 55 vs. 77 years, $p<0.05$). The sex ratio of our five cases showed a female dominance (male/female – 2/3) compared with the control group (male/female – 344/80; $p<0.01$). Following aneurysm repair, four patients continue to be followed up at our institution without any sign of recurrent aneurysm or other complications (mean 4.3, range 0.5–8.3 years).

The histopathologic features of the resected aneurysmal wall of the five patients with SLE are presented in Table 1. Intimal hypertrophy and medial atrophy were common findings compared to the usual atherosclerotic AAA. On the contrary, the extensive medial destruction in four cases, except for Case 2, was

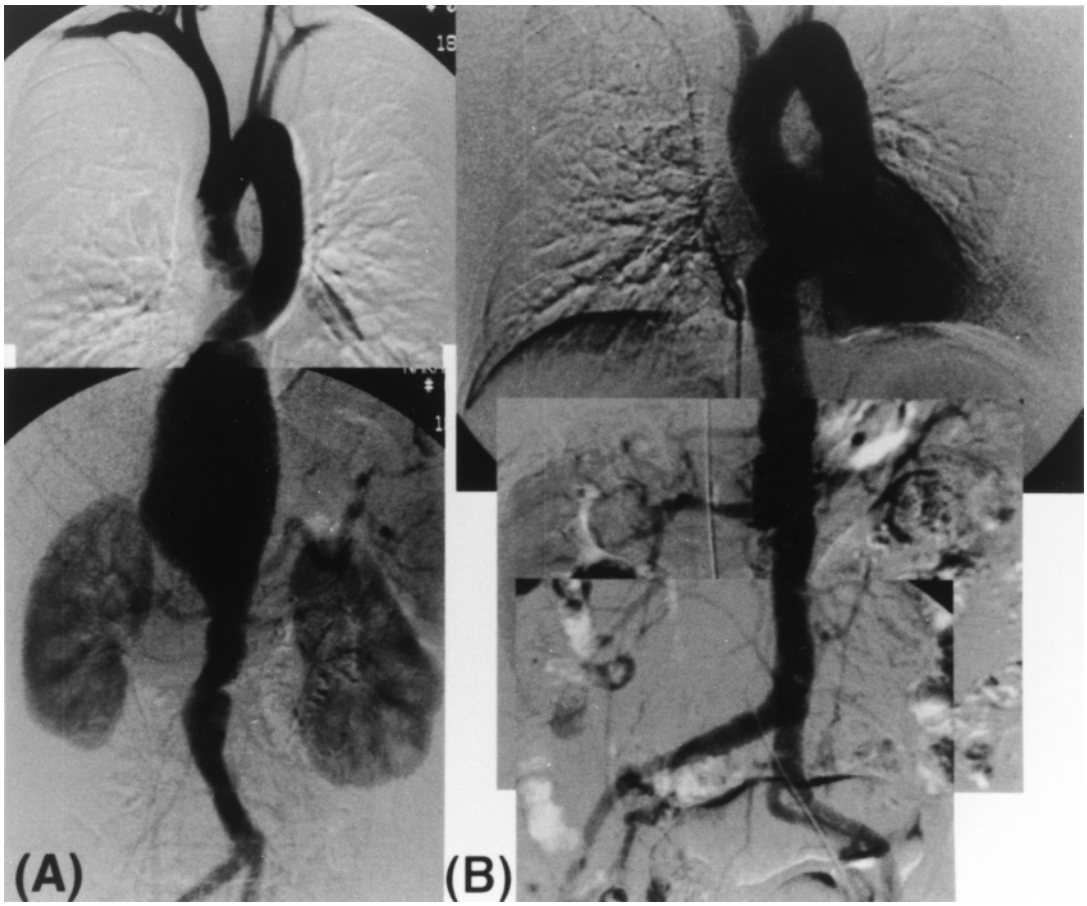

Fig. 1. (A) Angiogram in Case 5 revealed a 7.5-cm low thoraco-abdominal and a 4.5-cm infrarenal abdominal aortic aneurysm. At the level of the renal arteries, the aortic diameter was normal. (B) Postoperative angiography two months after repair of the aneurysms.

Table 1. Histopathologic findings of aortic aneurysms in patients with SLE.

Case	Intimal hypertrophy	Foamy macrophages	Destruction of medial elastic fibres	Medial atrophy	Adventitial fibrosis
1	+	+	++	+	+
2	++	++	+	++	−
3	++	+	++	++	+
4	+	+	++	++	−
5	+	+	++ (#)	+	+
Control group*	++	+	+	++	+

−: absent; +: moderately present; ++: present over wide extensive zone.
#: Worm-eaten-like destruction was present.
*: summarised findings of five consecutive cases with atherosclerotic abdominal aortic aneurysm without SLE.

observed in the patients with SLE. Particularly noteworthy was the abnormal worm-eaten-like medial destruction widely observed in the aneurysmal wall of Case 5 (Fig. 2). No necrotic microvasculitic findings accompanied by fibrinoid necrosis were observed, which is reported to be the characteristic pathological feature in organs of patients with SLE, such as kidney, adrenal gland, digestive tract, spleen, bladder and lung. Micro-

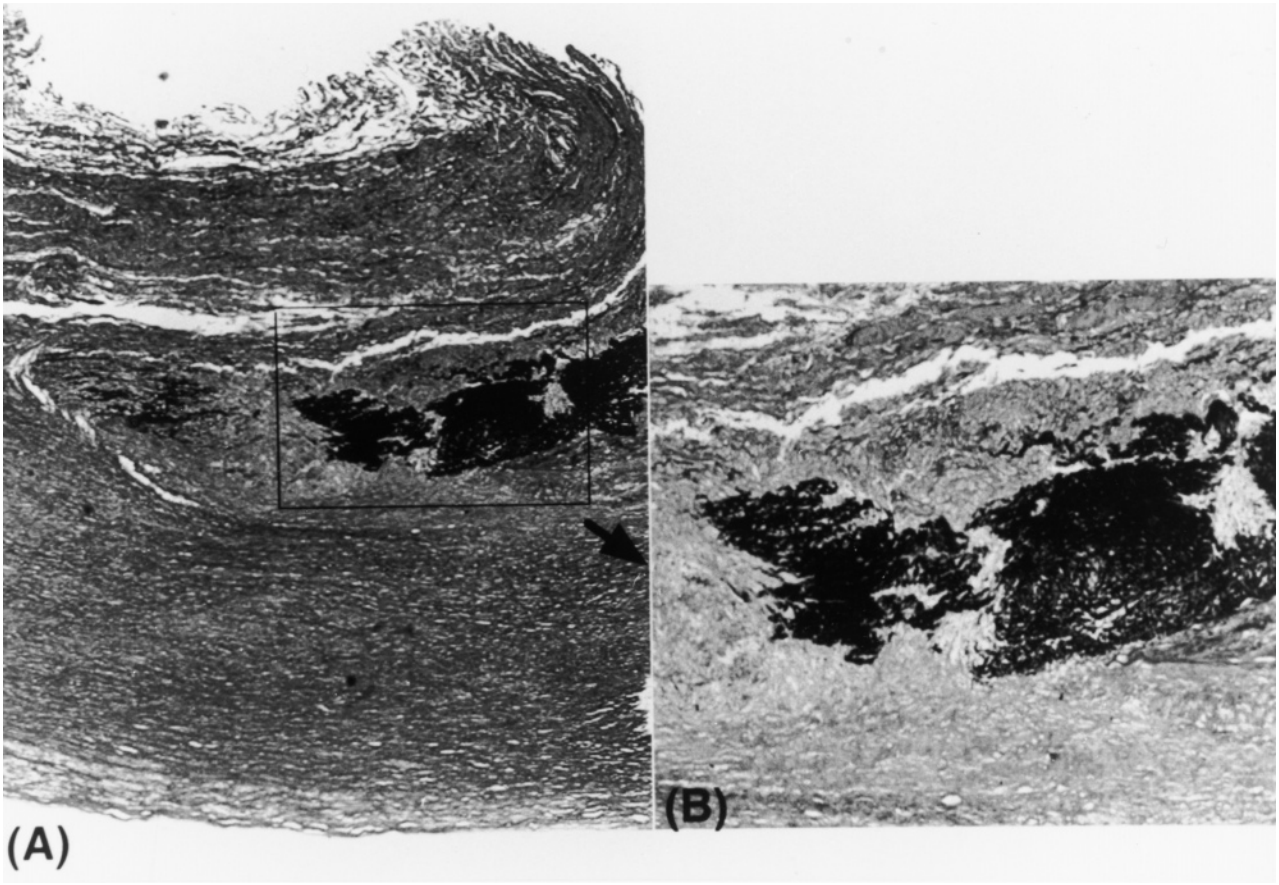

Fig. 2. Medial atrophy with wide zone and severe degree of destruction of medial elastic fibres, together with abnormal worm-eaten-like medial destruction are demonstrated in Case 5. (Elastic van Gieson stain, (A) ×40, (B) ×100.)

infarcts and marked vasculitis associated with granulation tissue formation suggesting primary arteritis were not present.

Discussion

During the past decade, we have experienced five patients with AAAs who have previously been diagnosed as having SLE. To our knowledge, only 16 cases of AA associated with SLE have been previously reported in the literature.[7–22] The clinical features of these patients are given in Table 2.

The age of reported cases ranged from 28 to 65 years old (mean 40 years), which was also about 30 years younger than the mean age of our patients of AAA without SLE. The patients included seven males and nine females, and the female dominance, also present in our series, may reflect the greater prevalence of this autoimmune condition in women. The location of the AAs varied: four in the ascending aorta, three in the aortic arch, three in the descending aorta, two in the upper abdominal aorta and two in the infrarenal aorta. In two cases, enlargement of the entire aorta was noted. There were no reports of multiple aneurysms. The type of aneurysm in the 16 reported cases consisted of twelve dissecting aneurysms, three fusiform aneurysms and one pseudoaneurysm. Characteristically, aortic dissections were well represented in the series (12/16, 75%), and almost all cases with dissection were fatal except for three patients.[15,18,21] In our series, only one case of acute aortic dissection was clinically diagnosed two years after the initial aneurysmectomy. This predominance of aortic dissection accounts for the difference in clinical results of reported cases from those in our treated patients.

As with our cases, the most common denominator in the reported series was also long-term corticosteroid therapy for SLE (range 1–22 years: mean 9 years). Adrenocorticosteroid administration has been recognised to be the main therapeutic option for SLE, the effects of which are well known, with inhibition of the formation of granulation tissue and chondroitin sulphate.[23] Administration has improved the overall

Table 2. Reported cases of aortic aneurysms associated with autoimmune disease.

Authors (year of publication)	Age/sex	Location	Type of aneurysm	Operability	Survival	Duration of steroid therapy (years)
Bernhard[7] (1969)	30/F	Asc	Dissection	+	Dead	4
Walts[8] (1977)	34/M	All	Dissection	−	Dead	22
Okiye[9] (1983)	33/M	Des	Dissection	+	Dead	6
Pazirandeh[10] (1988)	36/F	Arc	Dissection	−	Dead	2.5
Kimura[11] (1989)	38/F	Arc	Dissection	−	Dead	7
Seyama[12] (1989)	54/M	AAS	Fusiform	+	Alive	1.5
Yoshimato[13] (1989)	28/F	All	Dissection	−	Dead	11
Chakravarty[14] (1992)	43/F	Arc	Fusiform	+	Alive	1
Dugo[15] (1993)	29/F	AAS	Dissection	−	Alive	1
Stehbens[16] (1993)	56/M	AAI	Saccular	+	Alive	16
Roger[17] (1995)	31/F	Asc	Dissection	−	Dead	12
Ohge[18] (1995)	55/F	Asc	Dissection	+	Alive	11
Sclair[19] (1995)	30/F	Des	Dissection	−	Dead	13
Lam[20] (1997)	65/M	Des	Dissection	−	Dead	1
Hussain[21] (1998)	40/M	Asc	Dissection	+	Alive	22
Marubayashi[22] (1998)	40/M	AAI	Fusiform	+	Alive	18
	40.4±11.5 S.E.M.					9.2±7.7 S.E.M.

AAI: infrarenal abdominal aorta; AAS: suprarenal abdominal aorta; All: entire aorta; Arc: aortic arch; Asc: ascending aorta; Des: descending aorta.

prognosis of these patients, but may result in deleterious effects on the cardiovascular system.[24,25] Bulkley and Roberts reported an increased incidence of hypertension, left-ventricular hypertrophy and atherosclerosis in patients with SLE treated with steroid for over 1 year.[26] It can accelerate atherosclerotic change of the aortic wall, which is a well-noted complication of patients with SLE. The contribution of corticosteroids to the development of aortic lesions in patients with SLE has been difficult to assess, and there have been no reports concerning aortic aneurysmal formation due to corticosteroid administration in patients without SLE.

There have been only a handful of reports describing detailed findings of the aorta aneurysm histopathologically. Moreover, only one case report by Stehben *et al.*[16] gives a pathological description of a non-dissecting aortic aneurysm associated with SLE. They described the findings of thrombus with underlying atheromatous debris containing lipophages and remaining medial elastic fibres deep to the debris, which also did not differ from the findings in patients with atherosclerotic AAA without SLE. Moreover, the wide zone of medial destruction shown in our patients with SLE was not reported in the paper by Stehben. Nashel reported that accelerated atherosclerosis was associated with long-term corticosteroid treatment, in patients with rheumatoid arthritis.[27] The histological findings of our four patients on prolonged steroid therapy except for Case 2 demonstrated intimal atherosclerosis at a young age even though they had few other risk factors, e.g. of smoking (1/5), hypertension (1/5), ischaemic heart disease (0/5), diabetes mellitus (0/5) and hyperlipidaemia (0/5). The absence of necrotic microvasculitis accompanied by fibrinoid necrosis may also reflect the effect of long-term steroid therapy,[6,24,26] although it weakens the medial elastic lamina.[26]

In conclusion, prolonged corticosteroid administration seems to play a major role in accelerating atherosclerosis, which can result in aortic aneurysmal enlargement, possibly together with primary aortic-wall involvement and/or vasculitic damage, particularly severe medial destruction, in patients with SLE. However, the absence of fibrinoid necrosis, a characteristic finding in the organs of patients with SLE, supports the causal link between the prolonged corticosteroid therapy and the aortic aneurysmal enlargement.

References

1 Oh WMC, Taylor RT, Olsen EGJ. Aortic regurgitation in systemic lupus erythematosus requiring aortic valve replacement. *Br Heart J* 1974; **36**: 413–416.

2 Yetes DB, Scott JT. Cardiac valvular disease in chronic inflammatory disorders of connective tissue. *Ann Rheum Dis* 1975; **34**: 321–325.

3 MacLeod CB, Johnson D, Frable WJ. "Tree-barking" of the ascending aorta. *Am J Clin Pathol* 1992; **97**: 58–62.

4 Shearer MA. Review: the heart in systemic lupus erythematosus. *Am Heart J* 1959; **58**: 452–466.

5 Bonfiglio TA, Botti RE, Hagstrom JWC. Coronary arteritis, occlusion and myocardial infarction due to lupus erythematosus. *Am Heart J* 1972; **83**: 153–158.

6 Cervera R, Font J, Pare C *et al.* Cardiac disease in systemic lupus erythematosus: prospective study of 70 patients. *Ann Rheum Dis* 1992; **51**: 156–159.

7 Bernhard GC, Lange RL, Hensley GT. Aortic disease with valvular insufficiency as the principal manifestation of systemic lupus erythematosus. *Ann Intern Med* 1969; **71**: 81–87.
8 Walts AE, Dubois EL. Acute dissecting aneurysm of the aorta as the fatal event in systemic lupus erythematosus. *Am Heart J* 1977; **93**: 378–381.
9 Okie SE, Sterioff S, Schaff HV, Engen DE, Zincke H. Acute dissecting aneurysm of the aorta after renal transplantation. *J Urol* 1983; **129**: 803–804.
10 Pazirandeh M, Ziran BH. Dissecting aortic aneurysm in a patient with systemic lupus erythematosus. *J Rheumatol* 1988; **15**: 525–527.
11 Kimura K, Maeta T, Shitomi K *et al.* A case of systemic lupus erythematosus complicated with dissecting aortic aneurysm. *Nippon Naika Gakkai Zasshi* 1989; **78**: 591–592.
12 Seyama K, Muto J, Furuya H *et al.* A case of upper abdominal aortic aneurysm associated with systemic lupus erythematosus. *Jin to Touseki* 1989; **27**: 1139–1144.
13 Yoshimoto K, Saima S, Nakamura Y *et al.* A case of acute dissecting aneurysm of the aorta in systemic lupus erythematosus. *Nippon Jinzo Gakkai Shi* 1989; **31**: 1211–1216.
14 Chakravarty K, Scott DGI. Mycotic aneurysm of the aortic arch masquerading as systemic lupus erythematosus. *Ann Rheum Dis* 1992; **51**: 1079–1081.
15 Dugo M, Liessi G, De Luca M *et al.* Dissection of the thoracic-abdominal aorta in a young adult with systemic lupus erythematosus. *Clin Nephrol* 1993; **39**: 349–351.
16 Stehbens WE, Delahunt B, Shirer WC, Naik DK. Aortic aneurysm in systemic lupus erythematosus. *Histopathology* 1993; **22**: 275–277.
17 Guard RW, Graham IG, Edmonds JP, Thomas AC. Aortitis with dissecting complicating systemic lupus erythematosus. *Pathology* 1995; **27**: 224–228.
18 Ohge H, Imai K, Shirage K *et al.* A case of surgical treatment of acute aortic dissection without an intimal tear. *J Jpn Assoc Thorac Surg* 1995; **46**: 866–869.
19 Sclair M, Nassar H, Bar-Ziv Y, Putterman C. Dissecting aortic aneurysm in systemic lupus erythematosus. *Lupus* 1995; **4**: 71–74.
20 Lam KY, Cheung F, Yam LYC, Lee CH, Fung KH. Atypical manifestations in a patient with systemic lupus erythematosus. *J Clin Pathol* 1997; **50**: 174–176.
21 Hussain KM, Chandna H, Santhanam V *et al.* Aortic dissection in a young corticosteroid-treated patient with systemic lupus erythematosus. *Angiology* 1998; **49**: 649–652.
22 Marubayashi S, Sugi K, Ishiyama K *et al.* A case of abdominal aortic aneurysm associated with systemic lupus erythematosus. *Hiroshima J Med Sci* 1998; **47**: 85–87.
23 Lorenzen I. Corticosteroid and vascular connective tissue. *Acta Endocrinol* 1969; **62**: 67–76.
24 Bernhard GC, Lange RL, Hensley GT. Aortic disease with valvular insufficiency as the principal manifestation of systemic lupus erythematosus. *Ann Intern Med* 1969; **71**: 81–87.
25 Doherty NE, Siegel RJ. Cardiovascular manifestations of systemic lupus erythematosus. *Am Heart J* 1985; **110**: 1257–1265.
26 Bulkley BH, Roberts EL. The heart in systemic lupus erythematosus and the changes induced in it by corticosteroid therapy. A study of 36 necropsy patients. *Am J Med* 1977; **58**: 243–264.
27 Nashel DJ. Is atherosclerosis a complication of long-term corticosteroid treatment? *Am J Med* 1986; **80**: 925–929.

Accepted 1 July 1999