Journal of Korean Medical Science
Vol 6, No. 1, 75-82, March 1991

Thoracic Aortic Aneurysm Associated with Aortitis

—Case Reports and Histological Review—

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Ten cases of post-inflammatory aneurysm of the thoracic aorta were studied morphologically using aortic wall and aortic valve tissue resected during the surgical repair of the lesions. Four cases of aortic aneurysm in Behcet's disease showed massive perivascular infiltration of the lymphocytes and plasma cells in adventitia and vasa vasorum. Fibrous obliteration of the vasa vasorum was seen, and neutrophilic infiltration was also associated in two cases with recurrent prosthetic valve failure. Three cases of aortic aneurysm associated with Takayasu's arteritis showed similar histologic features, but giant cells and histiocytic reactions were additional findings. Plasma cell infiltration was more pronounced compared to the Behcet's aortitis. One case of luetic aortitis showed a non-specific chronic inflammatory reaction with florid endothelial cell proliferation. One case of ankylosing spondylitis showed fibrous thickening at the periannular portion of the aortic valve cusps, but this finding was also seen in an aortic valve of a patient with Behcet's disease. One case without any diasease association showed similar features of chronic inflammation with granuloma formation. The findings suggest that they have similar histologic features indistinguishable in terms of the clinical disease association, but a granulomatous reaction could be expected in Takayasu's arteritis.

Key Words : *Aortitis, Aortoannuloectasia, Thoracic aortic aneurysm Behcet's disease, Takayasu's arteritis, Ankylosing spondylitis, Luetic aortitis.*

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This study is supported in part by a Seoul National University Hospital Research Grant (Lee SK) (1988).
Excerpts of this paper were presented at the 13th Spring Meeting of the Korean Society of Pathologists on May 20, 1988.

INTRODUCTION

Histologic abnormality of the aortic initma and media has been implicated in the pathogenesis of ascending aortic aneurysm and dissection (Klima et al., 1983). It has been suggested that cystic medial degeneration is the most common histologic expression of aortic annuloectasia and ascending aortic aneurysm in patients with Marfan's syndrome (Roberts and Honig, 1982).

However, some cases showed primarily inflammatory change without a significant accompanying degenerative process. Syphilis was a common etiology of aortic aneurysm in the past (Heggtveit, 1964), but it has become a rare disease nowadays. Takayasu's arteritis is a well known example of post-inflammatory aortic aneurysm (Lindsay et al., 1990), and several cases of aortitis and aneurysms in Behcet's disease (James and Thomson, 1982) and anklosing spondylitis have been reported (Bulkley and Roberts, 1973). The etiology and pathogenesis of these lesions are unknown, but vasculitidis involving the vasa vasorum and adventitial vessels are most probably the morphogenetic mechanism of the lesions. We studied 10 cases of inflammatory aortitis syndrome with special emphasis on their histologic differences and possible histogenetic implications.

MATERIALS AND METHODS

Ten cases with clinicopathologic evidence of postinflammatory aortic wall disease were analyzed. They underwent surgical treatment of thoracic aortic aneurysm and aortic annuloectasia from 1986 to 1989 at the Seoul National University Hospital. The clinical features were analyzed to exclude the possibility of primary aortic valve lesion and aortopathy showing cystic medial degeneration with or without associated marfan's syndrome, as well as to categorize the cases into Behcet's disease, Takayasu's arteritis, luetic aortitis, ankylosing spondylitis, or others (Table 1). Both aortic wall and aortic valve tissue were available in 5 cases, but only the aortic wall was resected in two cases, while the aortic valve was resected in 3 cases. The specimens were fixed in formalin, embedded in paraffin, sectioned in 5μ thickness and stained with hematoxilin and eosin, Masson's trichrome and von Verhoeff's stain.

RESULTS

The clinical features of 9 cases could be categorized into Behcet's desease, Takayasu's arteritis, syphilis, and ankylosing spondylitis. However, clinical evidence of these disease associations was lacking in one case. The histology of the aortic wall showed

Table 1. Clinicopathologic Summary of the Cases.

Case No.	Age/Sex	Systemic Manifestations and History	Cardiovascular Manifestation
1	34/F	Pleural effusion 6 yr ago Incomplete Behcet's disease 4yr ago	Pericardial errusion. Aortic regurgitation with annuloectasia. Narrowing of carotid, left renal, and superior mesenteric arteries
2	34/M	Complete Behcet's disease, Repeated prosthetic valve failure(5 operations)	Aortic regurgitation Mitral stenoinsufficiency
3	36/M	Incomplete Behcet's disease, Repeated prosthetic valve failure(3 operations)	Aortic regurgitation
4	28/M	Incomplete Behcet's disease	Aortic regurgitation
5	30/M	Malignant hypertension 8 yr ago, Takayasu's disease	Dissecting aortic aneurysm. Aortic regurgitation. Occlusions of coronary arteries
6	31/F	Takayasu's disease	Dissecting aortic aneurysm. Tortuous and narrowed aorta with saccular aneurysms Renal artery origin stenosis
7	33/M	Aortic valve replacement due to aortic regurgitation, 3 yr ago. Takayasu's disease	Aneurysm and rupture of sinus Valsalva Fusiform aneurysm of ascending aorta Occlusions of LCCA, LSCA
8	57/M	Diabetes mellitus for 6 yr. Syphilitic aortitis	Multiple saccular aneurysms at thoracic and abdominal aortae
9	28/M	Ankylosing spondylitis 6 mo ago	Aortic regurgitation for 4 yr
10	31/F	Increased ESR, 2+ reactive CRP	Pericardial effusion Annuloectasia Thickening and dilatation of BCA

yr. : years
mo. : months
ESR : erythrocyte sedimentation rate
CRP : c-reactive protein
LCCA : left common carotid artery
LSCA : left subclavian artery
BCA : brachiocephalic artery

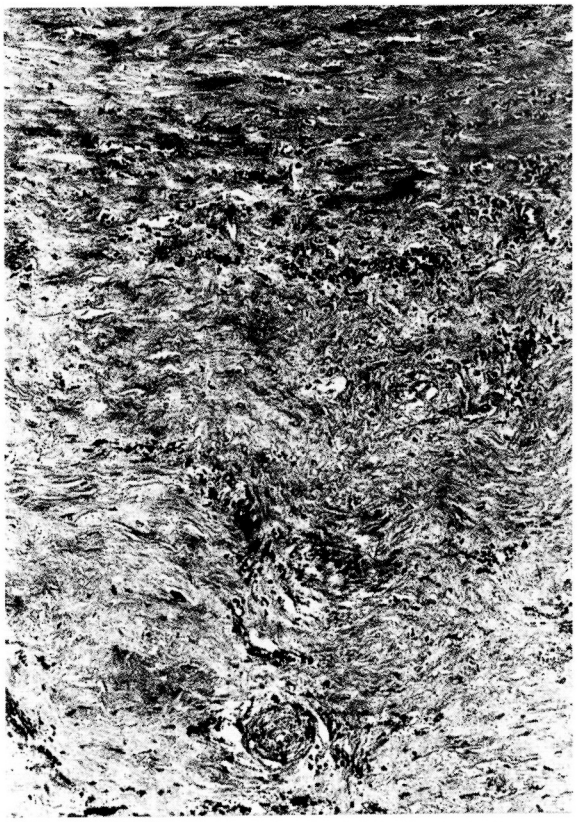

Fig. 1A. A common microscopic feature of the outer half of the aortic wall. Irregular fibrosis and multiple patchy collections of mononuclear cells are seen. (Hematoxylin & eosin, ×100).

Fig. 1B. Elastic fibers are markedly decreased and fragmented. (Von Verhoeff stain, ×100).

common features of dense fibrous scar, loss of elastic fibers, and patchy infiltration of the inflammatory cells without significant participation of myxoid degeneration (Fig. 1 A,B). Aortic valve leaflets showed increased thickness near the annulus and myxoid degeneration without increase of blood vessels (Fig. 2).

1. Aortitis with Behcet's disease

Four patients had clinical evidence of Behcet's disease. Three patients were male and one was female. The mean age at first operation was 33 years. Case 1 was a 34-year-old woman. She was diagnosed as Behcet's disease 4 years before the clinical presentation of cardiovascular lesions. Oral ulcers, skin lesions, and Raynaud's phenomenon were present, and mild fever and an elevated erythrocyte sedimentation rate were associated. Pericardial effusion, aortic insufficiency, and stenoses of the renal and mesenteric arteries were present. Case 2 was 34-year-old man. He had presented with aortic insufficiency, and mitral steno-insufficiency, and double valve replacement was performed. However, he underwent 4 additional ope-

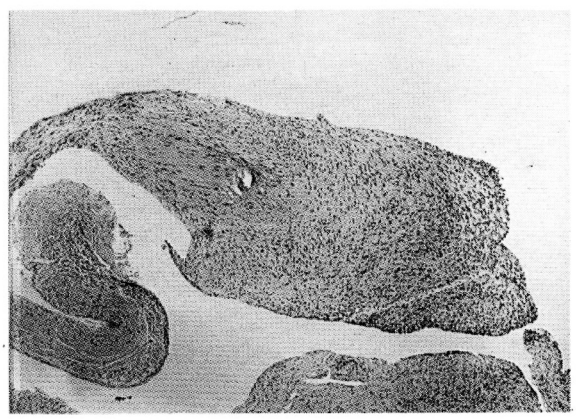

Fig. 2. Scanning view of the resected aortic valve shows fibrous thickening of leaflets and myxoid change, however, vascularization is not associated. (Hematoxylin & eosin, ×100).

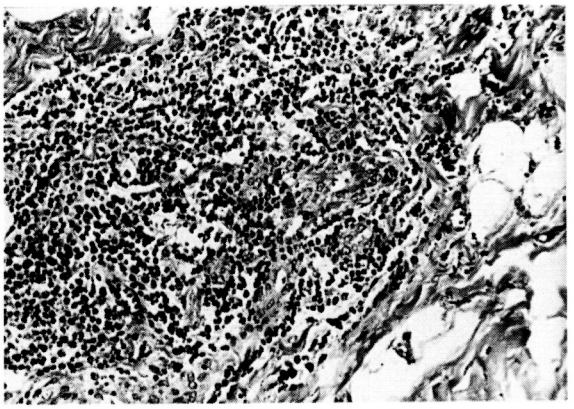

Fig. 3. Adventitial inflammation seen in Behcet's disease (Case 2). Perivascular cuffing by lymphocytes is seen. (Hematoxyllin & eosin, ×100).

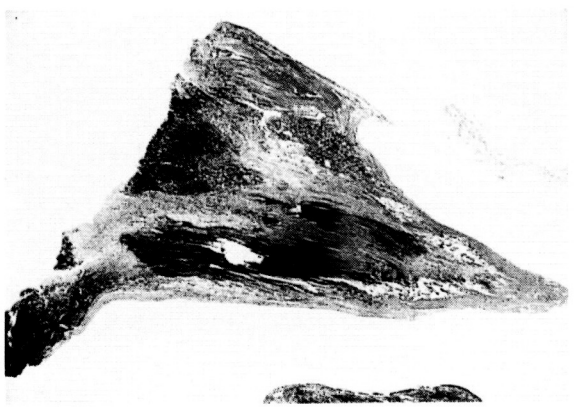

Fig. 4. Papillary muscle resected in Case 2 shows ischemic necrosis and hemorrhage. (Hematoxylin & eosin, ×10).

rations due to repeated aortic insufficiency and aortic graft failure during a 20-month period, but clinical evidence of Behcet's disease was detected only after the third operation. Oral and genital ulcers, skin lesions and uveitis were present. Case 3 was a 30-year-old man. He also underwent three operations during a 20-month period due to repeated failure of aortic valve prosthesis. Case 4 was a 28-year-old man. Aortic insufficiency manifested and aortic valve replacement and aortic wall biopsy were performed. The operative findings of these cases were very similar, being characterized by aortic annuloectasia and aneurysmal dilatation of the ascending aorta. Intimas of the aortas were edematous. Aortic valve leaflets were floppy without a significant increase in thickness and the commisures were intact.

The histology of the aortic wall in cases 2 and 4 showed irregular medial and adventitial fibrosis and infiltration of lymphocytes and plasma cells around the vasa vasorum Stenosis and sclerosis of the vasa vasorum were seen (Fig. 3). Masson's trichrome and von Verhoeff's stains revealed irregular disruption of the elastic fibers and fibrous replacement of media. However, myxoid degeneration of the wall was not pronounced and atherosclerotic change was meager. Giant cell reaction and fibrinoid necrosis were not associated. Case 2 showed an old infarct in the papillary muscles resected for mitral valve replacement (Fig. 4). Aortic valve cusps showed mild myxoid degeneration of the leaflets. Case 1 showed preferential thickening at the periannular regions of the cusps, but postinflammatory vascularization was not associated.

2. Aortitis with Takayasu's arteritis

Three cases were clinically diagnosed as having Takayasu's arteritis. Their mean age was 31 years, and 2 were female patients. Case 5 was a 30-year-old man who presented with acute chest pain after a history of malignant hypertension for 8 years. An echocardiogram revealed aortic regurgitation and left ventricular dysfunction, thickened aortic wall, and luminal dilatation in the ascending aorta, dilatation and thrombosis in the descending thoracic aorta, and severe stenosing lesion in the left common, left anterior descending and left circumflex coronary arteries. A coronary artery bypass graft and aortic valve graft were inserted, but the patient died postoperatively. Case 6 was a 30-year-old woman who presented with a mediastinal mass and hypertension. Aneruysmal dilatation and dissection of the descending thoracic aorta and narrowed tortuous abdominal aorta with saccular aneurysm were detected 3 years before her operation. The proximal portion of the renal artery was stenotic. Resection of the aneurysm and a bypass graft were performed. Her postoperative course was uneventful for 1 year except for persisting hypertension of 190/110㎜Hg. Case 7 was a 33-year-old man who had a history of aortic valve replacement 3 years ago. Coarctation of the aorta, aortic insufficiency, and narrowings of the left common carotid and left subclavian arteries were also detected. He presented recently with acute heart failure and continuous murmur. Aortography revealed a fusiform aneurysm of the ascending aorta and aneurysm and rupture at the sinus Valsalva.

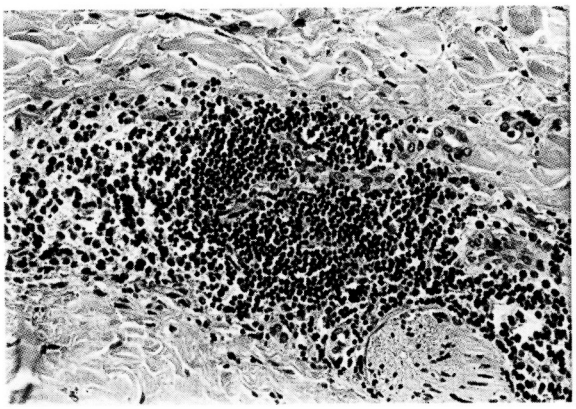

Fig. 5. A dense perivascular collection of lymphocytes is surrounded by plasma cell zone in Takayasu's disease (Case 7). (Hematoxylin & eosin, ×100).

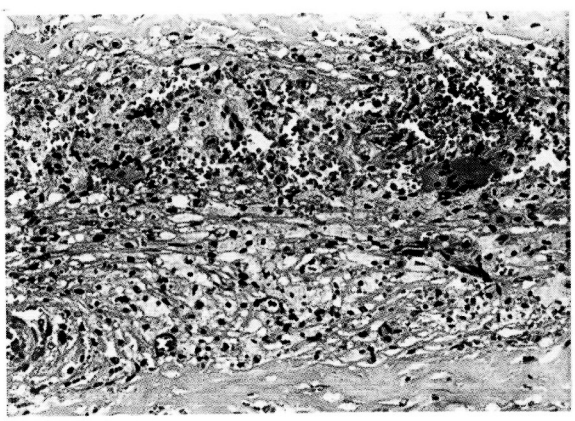

Fig. 6. A granuloma seen in Takaysu's disease (Case 6) consists of a few giant cells and a few histiocytes in loose edematous stroma. (Hematoxylin & eosin, × 100).

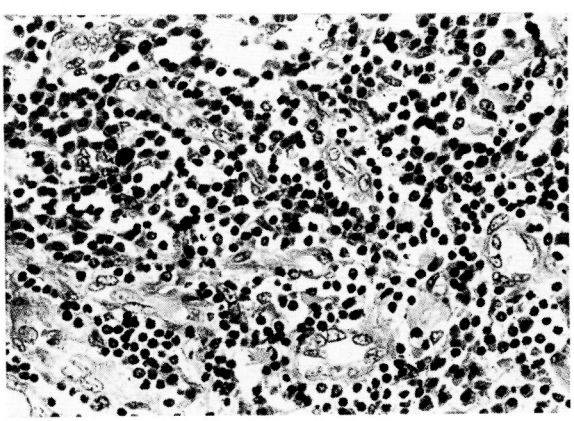

Fig. 7. Aortitis seen as syphilis (Case 8) shows florid proliferation of endothelial cells and inflammatory infiltrates mainly consisting of plasma cells. (Hematoxylin & eosin, ×200).

Benthal's operation was performed.

All three cases(case 3,5 & 6) showed multiple nodules of perivascular infiltration of lymphocytes and plasma cells. Inflammatory nodules were seen at the junction between the media and adventitia or at the junction of the inner compact collagen layer and outer loose areola layer of adventitia (Fig. 5). Two or the subintimal media in 1 case. The inflammatroy nodules were composed of central compact collections of lymphocytes and a peripheral plasma cell zone (Fig. 5).

3. Aortitis with clinical features of syphilis

Case 8 was a 57—year-old man. He was clinically suspected of having luetic aortic aneurysm, and both VDRL and TPHA were reactive. Multiple saccular aneurysms were seen at the thoracic and abdominal aortas. Histologic examination revealed marked proliferation of endothelial cells, fibrosis of adventitia, diffuse plasma cell infiltration in the adventitia and nodular inflammation around the vasa vasorum and fibrosis of the wall (Fig. 7). However, granulomatous lesion was not associated. Spirochetal organism could not be demonstrated in the lesion.

4. Aortitis with ankylosing spondylitis

Case 9 was a 28—year-old man. He had suffered from sacroiliitis and uveitis for 6 months. He had cardiac symptoms for the last 4 years. Aortic insufficiency was detected, and a resected aortic valve for valve replacement operation showed thickening of the leaflets were normal except for mild myxoid degeneration.

5. Aortitis without any other disease association

Case 10 was a 31—year-old woman. Serologic tests for syphilis were negative, and he had no previous or postoperative history of stigmata of Behcet's disease of Takayasu's disease, but his erythrocyte sedimentation rate was elevated to 60㎜hr and C-reactive protein was positive. Pericardial effusion and aortoannuloectasia were present. Bengthal's operation was performed when the brachiocephalic trunk showed a thickening and mild dilatation and the aortic intima was edematous.

Histologic features were similar to those with Takayasu's arteritis, being characterized by a few granulomatous lesions, plasma cell infiltration, and sclerosis of the vasa vasorum. Medial fibrosis was

Table 2. Summary of clinical

Case No.	Age/Sex	Systemic Manifestations and History	Cardiovascular Manifestation
1	34/F	pleural effusion 6 yr ago Incomplete. Behcet's disease 4yr ago	Thickening at periannular regions of the cusps
2	34/M	Complete Behcet's disease. Repeated prosthetic valve failure(5 operations)	Medial and adventitial fibrosis Infiltration of lymphocytes and plasma cells around the vasa vasorum
3	36/M	Incomplete Behcet's disease. Repeated prosthetic valve failure(3 operations)	Medial and adveutitial fibrosis Infiltration of lymphocytes and plasma cells around the vasa vasorum
4	28/M	Incomplete Behcet's disease	Medial and adventitial fibrosis Infiltratiou of lymphocytes and plasma cells around the vasa vasorum
5	30/M	Malignant hypertension 8 yr ago. Takayasu's disease	Multiple nodules of perivascular infiltration of lymphocytes and plasma cells
6	31/F	Takayasu's disease	Multiple nodules of perivascular infiltration of lymphocytes and plasma cells
7	33/M	Aortic valve replacement due to aortic regurgitation, 3 yr ago. Takayasu's disease	Multiple nodules of perivascular infiltration lymphocytes and plasma cells
8	57/M	Diabetes mellitus for 6 yr. Syphilitic aortitis	Proliferation of endothelial cell. Fibrosis of adventitia Diffuse plasma cell infiltration in adventitia
9	28/M	Ankylosing spondylitis 6 mo ago	Fibrous thickening at the periannular portin of aortic valve cusps
10	31/F	Increased ESR, 2+ reactive CRP	Chronic inflammation with granuloma formation

yr. : years mo. : months
ESR : erythrocyte sedimentation rate CRP : c-reactive protein

present, but myxoid degeneration was not conspicuous. The clinical features and histologic findings are summurized in Table 2.

DISCUSSION

Because Marfan's syndrome is by far the most common hereditary connective tissue disease affecting the aortic media, etiologic studies on this aortic aneurysm have been aimed to categorize Marfan's syndrome and nonMarfan group (Klima et al., 1983). Non-Marfan group consisted of cases with histological similarities to the Marfan's syndrome, showing myxoid degeneration of media and atherosclerotic aneurysm. However, myxoid degeneration perse is considered to be a phenomenon of injury and repair caused by hemodynamic events (Schlatmann and Becker, 1977). Aterosclerosis is the most common cause of abdominal aortic aneurysm, but it tends to spare the ascending portion of the aorta unless diabetes of type II hyper-lipoproteinemia are associated (Lindsay et al., 1990). Syphilitic aoartic aneurysm was considered to be a common cause of aortitis and aortoannuloectasia in the preantibiotic era (Heggtveit, 1964) but it is a very rare disease nowadays. Excluding aortic inflammation associated with primarily valvular aortic disease and dissecting aneurysm of either Marfan's syndrome or atherosclerotic aneurysm, primary inflammatory lesion of aorta is rare. Infectious lesions by organisms of the Salmonella group or tuberculosis may affect the aorta resulting in mycotic aneurysms (Johansen and Devin, 1983), but they are more commonly seen in the abdominal aorta. Takaysu's arteritis is a prototype of noninfectious postinflammatory aortic aneurysm, but Behcet's disease and several connective tissue diseases are also known to induce aortic lesions. Takayasu's arteritis is a disease characterized by inflammation and stenosis of large and medium sized arteries with frequent involvement of the aortic arch and its branches. (Hall et al., 1985). But the ascending aorta may be involved and the histology was granulomatous or sclerosing arteritis in the vasa vasorum or major branches of the aorta (Hall et al., 1985). Behcet's syndrome primarily affects small vessels and induces myocarditis in the cardiovascular system, but there are several reports of cases

associated with ascending aortic inflammation and annuloectasia (James and Thomsomn, 1982 ; Hills, 1967 ; Park et al., 1984).

The present cases with Behcet's disease had various clinical stigmata of oral ulcers, genital ulcers, uveitis, and skin lesions along with other minor manifestations (Behcet's disease research committee of Japan, 1974 ; Eun et al., 1984). Case 2 could be categorized into a complete type, but Cases 1, 3, and 4 were of the incomplete type. Cardiovascular manifestations of those cases were aortic insufficiency in all 4 cases, but stenosis of the aortic branches was present in Case 1, suggesting a possibility of associated or coexistent Takayasu's arteritis (Lakhanpal et al., 1985). Papillary muscle infarct was seen in Case 2, which would be related to the coronary arteritis in Behcet's disease as was documented by Schiff and his associates (1982). Repeated failure of the prosthetic aortic valve was seen in Cases 2 and 3, which may be related with the consistent surgical findings of edematous aortic intima. Histologic examination revealed occlusive vasculitis with heavy infiltration of the plasma cells and lymphocytes in the media and adventitia. Fibrosis and fragmentation of the elastic fibers were ween but giant cell and granulomatous reactions were not associated. The cases with Takayasu's arteritis had stenotic lesions in the aortic branches. Aortic insufficiency was present in Cases 5 and 7. Dissecting aneurysm was present in Cases 5 and 6. Histologic examination revealed similar features to that of Bechcet's disease, but granuloma formation was present in every case. Stigmata of Behcet's disease was denied by the patients. Aortic regrugitaion and aneurysm are well-known complications of Takayasu's arteritis, but the histologic features of theis lesion have rarely been studied. Granulomatous vasculitis is a main histologic feature, and that is one of the microscopic similarities to the aortitis in giant cell arteritis or polyarteritis nodosa (Ishikawa, 1987).

Behcet's disease and Takayasu's disease have distinct clinical manifestations, but some of the cases with Takayasu's arteritis have constitutional symptoms suggesting a possibility of other immune-mediated lesions including Behcet's disease. Our Case 2 had clinical features of both Behcet's disease and Takayasu's disease. Case 10 had an elevated erythrocyte sedimentation rate and positivity for C-reactive protein. Operative findings of edematous intima and a thickening of the wall in the brachiocephalic trunk suggested a possibility of an early manifestation of Takayasu's disease.

The histologic difference among the lesions is not expected to be evident, and differential diagnosis may be impossible in most cases. But we could find several histologic differences according to the cause of the lesions. Granuloma formation was seen in every case of Takayasu's disease and in one case suspected to be such. The granuloma was a minute collecton of one or two giant cells and a few histiocytes in the edematous stroma. Both Takayasu's disease and Behcet's disease showed perivascular cuffing in vasa vasorum. Plasma cells were mainly seen at the margin of the central lymphocytic zone, and the plasma cell reaction was more pronounced in Takayasu's disease. Behcet's aortitis seemed to be a rather acute process and repeated graft failure was present in two instances.

A diagnosis of syphilitic aortitis is rarely conclusive because bacteriologic demonstration of the organism is rarely successful. The clinical history and laboratory finding are also misleading in many cases (Heggtveit, 1964). However, serologic findings and multiple saccular aneurysms in the thoracic aorta of the present Case 8 strongly supported its luetic origin. The endothelial proliferation was much more pronounced, and loosely-arranged inflammatory cells mainly consisted of plasma cells, compared to other cases.

The aortic valve in one case of ankylosing spondylitis showed a characteristic feature of dense adventitial scar involving a periannular portion of the aortic valve (Bulkley and Roberts, 1973). But one case of Behcet's disease (Case 1) in the present study also showed similar histology to a mild degree.

These findings suggest that vascular obliteration is a major pathogenetic mechanism regardless of the cause of the lesions, but cellular response and the degree of inflammatory cellular infiltration showed minor differences according to their causes.

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