References

- Angelini A, Basso C, Nava A at al. *Endomyocardial biopsy in arrhythmogenic right ventricular cardiomyopathy.* Am Heart J 1996; 132: 203-206.
- Basso C, Thiene G, Corrado D at al. *Arrhythmogenic right ventricular cardiomyopathy: Dysplasia, dystrophy or myocarditis?* Circulation 1996; 94: 983-991
- Basso C, Thiene G, Nava A et al. *Arrhythmogenic right ventricular cardiomyopathy: A survey of the investigations at the University of Padua.* Clin Cardiol 1997; 20: 333-336.
- Corrado 0, Thiene G, Nava A et al. *Sudden death in young competitive athletes: Clinicopathologic correlation in 22 cases.* Am J Med 1990; 89: 588-596.
- Corrado 0, Basso C, Thiene G et al. *Spectrum ot clinocopathologic manifestations of arrhythmogenic right ventricular cardiomyopathy/dysplasia: A multicenter study* JAm Coil Cardiol 1997; 30:1512-1520.
- McKenna WJ, Thiene G, Nava A at al. *Diagnosis of arrhythmogenic right ventricular dysplasia/cardiomyopathy* Br Heart J 1994; 71: 215-218.
- Menghetti L, Basso C, Nava A at al. *Spin-echo nuclear magnetic resonance for tissue characterization in arrhythmogenic right ventricular cardiomyopathy* Heart 1997; 76: 467-470.
- Nava A, Thiene G, Canciani B et al. *Familial occurrence of right ventricular dysplasia: A study involving nine families.* J Am Coil Cardiol 1988; 12: 1222-1 228.
- Nava A, Rossi L, Thiene G. (Eds.). *Arrhythmogenic right ventricular cardiomyopathy/dysplasia.* Elsevier, Amsterdam 1997.
- Rampazzo A, Nava A, Danieli GA at al. *The gene for arrhythmogenic right ventricular cardiomyopathy maps to chromosome 14q23-q24.* Hum Mol Genet 1994; 3: 959-962.
- Rampazzo A, Nays A, Erne P at al. *A new locus for arrhythmogenic right ventricular cardiomyopathy (ARVD2) maps to chromosome 1q42-q43.* Hum Mol Genet 1995; 4:2151-2154.
- Rampazzo A, Nava A, Miorin M at al. *ARVD4, a new locus for arrhythmogenic right ventricular cardiomyopathy, maps to chromosome 2 long arm.* Genomics 1997; 45: 259-263.
- Richardson P, McKenna WJ, Bristow Mat al. *Report of the 1995 WHO/ISEC Task Force on the definition and classification of cardiomyopathies.* Circulation 1996; 93: 841-842.
- Thiene G, Nava A, Corrado 0 at al. *Right ventricular cardiomyopathy and sudden death in young people.* N Engl J Med 1988; 318: 129-133.
- Thiene G, Corrado 0, Nava A at al. *Right ventricular cardiomyopathy: is there evidence of an inflammatory aetiology?* Eur Heart J 1991; 12(Suppl. 0): 22-25.
- Thiene O, Basso C, Danieli GA atal. *Arrhythmogenic right ventricular cardiomyopathy: A still underrecognized dllnical entity* Trends Cardiovasc Med 1997; 7: 84-90.
- Valenta M, Calabrese F, Thiene O at al. *In vivo evidence of apoptosis in arrhythmogenic right ventricular cardiomyopathy* Am J Pathol 1998; 152: 479-484.

Pathology of large vessel vasculitides

R Bruneval

Service d'Anatomie Pathologique and INSERM 430,

Hôpital Broussais, Paris, France.

Vasculitides can be classified according to the size of the vessels involved. Large vessel vasculitides are found in Buerger's disease, temporal arteritis, Takayasu's disease, Behçet's disease, infectious arteritides, rheumatologic and miscellaneous diseases. The arterial involvement presents pathological characteristics which contribute to diagnosis of the disease.

Buerger's disease is a thrombotic arterial and venous disease which is is associated with smoking in young nonatherosclerotic patients and is prominent in lower and upper limb arteries of 1-5 mm diameter. Most arterial lesions are sampled during surgical bypass surgery at the stage of nonspecific organized thrombosis. However, a characteristic pattern of Buerger's disease is no or minimal arterial wall damage. Venous involvement is mainly superficial thrombophlebitides.

Temporal arteritis belongs to the giant cell arteritides. It prominently involves the branches of the external carotid artery, mainly the temporal artery. Other sites can be involved: the aorta in about 10% of cases, and large arteries of limbs, with a risk of thrombosis, aneurysms and rupture. Temporal artery biopsy is diagnostic in less than 50% of cases. It is a focal inflammatory process with or without giant cells prominent in the internal part of the media. Steroid treatment does not change inflammation in biopsies for up to 4 weeks.

Takayasu's disease, also called aortic arch syndrome or nonspecific aortoarteritis, belongs to the group of giant cell arteritides. It involves mainly the aorta, but also frequently the pulmonary, the subclavian, the carotid and the renal arteries. It is characterized by a marked thickening of the arterial wall. Aneurysms and stenoses are commonly observed, In the inflammatory stage, the inflammation is made of mononuclear and giant cells, and is prominent in the external part of the media where it destroys the elastic fibers. In the fibrous stage, thickening and stenosis are generated by fibrosis of the intima and mainly of the adventitia with a fibrous ring where inflammation may have disappeared.

Behçet's disease is based on a systemic vasculitis phenomenon. In addition to multiorgan involvement, vein involvement is frequent, and arterial lesions are observed in 2-30% according to the series. Both systemic and pulmonary arteries are involved. It is a very aggressive involvement destroying the vascular wall with a risk of arterial rupture, pseudoaneurysm and thrombosis. The inflammatory process is often massive with an infectious-like pattern.

Infectious arteritides: the most frequent concern in infectious vascular pathology is now infection after vascular surgery, mainly infection in prostheses. In native arteries, primary infectious arteritis is the bacterial involvement of a preexisting vascular lesion such as aneurysm or atherosclerosis, Gram-negative germs being frequently responsible; secondary infectious arteritis or mycotic aneurysm is now rare and depends on the septic embolism from endocarditis, Gram-positive germs being frequently responsible. It is a thrombotic and destructive phenomenon. Syphilitic and tuberculous aortitides are now very infrequent: they may be a diagnostic problem with rheumatologic disease-associated aortitis.

Rheumatologic and miscellaneous diseases: arteritis, mainly aortitis can be observed in rheumatologic or in systemic diseases such as rheumatoid arthritis, ankylosing spondylitis, Reiter's syndrome, relapsing polychondritis, and Cogan's syndrome. Kawasaki syndrome is mainly responsible for coronary artery involvement.

References

- Abu-Farsakh H, Mody 0, Brown RW at al. *Isolated vasculitis involving the female genital tract: Clinicopathologic spectrum and phenotyping of inflammatory cells.* Mod Pathol 1994; 7: 610-615.
- Achkar AA, Lie JT, Hunder GG at al. *How does previous corticosteroid treatment affect the biopsy findings in giant cell (temporal) arteritis?* Ann Intern Med 1994; 120: 987-992.
- Berry CL. *Kawasaki's disease.* Pediatr Cardiol 1983; 4: 233-234.
- Case Records ot the Massachussets General Hospital. *Case 6-1999.* In: Scully R. (Ed.). N Engl J Med 1999; 340: 635-641.
- Ewart JM, Burke M, Bunt T. *Spontaneous abdominal aortic infections. Essentials of diagnosis and management.* Am Surg 1983; 49: 37-50.
- Gravallese EM, Corson JM, Coblyn JS at al. *Rheumatoid aortitis: A rarely recognized but clinically significant entity* Medicine 1989; 68: 95-106.
- Hainer JW, Hamilton GW. *Aorticabnormalities in relapsing polychondritis : Report of a case with dissecting aortic aneurysm.* N Engl J Med 1969; 280:1166-1168.
- Hamza M. *Large artery involvement in Behçet's disease.* J Rheumatol 1987; 14: 554-559.
- Heggtveit HA. *Syphifitic aortitis. A cfinicopathologic autopsy study of 100 cases.* Circulation 1964; 29: 346-355.

- Heggtveit HA, Henniga GR, Morrione TG. *Panaortitis.* Am J Pathol 1963; 42: 151-172.
- Hunder GG, Arend WP, Bloch DA et al. *The American College of Rheumatology 1990 criteria for the classification of vasculitis: Introduction.* Arthritis Rheum 1990; 33:1065-1067.
- Ilstrup DM. *Cogan's syndrome: 18 cases and a review of the literature.* Mayo Clin Proc 1986; 61: 344-361.
- Jennette JC, Falk RJ, Andrassy K at al. *Nomenclature of systemic vasculitides. Proposal of an International Consensus Conference.* Arthritis Rheum 1994; 37: 187-192.
- Klein RG, Campbell RJ, Hunder GG at al. *Skip lesions in temporal arteritis.* Mayo Clin Proc 1976; 51: 504-510.
- Klein RG, Hunder GG, Stanson AW at al. *Large artery involvement in giant cell [temporal]arteritis.* Ann Intern Med 1975; 83: 806-812.
- Lakhanpal S, Tani K, Lie JT at al. *Pathologic features of Behçet's syndrome.* Hum Pathol 1985; 16: 790-795.
- Lavignac C, Jauberteau-Marchan MO, Liozon E at al. *Etude immunohistochimique des lésions d'arterite temporale de Horton avant et au cours de la corticothérapie.* Rev Med Interne 1996; 17: 814-820.
- Lê Thi Huong D, Wechaler 8, Papo T at al. *Arterial lesions in Behçet's disease: A study in 25 patients.* J Rheumatol 1995; 22: 2103-2113.
- Lie JT. *Vasculitis unlimited in rheumatoid arthritis: An illustrated review.* Cardiovasc Pathol 1998; 7:191-204.
- Lie JT. *Aortic and extracranial large vessel giant cell arteritis: A review of 72 cases with histopathologic documentation.* Semin Arthritis Rheum 1995; 24: 422-431.
- Lie JT. *Thromboangitis obliterans (Buerger's disease) revisited.* In: Rosen PP, Fechner RE. (Eds.). Pathology annual. Appleton and Lange, Norwalk 1989; 23(2): 257-291
- Lie JT, and members and consultants ot the American College ot Rheumatology Subcommitee on Classification ot Vasculitis. *Illustrated histopathologic classification criteria for selected vasculitis syndromes.* Arthritis Rheum 1990; 33:1074-1087.
- Lie JT, Brown AL, Carter ET. *Spectrum of aging changes in temporal arteries, Its significance, in interpretation of biopsy of temporal artery* Arch Path 1970; 90: 278-285.
- Lupi-Herrera E, Sánchez-Torres G, Marcushamer J et al. *Takayasu's arteritis clinical study of 107 cases.* Am Heart J 1977; 93: 94-103.
- Lupi-Herrera E, Sánchez TO, Horwitz S et al. *Pulmonary artery involvement in Takayasu's arteritis.* Chest 1975; 67: 69-74.
- Morgan SH, Asherson RA, Hughes GRV. *Distal aortitis complicating Reiter's syndrome.* Br Heart J 1984; 52: 115-116.
- Rao JK, Allen NB, Pincus T. *Limitations of the 1990 American College of Rheumatology classification criteria in the diagnosis of vasculitis.* Ann Intern Med 1998; 129: 345-352.
- Robinowitz M, Virwani R, Mc Allister HA Jr. *Rheumatoid heart disease: A clinical and morphologic analysis of thirty-four autopsy patients.* Lab Invest 1980; 42: 145-147.
- Vollertsen RS. McDonald TJ, Younge BR at al. *The vasculitis syndromes in aorta and large arteries.* In: Camilleri JP, Berry CL, Fiessinger JN et al. (Eds.). Diseases of the arterial wall. Springer-Verlag, Berlin 1989; 457-482.
- Wechaler J, Bruneval P, Capron F at al. *Las vascularites: Classification histopathologique.* Rev Med Interne 1988; 9: 507-515.

Myocarditis. How do we make a biopsy diagnosis?

U. Baandrup

Aarhus University Hospital, Aarhus, Denmark.

In a Swedish autopsy study the incidence of myocarditis was observed to be 1.06%, while in autopsies of children and young adults the incidence has been reported to be 17-21%. In fact, nobody knows the (true) incidence of myocarditis.

Presenting symptoms and physical examination are often non-specific. Nearly 90% of patients give a history of a flu-like syndrome, but in less than 50% is a Viral disease recognized within the preceding month. The initial presentation may be one of acute or chronic heart (allure or cardiogenic shock or symptoms mimicking acute myocardial infarction. Patients may have life-threatening arrythmias or remain asymptomatic.

Myocarditis is best defined morphologically as an inflammatory involvement of the heart muscle characterized by a leukocytic infiltrate and resultant nonischemic necrosis/degeneration at myocytes.

With the recent onset of unexplained cardiac heart failure, chest pain, or life-threatening arrythmias, of all patients who have endomyocardial biopsy, 5-10% have morphological myocarditis. In the 1995 Task Force of WHO/ISEC on the definition and classification of cardiomyopathies it is said that "inflammatory cardiomyopathy is defined by myocarditis in association with cardiac dysfunction. Myocarditis is an inflammatory disease of the myocardium and is diagnosed by established histological, immunological, and immunohistochemical criteria. Idiopathic, autoimmune and infectious forms of inflammatory cardiomyopathy are recognized". In my view, this means that myocarditis and inflammatory cardiomyopathy are synonyms.

It is evident that the gap between clinical symptoms/clinical suspicion and morphological changes of myocarditis is wide – and in fact so wide, that we should look for the missing link or reconsider our entire concept. The causes of myocarditis are summarized in Table 1.

Table 1. Summary of causes of myocarditis.

Infectious	All types of microorganism
Immune-mediated	Postinfectious Systemic disorders Drug hypersensitivity Transplant reiection
Toxic	Drug induced/toxins
Other/unknown	Sarcoidosis Giant cell myocerditis Idiopathic

Unknown causes include special types such as sarcoid heart disease or giant cell myocarditis. However, more often one is not able to explain the process and the case is then dropped in the basket of unknown/idiopathic myocarditis. This is either rational or sufficient investigations have not been carried out (or the methodology is inadequate).

What I think fit for attacking the problem when dealing with endomyocardial biopsies is the following (and of course it is my personal choice):

i) Most of the time the material is formalin fixed. The biopsies must be serially cut.

ii) Routine staining procedures include hematoxylin and eosin, elastic van Gieson's, and trichrome reactions.

ii) Having viewed these sections, special reactions for iron, amyloid, microorganisms etc. may be undertaken.

iv) Immunohistochemical reactions presently performed on fixed tissue nearly as well as on frozen material should include char-