References

- Rampazzo A, Nava A, Miron M et al. ARVD4, a new locus for arrhythmogenic right ventricular cardiomyopathy, maps to chromosome 2q long arm. Genomics 1997; 45: 259-263.

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, Behcet’s disease, infectious arteritides, rheumatological 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 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 predominantly 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 non-specific aortaorteritis, 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.

Behcet’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 arteritides 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 aortitides.

Rheumatologic and miscellaneous diseases: arteritis, mainly aortitides 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

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 arrhythmias 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/regeneration at myocytes.

With the recent onset of unexplained cardiac heart failure, chest pain, or life-threatening arrhythmias, 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/clini cal 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>
<thead>
<tr>
<th>Table 1. Summary of causes of myocarditis.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infectious</strong></td>
</tr>
<tr>
<td><strong>Immune-mediated</strong></td>
</tr>
<tr>
<td><strong>Drug hypersensitivity</strong></td>
</tr>
<tr>
<td><strong>Transplant rejection</strong></td>
</tr>
<tr>
<td><strong>Toxic</strong></td>
</tr>
<tr>
<td><strong>Other/unknown</strong></td>
</tr>
<tr>
<td><strong>Idiopathic</strong></td>
</tr>
</tbody>
</table>

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.

iii) 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-