Histochemical, ultrastructural and structural changes in primary cardiomyopathy and in cobalt cardiomyopathy

ECKHARDT G. J. OLSEN

The paper on 'The pathology of primary cardiomyopathy' (page 732) concentrated on the criteria useful for diagnosis. This paper deals with the histochemical and ultrastructural changes (Van Noorden, Olsen & Pearse, 1971)

Congestive cardiomyopathy (systolic pump failure)

Glycogen is patchily increased in the myocardial fibres surrounding the nucleus and may also be found between myocardial fibres. As a marker of mitochondrial activity, succinic dehydrogenase and NADH diaphorase are used which show a similar distribution to that of glycogen, i.e. increased activity can be seen in the perinuclear region and between fibres. Acid phosphatase and non-specific esterases used as markers for lysosomal activity show also increased activity. The distribution is patchy throughout biopsy material. The histochemical changes reflect hypertrophy of the myocardium but we have been unable to find a specific enzyme alteration pathognomonic for congestive cardiomyopathy.

Ultrastructural changes consist of an increase in mitochondria. In some instances mild mitochondrial swelling is evident with some degenerative changes in cristae and occasionally mitochondrial 'ghosts' are seen. An increase in lipofuscin granules and lipofuscin precursor granules has also been found. The contractile elements are preserved and long runs of fibres are seen.

Hypertrophic cardiomyopathy with or without obstruction (diastolic compliance failure)

The most striking feature on histochemical examination is the glycogen content. There is considerable increase, particularly in the perinuclear area. Usually, with moderate amounts of increase in glycogen, a granular appearance is observed, but in cases of hypertrophic cardiomyopathy with obstruction, the granularity is lost and large areas of 'smudges' are seen, the so-called pooling of glycogen. Figure 1 compares the glycogen content of the heart with that of ordinary hypertrophy.

Histochemical analysis of many other systems, such as succinic dehydrogenase, acid phosphatase and non-specific esterases reveals quantitative changes consistent with the extreme hypertrophy seen in some myocardial fibres.

Ultrastructural changes may be striking but are unfortunately in no way pathognomonic for the condition. The uniform parallel arrangement of the contractile elements is lost and fibres run in all directions (Fig. 2). Similar changes affecting fibres are seen at light microscopic level.

Dystrophic changes of contractile elements are often observed but a dystrophic fibril may lie adjacent to a normal fibril. This patchy distribution makes interpretation of the appearances, particularly on needle biopsy, extremely difficult.

Extreme apparent increases in mitochondria, the so-called mitochondrialosis, are frequently seen. Each of these is within the lower limit of normal dimensions. Cross-over of myofilaments has been demonstrated (Ferrans, 1971) and this network of crossing contractile elements may explain the clinical manifestations. These changes can however also be seen in ordinary hypertrophy.

The histochemical changes allow one to understand some of the processes which occur within the myocardial cell and electron-microscopic investigations show the morphological appearances at very high magnification. These changes are, however, descriptive, and future work should concentrate on biochemical analysis which might throw light on this puzzling condition. It has previously been emphasized that the asymmetric hypertrophy of the interventricular septum is usually evident, even if clinically the obstructive element had disappeared.

There is, however, a very small number of patients who do not fit into the category of the hypertrophic obstructive group, nor do they fit into the congestive group. These patients are extremely difficult to classify and usually have some clinical features of obstruction with dominant congestive failure (Karatzas, Hamill & Sleight, 1968).

At necropsy these patients show hypertrophy and often extreme dilatation of all the chambers, together with endocardial thickening with or without superimposed thrombus. Macroscopically they resemble the congestive group of cardiomyopathies but they differ from congestive cardiomyopathy on histological examination.

Histologically this rare group show foci of abnormal cells indetical to those described in the
Changes in cardiomyopathy and cobalt cardiomyopathy

hypertrophic obstructive cardiomyopathic group. These foci of abnormal fibres, which are not seen in typical congestive cardiomyopathies, are randomly distributed, usually in the left ventricular myocardium, including the lateral wall (Fig. 3). This group suggests that a spectrum of hypertrophic obstructive cardiomyopathy may exist. On the one end of the spectrum the typical asymmetric hypertrophy (which may disappear) is seen, but in these patients, the distribution of abnormal fibres is usually in one continuous band, most commonly in the interventricular septum. At the other end of the spectrum there are these small foci of randomly distributed abnormal cells, and it may be that the different distribution may explain the different clinical manifestations (Olsen, 1971).

Alcoholic cardiomyopathy in beer drinkers—the cobalt story

In 1967 a report from Quebec described a cardiomyopathy affecting patients who had taken up to 20 pints of beer a day (Morin et al., 1967). The causative agent was eventually traced to cobalt which had been added to the beer in order to make it more frothy. The Quebec group of workers have been able to examine twenty-five hearts at necropsy; the hearts weighed 350–690 g. There was some dilatation of the ventricles, the myocardium showed moderate hypertrophy and occasionally ventricular mural thrombi were present. Histological examination
showed characteristic changes (Bonfent, Miller &
Roy, 1967). Variation in the staining properties of
hypertrophic myocardial fibres was evident; the
size of the muscle fibres varied and there was a
decrease in myofibrils. Vacuolation within the myo-
cardial fibre, sometimes multiple and small and
sometimes large, was invariably present (Fig. 4). The
vacuoles were due, at least in part, to glycogen
accumulation. Intracellular oedema was observed in
myocardial fibres separating individual fibrils from
one another. Interstitial oedema is also seen. Focal
fibrosis of varying severity was present and a strik-
ing feature was the virtual absence of inflam-
matory change. Hyaline change of myocardial fibres
was observed. The nuclei were occasionally bizarre in
shape but the marked changes seen in cases with
hypertrophic cardiomyopathy with obstruction, and
the extreme hypertrophy of myocardial fibres were
not seen.

Experimental support for the hypothesis that
cobalt could be the underlying cause for the cardio-
mypathy was obtained by feeding rats on a protein-
deficient diet and administering cobalt (Rona &
Chappel, 1971). The features described histologically
by the Quebec workers were simulated in these
studies. At electron-microscopic level, swelling of
mitochondria and occasional distortion of cristae
and the outer membrane was noted. In addition to

the changes in mitochondria, a pathognomonic
feature for cobalt toxicity was found, consisting of
dense, osmophilic, intramitochondrial particles 0.3–
0.4 μm in diameter. It has been suggested that these
particles represent cobalt-protein complexes and not
calcium.

Acknowledgments

This work has been carried out in close collaboration
with Miss Susan Van Noorden and Professor A. G. E. Pearse.
I am grateful to Dr G. Miller for the material on cobalt
cardiomyopathy and to Professor G. Rona for electron-
microscopic preparations.

References

beer-drinkers’ cardiomyopathy. Pathological studies.
Canadian Medical Association Journal, 97, 910.
Ferrans, V.J. (1971) Personal communication.
Karatzas, N.B., Hamill, J. & Sleight, P. (1968) Hyper-
trophic cardiomyopathy. British Heart Journal, 30, 826.
Morin, Y.L., Foley, A.R., Martineau, G. & Roussel, J.
(1967) Quebec beer-drinkers’ cardiomyopathy. Forty-eight
cases. Canadian Medical Association Journal 97, 881.
Hypertrophic obstructive cardiomyopathy, a histological,
histochemical and ultrastructural study of biopsy material.
Cardiovascular Research 5, 118.
Olsen, E.G.J. (1971) Morbid anatomy and histology in
hypertrophic obstructive cardiomyopathy. In: Hyper-
trophic Obstructive Cardiomyopathy, Ciba Foundation
Histochemical, ultrastructural and structural changes in primary cardiomyopathy and in cobalt cardiomyopathy.

E. G. Olsen

Postgrad Med J 1972 48: 760-762
doi: 10.1136/pgmj.48.566.760

Updated information and services can be found at:
http://pmj.bmj.com/content/48/566/760.citation

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/