Virchows Arch A (1987) 412:27–29

Virchows Archiv A

Restrictive cardiomyopathy in children

Ultrastructural findings

M. Toussaint[1], C. Planche[2], E. Villain[3], and J. Kachaner[3]

[1] Laboratoire d'Histologie et Embryologie, Faculté de Médecine Necker-Enfants Malades, 156, rue de Vaugirard, F-75015 Paris, France
[2] Service de Chirurgie Cardiovasculaire, Centre Chirurgical Marie Lannelongue, Le Plessis-Robinson, France
[3] Service de Cardiologie Infantile, Hôpital Necker-Enfants Malades, Paris, France

Summary. Restrictive cardiomyopathy is usually related to fibrosis of the endocardium or to an infiltrative disorder. However, in few cases, it can be due to isolated pathology of the myocytes but such alterations are not well characterized. This paper reports the disease in two 7 year old patients. There was severe venous congestion and catheterisation revealed increased end diastolic pressure in the ventricles. Both pericardial and myocardial biopsies were performed, as the clinical and haemodynamic data were indistinguishable from constrictive pericarditis. The structure of the pericardium was normal. The endocardium was not thickened. The interstitium of the myocardial tissue was not increased. Electron microscopic examination revealed intracellular masses of disorganized myofilaments. These large deposits may have produced decrease compliance of the myocytes and of the ventricular walls.

Key words: Restrictive cardiomyopathy – Endomyocardial fibrosis – Infiltrative changes of the myocardium – Intracellular deposits

Introduction

Idiopathic restrictive cardiomyopathy is uncommon in children. Its clinical and haemodynamic profiles are usually indistinguishable from constrictive pericarditis, so pericardial and myocardial biopsies are necessary for the diagnosis (Batisse 1981). We report two patients whose stiffening of the ventricular walls was secundary to lesions of the myocytes.

Offprint requests to: M. Toussaint

Observations

Two seven year old children were admitted with an exertional dyspnoea. One of them had a recent history of previous viral infection. The clinical data were essentially the same. Examination disclosed engorgement of the jugular veins and enlargement of the liver. A systolic murmur was heard at the apex and an early third sound was audible. The electrocardiogram revealed a bilateral atrial hypertrophy and a right bundle branch block. The chest X ray showed an enlarged cardiac silhouette; the cardiothoracic ratio was 0.66. M-mode and two-dimensional echocardiography demonstrated enlargement of both atria and the inferior vena cava. The thicknesses of the ventricular walls were not increased. The pericardium was normal. Right and left catheterisation were performed: the mean right atrial pressure ranged from 10 mm Hg to 15 mm Hg, and the pulmonary arterial wedge pressure was 15 mm Hg and 17 mm Hg. The end-diastolic pressures of the right ventricle (10 mm Hg and 18 mm Hg) and of the left ventricle (17 mm Hg and 18 mm Hg) were increased, with dip-plateau morphology. A diagnosis of restrictive cardiomyopathy was made. However, in order to exclude the diagnosis of constrictive pericarditis, both pericardial and myocardial surgical biopsies were performed. Myocardial tissue was obtained from the apex of the right ventricle with a Tru-Cut* needle (Travenol Laboratories, USA). It was immediately immersed in 1% cold procaïne hydrochloride and fixed during 24 h in 2% cold glutaraldehyde in 0.1 M Sörensen's buffer, pH 7.3. After washing, the tissue was post-fixed in osmium tetroxyde, dehydrated and embedded in Epon. Semithin sections (1 μm thick) were stained with alkaline toluidine blue. The average transverse diameter of the myocytes was obtained by measuring the shortest diameter of at least 15 cells. The quantitation of interstitial tissue was obtained by analysing the micrographs with a digital planimeter (Digiplan*, Kontron). The diameter of the myocytes was subnormal in both cases (22 and 16 μm respectively, vs 19.4 μm in our laboratory). The ratio of interstitium was subnormal in one case (27%) and slightly increased in the other (36% vs 26%). No inflammatory cells were seen. The endocardium was not significantly thickened. Ultrathin sections were stained with uranyl acetate and Reynold's lead citrate and examined with a EM 300 electron microscope. The most striking lesion was the presence of large masses of electron dense material; they extended as apparent streams between adjacent myofibrils (Fig. 1). In some cells, these masses occupied the whole cytoplasm (Fig. 2). On high magnification, one could observe small

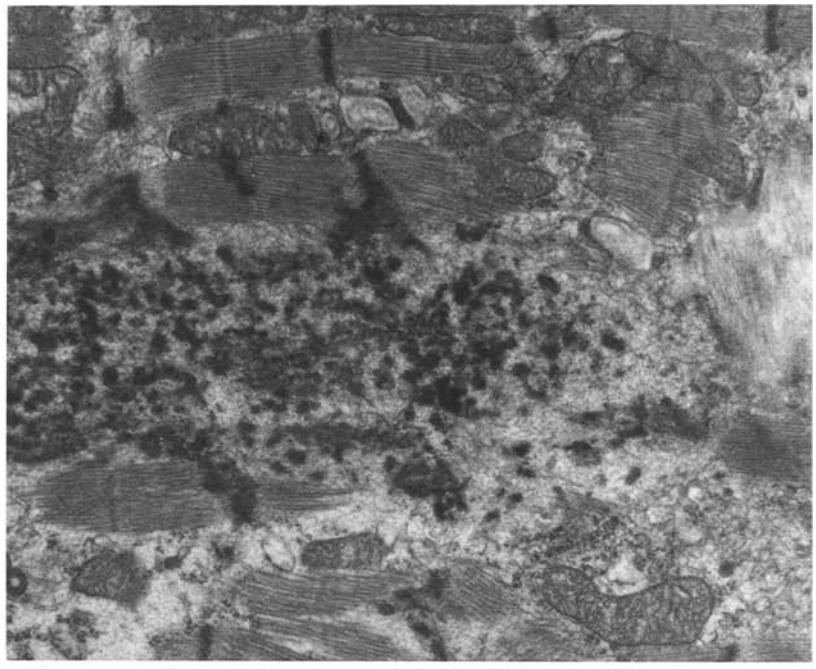

Fig. 1. Streaming of electron dense material between adjacent myofibrils. Longitudinal section (× 5400)

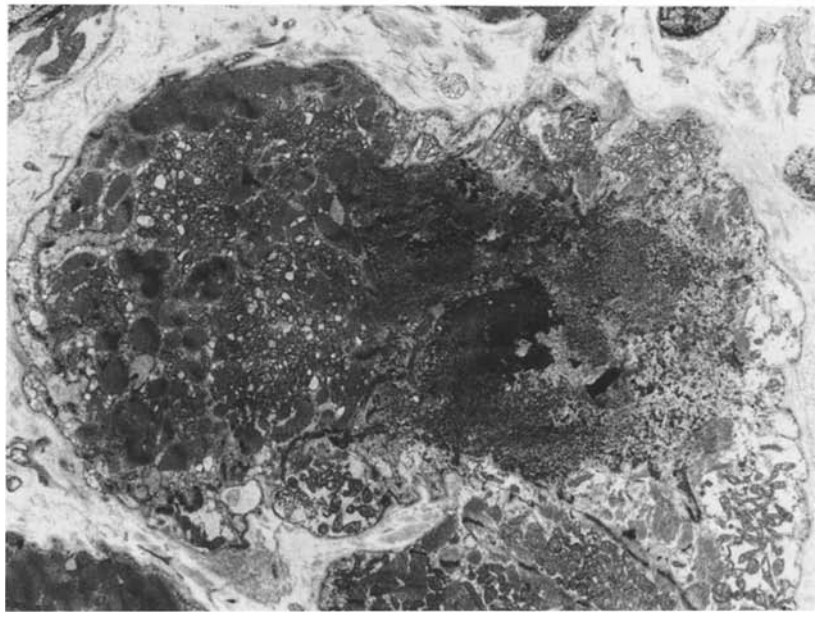

Fig. 2. Large masses of electron dense material. Transverse section (× 1710)

areas of dark material, scattered between large aggregates of highly disorganized filaments (Fig. 3). In other cells, these areas were amorphous and not homogenous. They were surrounded with many residual bodies. The other alterations were foci of myofibrillar disruption, and degenerative vesicles. The mitochondria were normal. The shape of the nuclei showed marked foldings and convolution of their membranes; the chromatin was condensed, and irregularly distributed. Light microscopic examination of the pericardium revealed normal thickness and structure.

Discussion

Restrictive cardiomyopathy is a form of myocardial disease characterized by an increased ventricular wall stiffness. The right and left end-diastolic pressures are increased, and the clinical consequence is systemic venous congestion (Benotti et al. 1980). The clinical profile is usually indistinguishable from a constrictive pericarditis, so pericardial and myocardial biopsies are generally helpful for the diagnosis (Batisse et al. 1981). Some specific heart muscle diseases restrict the filling of the ventricles. They are usually secondary to an infiltrative disorder such as amyloïdosis, haemochromatosis, glycogen storage disease, mucopolysaccharidoses, sarcoïdosis and sclerodermia (Siegel et al. 1984). Restrictive cardiomyopathy includes

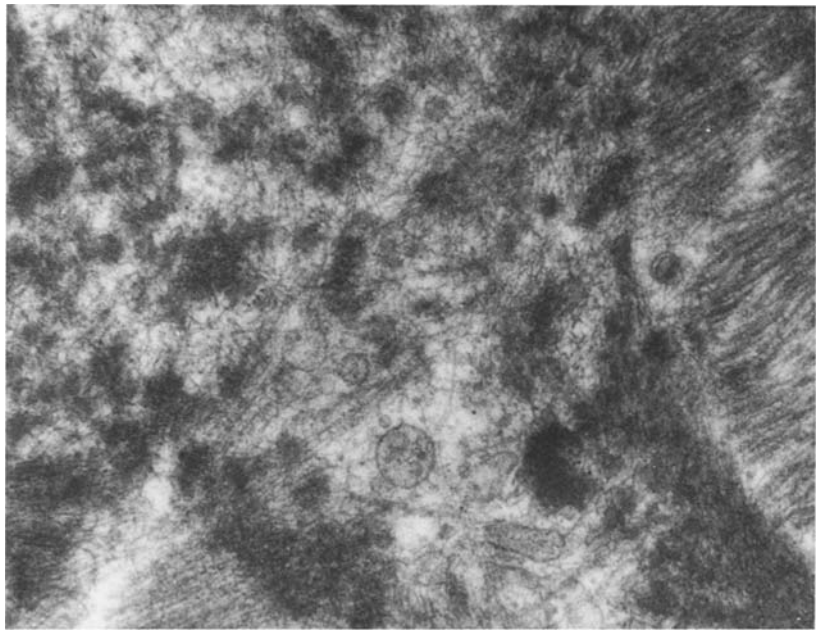

Fig. 3. Fine structure of the intracellular masses. Longitudinal section (×19800)

endomyocardial fibrosis and Löffler endocarditis which are essentially the same condition, related to an eosinophilic endomyocardial disease (Report of the WHO/ISFC task force). However, the present cases are different: their pathological basis is related to an abnormality of the ultrastructure of the cardiac myocytes. We believe that the intracellular deposits decrease their compliance. They may be highly disorganized sarcomeres: the small areas of electron dense material are probably Z band proteins, because their fine structures are identical. Furthermore they are continuous at some points with Z bands of normal myofibrils. The filaments are similar to actin (Fig. 3). Boffa (1983) reported two patients with necropsy histological examination of the heart and Arbutini (1983) one patient with endomyocardial biopsy; their findings were of cell disarray and an increased transverse diameter of the myocytes. We believe that these cases are not restrictive, but true hypertrophic cardiomyopathies with an increased stiffness of the left ventricular walls: cell disarray is a specific and sensitive marker of hypertrophic cardiomyopathy if it is widespread (Becker 1982; Maron 1981), so it can be accuratly judjed from necropsy sections. In the two cases of Benotti (1980), the histological structure of the myocardium is normal. In four patients described by Siegel (1984), the microscopic examination revealed an interstitial fibrosis and non specific alterations of the myocyte. Case reports by Dubost (1980) describe two patients with evidence of intracellular deposits of disorganised filaments. These two cases are similar to the present ones. Such a form of primary restrictive cardiomyopathy without endomyocardial fibrosis is observed exceptionaly, due to an ultrastructural alteration of the myocytes.

Acknowledgements. We wish to thank E. Donsez for her expert technical assistance.

References

Arbutini E, Buonanno C, Trevi G, Penelli N, Ferrans VJ, Thiene G (1983) Cardiac ultrastructure in primary restrictive cardiomyopathy. Chest 84:236–238

Batisse A, Kohout G, Fermont L, Kachaner J (1981) Myocardiopathies restrictives de l'enfant. Ann Pédiat 28:370–372

Becker AE, Caruso G (1982) Myocardial disarray. A critical review. Br Heart J 47:527–538

Benotti JR, Grossman W, Cohn PF (1980) Clinical profile of restrictives cardiomyopathy. Circulation 61:1206–1212

Boffa GM, Chioin R, Pellegrino PA, Scognamiglio R, Fasoli G, Razzalini R, Milanest O, Thiene G (1983) Cardiomiopatia restrittiva primaria. Rev Lat Cardiovas 4:263–275

Dubost C, Durand M, Camilleri JP, Deloche A (1980) Deux cas de myopathies restrictives primitives. Bull Acad Nat Méd 164:215–259

Maron BJ, Roberts WC (1981) Hypertrophic cardiomyopathy and cardiac muscle cell disorganisation revisited: relation between the two and significance. Am Heart J 102:95–110

Report of the WHO/ISFC task force on the definition and classification of cardiomyopathies (1980) Br Heart J 44:672–673

Siegel RJ, Sham PK, Fishbein MC (1984) Idiopathic restrictive cardiomyopathy. Circulation 70:165–169

Accepted July 27, 1987