Histiocytoid Cardiomyopathy in Infancy: A New Hypothesis*

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A case of histiocytoid cardiomyopathy in a ten-month-old boy is reported. Histologic and ultrastructural examinations led us to consider the possibility that the disease, rather than being a focal lesion of the common myocardium as it was heretofore considered, might be regarded as a diffuse lesion of the specific myocardium.

Histiocytoid cardiomyopathy in infancy (HCl)¹ is a rare heart syndrome first observed by Voth in 1962 and defined as arachnocytesis of the myocardium. Since then, 16 more cases have been reported under different names: isolated cardiac lipoidosis,² infantile cardiomyopathy with histiocytoid reaction,¹ infantile xanthomatous cardiomyopathy,³ focal myocardial degeneration,⁴ idiopathic infantile cardiomyopathy,⁵ and focal lipid cardiomyopathy.⁶ Its main trait is the recurrence of severe, often fatal, cardiac arrhythmias and paroxysmal tachycardia. The characteristic necroscopic finding is the moderate cardiac enlargement marked by a prevalently ventricular subendocardial distribution of foci of foamy histiocyte-like cells. Ultrastructural examination of their cytoplasm reveals myofibrils with Z lines which attest to their myocardial origin. There is no satisfactory interpretation of the significance of this lesion. The idea that this may be a focal metabolic disease, as suggested by some definitions of the lesion, has neither basis nor confirmation.

The opportunity of observing a case (the 18th) led us to some considerations which would suggest that the disease, rather than being a focal lesion of the common myocardium, is a diffuse lesion of the specific myocardium.

CASE REPORT

A ten-month-old boy weighing 8,800 gm, was the first-born of unrelated parents at term of a normal pregnancy. The mother did not take any drug during pregnancy. In an apparently healthy condition, the infant suffered a collapse and was rushed to Bambino Gesù Pediatric Hospital in Rome. On admission, the infant appeared seriously ill, pale, anxious and dyspneic. Physical examination revealed tachycardia, pulmonary edema, and hepatic enlargement. The ECG revealed paroxysmal junctional tachycardia with a rate of 300 per minute, anomalous intraventricular pathway with right bundle branch block and left posterior hemiblock, and retrograde conduction to the atrial 1:1 or 1:2. Pharmacologic treatment and vagal stimulation were ineffective. Ten hours after its onset, the arrhythmia subsided, and sinus rhythm resumed spontaneously. The following day the patient had a sudden attack of ventricular fibrillation, and died. Autopsy revealed a well-nourished male infant with cardiac enlargement, dilatation of the left ventricle, slight thickening of the parietal endocardium, pulmonary edema, and engorgement of spleen, liver, and kidneys. Weight of organs in grams was as follows: thymus 22, heart 58, right lung 100, left lung 76, spleen 46, liver 370, kidneys 80, and adrenals 8.

Lung fragments and samples of myocardium from the walls of the four cardiac cavities were examined. The conduction system was examined by the Lev method.⁷ For ultrastructural study, further myocardial samples were post-fixed with 1 percent osmium tetroxide in phosphate buffer dehydrate in alcohol, and embedded in mixtures of epoxy resins. For the histochemical study of the fats, cryostat sections of the myocardium fixed in 10 percent formalin were stained in Sudan III.

RESULTS

Histologic Examination

Myocardium was the site of the most relevant findings: in the numerous fragments taken from the cardiac walls and from interventricular septum, there were bundles of large fibrocells randomly oriented and distributed and showing vacuolated cytoplasms (Fig 1). Their distribution in the ventricles was predominantly subendocardial on both sides of the septum, but bundles of such fibers were much more numerous on the lateral wall of the left ventricle than of the right one. No bundles of vacuolated fibrocells were found on the atrial walls. In each single lesion, the morphologic characteristics of cells were uniform. No aspects of transition could be observed between normal myocardium and vacuolated fibers. These were separated from normal neighboring myocardium by interstitial connective tissue through which small blood vessels could run. There were no aspects of phlogosis or necrosis. In the cytoplasm of vacuolated fibrocells, fibrillar structures could barely be discerned by Mallory's PTAH method. The vacuoles tested PAS negative and appeared red with Sudan III.

Ultrastructural Examination

Ultrastructural examination of the vacuolated fibers of myocardium, fixed in nonbuffered formalin 24 hours after death, revealed, in spite of the grave autolytic phenomena, the unequivocal myocardial nature of the vacuolated fibrocells. This was proved (Fig 2) by rare-

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FIGURE 1. Group of fibers with foamy cytoplasm clearly separated from rest of the myocardium except for connective tissue (hematoxylin-eosin, original magnification × 175).
surrounded by cytomembrane. Their content, lacking electron density and apparently lacking structure except for occasional layers of cytomembrane, resembled mitochondrial crests. There were occasional findings of junctional complexes relevant to intercalated disks (Fig 2, arrow).

**Conduction System**

Examination by the Lev technique permitted systematic observation of the conduction system from the atrioventricular node to the bundles of His, including its divisions to right and left branches and the Purkinje's network on the left side of the interventricular septum. Figure 3, upper left, shows a transversal section of the bundle of His where arteries can be seen. This is composed of specific myocardial fibers prevalently of the small type. Among them there are bundles of fibers (Fig 3, upper right enlarged and lower left) with swelling and foaminess of the cytoplasm as observed in the bundles of the fibers in the ventricular walls. Examination of sections of the conduction system, identifiable with the...
subendocardial Purkinje's network on the left side of the septum (Fig 3, lower right) shows many specific myocardial fibers in the Purkinje's network with vacuolated cytoplasm.

**DISCUSSION**

The case reported is ascribable to the infantile histiocytoid cardiomyopathy for its clinical and especially histologic aspects.

The characteristics of this rare disease are as follows:

1. It occurs in children under two years of age, with sudden disturbances of rhythm.
2. It usually affects females. Only three patients out of 18 (two reported by Ferrans et al. and the present one) are male. The rarity of cases to date does not seem to permit genetic attribution as suggested by Bruton et al.
3. In some cases, association has been pointed out with neurologic or cardiac malformations.
4. A viral infection and/or vaccination is often cited in the recent history of almost every case, although no specific value can be attributed to it.
5. The lesions are evident as groups of altered cells mainly distributed in the ventricular walls as far as subepicardium. They have been observed as high as in the atrial walls.
6. Ultrastructural examinations performed to date have permitted, on the basis of the intracellular presence of myofilaments interposed with Z lines and existence of junctional complexes, the definition of myocardial nature of the xanthomatous cells constituting the essence of the lesion.
7. Histochernical examination, aimed essentially at showing intravacuolar fats in the xanthomatous cells, showed the presence of triglycerides which reveal no osmiophilia under the electron microscope since they are constituted of aliphatic saturated chains.
8. In the conduction system in the few cases observed, and in the present one, xanthomatous fibrocells were found identical to those observed in the other myocardial seats.

The involvement of the conduction system by the observed myocardial lesions might not be an occasional finding, as has been heretofore considered, but might reveal the true nature of the lesions. If a common denominator is to be found for the arrhythmia, the prevalent subendocardial distribution of the lesions, and the involvement of the conduction system, the possibility must be considered of an affection primarily or mainly concerned with the myocardial fibers of such peculiar functional and/or structural characteristics as those constituting the conduction system. This system has been thoroughly investigated even at the electron microscopic level with electromyographic correlation, and it has been possible to ascertain the existence of several cell types and their connection with common myocardial fibers without reaching definite conclusion about its pericardial distribution. The presence of xanthomatous fibers, both in the bundle of His and in the common myocardial fibrocells, might warrant consideration of a systemic lesion, involving the bundle of His to the outmost periphery of the Purkinje network. In this regard, the morphologic alterations to which the fibers are subject could behave as a marker of the peripheral distribution of Purkinje network giving the topographic identification and its distribution in the complex. This interpretation is strengthened by the fact that the lesions are focal and uniform, without grading toward the normal limitrophe myocardial fibers, from which they are clearly separated by connective spaces with blood vessels. The nature of the pathologic process involving the Purkinje network as a whole is not yet clear. The cellular lesions, as found in the ultrastructural examinations, show nothing specific and could therefore reflect a state of secondary cellular damage during the paroxysmal tachycardia and/or fibrillation occurred before death.

In conclusion, we hypothesize that this myocardial pathologic condition, rather than being a focal lesion of the common myocardium, is possibly a diffuse lesion of the specific myocardium.

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**REFERENCES**