Cardiology in the Young (2010), **20**, 115–123
doi:10.1017/S1047951110000181

Review Article

Changing concepts of endocardial fibroelastosis

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Abstract Endocardial fibroelastosis is not a disease but a reaction of the endocardium. I review the history of the term with emphasis on the gradual understanding of the many causes of this reaction. I include a comprehensive list of diseases or other cardiac stresses that authors have reported in association, and I try to explain the mechanism of the reaction. Although endocardial fibroelastosis is rare today, I issue a warning of a possible epidemic recrudescence of some of the associated diseases. My hope is for nosologic purity, therefore that outworn but surviving concepts will be firmly rejected.

Keywords: Endocardial fibroelastosis; mechanism; cardiomyopathy

Received: 13 October 2009; Accepted: 10 January 2010; First published online: 29 March 2010

The contemporary author of a report on the endocardial fibroelastosis is confronted by a perplexing literature; most of which was composed when much more was seen, but much less was understood. Confused outdated concepts need to be corrected. I begin with definitions, pathological findings, and a historical overview. I proceed to discuss the search for causes, clarified and unresolved issues, and speculate on mechanisms. I finish with a comment about nosology. I hope this review will arm future writers with updated facts.

Definitions

Endocardial fibroelastosis is a thickening of the endocardium by layers of collagenous and elastic fibres. Quantitatively, it is a right ventricular endocardium thicker than 10 micrometres or a left ventricular endocardium thicker than 20 micrometres.[1] This endocardial abnormality is unlike endomyocardial fibrosis, where there is a concomitant involvement of the sub-endocardial myocardium, often in association with hypereosinophilia.[2]

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Pathology

Gross examination

The endocardial fibroelastosis reaction is grossly identified as a pearly or opaque white appearance of the endocardium, especially of the ventricles, which normally appears pink as the colour of the myocardium shows through a transparent endocardium. The ventricles may be grossly, sometimes tremendously dilated, or more rarely, under developed such as in the hypoplastic left heart syndrome. A dilated ventricle may have its trabeculae stretched flat with shortened papillary muscles that are absorbed into the walls, leading to mitral valve regurgitation.

The endocardial fibroelastosis reaction is always found in hearts under stress and usually in the chamber most subject to stress, the left ventricle. The stress can be pressure overload from mechanical obstruction such as in coarctation of the aorta or aortic stenosis, or volume overload in ventricles failing secondary to cardiac-muscle disease. Its severity is related to the time of onset of the underlying cardiac stress. The periods of most rapid growth, foetal development, and early infancy are the times when the endocardial fibroelastosis reaction is the most active, when most cases are identified, and when most patients die.

Histology

The normal endocardium is transparent and only about 10 micrometres in thickness, and it is composed of five layers.[1] Starting at the ventricular cavity, the first of these is endothelium; next, loose connective tissue with a few cells; and then a layer of parallel elastic and collagen fibres. The next layer is of a few smooth muscle cells, and finally, just before the myocardium, there is a layer of loose connective tissue with capillaries, unmyelinated nerves, and a few cells. The first three layers are not apparently changed in the fibroelastosis reaction. The smooth muscle cell layer is the one, which becomes most involved in the reaction as it is thickened with elastin and collagen fibres. The sub-myocardial loose connective tissue layer becomes involved also but to a much lesser degree.

The histology of the myocardium varies depending upon the causal process. Thus, inflammation, scarring, or infiltration by metabolic byproducts may be noted; or the process may be so subtle as to be visible only by electron microscopy. Myocardial biopsies from infants and young children with a condition associated with the endocardial fibroelastosis reaction may suggest a near static process on light microscopy, whereas electron microscopy may reveal an active one.

Ultrastructural features

In 1973 at Childrens Hospital of Los Angeles, I began a programme of study of the paediatric cardiomyopathies based on a method of myocardial biopsy I developed to be especially safe for infants[3] and on close collaboration with our electron microscopist, Dr Harry Neustein. An important result of our study was elucidation of the ultrastructure of the endocardial fibroelastosis reaction.[1] So far, it remains the only ultrastructural study of endocardium from infants and children with active cardiomyopathy taken by biopsy and fixed immediately, retaining the fine structure of the cells actually producing the elastin and collagen fibres. This process has been confirmed in older patients with restrictive cardiomyopathy.[4]

The vast higher resolution of electron microcopy (Fig 1) reveals the endocardial fibroelastosis reaction as a chronologic sequence of hyperplasia of smooth muscle cells followed by their transformation and translocation from the inner, sub-endothelial layers to the outer, juxtamyocardial layers. From a stress stimulus, the immediate sub-endothelial smooth muscle cells, dark due to electron-dense cytoplasm, possessing many surface vesicles, myofilaments, and fusiform densities, proliferate. More deeply, other smooth muscle cells, lighter due to a less electron-dense cytoplasm, possessing fewer surface vesicles and fewer myofilaments, also proliferate. As the light smooth muscle cells translocate from the inner endocardial layers to the outer layers they transform into leiomyoid cells. The leiomyoid cells have characteristics of both light smooth muscle cells and fibroblasts. The leiomyoid cells proliferate, and those nearest to the myocardium become typical

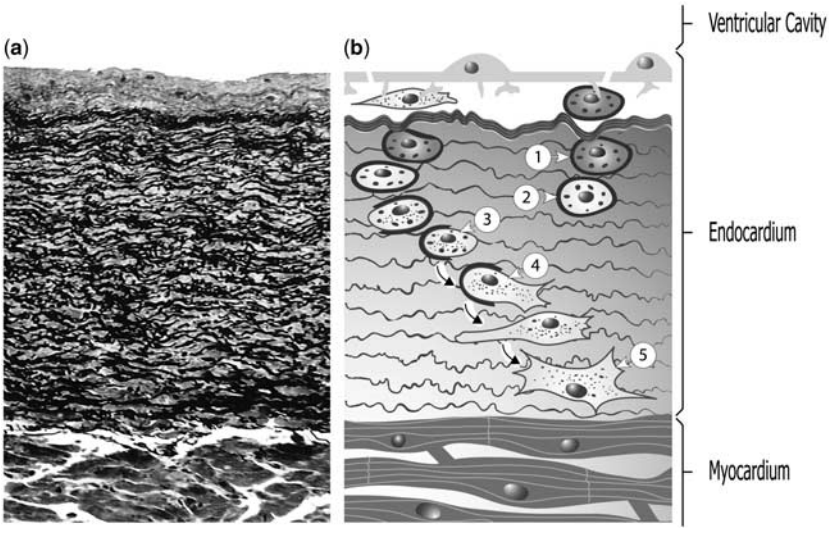

Figure 1.
*Endocardial fibroelastosis exposed! (**a**) Histologic stained section of endocardium (×420), showing dense fibres of collagen and elastin typical of endocardial fibroelastosis. Reproduced from Am J Pathol 1972; 66: 483–496, Figure 3; with permission from The American Society for Investigative Pathology and kind cooperation of Grover M. Hutchins, MD.[13] (**b**) In contrast is the parallel diagram derived from electron microscopy showing cellular activity that generates the fibroelastosis. Full description in text. 1. Dark smooth muscle cell; 2. Light smooth muscle cell; 3. Light smooth muscle cell with loss of basement membrane; 4. Leiomyoid cell; and 5. Fibroblast. Adapted from Archives of Pathology Laboratory Medicine 1979; 103: 218, Figure 8; Copyright 1979 American Medical Association. All rights reserved.*[1]

fibroblasts. The light smooth muscle cells and the leiomyoid cells appear to be the most prominent producers of elastin and collagen.

History

Even though a rational approach to clinical medicine blossomed in the late 19th and early 20th centuries, pathologists for a long time lumped all forms of congenital malformations of the heart as the result of foetal endocarditis, even dilated failing hearts without obvious malformations. As inflammation was not confirmed by histology, the concept that foetal endocarditis caused all cardiac malformations was eventually abandoned.[5] Still, heart muscle disease in the young was poorly understood. It was diagnosed simply by signs and symptoms of cardiomegaly and congestive cardiac failure with confirmation by chest X-ray. From autopsy examinations, pathologists grouped the conditions under various names such as idiopathic cardiac hypertrophy, cardiac enlargement of indeterminate cause, a congenital anomaly of the endocardium, or endocardial sclerosis. Such cases were common. In the pathology files of Buffalo Children's Hospital, Lambert and colleagues[6] found that the total of myocarditis and endocardial sclerosis nearly equaled the number of transpositions of the great vessels.

During my internship in 1942, our professor, Grover Powers, had recently written an article, "On the Idiopathic Hypertrophy of the Heart".[7] This article stressed the importance of ruling out anomalous origin of the left coronary artery from the pulmonary artery[8] and glycogen storage disease,[9] newly reported diseases then that had been found to accompany some cases of idiopathic hypertrophy. Even then, curious clinicians worried about finding the cause of this menace to the infant heart. We interns saw some of these infants die that year and were impressed by the mysterious nature of the phenomenon.

In 1943, pathologists at Sinai Hospital of Baltimore, upon examining hearts of such infants, noted that in most cases the endocardium was pearly white and microscopically showed the layering described above. They coined the term "endocardial fibroelastosis",[10] which they felt was more descriptive than endocardial sclerosis. The term was widely accepted becoming synonymous with the dilated, failing, heart of any infant if there were no other assignable cause. Autopsy was the only means of verifying the presence of endocardial fibroelastosis, yet the term was used as a diagnosis during life even though its presence could not be proven. Efforts were made to delineate criteria for the antemortem diagnosis of endocardial fibroelastosis, which then and for years to come, became a distinct disease.

The search for a cause

Over the decades following the 1940s, however, the concept of endocardial fibroelastosis as a disease was called into question as new evidence emerged. In 1957, Black-Schaffer[11] gave a devastating critique of the prevalent speculations. He postulated a simple mechanical explanation for endocardial fibroelastosis that would apply in all cases. The crux of his argument, stress on the ventricle causes the endocardial reaction, has been confirmed by years of accumulating evidence.

The role of infection gradually unfolded. Several observers had suspected an infectious cause of endocardial fibroelastosis. In 1962, Fruhling and associates at the University of Strasbourg published a 76-page report in French[12] that detailed studies over several years, which established the Coxsackie virus as a cause of endocardial fibroelastosis. The authors analysed a series of Coxsackie epidemics in the east of France that were each followed by an upsurge in the incidence of endocardial fibroelastosis. During one of these epidemics, the authors recovered the virus from the heart or other organs of 13 of 28 patients by injecting autopsy tissue into suckling mice. Their pathological material showed evidence of myocarditis, an intermediate state with both myocarditis and endocardial fibroelastosis, followed by disappearance of inflammation, leaving only the endocardial deposit. The findings by Fruhling were later supported by a study from Hutchins and Vie.[13] These authors reviewed autopsy specimens and also found cases of hearts with myocarditis, hearts with endocardial fibroelastosis, and hearts with both myocarditis and endocardial fibroelastosis. Hutchins and Vie did no virologic studies.

In 1963, Noren et al[14] set forth criteria for "primary endocardial fibroelastosis" in surviving patients. They reported a small series of patients with a history of maternal mumps or mumps exposure during pregnancy. They tested the patients intradermally and found delayed skin sensitivity to killed mumps virus. Noren concluded that the mumps virus was a cause of endocardial fibroelastosis. What began as a suggestion became a wave of enthusiasm and a countercurrent of doubt. Several reports denied the validity of the test because it was not repeatable or confirmable by other modalities.[15] At the same time, many others confirmed their findings. Controversy raged on the subject, finally leading one of the associates of Noren, the virologist St Geme,[16] to inject embryonated hens' eggs with mumps virus. The hearts in the resulting chicks went through the stages from acute myocarditis to finally, at age 1 year, typical endocardial fibroelastosis. The proponents of the mumps related theory

concluded with a wistful claim that some day Koch's postulates would be fulfilled and their hard work would be vindicated.[17]

Subsequently, mumps vaccine became widely used and the incidence of new cases of endocardial fibroelastosis took a sharp drop. Many years later, developments in genetics made it possible to detect viral genome in pathological material, first by *in situ* hybridisation and later by polymerase chain reaction. A prime example is the 1997 work by investigators in the genetics laboratory under the direction of Jeffrey Towbin.[18] They studied hearts with endocardial fibroelastosis that had been preserved in formalin from an era when mumps was still a widespread infection. They found mumps genome in the majority of the hearts they studied. After I eliminated their last three cases that had died after immunisation against mumps became widely adopted, over 80% of the autopsied hearts with endocardial fibroelastosis were positive for mumps. No one should doubt that transplacental mumps once was the most important aetiologic agent of the endocardial fibroelastosis reaction. Koch's postulates fulfilled!

Since the 1980s, the frequency of finding of endocardial fibroelastosis has diminished abruptly in the developed world. But a word of warning is appropriate. After years of numbers close to zero, there was an epidemic of mumps in England and Wales between 2004 and 2005 with a peak report of cases of 56,390 in 2005.[19] This number did not include many mild cases that were not reported. In the United States of America, several years of near zero reports were followed in 2006 with a peak of 6584 reports.[20] Both epidemics largely affected young people attending colleges. In Britain, this cadre was not immunised because during their infancy there had been a shortage of vaccine. In the United States of America, several factors including impotent vaccine were considered. The offspring of these young adults affected by mumps are at risk for endocardial fibroelastosis. Similarly, other epidemics like infections from the Coxsackie virus are potential risk factors. Paediatric cardiologists should pay attention to such epidemics.

Etiologies of endocardial fibroelastosis other than infection have also undergone intensive study. Gradually, etiologies are being assigned to the "idiopathic" diseases of heart muscle. The finding of endocardial fibroelastosis is now recognised in widely different diseases in foetuses, infants, children, and occasionally even in adults (Table 1).

In the course of compiling the Table 1, I found a virtually complete absence of the ventricular endocardial fibroelastosis reaction in hypertrophic cardiomyopathies. I am excluding fibrosis localised to the area of contact of the mitral valve with the hypertrophied septum, similar to the jet lesion accompanying a ventricular septal defect. No generalised involvement of typical left ventricular fibroelastosis is reported. One reference on Noonan's syndrome[21] notes that the reaction was found in the left atrium without involvement of the left ventricle.

Table 1. Diseases and other stresses associated with endocardial fibroelastosis.

- Cardiomyopathies
  - Dilated
    - Post-myocarditis (see myocarditis below)
    - Genetic
      - Known genes
        - Muscle LIM protein[43]
        - X-linked foetal cardiomyopathy (TAZ)[44]
        - Beta cardiac myosin heavy chain[45]
      - Familial but idiopathic
        - Autosomal recessive[46]
        - Autosomal dominant[32]
        - X-linked recessive[47]
  - Hypertrophic
    - Noonan syndrome (left atrium)[21]
  - Restrictive
    - Post-myocarditis[12]
    - Idiopathic[48]
  - Non-compaction
    - Barth syndrome[49]
- Congenital malformations
  - Aortic stenosis[50]
  - Coarctation of the aorta[51]
  - Anomalous coronary artery[8]
  - Hypoplastic left heart syndrome[35]
  - Intracranial arteriovenous fistula[52]
- Immunologic disease
  - Transplacental maternal antibodies[53]
  - Rhesus incompatibility[52]
- Myocarditis
  - Viral
    - Mumps[18]
    - Coxsackie[12]
    - Adenovirus[18]
  - Bacterial
    - Lactobacillus[54]
- Lysosomal storage diseases
  - Glycogen
    - Type II Pompe[55]
  - Mucopolysaccharides
    - Hurler's[56]
    - Maroteaux-Lamy[57]
  - Sphingolipids
    - Niemann-Pick's[58]
  - Gangliosides
    - Infantile sandhoff's[59]
- Other metabolic
  - Systemic carnitine deficiency[60]
- Physical injury
  - Post-electric shock[61]
- Vascular
  - Myocardial infarction[62]
  - Twin-twin transfusion[28]
  - Lymphatic obstruction[63]

https://doi.org/10.1017/S1047951110000181 Published online by Cambridge University Press

Infants of diabetic mothers exposed to hyperinsulinism that results in foetal ventricular hypertrophy lack the endocardial fibroelastosis reaction; even though foetal ventricular hypertrophy occurs at the very time *in utero* that the endocardial fibroelastosis reaction occurs most prominently in association with other stressors, This negative association has not been noted in the literature. During the preparation of this paper, I spoke to Barry J. Maron, MD, Director of the Hypertrophic Cardiomyopathy Center at the Minneapolis Heart Institute Foundation in Minneapolis. Dr Maron, an individual with likely the largest experience in the world with hypertrophic cardiomyopathy, had been unaware of this negative association. He had never seen endocardial fibroelastosis associated with hypertrophic cardiomyopathy at any stage. I also spoke with Jacqueline Noonan MD. She had not seen endocardial fibroelastosis in any case of her syndrome. To further explore the subject of the infants of diabetic mothers, I talked with Howard Gutgesell MD, an early writer on the subject. He also confirmed that he had neither seen nor was aware of a reported case of the generalised endocardial fibroelastosis reaction in infants with hypertrophic cardiomyopathy related to maternal diabetes.

In medicine, it behoves us all to avoid the word "never" but it seems warranted to invoke "rarely, if ever" for describing the lack of generalised endocardial fibroelastosis reactions in hypertrophic cardiomyopathy. I consider this an important observation that may have significance related to the mechanism of the reaction, as I discuss below. Also relevant here is another negative association, long recognised, that a diminutive ventricle that has no inlet or outlet and thus does no work, does not develop endocardial fibroelastosis. This was reported for aortic atresisa combined with mitral atresia by Noonan and Nadas in 1958.[22] Bryan and Oppenheimer 1n 1969[23] reported similar findings for tricuspid atresia combined with pulmonary atresia.

The modern concept of "the cardiomyopathies" took hold gradually as it evolved to include all diseases of cardiac muscle. Even though it is illogical to consider endocardial fibroelastosis as a specific disease, when the reaction can occur in conjunction with many cardiomyopathies and other stresses, nomenclature habits change slowly. It is still common in the clinical setting to find a patient diagnosed as "another case of endocardial fibroelastosis".

Mechanisms

Is there any better understanding today of just how the many kinds of stress on the heart end up with layers of collagen and elastin in the endocardium?

Some observations from foetal echocardiography provide interesting glimpses into the onset of the endocardial fibroelastosis reaction. Such early cases show some remarkable characteristics in speed of accumulation of endocardial fibroelastosis and ability of the rapidly growing heart to undergo fundamental changes in structure and function. Translating the work of others can be cumbersome, as invariably authors write about endocardial fibroelastosis as a disease. Some abstracted examples follow with my comments in italics.

1. In a foetus at 14 weeks,[24] the endocardium was already hyperechoic; thickened endocardium partially obstructed the aortic valve; the left ventricle contracted poorly; there was reversal of flow through the foramen; and the aortic valve appeared normal. At 16.5 weeks, the aortic annulus was further reduced and no flow through the aortic valve was noted. Pregnancy was terminated. The aortic valve was found at postmortem to be bicuspid and stenotic, and "far advanced" endocardial fibroelastosis was noted. *Extremely early onset of LV dysfunction and rapid progression of endocardial fibroelastosis, apparently involving aortic valve secondarily.*
2. Critical aortic stenosis was noted in a foetus at 27 weeks with hydrops.[25] The aortic valve was balloon dilated *in utero*. Cardiac failure improved but endocardial fibroelastosis appeared later, and it worsened with aortic valvotomy. The infant died at 1 day of age. *Aortic valve involved first, endocardial fibroelastosis apparently secondary.*
3. Routine obstetric echocardiogram led to a foetal echocardiogram at 20 weeks gestation.[26] The mitral valve and left ventricle were hyperechoic and left ventricle showed slightly reduced contractility, but the aortic valve and annulus appeared normal with normal aortic flow. At 22 weeks, the left ventricle was dilated, echo density had increased, but aortic flow remained normal. At 24 weeks, the left ventricle and aortic annulus were relatively smaller, but the aortic flow remained normal. Little change was noted over the remaining weeks, and the infant was born in good condition. Postnatal echocardiogram showed severe aortic valvar stenosis, hypoplasia of left ventricle and the aortic annulus. At catheterisation on day 2, a 70-millimetre of mercury transaortic gradient was found, valvuloplasty was performed, followed by a Norwood procedure, but the infant died a few days later without postmortem. *Endocardial fibroelastosis appeared while aortic valve seemed normal. Initial rapid evolution from dilated cardiomyopathy to aortic stenosis and finally, hypoplastic left heart syndrome.*
4. In a foetus at 20 weeks,[27] an echocardiogram showed endocardial fibroelastosis, a dilated left

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ventricle but no other abnormalities. Over the next 20 weeks, endocardial fibroelastosis rapidly increased while the left ventricle failed to grow, resulting in an idiopathic restrictive cardiomyopathy. *This case and others like it must be the result of very early clinical manifestation of cardiomyopathies yet to be identified*.

5. This report described two sets of monozygotic twins with twin–twin transfusion syndrome.[28] In each set, only the larger suffered congestive failure and developed endocardial fibroelastosis. *Environment trumped heredity!*
6. Two reports described foetal cardiomyopathies due to transplacental maternal antibodies that were completely reversed by treatment with steroids,[29,30] with reversal of endocardial fibroelastosis. *The first ever reports of reversal of endocardial fibroelastosis, by effective treatment of the cause when done early enough*.

Although these reports are few, they are not simply anecdotal; rather, they provide insights into the earliest stages of a process that heretofore has been clothed in mystery.

How do various cardiac stresses trigger endocardial smooth muscle cells to initiate the reaction that promotes layers of elastin and collagen? There is no direct evidence to answer this question. I will volunteer some hypotheses based on analogy with a similar problem facing researchers in pulmonary hypertension. That is a field where experimental manipulation and observation are easier than in studies of endocardial fibroelastosis. Pulmonary hypertension is a prominent clinical problem, and the condition has called forth considerable research effort. Fundamentally, both the endocardium and the vascular endothelium are at the interface between flowing blood and solid elements of the circulation. In both, the various stressors trigger smooth muscle cells to produce elastin and collagen. In the case of endocardial fibroelastosis the stressors are listed in the Table 1. In pulmonary hypertension, the stressors include excessive pressure and flow from left-to-right shunts, hypoxaemia as in altitude sickness, genetic aberration in idiopathic pulmonary hypertension, and others. It was hoped that this analogy would provide a simple answer to take from pulmonary hypertension and apply to endocardial fibroelastosis. But many studies of pulmonary hypertension over the years have revealed a complex system, a network of signalling molecules, both stimulatory and controlling, complexities impossible to relate here. A recent review illustrates this.[31]

Nevertheless, on the basis of the analogy with pulmonary hypertension, I offer three hypotheses: the same order of complexity as in pulmonary hypertension is at work in endocardial fibroelastosis; potent stimuli of smooth muscle cell proliferation and migration such as tenascin C and endothelin increase abnormally in the subendothelium in endocardial fibroelastosis as they do in pulmonary hypertension; and as the hypothetical network of control involves genes, it is logical to assume that genetic variation is the reason why some individuals develop deposits of endocardial fibroelastosis in their hearts while others undergoing similar stress do not. Considering the negative association of the endocardial fibroelastosis reaction with a variety of hypertrophic cardiomyopathies, leads to another hypothesis, that is, the ultimate physical trigger of the endocardial fibroelastosis reaction may well be an automatic ability to assess the contractility of the myocardium that most likely resides in the endocardium. All of the associated diseases and other stresses decrease contractility. The conditions that increase contractility, at least in early systole, inhibit the endocardial fibroelastosis reaction. It is this putative assessment of decreased contractility that initiates the biochemical triggering. I do not expect that these hypotheses will be confirmed or denied soon.

Some issues clarified

A fascinating relationship exists between endocardial fibroelastosis and non-compaction. In contrast to the long history of endocardial fibroelastosis, non-compaction was recognised as recently as 1990. It seems counterintuitive that, at autopsy, a failure of development should be found alongside an overdevelopment, but such is the case. In reports of endocardial fibroelastosis published before non-compaction was recognised, pathological pictures have demonstrated and authors have commented on marked trabeculation. (an example is Westwood's Family 1, case 3).[32] After recognition of non-compaction, Burke et al[33] Searched their vast autopsy material and reported on 14 cases. They all had some degree of the endocardial fibroelastosis reaction. Others have reported endocardial fibroelastosis in non-compaction as well. The reaction appears thickest at the apices of the long trabeculae, where ischaemic stress is likely the greatest, being the farthest from the epicardial coronary arteries and fed over a long and tortuous supply line. Previously in this journal, I declared that all non-compaction is congenital.[34] The failure of compaction in foetal life is contemporaneous with the most rapid deposition of endocardial fibroelastosis. Thus, the association is not so surprising.

Another interesting facet of the endocardial fibroelastosis story is its relation to hypoplastic left heart syndrome. The studies by Fruhling et al,[12] besides the major findings described above, also

https://doi.org/10.1017/S1047951110000181 Published online by Cambridge University Press

revealed a few cases in which Coxsackie virus was recovered from hearts with very thick endocardial fibroelastosis and very small left ventricles. Similar pathologic findings without the virology were noted in a review, undertaken by Ursell et al,[35] of autopsied neonatal hearts from three British hospitals. They found 46 cases of endocardial fibroelastosis with significant malformations of the left ventricle or aortic tract. But distinct from these 46 cases, there were three with endocardial fibroelastosis and left ventricular hypoplasia and no other lesions. Some of the more severe ones like those reported by Ursell are clearly hypoplastic left heart syndrome, whereas less severe ones survive as examples of what in the 20th century was called "the rare constrictive form of endocardial fibroelastosis". Thus, while most foetal hearts with cardiomyopathy or infection progress to dilatation, a few go the path of constriction, perhaps due to genetic variability. The foetal echocardiographers have now observed these changes literally as they occur, as shown above. I hope that the attention of geneticists will be attracted to study such hearts and remove some of the mystery.

Unresolved issues

Does endocardial fibroelastosis itself have a pathological significance other than as a reaction to an underlying cause? Some believe that the fibroelastic layer impedes both systolic contraction and diastolic filling. Others, like Black-Schaffer,[11] believe that the fibroelastic layer is protective against further dilatation. The difficulty in studying this is obvious. The diseases with which the endocardial fibroelastosis reaction is associated also affect systolic and diastolic function, rendering it impossible to distinguish the effects of the disease from those of the endocardial fibroelastosis reaction. In extreme situations such as congenital aortic stenosis that is not responding to valvotomy and a thick layer of endocardial fibroelastosis is apparently limiting function, a few surgeons have resorted to sharply resecting the fibroelastic layer from the myocardium with benefit to both function and growth.[36] When this procedure is performed in combination with a Ross-Konno operation or other valve replacement,[37] evaluation of the independent effect of the resection becomes difficult.

Much has been said in the past about endocardial fibroelastosis in the adult. There has been controversy about how much is a latent process from childhood, how much has been gradually acquired over many years, and how much has been recently acquired. All of these possibilities now seem valid. Though at one time this may have been a hot topic, the fact that the current edition of a major adult cardiology textbook does not discuss endocardial fibroelastosis, merely mentions it only once, in connection with childhood disease, it would seem unimportant to do any more than mention it here.

A brief lecture on nosologic purity

In the early days of endocardial fibroelastosis, a convention was established dividing cases into "primary" where no obvious cause was found and "secondary" where a congenital malformation such as a coarctation or other cause was evident. As it is now clear that all endocardial fibroelastosis is secondary to some factor, known or not yet known, the distinction has no merit. It is better to use the term "idiopathic" when the cause is not known rather than "primary", which implies some magical *de novo* phenomenon.

The authors of the first international classification of the cardiomyopathies placed endocardial fibroelastosis in the unclassifiable category. When the classification was revised in 1995,[38] endocardial fibroelastosis remained unclassified. There have been other more recent attempts at classification of the cardiomyopathies, but the most practical continues to be the 1995 work in which endocardial fibroelastosis remained unclassified. There is good reason for this, though it may not have been recognised by the authors of that document. The reason is simply that endocardial fibroelastosis does not logically belong on the tree of classification, because it may occur throughout the tree as a secondary feature. The logic of classification is well treated in a critique by Colan.[39] The North American Pediatric Cardiomyopathy Registry does not have an aetiological category for endocardial fibroelastosis. Rather, the registry applies it as modifying characteristic that may apply to many etiologies of cardiomyopathy. I assisted Steven Colan, Steven Lipshultz, and others to found that registry and its system of classification.[40] In a 2007 review written for the registry, Alvarez and Lipshultz restated the rationale for placing endocardial fibroelastosis as a reaction within dilated cardiomyopathy.[41]

It is difficult to abandon old habits of thought, speech, and writing, especially when they come so naturally. The endocardial fibroelastosis reaction can be detected non-invasively by echocardiography, and it can be directly visualised at surgery or at postmortem. As the observer, you should remember that the endocardial fibroelastosis reaction is not the disease; rather, you should question what underlying disease associated with cardiac stress caused the reaction.

There are reasons why it is important to use the right terminology. The best reason is that it is correct. Continued use of outdated thinking delays forward progress. It leads to textbooks with back-to-back

sections on dilated cardiomyopathy and endocardial fibroelastosis with almost identical texts, and to authors attempting to segregate cases with endocardial fibroelastosis from other cases of the same disease. Descriptions of endocardial fibroelastosis, as a distinct disease entity, continue to appear in reports in the 21st century. New investigators reference the medical literature of the 20th century and perpetuate confused concepts. Responsible senior paediatric cardiologists must put a stop to this by correcting their younger colleagues, and by providing advice to authors in their roles as editors of journals and textbooks. I tried to make this point in 1988.[42] Two decades later, with even more supporting evidence, the point still needs to be made. There is much to be done. But it is not difficult. It only requires vigilance and kind words of advice.

Acknowledgements

William N. Evans, MD, persuaded me to pursue this and when the task seemed done made it readable by his skilful editing. Ruben J. Acherman, MD, was indispensable in the role of medical artist. The author also thanks three people who kindly responded to my phone calls asking for their experience in various forms of hypertrophic cardiomyopathy: Barry J. Maron, MD (genetic), Jacqueline Noonan, MD (her syndrome), and Howard Gutgesell, MD (infants of diabetic mothers).

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