

Endocardial fibroelastosis and Niemann-Pick disease

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The concurrence of endocardial fibroelastosis and Niemann-Pick disease is described. This appears to be the first described case of endocardial fibroelastosis in association with a lipid storage disorder.

Endocardial fibroelastosis may be associated with many congenital heart malformations (Andersen and Kelly, 1956). Some cases occur in families in which the inheritance appears to be either multifactorial (Chen *et al.*, 1971) or of a more clearly defined pattern of inheritance, e.g. autosomal recessive (Rosahn, 1955), autosomal dominant (Hunter and Keary, 1973), and X-linked recessive (Westwood *et al.*, 1975). Endocardial fibroelastosis has also been described in association with some in-born errors of metabolism, notably the mucopolysaccharidoses (Krovetz and Schiebler, 1972) and type II glycogen storage disease (Pompe's disease) (Stanbury *et al.*, 1972). It has not to my knowledge been described in association with a lipid storage disease. I wish to describe a case of endocardial fibroelastosis in Niemann-Pick disease.

Case report

This female infant was born to a 17-year-old single mother by breech delivery at 32 weeks' gestation and weighed 2295 g (5 lb 1 oz). The parents were gentle but unfortunately a detailed family history was not obtained. The child appeared to develop normally until the age of 2 months when it was noted that she was not acquiring normal head control. She lost interest in her surroundings, fed poorly, and failed to thrive over the next few months. At 6 months of age, while being treated for bronchopneumonia in hospital, gross hepatosplenomegaly was first noted. Before this there was no acute illness or overt evidence of myocarditis. She was referred for further investigation.

She was a small, thin, retarded 7-month-old infant. There was increased tone in the lower limbs, gross hepatosplenomegaly, and the heart was clinically enlarged. Blood pressure was 90 mmHg and the femoral pulses were palpable. There was an apical pansystolic murmur. Her fundi were normal.

INVESTIGATIONS

Haematology

Hb 10.5 g/dl; other haematological tests were normal.

Bone marrow

Bone marrow was cellular with storage cells with an amorphous cytoplasm suggestive of a lipid storage disease.

Liver function tests

Serum aspartate aminotransferase was 350 IU/litre; and serum alanine aminotransferase was 390 IU/litre. Other liver function tests gave normal results. Serum lipids were normal.

Chest x-ray

The radiograph showed cardiac enlargement with normal lung fields.

Electrocardiogram

There was pronounced left ventricular hypertrophy.

She developed pneumonia in hospital and died at 7½ months of age.

NECROPSY AND MORPHOLOGICAL FINDINGS

The liver and spleen were enlarged and contained foam cells which were also present in the bone marrow, adrenals, thymus, and alveoli. The lungs showed patchy collapse and consolidation. The heart was enlarged, weighing 75 g (normal 37 g). The left ventricular wall was thickened and showed endocardial fibroelastosis but there was no mononuclear infiltration of the myocardium. The aortic and mitral valve were not involved. There were no storage cells in the heart and the coronary arteries were normal. The brain was small, with atrophy of the white matter, and histology showed lipid in the nerve cells.

BIOCHEMICAL ANALYSES

Sphingomyelin was increased in both grey and white matter in the brain as well as in the visceral organs (see Table). Cholesterol and cerebroside were decreased in white matter. These findings are typical of Niemann-Pick disease (Stanbury *et al.*, 1972). In addition, the thin layer chromatograms of gangliosides from cerebral cortex showed an increase in the G_{M_2} band and a faster-running NANA-containing glycolipid (probably G_{M_3}).

Discussion

This case includes all the typical features of type A Niemann-Pick disease (acute neuronopathic form) with early central nervous system involvement, gross hepatosplenomegaly, and death within the first four years of life (Stanbury *et al.*, 1972). The disease results from a defect in the activity of sphingomyelinase which results in the accumulation of sphingomyelin in brain and visceral organs. Though the enzyme assay is now widely used, unfortunately it was not available at the time these studies were conducted.

Our case is distinguished from others with type A Niemann-Pick disease by the concomitant occurrence of endocardial fibroelastosis. To our knowledge the association is unique. It has not been described in the excellent review by Fredrickson and Sloan (Stanbury *et al.*, 1972). Two further cases in Manchester, England, and 13 patients reviewed from the files of the Hospital for Sick Children, Toronto, Canada, had no cardiac involvement.

Theories on the aetiology of endocardial fibroelastosis include hereditary, viral, and mechanical. Other theories include myocardial hyperplasia, mitral regurgitation, anoxia, and a myocardial metabolic abnormality (Hutchins and Vie, 1972). Black-Schaffer (1957) originally proposed the mechanical hypothesis suggesting that endocardial fibroelastosis was a non-specific reaction of the endocardium to increased mural tension of whatever cause. Hutchins and Vie (1972) combined the

viral and mechanical tension theories in his study of a series of cases developing endocardial fibroelastosis after myocarditis (possibly caused by Coxsackie B but not proven). They proposed that these patients developed ventricular dilatation as a result of myocarditis. While the inflammatory condition subsided the ventricular dilatation and compensatory hypertrophy continued, with subsequent mitral regurgitation and endocardial fibroelastosis developing secondary to the ventricular dilatation and increased mural tension. Endocardial fibroelastosis in association with mucopolysaccharidoses or type II glycogen storage disease probably results from infiltration of the myocardium by the mucopolysaccharides and glycogen, respectively, resulting in impaired myocardial function and ventricular dilatation.

The cause of endocardial fibroelastosis in our case is puzzling. There was no infiltration of the subendocardium or myocardium by foam cells, which could result in impaired myocardial functions and ventricular dilatation. There were also no cardiovascular abnormalities to account for the endocardial fibroelastosis and no mononuclear infiltrate in the myocardium.

Hutchins and Vie (1972) found mononuclear infiltrates in 70 per cent of their cases of endocardial fibroelastosis. They thought that these cases had had a prolonged illness which had begun with an unrecognised myocarditis. The inflammatory lesion had resolved at the time of death. It is difficult to suggest that our case can be explained in this fashion, however, for the total duration of the illness was only a few months and there was no mononuclear infiltrate of the myocardium.

Endocardial fibroelastosis in this case of Niemann-Pick disease may be related to the underlying disease though there is no microscopical evidence of this. It may have followed myocarditis or it may represent the idiopathic type and be purely the coincidental occurrence of 2 rare diseases. A genetic aetiology for endocardial fibroelastosis can still not be excluded because a detailed family history was

Table Lipid composition of organs from child with Niemann-Pick disease (mg lipid/100 mg dry wt)

Tissue	Total phospholipid		Sphingomyelin		Total cholesterol		Total cerebroside	
	Patient	Normal*	Patient	Normal*	Patient	Normal*	Patient	Normal*
Cerebral white matter	23.9	32.6	13.22	7.5	6.88	10.53	5.11	—
Cerebral grey matter	27.8	33.0	15.52	4.5	6.52	5.14	4.23	—
Liver	29.0	12.0	21.96	1.6	7.10	—	1.41	—
Spleen	29.7	15.0	25.19	3.2	7.95	—	1.43	—
Kidney	19.6	—	12.90	—	3.01	—	2.24	—

*Normal values from Lowden *et al.* (1967).

not obtained. If the parents were consanguineous, the possibility of the simultaneous occurrence of 2 rare genetically determined diseases would be considered.

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