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Brief Report

An Infant With Mucolipidosis-II And an Atretic orifice of the Left Coronary Artery

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Abstract A one-month-old boy, with type-II mucolipidosis, presented with congestive heart failure and elevated cardiac enzymes. The atretic nature of the orifice of the left coronary artery was revealed by retrograde flow on color Doppler and selective coronary angiography. Type-II mucolipidosis and atresia of the left coronary artery are rare. To the best of our knowledge, this is the first report of their combined occurence, suggesting a possible causal relationship.

Keywords: Dilated cardiomyopathy; I-cell disease; lysosomes; metabolism

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Mucolipidosis II, I-cell disease, or MIM 252500, results from deficiencies of either the alpha or beta subunits of N-acetylglucosamine-1-phosphotransferase, both of which derive from a single mRNA transcribed from the GNPTAB gene on chromosome 12q23.3. This enzyme attaches N-acetylglucosamine-1-phosphate to mannose residues of newly-synthesized lysosomal enzymes, an essential step in the maturation of their carbohydrate side chains. The mannose-1-phosphate residues that ultimately result are essential for lysosomal uptake and targeting of the hydrolases.[1] The biochemical phenotype is characterized by generalized deficiency of lysosomal hydrolases in cells, contrasting with elevated levels of catalytically-active hydrolases in the plasma. The clinical phenotype arises from the deficiencies of multiple lysosomal hydrolases. Patients have signs of multisystemic storage, such as marked bony abnormalities, restricted movement of the joints, gingival hypertrophy, and psychomotor retardation, all of which may be evident within days of birth.[2] Fetal hydrops[3] has also been reported. Cardiovascular manifestations are described in most patients, including cardiomegaly and valvar disease.[4,5] In this report, we describe a 1-month-old male infant with I-cell disease and an atretic left coronary artery.

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Clinical History

A one-month-old French-Canadian boy was transferred for tachypnoea and tachycardia. Physical examination suggested congestive heart failure, and cardiomegaly was found on the chest X-ray. There was no contributory personal or familial medical history. Electrocardiography suggested anterolateral ischaemia, and levels of troponin-T were elevated to 0.601 μg/l, our normal range being from zero to 0.050 μg/l. Echocardiography showed severe left ventricular dysfunction and left coronary arterial hypoplasia. Colour Doppler interrogation of the main stem of the coronary artery demonstrated reverse flow (Fig. 1). Cardiac catheterization showed proximal atresia of the artery, and hypoplasia of its main segment, which was confirmed by retrograde filling during selective right coronary angiography (Fig. 2).

The patient was admitted to the intensive care unit and treated with nitroglycerin and inotropic

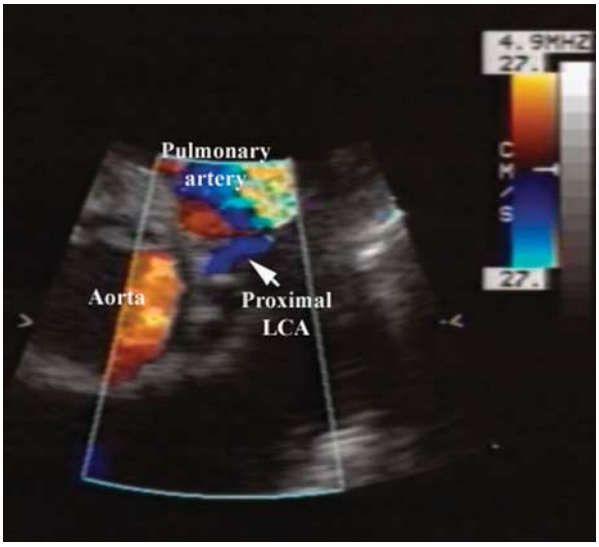

Figure 1.
Low velocity colour flow mapping in the parasternal short axis shows retrograde filling of the main stem of the left coronary artery (LCA). A filling defect is evident between the LCA and the aorta, due to the non-patency of the proximal part of the coronary artery (arrow).

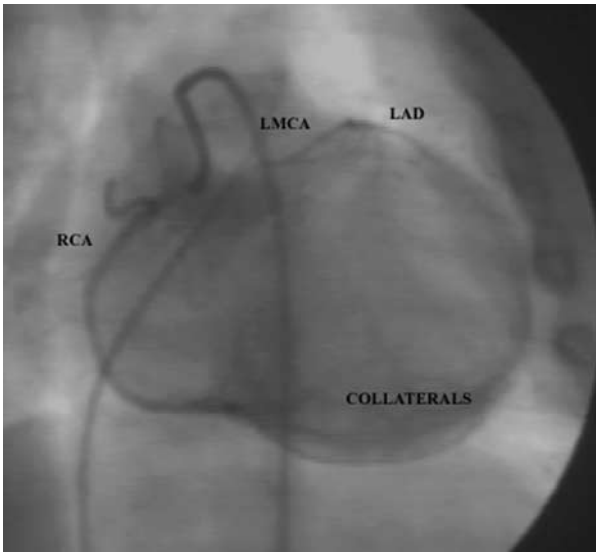

Figure 2.
Right coronary artery (RCA) angiography. Collateral branches arising from the right coronary artery anastomose with the left anterior descending artery (LAD). In sequential images, the main stem of the left coronary artery (LMCA) was opacified in a retrograde direction.

drugs. Physical examination showed gingival hypertrophy and a narrow thorax. The chest X-ray revealed broad osteopenic ribs. The diagnosis of I-cell disease was suspected clinically, and by the demonstration of reduced activity of lysosomal hydrolases in leukocytes, with elevated activity of these enzymes in the plasma (Table 1).

On the fourth day of hospitalization, he developed acute abdominal signs and haemodynamic instability. Laparotomy demonstrated volvulus and intestinal ischaemia. Given the severe underlying metabolic disorder, and the extreme clinical instability, heart transplantation was not felt to be indicated. The parents elected to withdraw life support and the patient died soon thereafter. Autopsy was declined.

In cultured fibroblasts, a generalized lack of intracellular retention of enzymatically-active lysosomal hydrolases was subsequently demonstrated, confirming the diagnosis of I-cell disease (Table 1).

Discussion

Cardiac involvement reported in I-cell disease includes cardiomegaly, mitral and aortic valvar deformation, hypertrophic and dilatated cardiomyopathy of the left ventricle, and is usually diagnosed when the infants are aged from 6 to 12 months.[5] These findings, resulting from the stored intracellular material, are progressive and often more severe than suspected clinically. Non-immune hydrops may also be present in the fetus,[3] but cardiac function has not been described in these cases. I-cell disease is typically fatal during early childhood.[4] In addition to medical therapy, cardiac surgery has been offered to reduce mortality, and to improve the quality of life in cases with valvar disease.[6,7]

The primary anatomic differential diagnosis of dilated cardiomyopathy in newborns and infants is an abnormal origin of the left coronary artery. Coronary arterial anomalies make up around 2% of congenital cardiac malformations. The commonest lesion is anomalous origin of the left coronary artery from the pulmonary trunk. Congenital atresia of the left coronary artery is extremely rare, with only 28 cases collated in a review from 1997.[8] Its clinical manifestations reflect the secondary myocardial ischaemia. In the collected series,[8] half of the patients presented in childhood with syncope, sudden death, ventricular tachycardia, or myocardial infarction. From a developmental standpoint, it is expected that atresia of the orifice of the left coronary artery would be compensated by a rich collateral vasculature from the right coronary artery. Hence, the delay until adulthood in the clinical presentation of half of the patients is remarkable. Presumably, various degrees of compensation by collateral channels prevent the fetal and neonatal onset of attributable signs and symptoms. The relatively delayed cardiac presentation suggests a progressive stenosis leading to total coronary arterial obstruction, potentially secondary to vascular mural storage. Although it has not been

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Table 1. Lysosomal hydrolase activities in cells (nmol/h/mg protein) and plasma or culture medium (nmol/h/mL). Reference values are presented between parentheses.

	In vivo		*In vitro*	
Enzymes	**Leucocyte**	**Plasma**	**Fibroblast**	**Culture medium**
Total hexosaminidase	1,068 (2,019)	14,848 (1,009)	518 (2,831)	3,655 (450)
ß-galactosidase	88.8 (176.9)	282 (63.9)	12 (933)	9.92 (2.06)
α-fucosidase	68.1 (108.4)	1,072 (352)	14 (79)	7.31 (1.46)
ß-glucosidase	75.5 (21.4)	13.3 (6.4)	44 (309)	5.39 (1.81)

emphasized in the literature, marked coronary arterial narrowing has been reported in other storage diseases, like mucopolysaccharidosis.[9,10] In one report on five subjects with the Hurler syndrome, the thickened intimal layer of the coronary arteries contained granular cells with clear vacuoles and substantial increase in collagen fibrils, with the interstitial layer containing heavy collagen deposits, as well as fine spicules of acid mucopolysaccharides and glucolipid deposits.[9] In addition, the smooth muscle cells of the medial layer contained lamellar bodies, clear vacuoles and amorphous densities. In all cases, these deposits and infiltrates resulted in diffuse luminal narrowing, greater than three-quarters of the extramural coronary arteries, and to a lesser degree in the intramural segments. Small focuses of myocardial necrosis and fibrosis were described in all patients, mainly in the left ventricular subendocardial region and the papillary muscles. Another multimodal imaging report involving three children with Hurler syndrome, and one with Scheie syndrome, documented marked narrowing of the abdominal aorta, as well as multiorgan arterial stenoses, leading to abdominal coarctation in three and hypertension in all.[10] Of the latter series, a severe coronary arterial stenosis was confirmed in one.[10] The age of the patients in these reports varied between 4 and 16 years old. We are unaware of similar reports in the neonate, either with mucopolysaccharidosis or with mucolipidosis.

To our knowledge, ours is the first report of a congenital abnormality of the coronary arteries in I-cell disease. Both entities are rare, and their concomitant occurrence suggests a possible connection between them. The severe coronary arterial abnormality found in our patient raises the important question of whether the dilated cardiomyopathy described in other patients with I-cell disease may be a consequence of undiagnosed and progressive coronary arterial involvement. It seems prudent to suggest that the development of atresia of the coronary arteries be considered in patients with I-cell disease and cardiomyopathy, especially if valvar pathology is absent or minor. Conversely, signs of I-cell disease may be searched for in rare children found to have atresia of the left coronary artery.

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