G90 Inborn Errors of Metabolism Explain a Suspected SIDS Case

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The goal of this presentation is to underline the difficulty of diagnosis of SIDS. According to San Diego SIDS diagnostic criteria, a clinical, anamnestic, circumstantial, and autoptic investigation must be performed. In most of cases death remains unjustified after the diagnostic procedures and SIDS is unresolved. This presentation concerns a case of resolved SIDS, in which the postmortem investigation led to diagnosis of dilated cardiomyopathy (DCM) with endocardial fibroelastosis, associated to tubular hypoplasia of the aorta and inborn errors of metabolism.

This presentation will impact the forensic science community by showing the difficulty to diagnose clinical silent cardiomyopathy in children younger than one year old, and so an accurate clinical, anamnestic, circumstantial and instrumental investigation can lead to a timely diagnosis of DCM in life.

A 10-month-old female infant was born full term (41+2 gestational week) at a weight of 3,800g. She had no neonatal complications. She was exclusively fed with formula and her mother had familiar history of Celiac disease. At 4-months-old, growth retardation and several generalized convulsive seizures, without fever, appeared. Laboratory investigation and electroencephalogram were unremarkable. When she was 10 months-old, the infant reported recurrent convulsive crisis (twice a night) and she was admitted into the hospital, where, on clinical examination, she appeared a very small infant (weight 6720g, length 70cm, CC 43cm). Electroencephalogram revealed paroxystic activity and decelerated rhythm on right occipital area. Laboratory blood values demonstrated reduced red cells count, respiratory acidosis (pH 7.333, pO2 37.1 mmHg), increased liver enzymes. Celiac disease HLA haplotypes examination was negative. Aminoacids dosage in blood revealed above all high citrulline levels. The ECG showed inverted T-waves in all derivations. In the following days the infant returned home to continue anticonvulsant therapy, but in the night she had recurrent convulsive crisis and she was admitted to the Emergency Department for blue lips, generalized hypotony, and cardiorespiratory arrest. Cardio-pulmonary resuscitation was unsuccessful and the infant was declared dead.

The external examination was unremarkable. The internal examination revealed heart increased in size (7.5x7.5x3.8cm) and weight (161g). The left ventricle showed a marked dilatation with an anterior wall thickness of 1.2cm, a lateral wall thickness of 1.4cm and an interventricular septum thickness of 1.2cm. At the transverse section the myocardium showed white areas, extended from atrio – ventricular plane to apex, with increased consistence. The right ventricular chamber was dilated with increased wall thickening. The left and right ventricular endocardium was shining and brightness. The descending aorta showed a short tract of tubular hypoplasia with vascular constriction to a minimum vascular diameter of 0.2cm, at 2.5cm from the left subclavian artery. Macroscopical examination of other organs was unremarkable, although liver showed hepatomegaly (size 15x9x4cm and weight 256g).

Histological examination of the heart revealed diffuse fibrosis mainly interstitial and with an undulating aspect, and fields with patchy fibrosis, rare foci of contraction band necrosis, disarray and disappearance of myofibrils with intramyocardial oedema resulting in empty sarcolemmal tube and with any type of reaction (colliquative myocytolisis grade 1) in the subendocardial layers. Left ventricular examination revealed a diffuse and considerable thickening of the endocardium resulting from proliferation of fibrous and elastic tissue representing a diffuse subendocardial fibroelastosis. Liver histological findings were suggestive of diffuse microvesicular steatosis. Non-identified metabolic disease was characterized by the following laboratory data: citrulline *38 mmoli/l (VN 9.50-33.61)*. The urinary acid dosage offered many alterations: methylmalonic acid *12 (VN <7)*. The complete aminoacidogram presented: *taurine 202.763 (vn 38-127), aspartic acid 29.335 (vn 3-9), serine 185.407 (vn 92-181), cystine 5.645 ↓ (vn 25-62), ethanolamine 7.841 (vn 0-6)*. The urinary amino acid dosage presented: "*aspartic acid 41.524 (vn 3-10), glutamine 66.581 ↓ (vn 74-197), glycine 96.764 ↓ (vn 114-445), valine 5.770 ↓ (vn 6-19), cystathionine 0.141 (vn 0-0), leucine 3.564 ↓ (vn 4-16), fenylalanin 8.754 ↓ (vn 11-28), 1-metyl-histidine 17.889 (vn 0-0), histidine 69.135 ↓ (vn 92-278).*"

These data show the close correlation between cardiomyopathy and metabolic-genetic disease, supported by the presence of hepatomegaly and reduction in cranial diameters.

The dilated cardiomyopathy is a myocardial disorder characterized by dilated left ventricular (LV) chamber and systolic dysfunction that commonly results in congestive heart failure. DCM shows an incidence of 0.34 cases per 100,000 children and it represents the half of all the pediatric cardiomyopathies. Age younger than one year is the most common age at diagnosis of DCM. In the most severe cases, the affected children are clinically silent until they suddenly present signs and symptoms of heart failure (breathlessness at rest, orthopnoea, early onset fatigue, abdominal pain, pallor). DCM is prevalent with 66% in the first year of life and it is correlated with metabolic diseases in 9% of cases. The main characteristics of this pathology are: increasing of size and weight of the heart, expansion of cardiac cavities and fibrosis. Metabolic diseases cause many alterations that involve mainly the brain, the hearth and multiorgans deficit generically leading to hepatopathy, kidneys, ocular and cutaneous alterations.

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In conclusion, the cause of death was a dilated cardiomyopathy associated with tubular hypoplasia of the first tract of descendant aorta in a small female infant affected by inborn errors of metabolism.

Dilated Cardiomyopathy, Inborn Errors of Metabolism, Sudden Infant Death Syndrome

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