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Case Report

Pompe Disease and Infantile Spinal Muscular Atrophy: Association or Coïncidence?

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ABSTRACT

Background: Pompe disease (P.D.), also known as Glycogen storage disease type II, is an autosomal recessive lysosomal storage disease caused by a deficiency of acid alpha-glucosidase (AAA) or maltase acid. This enzyme allows the hydrolysis of lysosomal glycogen. Patients with infantile-onset P.D. (IOPD) exhibit a nearly complete absence of AαGlu activity; moreover, they develop hypotonia and hypertrophic cardiomyopathy during infancy. Patients with IOPD eventually die of cardiorespiratory failure due to the accumulation of massive amounts of glycogen in their skeletal and heart muscles.

Case report: T.M. is a 4-month-old female infant, the second of two siblings, hospitalized at the Neonatology and Nutrition Center in Rabat, Morocco, for severe respiratory distress with generalized congenital hypotonia.

Conclusion: Spinal muscular atrophy (SMA) is an autosomal recessive genetic disorder characterized by the degeneration of alpha motor neurons within the spinal cord. The disease is linked to a mutation in the survival motor neuron (SMN)1 gene on chromosome 5 (5q13.2), which prevents the synthesis of SMN protein. No case of association has been reported between these two diseases to date. We present a case of Pompe disease associated with spinal muscular atrophy.

Keywords: SMN1, Glycogen storage disease type II, Neonatal hypotonia

Introduction

Pompe disease, glycogenosis type II or acid maltase deficiency, is a rare genetic disease of autosomal recessive transmission. This disease was one of the first lysosomal storage diseases to be described at the onset of the 20th century. Pompe disease, which is caused by an acid α-glucosidase enzyme deficiency (GAA; EC 3.2.1.20) due to pathogenic variants in GAA, is characterized by intralysosomal accumulation of glycogen throughout bodily tissues, most notably within cardiac and skeletal muscle (1). Infantile spinal muscular atrophy (SMA) is an autosomal recessive disease identified by primary degeneration of spinal cord anterior horn cells, leading to progressive muscle weakness (2, 4). The disease was first described by Werdnig and by Hoffmann in the 1890s. The genetic defect was localized to 5q11.2-q13.3 a century later with the identification of the survival motor neuron (SMN) as the disease-causing gene in 1995 (3).

The present report aims to highlight the absence of any case of association between these two diseases to date. We report a case of Pompe disease associated with spinal muscular atrophy to help all medical staff involved in the newborn screening process. It can significantly help medical geneticists, primary care pediatricians, and neonatal intensive care staff to better understand the complexities of screening for a heterogeneous genetic disorder.

Case report

T.M. is a 4-month-old female infant, the second

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of two siblings, hospitalized at the Neonatology and Nutrition Center in Rabat, Morocco, for severe respiratory distress with generalized congenital hypotonia. She had a 32-year-old mother, a 35-year-old father, and a healthy 5-year-old brother. The patient was the result of a well-monitored pregnancy carried to term by non-consanguineous parents. Stress tests were inconclusive, and there were no maternal serum or ultrasound abnormalities. Labor was induced at 38 weeks, and delivery was uncomplicated. The neonate took several seconds to begin breathing following the clamping of the cord, and she was then admitted to the neonatal intensive-care unit (NICU), where she received oxygen. Initial Apgar scores were 7 at 1 min and 8 at 5 min.

The NICU staff noted that she was floppy and had a chest deformity consistent with respiratory muscle weakness requiring intubation, and she received empiric antibiotics. She had a bright and alert disposition despite slight hypotonia. Her suck was weak, her tongue appeared tremulous, and she required nasogastric feeding. Moreover, clinical examination revealed generalized hypotonia with areflexia, accompanied by hepatomegaly. The biological assessment objectified elevated transaminases: ASAT: 200 IU / l; ALAT: 166 IU / l PAL: 350 IU / l with CPK: 3170 IU / l

The metabolic balance returned to normal:

*Ammonemia: Normal

* Lactatemia: 279

* A.A. chromatography in blood and urine: Normal

* Profile of acylcarnitine: Elevation of c2-carnityl

* Homocysteinemia: normal

Echocardiography demonstrated hypertrophic cardiomyopathy of the left ventricle(LV). The LV function is preserved and hyperkinetic with an ejection fraction of 97%. This clinical finding raised suspicion about the presence of Pompe disease, and the enzyme assay objectified an AGA deficiency and confirmed the diagnosis. The patient received an enzyme replacement therapy with MYOZYME four times as an intravenous infusion of 20 mg/kg every two weeks. Due to the lack of improvement in the clinical picture, spinal muscular atrophy was also suspected; therefore, the polymerase chain reaction was carried out and showed homozygous deletion of exon 7 of the SMN gene in favor of spinal muscular atrophy. The evolution was marked by the occurrence of cardiorespiratory failure after four months of hospitalization.

Discussion

Pompe disease, which is one of the first lysosomal storage diseases, is a rare genetic disease of autosomal recessive transmission described at the beginning of the 20th century. It has a broad clinical spectrum: the infantile form is characterized by early cardiomyopathy, macroglossia, hepatomegaly, and hypotonia. Death from cardiorespiratory failure occurs before the age of 2 years. Juvenile and adult forms are identified by proximal and axial muscle deficits, with or without diaphragmatic involvement. The prevalence of the infantile form, as in our case, is estimated at 1 in 138,000. (5,6)

This report highlights a positive case of a neonate in Rabat, Morocco, screening positive for Pompe disease. Clinical, biochemical, and molecular confirmatory testing ultimately identified a diagnosis of late-onset Pompe disease. The diagnosis of the classic infantile form is made between 0 and 9 months of age in the presence of respiratory insufficiency, cardiomegaly (hypertrophic cardiomyopathy, sometimes of prenatal onset), or hypotonia. The initial evaluation may also reveal a history of repeated respiratory infections, hypo mobility, feeding difficulties from the first weeks of life, growth deficiency, absence of osteotendinous reflexes, hepatomegaly, and macroglossia.

Infantile spinal muscular atrophy is one of the most frequently fatal autosomal recessive hereditary diseases, with an incidence varying from 1/6000-1/10000 births. This disease was first described by Werdnig and Hoffmann in 1890 (2, 4). It is often revealed during the antenatal period by a decrease in active fetal movements and hydramnios; thereafter, at birth, axial and peripheral hypotonia appears associated with swallowing disorders and osteotendinous areflexia. Bulbar involvement is frequent with swallowing disorders. The mimic is respected, and no central neurological involvement is observed. Sitting is never acquired. Death usually occurs in the first two years due to the damage inflicted on the intercostal muscles responsible for restrictive respiratory failure.

In our patient, the symptomatology was revealed from birth by the development of generalized hypotonia, areflexia, and hepatomegaly with severe respiratory distress. The biological workup showed elevated transaminases with elevated creatine phosphokinase (CPK). The metabolic panel was normal. Echocardiography

displayed hypertrophic cardiomyopathy of the left ventricle. The AGA enzyme assay illustrated a deficit, confirming the diagnosis of Pompe disease. The patient was put on enzyme replacement therapy: alglucosidase alfa (Myozyme®) at a dosage of 20 mg/kg /2 weeks by intravenous infusion. This treatment limits the accumulation of lysosomal glycogen, limiting the evolution of the disease (7). non-improvement of the patient and the clinical picture raised suspicion about the presence of spinal muscular atrophy, and the PCR method objectified the deletion of exon 7 of the SMN gene, which confirmed the disease. The evolution was marked by the occurrence of cardiorespiratory failure after four months of hospitalization. Genetic counseling has been offered to parents.

Acknowledgments

None.

Conflicts of interest

The authors declared no conflict of interest.

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