Partial Merosin Deficiency and Precocious Puberty

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ABSTRACT

The congenital muscular dystrophies (CMD) are autosomal-recessive disorders. Classical congenital muscular dystrophy is grouped as merosin-positive and merosin-negative (MN-CMD). Precocious puberty in girls has been defined by Marshal and Tanner in 1969. In most of the cases, precocious puberty is idiopathic and is related to premature release of gonadotrophins. So far, the association between merosin deficiency and precocious puberty has not been identified. We report a case of a child with precocious puberty who was diagnosed with merosin deficiency in infancy.

Key words: Precocious puberty, merosin deficiency, child

INTRODUCTION

The congenital muscular dystrophies are autosomal-recessive disorders. They are clinically heterogeneous group, show similar dystrophic findings on muscle biopsy. They are characterized by the early onset of hypotonia, weakness, and joint contractures. By the definition of a deficiency in the laminin-2 chain of merosin, classical congenital muscular dystrophy was grouped as merosin-positive and merosin-negative (MN-CMD) (1). Merosin is a heterotrimeric glycoprotein consisting of a heavy chain (laminin-2) and two light chains and expressed in extracellular matrix. Mutations in the LAMA2 gene located on chromosome 6q22-23 are shown. This gen encode the laminin-2 chain of merosin (2). Laminin-2 is expressed in skeletal and cardiac muscles, pancreas, lungs, spleen, kidneys, adrenal glands, skin, testes, peripheral nerves and brain (3). Clinical findings of MN-CMD present at birth and include severe muscle hypotonia, weakness, delayed motor development, severe and early contractures associated with joint deformities and elevated serum creatinine kinase (4).

Precocious puberty in girls has been defined by Marshal and Tanner in 1969 as “the presence of any secondary sex characteristic in a girl before the age of 8, or the onset of menstruation prior to 10 years of age” (5). So far, the association between merosin deficiency and precocious puberty has not been reported. We report a case of a child with precocious puberty who presented at infancy with marked generalized hypotonia and normal mental development and was diagnosed with merosin deficiency.
CASE
An eight year old girl admitted to pediatric endocrinology department with the complaint of breast development for four months. She has healthy parents and two siblings. She was born of non-consanguineous marriage by cesarean section after full term gestation. Her birth weight was 2000g. She had hypotonia, neurological developmental delay and short stature. In her past history it was learned that she diagnosed as partial merosin deficiency. The clinical diagnosis hasn’t been confirmed by detection of mutations on LAMA2 gene because of social reasons. Serum creatinine phosphokinase (CPK) level was slightly elevated. In physical examination her height was 116 cm (-2.27 SDS), weight was 25.7 kg (-0.13 SDS), breast development was at Tanner stage 3 and pubic hair was at Tanner stage 2. She had reduced muscle tone and slightly decreased deep tendon reflexes. Cognitive development and other systemic examinations were normal. She could walk unsupported but gets tired easily. Basal LH, FSH and estradiol levels were 9.52 m IU/ ml, 3.5 m IU/ml and 10 pg/ml, respectively. Her bone age was 11 years and predicted adult height was 131.3 cm. Rutine chromosome analysis was normal. Ultrasonographic examination of internal genitalia showed increase in uterine and ovarian sizes for her age. Cranial MRI was normal. With clinical and biochemical findings she was diagnosed as idiopathic precocious puberty and begun intramuscular injections of GnRH analogue monthly.

DISCUSSION
Congenital muscular dystrophy is an autosomal recessive disease that is present at birth or manifests by the age of 6 months. The disease is characterized by early onset of hypotonia and weakness. CMD was first described by Batten in 1903, but the disease was named as ‘dystrophia muscularis congenita’ by Howard (1,6). This is a group of muscle diseases include the Fukuyama type, Walker Warburg syndrome, muscle eye brain disease, Duchenne and Becker congenital muscular dystrophy. Almost 50% of diseases are caused by primary deficiency of a protein named merosin, and present with a severe motor and respiratory involvement. The merosin negative subtype comprises about 30% of CMD (1,7). It is a heterogeneous disorder with complete and partial deficiency of merosin chains. Patients with complete merosin deficiency have neonatal onset; however, those with partial merosin deficiency can manifest the disease from birth to adulthood. Patients with complete enzyme deficiency are unable to walk or stand independently, whereas those with partial enzyme deficiency can often walk with no support (5). It present with delayed motor development and generalized muscle atrophy. In contrast with other CMD patients, those with merosin deficiency have high creatinine phosphokinase levels (1).

Our patient admitted to hospital with hypotonia and developmental delay at the age of 8 months. She had slightly increased serum creatinine phosphokinase levels and normal brain MRI; with this clinical and laboratory findings she was diagnosed with partial merosin deficiency. The normal brain MRI and normal cognitive development distinguish this form from Fukuyama CMD, muscle-eye-brain disease or other forms of CMD with secondary partial merosin deficiency and abnormal brain MRI and/or mental retardation. Prenatal diagnosis can be made by immunocytochemical studies of chorionic villous samples and genetic linkage analysis (7). Our patient had early pubertal findings. Her breast development was at Tanner stage 3 and pubic hair development was at Tanner stage 2. Bone age was 11 years. She was diagnosed with central puberty precocious with these findings. In most of the cases, precocious puberty is idiopathic and is related to premature release of gonadotrophins (4). Bone maturation is accelerated in precocious puberty, leading to premature epiphyseal closure and curtailed stature. In addition, pituitary suppression with GnRH antagonists is indicated to delay pubertal development (8).

We report a child with partial merosin deficiency and central puberty precocious. In our knowledge the association of these two disease was not reported before. However, this needs to be investigated if there is an association or this is a coincidental event.

REFERENCES


