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DELAYED DIAGNOSIS OF SPINAL MUSCULAR ATROPHY TYPE IIIA IN A CHILD PRESENTING WITH ABNORMAL WALKING

YÜRÜME BOZUKLUĞU İLE GELEN BİR ÇOCUKTA GECİKMİŞ SPİNAL MUSKULER ATROFİ TİP IIIA TANISI

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ABSTRACT

Out-toeing is one of the most common gait disturbances in children that cause parents to seek medical advice from their doctor. Spinal muscular atrophy (SMA) type III usually presents with an abnormal gait like waddling. The key to an accurate diagnosis of SMA type III is a careful history including subtle motor milestones. We report a 10 year-old-girl with SMA type IIIa presenting with abnormal gait. Past medical history revealed that the patient had been admitted to the department of orthopedic surgery for out-toeing and delayed walking at the age of 6. She had been diagnosed as flat foot and treated with modified shoes for 4 years. On admission, she had waddling gait, Gowers sign and fasciculation in her tongue. The creatine kinase was 462 U/L (N: 5-130 U/L). The electromyogram showed signs of anterior horn cell disease. She had had deletion of exon 7 of SMN gene. Any information about delayed walking obtained from the medical history of a patient with out-toeing related flat foot should alert the physician to diagnose a neuromuscular disease like SMA type IIIa.

Key words: Spinal muscular atrophy, out-toeing, childhood

ÖZET

Çocuklarda dışa basarak yürüme, ailelerin doktora başvurmasına neden olan en yaygın yürüme bozukluklarından biridir. Spinal muskuler atrofi (SMA) tip III de, genellikle yalpalayarak yürüme şeklinde ortaya çıkar. İnce motor gelişim basamaklarını içeren ayrıntılı öykü, SMA tip III tanısında anahtar rol oynamaktadır. Bu makalede anormal yürüme yakınması ile başvuran SMA tip III tanısı alan 10 yaşında bir kız olguyu sunduk. Olgunun özgeçmişi sorgulandığında, 6 yaşında ortopedi polikliniğine dışa basarak yürüme ve yürümede gecikme yakınmaları ile başvurduğu ve düztabanlık tanısı ile 4 yıl süresince modifiye ayakkabı ile tedavi edildiği öğrenildi. Kliniğimize başvurusunda olgunun fizik bakısında, yalpalayarak yürüme, Gowers işareti ve dilinde fasikulasyonlar mevcuttu. Laboratuvar parametrelerinden kreatin kinaz 462 U/L (N: 5-130 U/L) olarak saptandı. Elektromiyogram incelemesinde, ön boynuz hücre hastalığı ile uyumlu bulgular tespit edildi. SMN geni 7. eksonunda delesyon saptandı. Yürümede gecikme ve düztabanlığa bağlı dışa basarak yürüme yakınmasıyla başvuran olgularda SMA tip III gibi nöromuskuler hastalıklar akılda tutulmalıdır.

Anahtar kelimeler: Spinal muskuler atrofi, dışa basma, çocukluk çağı

INTRODUCTION

Spinal muscular atrophy (SMA) is a neurodegenerative, genetic disease with a frequency of 10-15 per 100000 live births. It is the second most common neuromuscular disease, following Duchenne muscular dystrophy. The progressive degeneration of anterior horn cells begin in fetal life and continue to infancy and childhood (8). SMA is classified into 4 types based on age at onset of symptoms and clinical course: SMA type I (Werdnig-Hoffmann disease), type II, type III (Kugelberg-Welander disease) and type IV (1).

Spinal muscular atrophy is a clinically heterogeneous disease characterized by loss of motor function and muscle atrophy. The initial feature of SMA type III is gait instability caused by proximal weakness. Disease progression is very slow and often seems arrested. These patients are noteworthy because typically clinical picture of SMA type III may exist several years after initial insidious presenta-

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tion. In more than 90% of the cases, the diagnosis is established by showing the gene abnormality on chromosome 5. Muscle biopsy is not needed if genetic analysis shows the appropriate mutation (2,3).

In this paper, we discuss a case who had been followed as flat foot presenting with out-toeing for 4 years by the department of orthopedic surgery and diagnosed as SMA type IIIa in the department of pediatrics. Although SMA type IIIa patients rarely present with out-toeing, we emphasize the importance of careful neurologic evaluation in patients with gait abnormality.

CASE

A 10-year-old girl who had experienced disability of climbing stairs and rising from the floor was referred from department of orthopedic surgery. In her past history, she was born with cesarean delivery at the 39th week of gestation and weighed 3500 g at birth. Information about her motor milestones was learnt from her parents: To hold her head steady in sitting was maintained at 3 months of age; the age when sitting without support was 7 months; walking was achieved at 30 months of age. When she was 6 years old, she had been admitted to the department of orthopedic surgery because of out –toeing due to flat foot and used modified shoes for 4 years. The patient then was transferred to our department at 10 years of age, as her complaints have continued and some extra symptoms had also begun to occur due to progressive weakness in this period. Her parents were second degree relatives and she had a twenty year old brother. All of them were asymptomatic.

On admission, her body temperature was 36.5 °C; heart rate 90 beats/min; respiratory rate 16 breaths/min; blood pressure 110/80 mmHg; body weight 33 kg (25-50 percentiles); height 139 cm (50-75 percentiles). Her gait was of waddling type. Upon neurologic examination, mental status and higher cerebral functions were normal. All cranial nerves appeared intact except fasciculations of the tongue due to hypoglossal nerve involvement. The tendon reflexes were normal in the upper extremities and absent in the lower extremities. Bilateral Babinski reflexes were negative. In her motor examination, muscle power was graded 4/5 for upper extremities and 3/5 for lower extremities. She showed a typical Gowers manoeuvre. Her calves were not hypertrophic. Findings of cerebellar and sensory functions were in normal range. There were not any abnormal findings on physical examinations of other organ systems. Except for creatine kinase (CK) level which was 462 U/L (normal range; 5-130 U/L), results of routine laboratory testing (CBC, blood biochemistry, urinalysis), chest radiograph, MRI of spinal cord and echocardiography were all in normal limits. Electromyography (EMG) study showed fibrillations and fasciculations as well as denervation potentials and high-amplitude polyphasic motor potentials at muscles of upper and lower limbs. Motor nerve conduction velocity was normal. DNA analysis by PCR showed that the telomeric copy of survival motor neuron gen (SMN) was deleted for exon 7, so the patient was diagnosed as having SMA type III.

DISCUSSION

Out-toeing is one of the common gait disturbances that cause parents to seek medical advice. In most cases, this complaint is a variation of normal growth and development. The problem resolves without treatment as the child grows. One of the common causes of out-toeing is flat foot. Flat foot is usually secondary to laxity and muscle weakness, which allows sagging with weight bearing (5,9,11) In our patient's first admittance to department of orthopedic surgery, she had presented with out-toeing. She had diagnosed as having flat foot and treated with modified shoes for 4 years, unsuccessfully. We think that in this patient, while clinically the child did not appear neurologically disturbed, there were developmental signs that pointed to a neuromuscular disease. In children with gait disturbances, as seen in our patient, evaluation of the present and delay of developmental milestones is very important (2,7,11). In her past medical history, she had achieved walking with delay (30 months of age). Rudnik-Schöneborn et al. (7) have found that 16% of SMA IIIa patients showed delayed walking. It has been reported that median age at walking is 13 months (range: 9-53 months) in SMA type IIIa patients. This is an important clue for diagnosis of gait abnormality due to neuromuscular diseases. In our patient, however, information about delayed walking had not been taken into account between 6 and 10 years of age. We thought that in this patient the condition remained stable for a long time and a gradual worsening of motor abilities has occurred. Maybe, subtle features of SMA at the first admittance were confused with flat foot and contributed to the misdiagnosis.

An abnormal gait can be a first sign of either proximal or distal leg weakness. Juvenile SMA is the only chronic denervating disease in which weakness is more proximal rather than distal (2). Neurological examination of the patient at 10 years of age revealed several symptoms due to symmetric proximal muscle weakness including waddling gait and positive Gowers sign. Symptoms of leg weakness were more prominent than arms. Deep tendon reflexes were decreased but sensation was intact. In additional, we observed fasciculations in her tongue as a sign of muscle denervation.

Serum CK estimation is a single outpatient test which should be carried out on any patient with abnormal gait (5). About a quarter of type III SMA patients are reported to have a dystrophic phenotype with mild to moderately elevated serum CK levels and "myopathic" histopathology. Hence, it may easily be confused with a muscular dystrophy (4,6) However, our patient showed no muscle hypertrophy but the CK level was three-fold high.

In most patients, SMA is readily distinguished from myopathic disorders by EMG and muscle biopsy, but the most definitive diagnostic test is a molecular genetic marker in blood for the SMN gene (2,4,8). It has been reported that

SMN1 was deleted for exons 7 or 8 in 85% of Turkish SMA patients (10). In our patient, EMG showed fibrillation potentials and other signs of denervation of muscles of all extremities. The SMN gene analysis also revealed deletion of exon 7, and confirmed the diagnosis.

In all classification systems, achieved motor milestones are the most important criteria apart from age onset. The mild form of childhood or juvenile SMA (type III) is known as Kugelberg-Welander disease and shows a wide range of clinical onset from the first year of life until the 3rd decade. Patients with SMA type III learn to walk without support which distinguishes them from SMA type II. Type IIIa has age of onset before 3 years, and IIIb has age of onset 3 to 30 years (7). Because delayed motor development is not a feature of SMA type IIIb, our patient was diagnosed as SMA type IIIa.

Early diagnosis of SMA with DNA analysis can provide a basis for prenatal diagnosis which is of great importance in preventing SMA. In addition, this policy can help to decrease the disability and parental anxiety (2).

In conclusion, gait disturbances are one of the most common parental concerns in children. If any information about delayed walking could be obtained from the medical history of a patient with out-toeing related flat foot, SMA type IIIa should be kept in mind. Hereby, the diagnosis can be established as early as possible by raising the awareness of the potential pitfalls in diagnosing of SMA type III.

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