

Diagnostic Difficulties of Duchenne Muscular Dystrophy in Madagascar

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Abstract – Duchenne muscular dystrophy is a rare genetic disease characterized by a deficiency of dystrophin. It is serious because of its functional impact, and secondarily vital. An observation in a boy of ten years of a clinical myogenic syndrome is reported. This condition involves a diffuse atrophy with predominantly proximal muscle weakness without sensory impairment. Serum creatine kinase is high. Rarefaction with unequal muscle fiber size was found on histological examination. On the occasion of this singular observation, the authors recall the main features of the disease and highlight the technical difficulties in diagnosis in Madagascar.

Keywords – Myopathy, Genetic, Creatine Kinase, Muscle Biopsy, Duchenne.

I. INTRODUCTION:

Duchenne de Boulogne myopathy is a form of progressive muscular dystrophy. It is a hereditary and familial condition characterized by slow muscle degeneration without damage to the nervous system. The disease is an X-linked recessive transmission, expressed in the male homozygous. Its incidence is 1 case per 3,500 male births in developed countries with a prevalence of 3 cases per 100,000 inhabitants (1). There is currently no effective curative treatment for Duchenne muscular dystrophy. The aim of our work is to report a case observed at the Joseph Raseta paediatrics service of Befelatanana Antananarivo, which is the first case observed in the service, to compare it with the data in the literature, and to underline the technical difficulty to diagnose it in our country.

II. DESCRIPTION

RS is a young boy, born on August 11, 2006, hospitalized for a walking disorder. Four months before her consultation, the mother noticed that the child presented a slow, waddling gait, with fatigability of the lower limbs.

He frequently fell, and to get up he had to lean on his thighs. He presented a fatigability of the upper limbs, without functional impotence. The evolution was towards a slimming first at the level of the buttocks, then at the level of the thighs and the stumps of the shoulders. On the day of his admission, he could no longer walk and presented a vicious attitude with tendon retraction of both knees fixed in flexion.

His personal history was not unusual: the pregnancy and delivery were uneventful. RS showed normal neuromotor development: he walked at 15 months and spoke normally at 2 years of age. His vaccinations are up to date, especially

against polio. He is the sixth of seven siblings, including an 8-year-old brother who has the same clinical symptoms with enlarged calves. The latter could not be explored for financial reasons. His parents are not inbred.

At the clinical examination of March 2, 2016, he is a 10-year-old boy, weighing 20 kg and measuring 1.27 m, afebrile and not dyspneic. He is unable to stand or walk (stage VII of WALTON and GARDNER MEDWIN). In supine position, lifting is difficult: he can only sit down after turning sideways to support himself on his elbows and needs the help of a third person to lift his shoulders. He has no functional limitation of the upper limbs but fatigability when the arms are stretched over his head. The muscular and articular balance sheet shows a marked amyotrophy, predominant in the pelvic and scapular belts. The lower limbs are bilaterally equinovag with a 45° flexum of the knees (Figure 1). There is hypertrophy of the calves (Figure 2). The feet are fixed with a vicious varus equinus attitude. The toes are not clawed. There is no muscular pain or inflammatory signs in the muscles involved. Both deep and superficial sensitivity is preserved and there is no sphincter disorder. Patellar and achilles reflexes are diminished, bicipital and stylo-radial reflexes are normal and symmetrical. Facial muscles are unharmed and there is no strabismus. Cranial pairs are normal (absence of dysphagia,

normal visual acuity). Cardiorespiratory examination is normal. Trunk tone is preserved and no spinal column deformity has been detected so far. At the level of higher functions, language is normal, as is memory. However, the patient has a difficulty at school, especially in comprehension. The rest of the clinical examination is without abnormalities.

The biological examinations did not show any inflammatory syndrome. Serum creatine kinase (CK) levels were found to be 1800 IU/l, 10 times normal. Cerebrospinal fluid (CSF) study showed normal results. Chest X-ray and dorsal lumbar spine X-ray in frontal and profile views did not show any deformity. The electrocardiogram showed a normal pattern; cardiac ultrasound could not be performed. The electromyogram could not be performed because it is not currently available in Madagascar. A muscle biopsy was performed on the vastus lateralis muscle. Analysis of the biopsy fragments showed muscle fibers of different sizes, generally atrophied, separated by more or less abundant adipose tissue, without inflammatory infiltrates, compatible with Duchenne muscular dystrophy (Figure 3, 4). Respiratory Functional Investigation was requested but could not be performed due to financial problems.



Figure 1: Flexum of Both Knees



Figure 2: Enlarged calves in the brother



Figure 3: Normal muscle fiber.

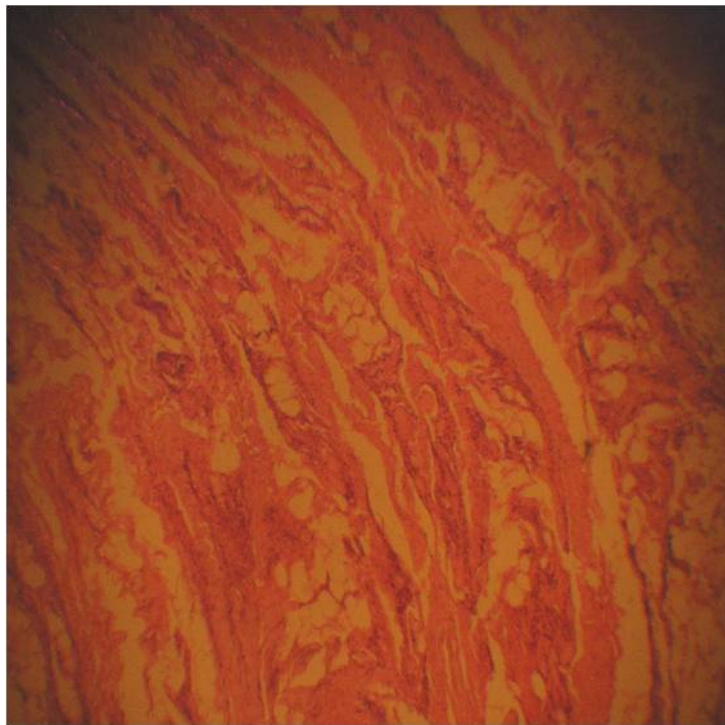


Figure 4: Myofibrillar disorganization and fatty invasion.

The drug treatment is based on multi-vitamin compositions. Functional treatment was the main part of the patient's treatment. It was carried out at the Centre d'Appareillage de Madagascar (CAM), at the rate of one session every two days for one month, then one session per week as a continuous cure. Apart from the treatment carried out and supervised at the centre, rehabilitation exercises using simple techniques were carried out every day at the hospital, thanks to the cooperation of the patient and his family, and were continued at home.

During the hospitalization, the clinical evolution was stable. There were no respiratory difficulties, no smooth muscle damage, in particular no cardiac damage. He had good cooperation during functional rehabilitation exercises. After one month of hospitalization, the child was released at home and underwent outpatient physiotherapy sessions. He was to be seen regularly on an outpatient basis, but unfortunately, he was lost to the outside world and no contact with the parents was possible.

III. DISCUSSIONS :

Described for the first time in 1868 by the French neurologist Duchenne de Boulogne, the disease that bears his name is X-linked recessive transmission (2). In siblings, girls are healthy carriers. The parents of sick boys are always healthy, with rare exceptions. However, affected

boys can be found among the mother's brothers, uncles, great-uncles, or nephews (3). The disease starts between 3 and 6 years of age (4). In the state phase, the muscle deficit affects, in order of decreasing intensity, the pelvic girdle, the trunk, the scapular girdle, the back muscles, the thigh and arm muscles. Amyotrophy is of particular interest in very deficient limbs, where the idiomuscular reflex is abolished. This reflects the myogenic, rather than neurogenic, nature of the manifestations observed (5).

Pseudohypertrophy expresses the scleroadipal proliferation of connective tissue. Late in life, muscle fibres become scarce, invaded by fibrosis, associated with fat involution (1). Loss of gait occurs after the age of 10 years and is followed by the onset of orthopaedic deformities that will worsen thereafter (5). Breathing damage becomes more evident after loss of gait. Cardiac damage, on the other hand, is almost constant, early, but is often clinically latent. They may include cardiomyopathy, rhythm disturbances, or mitral prolapse. In 1/3 of cases, cardiomegaly without hemodynamic consequences at the beginning is found, but can evolve into high output cardiac failure (1). The diagnosis is affirmed by the determination of the serum level of muscle enzymes, the most characteristic of which is that of creatine kinase, with a level that can reach up to 150 times normal. Between Walton Gardner stages IV, there and I appears to be an exponential decrease in serum creatine

kinase to near-normal values in the advanced stage (3). Classical histology shows necrotic-regenerative lesions with adipose involution. The differential diagnosis is mainly made with progressive spinal muscular atrophy, such as Wernig Hoffmann's disease or Kugelberg Welanders disease, and atrophic fat paralysis in children. The treatment of Duchenne's disease is only palliative through functional rehabilitation. The curative treatment of Duchenne's disease is still at the research stage.

In Madagascar, no study has yet been undertaken to determine the exact prevalence of this pathology. Our patient is the first case observed in the Befelatanana Pediatrics Department. Nevertheless, studies have shown the existence of Duchenne muscular dystrophy in Madagascar, including a case reported by Soja in Toliary in 1996 (6).

Concerning our patient, his mother is clinically healthy with a serum creatine kinase level of 180UI/l. This level is indeed normal in 1/3 of female drivers (1).

None of our patient's three sisters had any obvious signs of the disease. In the literature, there are a few cases of authentic Duchenne in girls. This is related to a variable expressivity of the disease in a female carrier. Most female drivers have high muscle enzyme levels and about 10% have clinical manifestations such as muscle deficits or calf hypertrophy (1, 7). Duchenne de Boulogne described two female cases out of thirteen observations (8), and out of the 104 myopathies of the Duchenne type, Penn et al. retained 19 girls, 66% of whom were sporadic (9). Difficulties encountered in making the diagnosis in our patient were due to the failure to complete the family tree, which would have been a useful contribution in the context of a more complete family survey in search of possible, other carriers of the defect. The age of discovery was later in our patient. This can be explained by the fact that the preclinical phase would have been silent. Nevertheless, biological and histological signs that should have been sought (10) may characterize it. Difficulty of access to specific complementary examinations limits the diagnostic approach: the Exploration Fonctionnelle Respiratoire (EFR) could not be carried out although it would have provided useful information on the respiratory state, electromyography is not available, and immunohistochemistry on frozen sections for DNA study which would allow the definitive diagnosis to be made. In addition, treatment could not be followed on a regular basis due to the geographical remoteness of the rehabilitation centre. Thus, we suggest a relatively simple and clear explanation of the disease in order to combat superstitious beliefs and practices that will only delay diagnosis and treatment. Future consanguineous couples should be

informed of their risk of having myopathic children. Efforts should focus on prevention through genetic counselling.

This requires an accurate genealogical study, supported by other explorations such as DNA and genetic linkage studies. As far as possible, the child should be provided with a life comparable to that of normal children and should be allowed normal schooling for as long as his or her motor skills permit.

IV. CONCLUSION

This observation has the interest of reporting a rare case of a severe, disabling and little-known disease in Madagascar where the level of education is low. In developing countries, superstitions and beliefs still occupy an important place. The means of diagnosis are therefore limited, making treatment even more difficult.

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