OPEN ACCESS

GAVIN PUBLISHERS

Academic Orthopedic Research and Rheumatology

Pamanta IS, et al. Acad Orthop Res Rheum 2: 112.

DOI: 10.29021/2688-9560.100012

Research Article

Duchenne's muscular dystrophy: Clinical, Biological and Evolutionary Aspects about Five Cases in Rheumatology Department at Teaching Hospital of Point G

Ibrahim Sory Pamanta, Boureima Kodio, Sidi Toure, Abdoulaye Karembe, Idrissa Ah Cisse*

Department of Rheumatology, University Hospital of Point G, Bamako, Mali

***Corresponding author:** Idrissa Ah Cisse, Department of Rheumatology, University Hospital of Point G, Bamako, Mali. Tel: +22376379158; Email: idicisse@hotmail.com

Citation: Pamanta IS, Kodio B, Toure S, Karembe A, Cisse I Ah (2018) Duchenne's Muscular Dystrophy: Clinical, Biological and Evolutionary Aspects about Five Cases in Rheumatology Department at Teaching Hospital of Point G. Acad Orthop Res Rheum 2: 112. DOI: 10.29021/2688-9560.100012

Received Date: 29 January, 2018; **Accepted Date:** 12 February, 2018; **Published Date:** 21 February, 2018

Abstract

Introduction: Duchenne's muscular dystrophy (DMD) caused by non dystrophin expression is linked to X chromosome. Described in the 19th century, it is the most common muscular dystrophy of the child [1,2]. The incidence is estimated at 30 cases per 100 000 births [1,2]. Goal - Study clinical, biological and evolutive aspects of the Duchenne's Muscular Dystrophy.

Patients and Methods: It was a retrospective study about 5 cases of DMD, collected in 7 years [2005-2012]. The diagnostic criteria were: (1) The static disorders (Lumbar dysbasie), walking ("gallinacée") and balance (repeated falls), (2) The calf hypertrophy and Gower's manoeuver, (3) Biological myolysis: creatinine kinase (CPK) greater than 3 times normal, (4) Anatomopathological and immunohistiochemical confirmation when it was possible.

Results: During our study from the period of 2005 to 2012, we had 5 cases of boys with an average age of 7 years and the extreme age from 1 year to 12 years. The calf's hypertrophy and the presence of a Gowers's sign in 4/5 patients. Family characteristic was present in two boys aged 5 and 10 years with a consanguineous marriage. Muscular Histological examination concluded dystrophic lesions. The immunohistiochemistry found no expression of dystrophic. Corticosteroids early established at 0.5 mg / kg / day combined with physiotherapy rehabilitation maintained the autonomy of patients.

Conclusion: Corticosteroids would slow down cardiopulmonary complications. Associated with the physiotherapy rehabilitation and practical advice, it has decreased falls.

Keywords: Bamako; Duchenne's Muscular Dystrophy; Rheumatology

Abbreviations:

CPK	:	Creatinine Kinase
CRP	:	C - reactive protein
DMD	:	Duchenne's Muscular Dystrophy
ECG	:	Electrocardiogram
EMG	:	Electro - Myogramme
LDH	:	Lactate Dehydrogenase
CBC	:	Complete Blood Count
QI	:	Intellectual Quotient
UI/L	:	International unit per liter
ESR	:	Erythrocyte Sedimentation Rate

Introduction

Duchenne's Muscular Dystrophy (DMD) was described for the first time in the late 19th century by Guillaume Benjamin Amand Duchenne. This is the most common form of muscular dystrophy of the child [1-2]. DMD belongs to the group of hereditary progressive diseases. It is a neuromuscular disease leading to atrophy and progressive muscle weakness due to degeneration of skeletal, soft and cardiac muscles. It is characterized by a recessive disorder linked to X, sometimes called pseudo-hypertrophic

muscular dystrophy. DMD is caused by the absence of a protein of muscle fibers called dystrophin. Dystrophin, a membrane protein of sarcolème, is encoded by a gene on the short arm of the X chromosome in p21-2 position. This allelic disorder linked X to results from a mutation in the large dystrophin gene at this position. DMD primarily affects boys with an incidence of about 30 per 100 000 of living males. The mutation rate is close to 1 in 10 000 [2]. Girls are usually asymptomatic, but there are a small percentage of women conducting these moderate forms of the disease (Symptomatic form of muscular dystrophy in female). It is most often girls with Turner syndrome (XO) or a turnerian mosaic (X / XX or X / XX / XXX), an abnormal X chromosome or an X-autosomal translocation. In some heterozygous women, the disease occurs due to an incomplete activation of the maternal X chromosome.

Although it is present at birth, the disease begins in boys during childhood (3-5 years) with delayed motor development and overall development. In general, boys with DMD are unable to run or jump. The disease progresses rapidly and the child develops a waddling gait with calf hypertrophy (Gower's positive sign). Climbing stairs becomes difficult and the child falls frequently. Walking becomes impossible between 6 and 13 years, with an average of 9.5 years in patients not treated with steroids. The complication may be too restrictive cardiomyopathy and respiratory failure that can lead to death during adolescence [1,2].

Diagnosis is based on clinical presentation, family history and laboratory results (100-200 times higher than normal levels of serum creatinine kinase). Muscular biopsy shows a dystrophy and a total absence of dystrophic. Molecular analysis shows most frequently deletions frame-shift (A shift of the reading frame), duplications or missense mutations in the DMD gene. Care is multidisciplinary. Medical treatment consists of corticosteroids and the support of locomotors deficits. Exon skipping is a promising therapeutic approach for DMD.

We report five cases in addition to previously published studies.

Patients and Methods

It was a retrospective study of 5 cases of DMD, collected in 7 years [2005-2012]. The diagnostic criteria were:

- The static disorders (Lumbar dysphasia), of the (gallinacean) walk and balance (repeated falls).
- The calf hypertrophy and Gowers's manoeuver,
- Biological myolysis: creatinine kinase (CPK) greater than 3 times normal .
- Anatomo-pathological and immunohistiochemical confirmation when it was possible.

Observation 1

Mr T I. 5 years old, seen in consultation for trouble in standing up for a year. Parents found the child in a walking gradually tiptoe with frequent falls. No family history has been reported.

Physical examination:

- It has allowed the Gower's manoeuver; he waddled in addition to hyperlordosis.
- The intellectual Quotient (QI) seems normal.
- The thorax is smooth, cardio - pulmonary auscultation did not find any sign of cardiomyopathy, nor pulmonary disease, despite episodic cough reported by the family.

The biological results showed:

- A large increase in CPK 17780 International unit per liter (IU) / L [N <175 IU / L].
- The rate of lactate dehydrogenase (LDH) increased to 2700 IU / L [N 228-456 IU/L].
- A normal electrocardiogram (ECG), spirometry made with a mask found lying 1 liter 230CC; so concordant normal vital capacity with age.
- The rest of the routine laboratory tests are normal: Complete Blood Count (CBC), Erythrocyte Sedimentation Rate (ESR), C - reactive protein (CRP), transaminases, creatinine, and glycemy.
- Muscle biopsy performed showed dystrophic lesions with presence of endomysial fibrosis. Immunohistochemistry study is for a DMD with absence of dystrophic expression.

The treatment included:

- Glucocorticoid therapy with a vitamin and calcium intake.
- The physiotherapy rehabilitation.

The evolution is characterized by:

- A locomotors stationary state
- A slight decrement of CPK with corticosteroids (7.5 mg of prednisone), the last check dated from 05/10/2011 (CPK rate was 13,500 IU / L)
- The rate of LDH remained stable between 2700 - 2600 IU / L [N 228-456 IU / L].

Observation 2

Mr AT 10 months old is the younger brother of IT seen in consultation for possible early detection due to the final diagnosis with his the senior brother. Clinical examination is almost normal,

electrocardiogram (ECG) also. Muscle enzymes (CPK) were 288 IU / L [N <175 IU / L] and 588 LDH rate IU / L [N: 228-456 IU / L].

Control after two months shows a slight increase in CPK and LDH respectively 233 IU/L and 250 IU/ l. However, our attention was focused on increased CPK and LDH although discreet in addition to family history of DMD in siblings. The patient is monitored.

Observation 3

Mr MD 12 year's old, family history of probably Duchenne's myopathy dystrophy. Two uncles had presented a striking symptomatology. The first in 1975 at age 6 years died at 13 years and the second in 1976 at the age of 5 died in 10 years. He has consulted for musculoskeletal disorders found for more than 5 years of installation and progressive aggravation. The interview notes limb weakness with difficulty load, frequent falls and swallowing difficulties.

Physical examination:

A clinical examination was found: an equinus and muscular arms, calf hypertrophy, a pronounced flexion of the lower limbs, the Gower's manoeuver, a lordotic dysbasia, and gallinacée approach. Psycho mental retardation is determined on the basis of a simple QI test; osteo-tenduneous reflexes are effective at four members. The cardio-pulmonary auscultation is normal. He weighed 30kgs.

The biological results showed:

- The determination of CPK increased to 7007 IU / L [N <175 IU / L]. CBC, ESR, creatinine, blood glucose is normal.
- CRP is positive at 13 mg / l
- The ECG is normal
- The chest radiograph showed a cardiomegaly and pulmonary right.

The EMG and Western Blot are not feasible in Bamako for the identification of the deficit dystrophy and eventual analysis of mutations carried by leukocytes. The probable diagnosis of DMD is retained. The treatment consisted of: the administration of 15 mg /days of prednisone, associated with vitamin D and calcium supplementation.

The evolution is characterized by:

- A stationary clinical symptoms despite the physiotherapy rehabilitation
- A decrease of CPK 7007 - 4593.

Observation 4

Mr SP 9 years old, without significant family history consults for instability of the lower limbs with falls recorded by parents for two years; installed progressively getting worse.

A physical examination:

We found: calf hypertrophy, Gowers's manoeuver, a lordotic dysbasie, and gallinacée walk. QI is normal, cardio-pulmonary auscultation is normal. It weighed 19 kgs.

- **The balance sheet showed:**
- CPK largely increased to 13,576 IU / L [N <175 IU / L].
- The CBC, ESR, CRP, creatinine, glucose, normal transaminases.
- The normal ECG
- The chest radiograph is normal.
- Radiography of the lumbar spine showed a hyperlordosis and scoliosis.

Electro-myogramme (EMG), Western Blot has not been possible. The diagnosis of DMD was selected. Treatment consisted of prescription of prednisone at the dose of 10 mg / day, after five months CPK were 8.245UI. Vitamin D – calcium supplementation was associated. The physiotherapy rehabilitation was indicated. Parents reported an improvement of 20%.

Observation 5

Mr SD 8 year's old consults for repeated falls more and more frequent. The interview notes a poorly systematized irradiation of the lumbar.

A physical examination:

It was found: calf hypertrophy, a walk on tiptoe. The cardio - pulmonary auscultation and the rest of the clinical examination were normal. He weighed 22 kgs.

The examination showed:

CPK increased to 4690 IU / L [N <175 IU / L].

- The CBC, ESR, creatinine, glucose and CRP are normal.
- The EMG and genetic testing are not feasible in Bamako.
- The diagnosis of DMD was selected.

The treatment was:

Prednisone prescribed 5 mg / day, combined with calcium supplementation and vitamin D3.

The evolution is characterized by a stationary clinical condition. Repeated checks CPK showed a steady climb up to 10,581 IU. The increase to 15 mg / day of prednisone diminished the rate.

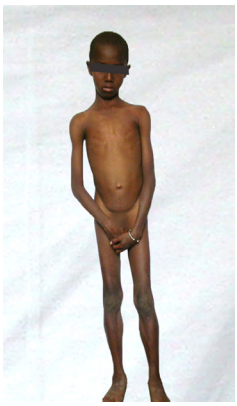
Comments and Discussion

The limitations of our study were:

- ✓ The only hospital recruitment
- ✓ The absence of genetic testing in the majority of patients due to:
- ✓ Insufficient technical platform for specific tests
- ✓ Low income patients' parents, limiting examinations
- ✓ Irregular monitoring

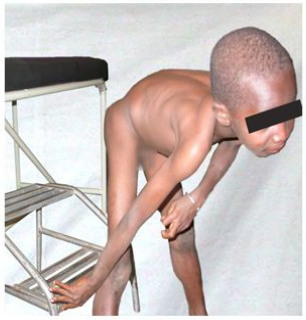
Five cases of DMD have been identified in seven years on 5071 patients seen in the department of Rheumatology at the teaching Hospital of Point G. It represents approximately 0.1% of all registered patients. This reinforces the scarcity of DMD reported in several studies [1-3] with an incidence of 1/3500 live births male. All patients were boys. DMD primarily affects boys [1,2,4]. The age of patients is between 1 and 12 years, with an average age of 7 years.

The reason of consultation was most often a walk disturbance with frequent falls. These symptoms are the earliest signs, motivating consultation in DMD [1-3]. Two patients had a family history of DMD. The disease begins in young boys with delayed motor development and overall development, the aggravation is increasing with age. Pseudo hypertrophy of the calf muscle is classic. The clinical manifestations were observed at the age of 5 years in 4 patients. Only one year old patient was asymptomatic however, he has a family history of DMD. The child shows little signs before the age of 3 years [1,2]. Clinical examination revealed: calf hypertrophy, Gowers's manoeuver, and all had a waddling gait. These clinical signs are constant in DMD [1,2] (Sée figures A,B,C below).



A: The calf and thigh have almost the same diameter.

B: Calf Hypertrophy.



C: The charging is only possible with support.

Concerning the locomotion: Two patients have a lordotic dysphasia. They were the older with 9 and 12 years, the second suffering of reducible members bending. Four out of five patients had a walking disorder. A Delaubier et al. [5] reported that the average age of walking trouble is 12 years

We have not noticed a heart or lung disease clinically. According Delaubier A et al. [5] in adulthood vital respiratory status varies between 6 and 41% of theoretical capacity. They reported in the same study that 25 out of 42 patients have cardiac disease, but symptomatic in only two patients. Would the age of our patients explain the absence of cardiac and respiratory diseases? Functional exploration was normal in case No. 1. This reinforces the findings of Duboc D et al. [6] which in a series of 57 children aged 9.5 to 13 years diagnosed DMD cardiological examination was normal. A 12-year-old child had swallowing difficulty, compatible with Broncho - pneu monia associated (Mendelson's syndrome). A patient suffering from mental retardation (patient 12 years old). QI concludes with mental retardation in 30% of cases [7]. Increased CPK is constant and is the first biologically oriented element. A rate of serum creatinine kinase 100-200 times higher than normal may be reported [1,2,8] LDH were also high in our serie. A case of broncho - bacterial pneumonia associating a cardiomegaly has regressed with antibiotics. Inspiratory muscles lesions cause a restrictive syndrome with episodes of pulmonary iterative [1,2,4,8].

The diagnosis was bio-clinical. Muscle biopsy of patient number 1 showed: dystrophic lesions with marked with presence of endomysial fibrosis. Immunohistochemical study concludes a Duchenne's muscular dystrophy with lack of dystrophin's expression. Muscle biopsy has a prominent place for the certified diagnosis [1,2,9,10].

The treatment can be basically summarized to the co - prescription corticosteroids and physiotherapy rehabilitation in all patients. A vitamin D and calcium intake was systematic in all patients. This treatment improved the patients and decreased the rate of CPK. Corticosteroid keeps a place in the treatment of DMD [1,2]. I Desguerre [3] state that steroids delay the age of loss

of walking abilities from 6 months to 2 years and am related to the age and the severity of scoliosis. The pharmacogenetics action (Fuitage of codons stop, Exon skipping) is the issue in recent years [3,11-13]. Clinical monitoring was to prevent the complications of corticosteroid, especially cardiovascular. Clinical and biological evolution was satisfactory in 4 patients.

Conclusion

DMD primarily affects boys, it manifests in childhood. Disorders walking, calf hypertrophy and maneuver Gowers are constant. At the age of 12, cardiovascular and respiratory complications are present. Genetic testing required for definitive diagnosis remains a bargain in our country. Clinical signs associated with high CPK led to the diagnosis. Corticosteroid therapy improves clinical symptoms and decrement CPK.

References

1. Bennett JC, Plum F, Gill GN, Kokko JP, Mandell GL, Ockner RK, Thomas Smith Wood wart Muscular dystrophies: In CECIL Treaty of Internal Medicine; Flammarion edict 1997: 2161-2164.
2. Mendell JR, Griggs RC, Patcek LJ (1996) Muscle diseases: Chap. 383 Mc Graw-Hill. in Harrison internal medicine 14th Ed 1996: 2852-2854.
3. Desguerre I, Barnerias C (2013) New therapies in Duchenne muscular dystrophy Arch. of Pediatrics 20: 102-103.
4. Mompoint D, Carlier RY, Orlikowski D (2010) Neuromuscular diseases: imaging chest complications, digestive and urinary J Radiol 91: 1419-1436.
5. Delaubier A, Guillou C, Rideau Y (1998) Duchenne muscular dystrophy: life after 20 years An of Rehabilitation and physical med 41: 303.
6. Duboc D, Meune C, Lerebours G, et al. (2005) Effect of perindopril on the onset and progression of left ventricular dysfunction in Duchenne muscular dystrophy. J Am Coll Cardiol 45: 855-857.
7. Guillou C, Delaubier A, Rideau Y (1998) Duchenne muscular dystrophy: what changes after 20 years? Annals of Physical Medicine and Rehabilitation 41: 303.
8. FORT P. Role of dystrophin Dp71 in the eye: phenotypic Impacts Thesis of Medicine, Strasbourg, July 2005.
9. Feasson L, Gautheron V, Mosnier JF, Antoine JC, Damon G, et al. (1997) Interest in muscle biopsy clamp in the etiological diagnosis of neuromuscular diseases Ann Phys Med Rehab 1997; 40: 527-533.
10. Muntoni F, Torelli S, Ferlini A (2003) Dystrophin and mutations: one gene, several proteins, multiple phenotypes. Lancet Neurol 2: 731-740.
11. Schram G, Fournier A, Leduc H, Dahdah N, Therien J, et al. (2013) All-causes mortality and cardiovascular outcomes with prophylactic steroid therapy in Duchenne muscular dystrophy. J Am Coll Cardiol 2013; 61: 948-954.
12. Cirak S, Arechavala- Gomeza V, Guglieri M, Feng L, Torelli S, et al. (2011) Exon skipping and dystrophin restoration in patients with Duchenne muscular dystrophy after systemic phosphorodiamidate morpholino oligomer treatment: an open- label, phase 2, dose- escalation study. Lancet 378: 595-605.
13. Adkin CF, Meloni PL, Fletcher S, Adams AM, Muntoni F, et al. (2012) Multiple exon skipping strategies to by-pass dystrophin mutations. Neuromuscular Disorders volume 22 (2012) 297-305.