Two cases of Becker's muscular Dystrophy

GANESAN KANAGASABAPATHI
Department of General Medicine,
K.A.P. VISWANATHAN GOVERNMENT MEDICAL COLLEGE

Abstract:
Becker's muscular Dystrophy is an X-linked recessive disorder results from allelic defects of the gene that encodes dystrophin, a 427-kDa protein localized to the inner surface of the sarcolemma of the muscle fibre. It is less frequent than Duchennes and women may be affected due to mosaicism. We present two cases of Beckers muscular dystrophy in a brother and sister. They presented with weakness of proximal muscles of both upper and lower limbs. The CPK levels were markedly elevated. The EMG showed mixed myopathic pattern in proximal muscles of lower limbs and the Nerve conduction studies were normal. Muscle biopsy confirmed the diagnosis by focal atrophy and replacement by fatty and fibrous tissue.

Keyword: Becker's muscular Dystrophy, Dystrophin, Duchenne's muscular dystrophy

Introduction
BMD(Becker's muscular Dystrophy) is an inherited disease and it is generally milder than DMD (Duchenne's muscular dystrophy) and the onset of symptoms usually occurs later. The incidence and prevalence of BMD are lower than those of DMD and the mean age for symptom onset is to be 12 years, and the range is 5 to 45 years. Given the transmission pattern, the disease affects primarily males. Translocations may allow the possibility of a female presentation of the BMD phenotype. The pelvic girdle, gluteal and thigh muscles affected first. It is not uncommon for those with Becker Dystrophy to walk well into adult life. We report two cases of BMD with the onset of symptoms around 10 years of age, progressive and associated with weakness of proximal muscles than distal and lower limbs more involved than upper limbs.

CASE REPORTS
The first case is Mr. MURUGAN, 16yr old male presented with history of difficulty in getting up from floor and progressive difficulty in running for 9 years. With tremulousness of hands and feet for 7 years. These proximal muscle weaknesses of lower limbs were of gradual onset, progressively worsening and were associated with tripping of toes and frequent falls but there were no weakness of trunk muscles or of both upper limbs and also there was no diurnal variation in weakness. There was a history of muscle twitching present in arms, chest and upper back but not in lower limbs. There was no difficulty in vision and speech, no sensory disturbances and bowel, bladder disturbances. In the past history there was no history of DM, HTN, TB, trauma, vaccination, dog bite and any drug intake or addiction.

Antenatal, natal histories were normal but there was mild delay in motor milestones. He is born of nonconsanguineous marriage, the eldest daughter had unnatural death at the age of 19 and another elder sister is suffering from similar complaints. His half brother and sister were apparently normal. On examination, patient was moderately nourished and built, conscious, oriented, afebrile, short statured. There were no pallor or cyanosis, no lymphadenopathy or neurocutaneous markers or thyromegaly. CNS Examination: Higher functions and cranial nerves were normal. Optic Fundus was normal. Examination of the motor system showed mild wasting present in bilateral suprascapular region, gluteal region and marked wasting in front and back of thigh in both sides. Fasciculations seen over both the arms, both sides of the chest. Tone was normal in all the limbs. Hypertrophies of calf muscles were present bilaterally. Power of Muscles of shoulder were 4/5 in both Deltoid, Supraspinatus, Infraspinatus, Serratus anterior and Pectoralis major and 4/5 in Lattisimus dorsi and Rhomboideus in both sides. It was 4/5 in muscles of elbow and forearm. Power was normal in neck, trunk and hand muscles Iliopsoas, Gluteus maximus, Gluteus medius, Gluteus minimus and hip adductors of right side showed the power of 4/5 and on left side 4-/5. Power was 4-/5 in both hamstrings and quadriceps. In the legs and in feet the power was 4/5 on both sides. Superficial reflexes were normal and Plantar was flexor bilaterally. Of the Deep Tendon Reflexes bilateral Biceps, Triceps, Supinator, Pectoral jerks diminished both sides. Knee jerk was absent and Ankle jerk was preserved. Coordination was normal. Fine tremors were present on extended upper limbs and lower limbs. Gait resembled Waddling gait. Sensory system was intact on both sides. Autonomic nervous system, bowel, bladder were normal. There were no signs of meningeal irritation. Spine and cranium were normal, Cerebellar functions were normal. Other systemic examinations were normal. Investigations showed elevated CPK of 842u/L (normal 51-294u/L). CBC, Blood Sugar, Urea, Creatinine, Electrolytes, LFT were within normal limits. ECG, ECHO,
USG Abdomen were also Normal. EMG study from both LL muscles showed fibrillations, fasciculations, complex repetitive discharges and a mixed myopathic denervation pattern more prominent in proximal muscles when compared to distal muscles. **Nerve conduction studies** in both lower limbs showed normal sensorimotor conduction. **Muscle biopsy** Section studies showed wavy muscle bundle with mild variation in fibre size and minimal intermuscular adipose tissue with increased endomysial fibrosis. In places show focal crowding of nuclei with muscle contracture. Overall picture were suggestive of muscular dystrophy.

Next we move on to SATYAPRIYA, 17 years, elder sister of Murugan presented with Pain both legs and hands for 7 yrs which was gradual in onset, by doing household work aggravated by walking and associated with difficulty in walking and frequent falls. There was proximal muscle weakness of both upper and lower limbs and associated with twitching of muscles of both arms, upperback, thighs, legs for 1yr. There was no history of weakness of trunk and neck muscles and no diurnal variation of weakness. No history of LOC, seizures, headache, blurring of vision, speech disturbances. No histories of cranial nerve abnormalities, sensory disturbances, difficulty to walk in narrow pathways or in the dark. Bowel and bladder were normal. Past history was uneventful.

On examination patient was conscious, oriented, afebrile, build and nourishment were normal, no pallor, cyanosis, lymphadenopathy, neurocutaneous markers and no thyromegaly. **CNS Examination** showed higher functions, cranial nerves were within normal limits. Examination of motor system showed wasting in suprascapular, infrascapular and interscapular region bilaterally and the tone was normal in all the limbs. Power of muscles of shoulder were 4-/5 in both Del-toid, Supraspinatus, Pectoralis major and Lat-tisimus dorsi. It was 4-/5 in Infraspinatus and in Rhomboideus in both sides. There was mild winging of scapula due to weakness of Serratus anterior. The power was normal in muscles of elbow, forearms, hands and in neck, trunk. Iliopsoas, Gluteus maximus, Gluteus medius, Gluteus minimus of both sides showed the power of 4-/5 and adductors were 4/5. The power of quadriceps was 4-/5 and hamstrings 4/5 on both sides. The muscles of the legs and feet were 4/5. Superficial reflexes were normal bilaterally and plantar were flexor. Of the Deep Tendon Reflexes biceps, triceps, supinator, pectoral, knee jerks were diminished and ankle jerk was present bilaterally. Coordination was normal. There were fine tremors present in extended upper limbs. Gait resembled Waddling gait. Hypertrophy of calf muscles seen. Sensory system was intact on both sides. The cerebellar functions, spine and cranium were
Investigations revealed elevated CPK of 326U/L (normal 39-238u/L). Other blood tests were normal. ECG, echocardiogram were within Normal limits. Other system examinations were normal. EMG showed Proximal muscles of both lower limbs and upper limbs had mixed myopathic and neurogenic features. Distal muscles showed normal findings. Nerve conduction studies in both lower limbs showed normal sensorimotor conduction. Muscle biopsy Section studies showed striated muscle bundles with focal atrophy & replacement by fatty & fibrous tissue. In places they showed nuclear crowding & hyaline bodies suggestive of muscular dystrophy with atrophic changes.

Discussion
The findings in our cases are consistent with a clinical diagnosis of Becker’s muscular Dystrophy. The onset was around the age of 10 years and slowly progressive with involvement of proximal muscles of both lower and upper limbs. There was elevated CPK levels in both cases and calf muscles hypertrophy present in both patients. Nerve conduction studies were normal and EMG showed mixed myopathic pattern. Finally muscle biopsy confirmed the diagnosis by atrophic changes in the muscles and replacement by fatty fibrous tissue. In 1955 Becker and Keiner proposed this separate disease the less severe form. It is inherited as X-linked recessive disease. In 30% of cases there is no family history and may be due to spontaneous mutations. BMD results from allelic defects of the same gene responsible for Duchenne dystrophy and 10 times less frequent than Duchenne, with an incidence of about 3 per 100,000 live-born males. The affected gene is Dystrophin which is present but structurally abnormal in Becker’s dystrophy. The histological changes are loss of muscle fibres, which are replaced with residual fibers of small and large size with haphazard arrangement associated with increase in lipocytes and fibrosis. The Pseudo hypertrophy is due to lipocytic replacement of degenerated muscle fibres. Patients first experience difficulties between ages 5 and 15 years although onset is in the third or fourth decade or even later can occur. Clinical features are indisposition to walk or run normally, appear less active than expected, prone to falls. Becker dystrophy patients walk beyond age 15 and most survive into the fourth or fifth decade. The muscle wasting closely resembles that seen in Duchenne’s. There is progressive symmetric muscle weakness and atrophy (proximal greater than distal) is present. Sometimes the weakness of quadriceps femoris may be the only sign which is present. Proximal muscles, especially of the lower extremities, are prominently involved. The iliopsoas, quadriceps and gluteal muscles are involved early. Later pretibial muscles are affected which leads to foot drop and toe walking. The muscles of pectoral girdle and upper limbs are affected after pelvicrural muscles. As the disease progresses, weakness become more generalized but significant facial muscle weakness is not a feature. Hypertrophy of muscles, particularly in the calves, is an early and prominent finding (pseudo hypertrophy), feels rubbery, weaker, more hypotonic. Due to the weakness of abdominal and paravertebral muscles patient assumes lordotic posture. The weakness of extensors of hip and knee interferes with activities like climbing stairs, rising from a chair or from stooped posture. EMG shows fibrillations, positive waves and brief polyphasic motor unit potentials. Female carriers may display the same abnormality.
with milder degree (Lyon hypothesis). EMG and muscle biopsy help to exclude SMA. Other investigations are analysis of dystrophin gene in DNA of WBC’s, immunostaining of muscle for dystrophin and ELISA to measure dystrophin levels in muscle biopsy samples.

Heart failure from DCM is the common cause of morbidity and the most common cause of death in Becker’s muscular Dystrophy. Treatment The use of glucocorticoids has not been adequately studied. Preventive measures are more successful. Ambulation and upright posture delays scoliosis. Avoid prolonged bed rest and encourage the patient to maintain a full and normal life. Prevention can be by prenatal counseling. Injection of human myoblasts, stem cells and Viral mediated gene delivery are under trial

**Conclusion:**
We are presenting these cases of Becker's muscular Dystrophy because of its rarity.

**References:**
Harrison’s Principles of Internal Medicine, 18th edition.

Adams and Victor’s Principles of neurology

Dystrophinopathies by Basil T Darras, MD David T Miller, MD, PhD, David k Urion, MD

Beggs AH. Dystrophinopathy, the expanding phenotype. Dystrophin abnormalities in X-linked dilated cardiomyopathy. Circulation. 1997; 95:2344