LIMB GIRDLE MUSCULAR DYSTROPHY

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INTRODUCTION

Limb girdle muscular dystrophy (LGMD) is one of the hereditary myopathies [1]. It may present with autosomal dominant or autosomal recessive mode. The onset varies from early childhood to early adulthood with progressive course. When limb-girdle muscular dystrophy begins in childhood, the progression is usually faster and the disease more disabling. The syndrome of limb girdle muscular dystrophy represents more than one disorder [2]. Both males and females are affected. The limb girdle muscular dystrophy typically manifests with progressive weakness of the pelvic and shoulder muscles. Respiratory insufficiency from the weakness of diaphragm may occur, as may cardiomyopathy. Over time, the person with LGMD loses muscle bulk and strength. Eventually, he may need a power wheelchair or scooter, especially for long distances [3].

CASE REPORT

A 45 year old male presented with gradual onset weakness of both upper and lower limbs of 6 year duration. The weakness was more marked at the proximal portions of the limbs mainly involving the muscles of the shoulder and pelvic regions. It was difficult for patient to raise his arms over head and stand from squatting position. Gradually the weakness became so marked that patient was not even able to walk around without support. There was no history of pain or tenderness in the affected muscles, visual deterioration, and weakness of the face or scapular region, palpitations, breathlessness, oedema, involvement of sphincters or any other neurological complaints. On examination, he had waddling gait. He was having wasting of the shoulder and pelvic girdles. Tone of the muscles on both sides was equal. Power of the muscles in the proximal group of muscles of both the upper and lower limbs was 3/5 and in the distal group of muscles was 4/5. There was no sensory deficit, nystagmus or diplopia. Romberg was negative. Muscle enzymes including creatine kinase and Aldolase were raised in serum. Creatine Kinase (CK) was 1149 (25-125) U/L and Serum Aldolase was 15 (< 7.6) U/L. Electromyography (EMG) revealed myopathic changes. Muscle biopsy revealed atrophic changes. Echocardiography and other routine investigations were normal. Keeping in view the clinical picture and lab studies the diagnosis of LGMD was made.

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DISCUSSION

The earliest descriptions of limb-girdle weakness are ascribed to Leyden and Möbius in 1876 and 1879, respectively. In 1954, when Walton and Nattrass reported 105 cases of limb-girdle weakness associated with many other disorders, the nosological entity of limb-girdle dystrophy was formally established [4].

Skeletal muscle consists of two major components, the sarcolemma and sarcomeres. Sarcolemma is the membrane which covers sarcomers, which are the contractile units of the muscle cell [5]. Sarcolemma consists of different structural proteins which are genetically coded. Amongst these proteins, dystrophins, glycoproteins and sarcoglycans are the important ones. Dystrophins combine with glycoproteins and different the sarcolemmal proteins to form the dystrophin-glycoprotein complex which gives strength and stability to the sarcolemma (see figure). Absence of any one these structural proteins results in rupture of the sarcolemma resulting in death of the underlying muscle fiber.

Limb girdleweakness affects both males and females, with onset ranging from late in

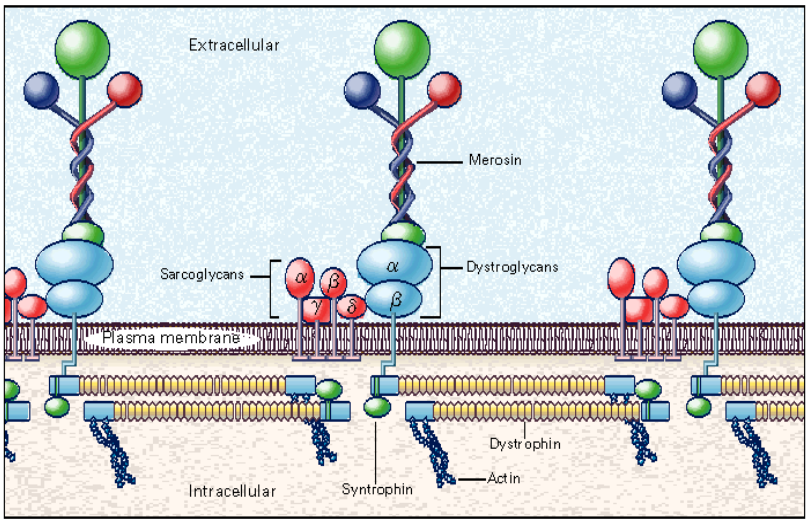

Figure: Pathophysiology of limb girdle muscular hystrophy.

the first decade to the fourth decade [6]. Most limb girdle muscular dystrophies are progressive and affect primarily the pelvic and shoulder girdle muscles. Respiratory insufficiency from weakness of the diaphragm may occur. The distribution of weakness and the rate of progression vary from family to family. Similar to the dystrophinopathies, cardiac involvement may result in congestive cardiac failure or arrythmias, occasional patients present with a cardiomyopathy. Intellectual functions remain normal [7].

The frequency of LGMD in the general population cannot be estimated because of the heterogenous nature of this group of disorders. LGMD is associated with low mortality but it gives rise to significant disabilities. LGMD may show an autosomal recessive or sporadic method of inheritance. Some forms of LGMD dramatically affect young adults, while other types progress so slowly that they are not detected until much later in life [8].

These syndromes are now classified on the basis of at least 15 identified genes—5 autosomal dominant and 10 autosomal recessive [9]. The 5 dominant genes are associated with the components of sarcomeres. The 10 recessive genes are associated with the plasma basement membrane and the adjacent reticular lamina, which contains the fibrillary collagen.

The single biochemical abnormality in LGMD syndrome is the elevation of the CK level. The CK elevation in the recessively inherited varieties is significantly higher than in the rest of the spectrum of LGMDs [10]. However, the CK level is usually significantly lower than in patients with Duchenne or Becker dystrophy. Individuals with Duchenne or Becker dystrophy may have elevated creatine in the urine, but they do not have myoglobinuria. Muscle biopsy findings are characterized by necrotic fibers with endomysial perivascular or perimysial mononuclear infiltration.

The goal of therapy is aggressive prevention of contractures at the hip and shoulder girdle, via stretching. Very few studies detail the effectiveness of an exercise regimen in limb-girdle syndrome. Given the slowly progressive nature of the disease, the prudent approach to exercise therapy is to prescribe active-assistive and resistive movements and preserve and maintain muscle strength in the pelvic and shoulder girdle musculature [11]. This therapy can prevent the rapid development of orthopedic deformities of hyperlordosis, pelvic forward rotation, and flexion/abduction contracture. If the patient becomes nonambulatory, wheelchair mobility is essential.

The wheelchair should complement the patient's lifestyle, providing comfort, safety, and functionality. Patients who develop an equinus foot deformity can benefit from tendon-lengthening surgery and/or knee-ankle-foot orthoses or ankle-foot orthoses to maintain mobility.

A surgical approach has been attempted to correct the flexion contractures and scoliosis only in persons with Duchenne dystrophy. Results have been conflicting because, after surgery, patients often are unable to maintain their ambulatory status. In exceptional cases of shoulder-girdle involvement, the patient may benefit from scapulopexy (attaching the inner border of the scapula to the fourth rib using either Mersilene tape or fascia lata).No medication is used for the specific treatment of LGMD [12]. The mortality ascribed to the disease and/or the complications thereof is negligible. However, the prognosis with regard to mobility, self-care, and maintenance of the ability to work is dependent on the aggressive, goal-directed management.

CONCLUSION

Evaluation of a patient with muscular dystrophy must take into consideration an accurate clinical history with special emphasis on family history; a detailed physical examination; laboratory investigations including CK, EMG, and, possibly muscle biopsy, molecular genetic studies, and an evaluation of the absence or alteration of dystrophin. Incidence of such debilitating disorder can be reduced by genetic counseling and family screening.

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