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Emery-Dreifuss Muscular Dystrophy: A Difficult Diagnosis

KEYWORDS: Muscular dystrophy, x-linked recessive, emerin, a-v block

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ABSTRACT *The Emery-Dreifuss muscular dystrophy is a form of dystrophy that frequently presents early contractures and cardiac conduction defects, caused by emerin deficiency in the inner nuclear membrane of the muscular fibers. A 11 year old male child came with complaint of chest pain. He was having muscle weakness and hypotrophy of limb muscles as long as contracture of limb. Electrocardiogram shows av block. CPK borderline raised and muscle biopsy disclosed features of muscular dystrophy.*

INTRODUCTION:
Emery-Dreifuss Muscular Dystrophy (EDMD) clinically manifests with triad of weakness and wasting of humero-peroneal muscles, early contractures of elbow flexors, tendo-achilles and paraspinal muscles and cardiac abnormalities[1,2]. Cardiac involvement is the most serious and important aspect of the disease. It usually becomes evident as muscle weakness progresses, but may exceptionally occur before there is any significant weakness. Two main modes of inheritance seen: X-linked and autosomal dominant. Rare autosomal recessive inheritance has also been described [3]. The disease course of the AD-EDMD is generally slow. But the x-linked EDMD has severe phenotypic features.

CASE REPORT:
A eleven year male child came with history of chest pain for 3 months. He was having occasional chest pain since 3 years. There were no previous histories of hospital admission due to the repeated respiratory tract involvement. He was having normal birth history and no developmental delay. There was no significant family history. The child was having triangular face, winging of scapulas, atrophy of chest musculature and arm causing drooping of left arm. Bilateral thenar muscles were atrophied, thumb was abnormally placed (fig-1,2). Lower limbs were having atrophied distally bilaterally. Right foot muscles were having contractures leading to halux varus. The vitals were normal. On systemic examination there was a pansystolic murmur in LLSB. All other systemic features were within normal limits. On investigation blood tests were found to be normal, ECG revealed A-V block (fig-3), echocardiography showed medium sized vsd with ejection fraction normal. Cpk was mildly raised. X-ray limbs showed no significant anomaly. Chest X-ray showed mild cardiomegaly with CT ratio to be 56%. Muscle biopsy confirmed the diagnosis (fig-4). From the clinical pictures, a-v block, features of muscular dystrophy in muscle biopsy it was diagnosed to be a case of emery-dreifuss muscular dystrophy.

DISCUSSION:
Emery had described this entity with triad of humero-peroneal weakness, early contractures and cardiac disturbance.[1]

Early contractures, often before there is any significant weakness, of elbows, Achilles tendons, and post-cervical muscles .

Slowly progressive muscle wasting and weakness with a distinctive humero-peroneal distribution (i.e. proximal in the upper limbs and distal in the lower limbs) early in the course of the disease. Weakness is rare.

Cardiac conduction defects (ranging from sinus bradycardia, prolongation of the PR interval on electrocardiography to complete heart block). A generalised cardiomyopathy may also occur simultaneously. First-degree AV block and complete heart block are common followed by paroxysmal atrial tachycardia, AF, atrial flutter, bundle branch block, second-degree AV block and VT.

Miller et al[4] proposed diagnostic criteria:

(a) early contractures of Achilles-heel, elbows and spine;
(b) slow progression and symmetric weakness prominent in humero-peroneal muscle;
(c) cardiac conduction abnormality and/or cardiomyopathy;
(d) myopathic features;
(e) X-linked inheritance.

Contractures occur even before onset of weakness and are attributed to primary abnormality of the tissue that surrounds the joints or secondary to dystrophic changes in the muscle. Cardiac involvement is the most serious and important aspect of the disease. It usually becomes evident as muscle weakness progresses, but may exceptionally occur before there is any significant weakness. Two main modes of inheritance exist: X-linked and autosomal dominant. Rare autosomal recessive inheritance has also been described. Most X-linked EDMD patients become symptomatic in early childhood (<15 years) with mild weakness, followed by contractures[3,5]. EDMD arises from genetic defects in nuclear proteins (emerin and lamin A/C). To date, around 100 mutations in the *STA* gene have been reported. They are approximately composed of 39.5% of small deletions, 31% of non-sense mutations, 15.5% of mutations in splice sites. The X-linked variant is caused by defects in the STA gene on Xq 28 (codes for 34 KD), a protein called emerin while the AD/AR is due to defects in the LMNA gene located at

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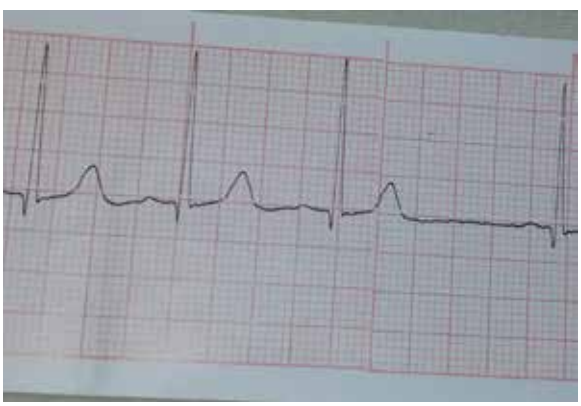
1q21 that encodes lamin A and C[6]. Emerin, the product of the EMD gene, is a ubiquitous protein that decorates the nuclear rim of many cell types. These findings could not explain, however, the role of emerin nor account for the skeletal muscle- and heart-specific manifestations associated with the disorder. Using 2 antisera against synthetic peptide fragments predicted from emerin cDNA, Nagano et al. (1996) found positive nuclear membrane staining in skeletal, cardiac, and smooth muscles in normal controls and in patients with neuromuscular diseases other than EDMD. In contrast, a deficiency in immunofluorescent staining of skeletal and cardiac muscle from EDMD patients was observed[7]. In heart, the specific localization of emerin to desmosomes and fasciae adherentes could account for the characteristic conduction defects described in patients with Emery-Dreifuss muscular dystrophy[8].

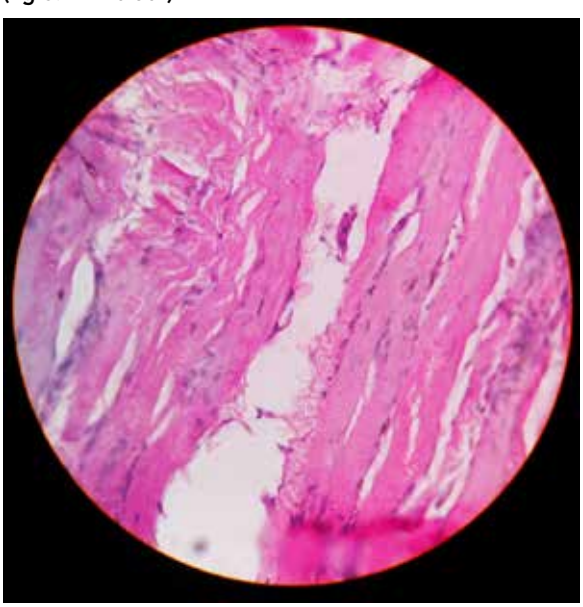
There is no specific treatment. Management of complications are the main modalities. Great care should be given to proper diagnosis and follow-up of patients with EDMD. All patients should have a detailed cardiac investigation and regular follow-up by cardiologist since sudden death can be seen in these patients and early detection of arrhythmias can be lifesaving by pacemaker or defibrillator implantation. Proper care and management can prolong their life expectancy well.

(Fig-1: syndromic facies, drooping of left shoulder, hypotrophy of left pectoralis major)

(fig-2: abnormal thumb and thenar atrophy)



(fig-3: A-V block)



(fig-4: features of muscular dystrophy in slide of muscle biopsy)

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