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Original Article

Pathology Section

Clinicopathological Study of Spectrum of Muscle Disorders in a Tertiary Care Hospital

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ABSTRACT

Introduction: The diagnostic approach to muscle disorders is often challenging due to paucity of literature, unavailability of ancillary facilities, affordability and improper sample collection. The role of pathologist in terms of categorising the muscle biopsy interpretation with limited resources plays an imminent role in guiding clinicians for further therapeutic approach.

Aim: To analyse spectrum of various muscle disorders and to relate their clinical and histopathological findings.

Materials and Methods: This was observational retrospective as well as prospective study of 63 muscle biopsies received during 10 years period from June 2009 to June 2019, at Department of Pathology in Grant Government Medical College, Mumbai, India. Slides of muscle biopsies received prior to June 2017 were restained and reviewed while muscle biopsies after this period were studied prospectively. Various histomorphological and histopathological (fascicular architecture, variation in size and shape of fibers, necrosis and degenerative/regenerative changes, nuclear characteristics, type and distribution of inflammatory cells along with interstitial changes) features were studied in detail and the findings were compared with similar previous studies. These findings when clubbed together with clinical, biochemical and Electromyography (EMG) findings, to guide the path towards appropriate diagnosis.

Results: The present study evaluated and analysed 63 muscle biopsies, clinically, histopathologically and histomorphologically. Mean age was 30.6 years, 43 (68.25%) patients were males and 20 (31.75%) patients were females. A number of 12 (19.04%) patients were clinically diagnosed as having limb-girdle muscular dystrophy, followed by 9 (14.28%) patients as inflammatory myositis. Eight patients (12.69%) were diagnosed as Polymyositis (PM), five (7.93%) as Dermatomyositis (DM), one (1.58%) patient each of juvenile DM and inclusion body myositis. Histopathologically, the cases diagnosed were PM-14 cases (22.22%) followed by muscular dystrophy (excluding limb-girdle muscular dystrophy)- 12 cases (19.04%) and limb-girdle muscular dystrophy- 9 cases (14.28%).

Conclusion: Although molecular and genetic studies are need of hour, histomorphological features helps in proper categorisation of cases, however close liaison between pathologist and clinicians is essential and histopathological findings should only be interpreted in light of clinical manifestations and laboratory findings.

Keywords: Muscle biopsy, Muscle diseases, Muscle dystrophies, Polymyositis

INTRODUCTION

The diagnostic approach to muscular disorders is often challenging as they are phenotypically and genetically heterogenous. The muscle biopsy is indicated in suspected neuromuscular disorders with various signs and symptoms including pain, cramps, stiffness, paresthesia, weakness and hypotonia [1]. Medical history, clinical examination, laboratory tests, Electromyography (EMG) and muscle biopsy are important components for the diagnosis of muscular diseases whilst imaging and genetic testing are increasingly gaining importance. However, not all centers are equipped with these advanced diagnostic modalities and not all patients can afford these. Mainstay of diagnosis, in such instances, continues to remain histopathology, enzyme, and immunohistochemistry. There is a paucity of literature, analysing the broad spectrum of muscular disorders such as muscular dystrophies, inflammatory myopathies, muscle atrophies and secondary myopathies in the light of histopathological findings. Even categorising the muscular disorders into broad categories helps the clinician to decide the course of treatment since in most of the muscular dystrophies, the management is only supportive.

The aim of this study was to analyse spectrum of various muscle disorders and highlighting role of histopathology and basic laboratory tests in their diagnosis and treatment.

MATERIALS AND METHODS

This was observational retrospective as well as prospective study of 63 muscle biopsies received at Department of Pathology in Grant Government Medical College, Mumbai, Maharashtra, India, over the period of 10 years from June 2009 to June 2019. Ethical clearance was obtained from Institutional Ethics Committee (letter No.IEC/PG/464/Dec/2018) dated 17/12/2018.

Inclusion criteria: All adequate biopsy samples without any fixation and processing artefact, received during the study period were included in the study.

Exclusion criteria: Steroid induced myopathies and inadequate samples were excluded.

The detailed clinical histories of all samples were obtained from departmental records as well as hospital medical record system. Biopsies received during June 2017 to June 2019 were studied prospectively, however, the slides of the samples received during the period June 2009 to May 2017 were reviewed. Muscle biopsy samples received in 10% formalin were processed in automated tissue processor and stained with routine Haematoxylin and Eosin (H & E) stain. Special stains were used wherever required. Various histopathological features were noted as fascicular architecture, variation in size and shape of fibers, necrosis and degenerative/regenerative changes, nuclear characteristics, type and distribution of inflammatory cells along with interstitial changes.

STATISTICAL ANALYSIS

The data of every case was recorded in a separate case record form and later entered and analysed in Microsoft Excel 2010. Frequency (n) and percentage (%) analysis was carried out in the collected data.

RESULTS

In the present study, most common age group of patients was 31-40 years (28.57%) followed by 21-30 years (26.98%). While, the

least common age group was 51-60 years (7.93%). Mean age was 30.6 years [Table/Fig-1]. We observed male to female ratio of 2.15:1 where 43 (68.25%) patients were males and 20 (31.75%) patients were females. The most common chief complaint observed was proximal limb weakness with or without swelling followed by difficulty in getting up from sitting position. Other complaints were swelling with or without rash, paraplegia and foot drop. Headache and swelling of eyes were also observed in one case of inflammatory pseudotumour [Table/Fig-2].

Age range (years)	No. of patients (n)	Percentage (%)
1-10	7	11.11%
11-20	7	11.11%
21-30	17	26.98%
31-40	18	28.57%
41-50	9	14.28%
51-60	5	7.93%
Total	63	100%

[Table/Fig-1]: Age-wise distribution.

Chief complaints	No. of patients (n)	Percentage (%)
Proximal limb weakness	34	53.96%
Proximal limb weakness with swelling	7	11.11%
Difficulty in getting up from sitting position	6	9.52%
Swelling with rash	4	6.34%
Foot drop	3	4.76%
Swelling over limbs	3	4.76%
Swelling over limbs with pain	2	3.17%
Proximal limb weakness with rash	1	1.58%
Painful paraplegia	1	1.58%
Anasarca	1	1.58%
Headache and swelling of right eye	1	1.58%
Total	63	100%

[Table/Fig-2]: Distribution of study subjects according to chief complaints.

The levels of Creatine Kinase (CK) were found increased in 48 patients (76.19%), majority of these had levels in range of 1001-5000 IU/L and two patients of muscular dystrophy had CK levels as high as 15000 IU/L. The remaining 15 (23.81%) patients had levels within normal range.

In the present study, 12 (19.04%) patients were clinically diagnosed as having limb-girdle muscular dystrophy, followed by 9 (14.28%) patients as inflammatory myositis. Eight patients (12.69%) were diagnosed as PM, five as DM, one patient each of juvenile DM and inclusion body myositis [Table/Fig-3].

Clinical diagnosis	No. of patients (n)	Percentage
Primary muscular disease	5	7.93%
Limb-girdle muscular dystrophy	12	19.04%
Muscular dystrophy	5	7.93%
Duchene muscular dystrophy	3	4.76%
Becker's dystrophy	1	1.58%
Inflammatory myositis	9	14.28%
Polymyositis	8	12.69%
Dermatomyositis	5	7.93%
Juvenile dermatomyositis	1	1.58%
Inclusion body myositis	1	1.58%
Abscess	2	3.17%
Congenital myopathy	1	1.58%
Compartment syndrome	2	3.17%
Hoffman syndrome	2	3.17%
Koch's	1	1.58%
Spinal muscular atrophy	1	1.58%
Inflammatory pseudotumor	1	1.58%
Hansen's disease	1	1.58%
Fragile X syndrome	1	1.58%
Systemic lupus erythematous associated myopathy	1	1.58%
Total	63	100%

[Table/Fig-3]: Distribution of study subjects according to the clinical diagnosis.

The commonest histopathological diagnosis observed was PM- 14 cases (22.22%) followed by muscular dystrophy (excluding limb-girdle muscular dystrophy)- 12 cases (19.04%) and limb-girdle muscular dystrophy- 9 cases (14.28%). Twelve out of 63 cases (19.04%) showed normal muscle without any specific pathology. The histopathological diagnosis of remaining cases is shown in [Table/Fig-4].

Histopathological diagnosis	No. of patients (n)	Percentage
Normal muscle	12	19.04%
Muscular dystrophy	12	19.04%
Limb-girdle muscular dystrophy	9	14.28%
Polymyositis	14	22.22%
Dermatomyositis	4	6.34%
Hypothyroid myopathy	2	3.17%
Compartment syndrome	2	3.17%
Juvenile dermatomyositis	1	1.58%
Granulomatous myositis	1	1.58%
Spinal muscular atrophy	1	1.58%
Chronic inflammation	1	1.58%
HIV associated myopathy	1	1.58%
Inflammatory pseudotumor	1	1.58%
Abscess	1	1.58%
Focal atrophy	1	1.58%
Total	63	100%

[Table/Fig-4]: Distribution of study subjects according to histopathological diagnosis.

Detailed evaluation of Haematoxylin and Eosin (H&E) stained slides revealed various features as illustrated in [Table/Fig-5-8]. Variation in size and shape of muscle fibres was most common but non specific microscopic finding seen in almost all cases of muscular dystrophies and myositis. Diffusely distributed atrophic fibers were more commonly seen in muscular dystrophies. Three out of five (60%) cases of DM showed perifascicular atrophy. Three out of nine (33.33%) cases showed hypertrophy of fibers in limb-girdle muscular dystrophy [Table/Fig-5].

Many cases of muscular dystrophies and myositis showed necrosis and degenerative/regenerative changes. Almost all cases of muscular dystrophies showed myophagocytosis. Loss of cross striations and presence of rounded hyaline fibers were also noted in cases of muscular dystrophies. Regenerating fibers showed presence of vesicular nuclei with prominent nucleoli [Table/Fig-6].

Internalisation of nuclei were seen more frequently in muscular dystrophies than other muscular disorders [Table/Fig-7].

Many cases of muscular dystrophies especially, limb-girdle muscular dystrophies showed presence of inflammatory cells in addition to inflammatory myositis. Perivascular and perimysial inflammatory infiltrate was seen more commonly in cases of DM while inflammatory infiltrate in PM and muscular dystrophy was in endomysium [Table/Fig-8]. Adipose tissue infiltration and fibrosis were seen in muscular dystrophies as well as in inflammatory myositis contributing to loss of fascicular architecture in many cases. Pericellular fibrosis was more evident in muscular dystrophies [Table/Fig-9].

Muscular disorders	Variation in size and shape (n)	Atrophy (n)	Hypertrophy (n)
Muscular dystrophy (excluding limb-girdle muscular dystrophy)	12 (100%)	12 (100%)	5 (41.66%)
Limb-girdle muscular dystrophy	9 (100%)	9 (100%)	3 (33.33%)
Polymyositis	14 (100%)	14 (100%)	1 (7.14%)
Dermatomyositis	3 (75%)	3 (75%)	-
Hypothyroid myopathy	2 (100%)	2 (100%)	1 (50%)
Compartment syndrome	-	-	-
Juvenile dermatomyositis	1 (100%)	1 (100%)	-
Granulomatous myositis	-	-	-
Spinal muscular atrophy	1 (100%)	1 (100%)	1 (100%)
Chronic inflammation	-	-	-
HIV associated myopathy	1 (100%)	1 (100%)	-
Inflammatory pseudotumor	-	-	-
Abscess	-	-	-
Focal atrophy	1 (100%)	1 (100%)	-

[Table/Fig-5]: Variation in size and shape/atrophy/hypertrophy of muscle fibers.
n: Number of patients; HIV: Human immunodeficiency virus

Muscular disorders	Internalisation of nuclei (n)
Muscular dystrophy	12 (100%)
Limb-girdle muscular dystrophy	7 (77.77%)
Polymyositis	7 (50%)
Dermatomyositis	1 (25%)
Hypothyroid myopathy	1 (50%)
Compartment syndrome	-
Juvenile Dermatomyositis	-
Granulomatous myositis	-
Spinal muscular atrophy	-
Chronic inflammation	-
HIV associated myopathy	-
Inflammatory pseudotumor	-
Abscess	-
Focal atrophy	1 (100%)

[Table/Fig-7]: Internalisation of nuclei.
n: Number of patients; HIV: Human immunodeficiency virus

Out of total 19 cases of autoimmune myositis, 14 (73.68%) cases were of PM; 4 (21.05%) cases were of DM and 1 (5.27%) case was of juvenile DM. In present study, exact correlation between

Muscular disorders	Necrosis (n)	Degenerative/regenerative changes (n)
Muscular dystrophy	7 (58.33%)	12 (100%)
Limb-girdle muscular dystrophy	8 (88.88%)	9 (100%)
Polymyositis	9 (64.28%)	12 (85.71%)
Dermatomyositis	4 (100%)	2 (50%)
Hypothyroid myopathy	-	1 (50%)
Compartment syndrome	2 (100%)	2 (100%)
Juvenile Dermatomyositis	1 (100%)	1 (100%)
Granulomatous myositis	1 (100%)	-
Spinal muscular atrophy	1 (100%)	-
Chronic inflammation	-	-
HIV associated myopathy	1 (100%)	-
Inflammatory pseudotumor	-	-
Abscess	-	-
Focal atrophy	-	-

[Table/Fig-6]: Necrosis and degenerative/regenerative changes.
n: Number of patients

clinical diagnosis and final histopathological diagnosis was seen in 74.60% of cases (47 out of 63 cases). The histopathological findings and Electromyography (EMG) changes were compared in terms of number of cases both in 48 cases of raised and 15 cases of normal CPK levels, respectively. The flow chart [Table/Fig-10] illustrates how the cases were divided in terms of EMG findings like presence or absence of myopathic changes. Furthermore, the cases were divided whether significant histopathological changes were observed or not.

DISCUSSION

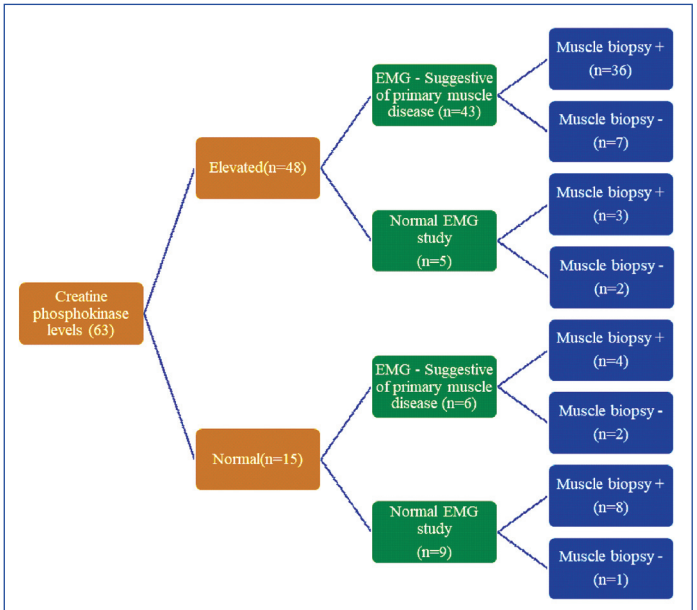
The present study is an institutional clinical and pathological overview of 63 cases of muscle biopsies received during a period of ten years in a tertiary healthcare center. The histopathological findings in muscular disorders are often non specific, making clinical input a prerequisite to reach a specific diagnosis. A pathologist play imminent role to identify a diagnostic category such as normal, non specific, dystrophic, inflammatory or neoplastic. Since, the biopsy report serves as therapeutic guidelines for the clinicians; even exclusion of a diagnosis is important [2]. In this study (n=63), the mean age of muscular disorders was 30.6 years. This correlated with the study of Owji M et al., (n=40) whose study depicted a mean age of 34 years [3].

Histopathological diagnosis	Type of inflammatory infiltrate			Distribution of inflammatory infiltrate		
	Polymorphonuclear	Lymphoplasmacytic	Mixed	Perivascular	Endomysial/Perimysial	Diffuse
Muscular dystrophy	-	2 (16.66%)	-	2 (16.66%)	-	-
Limb-girdle muscular dystrophy	-	3 (33.33%)	-	2 (22.22%)	1 (11.11%)	-
Polymyositis	-	12 (85.71%)	2 (14.28%)	7 (50%)	11 (78.57%)	2 (14.28%)
Dermatomyositis	-	4 (100%)	-	4 (100%)	4 (100%)	-
Hypothyroid myopathy	-	-	-	-	-	-
Compartment syndrome	2 (100%)	-	-	-	-	2 (100%)
Juvenile Dermatomyositis	-	1 (100%)	-	1 (100%)	1 (100%)	-
Granulomatous myositis	-	1 (100%)	-	-	-	1 (100%)
Spinal muscular atrophy	-	-	-	-	-	-
Chronic inflammation	-	1 (100%)	-	-	-	1 (100%)
HIV associated myopathy	-	1 (100%)	-	1 (100%)	1 (100%)	
Inflammatory pseudotumor	-	-	1 (100%)	-	-	1 (100%)
Abscess	-	-	1 (100%)	-	-	1 (100%)
Focal atrophy	-	-	-	-	-	-

[Table/Fig-8]: Type and distribution of inflammatory infiltrate.
HIV: Human immunodeficiency virus

Clinical diagnosis	Interstitial changes (Histopathological changes)			
	Fibrosis	Adipose tissue infiltration	Haemorrhage	Intermuscular spaces widening/ mucin deposition
Muscular dystrophy	8 (66.66%)	6 (50%)	-	-
Limb-girdle muscular dystrophy	8 (88.88%)	3 (33.33%)	-	-
Polymyositis	11 (78.57%)	1 (7.14%)	-	-
Dermatomyositis	2 (50%)	2 (50%)	-	-
Hypothyroid myopathy	1 (50%)	1 (50%)	-	2 (100%)
Compartment syndrome	-	-	2 (100%)	-
Juvenile dermatomyositis	1 (100%)	-	-	-
Granulomatous myositis	-	-	-	-
Spinal muscular atrophy	-	-	-	-
Chronic inflammation	-	-	-	-
HIV associated myopathy	-	-	-	-
Inflammatory pseudotumor	1 (100%)	-	-	-
Abscess	1 (100%)	1 (100%)		
Focal atrophy	-	-	-	-

[Table/Fig-9]: Relation of clinical diagnosis with histopathological findings.



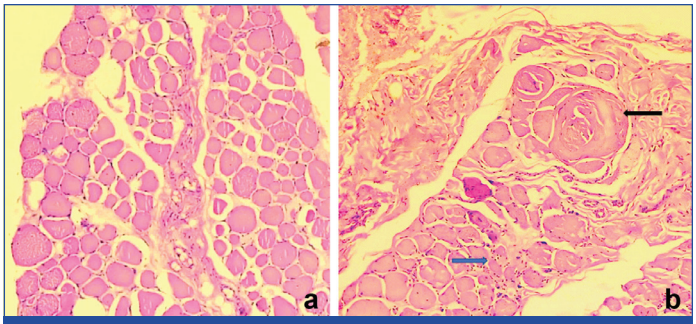
[Table/Fig-10]: Flowchart showing changes in creatine phosphokinase levels, electromyography study and histopathological diagnosis.
(Muscle biopsy+: Myopathic changes in muscle biopsy, Muscle biopsy -: no specific pathological findings)

The male to female ratio was found to be 2.15 (43 males:20 females) in present study which correlated with the study of Hafner P et al., (n=83) [4]. Proximal muscle weakness is the most common symptom in a myopathic disorder [5]. In this study also, progressive proximal limb weakness was the most common chief complaint observed in 34 cases (53.96%), other common complaints were swelling over limbs, difficulty in getting up from sitting position and rash.

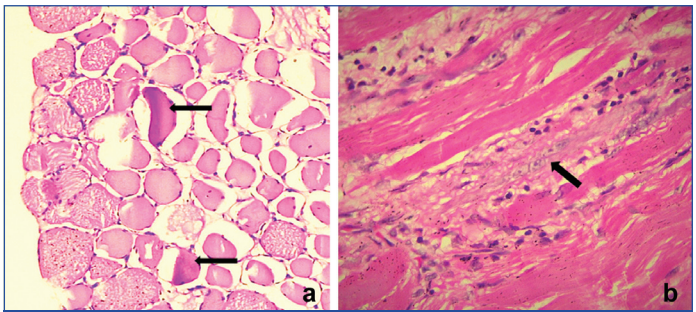
Abnormal CK was seen in 48 cases (76.19%) which correlated with study done by Nilopor et al., who reported the same findings in 66% of cases (n=100) [6]. Muscular dystrophy including limb-girdle muscular dystrophy constituted highest of all other disorders 33.32%) which was well correlated with Owji M et al., [3]. On the contrary, study performed by Skram M et al., showed only 16% cases of muscular dystrophy. [Table/Fig-11a] [1]. It was observed that, PM was the most common inflammatory myopathy in adults [7] which was similar to the findings in this study (PM-73.68%, DM-21.05%, Juvenile dermatomyositis-5.27%).

In this study, CK levels were raised in 100% cases of muscular dystrophy signifying that muscle destruction is an integral part of muscular dystrophy. In initial stages of the disease, CK levels are raised to as high as 20-300 times followed by fall in the levels with disease progression [8].

Nine cases (14.28%) of Limb Gridle Muscular Dystrophy (LGMD) were found in this study which is similar to the study done by Constantinides V et al., (14 out of 89 cases, 15.73%) [9]. On the other hand, limb-girdle muscular dystrophy constituted only 4.67% and 9.67% cases in the studies performed by Owji M et al., and Chang J et al., respectively [3,10]. The first symptoms include abnormal gait (waddling gait, walking on the feet balls) and difficulties in running and standing up [11]. This was similar to the observations in this study in which six cases (66.66%) showed abnormal gait (most commonly waddling gait) as a first symptom [Table/Fig-11b,12a,b,13a,b].

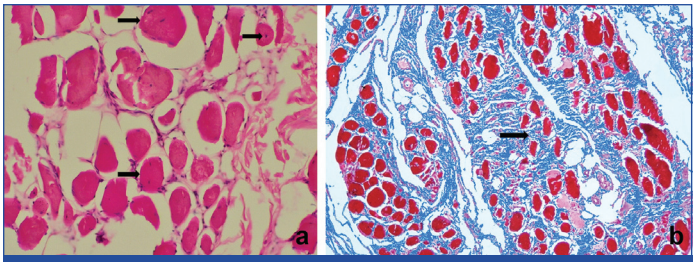


[Table/Fig-11]: a) Muscular dystrophy- Variation in size and shape of fibers (Transverse section, H&E, X100); b) Limb-girdle muscular dystrophy- Hypertrophic fibers showing whirling (black arrow) and atrophic fibers (blue arrow) (Transverse sections, H&E, X100).



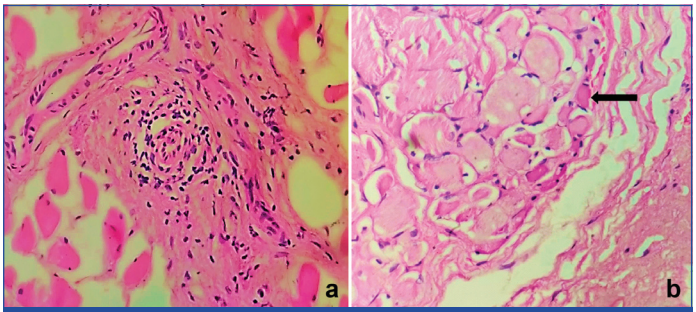
[Table/Fig-12]: a) Muscular dystrophy- Regenerating fibers (black arrow) characterised by basophilic cytoplasm reflective of increased messenger Ribonucleic Acid (mRNA) content (Transverse section, Haematoxylin and Eosin (H & E), X100); b) Muscular dystrophy- thin regenerating myotubes (black arrow) (Longitudinal section, H&E, x400).

In this study, 7.9% cases of DM were found which was consistent with the studies of Owji M et al., and Prayson R [3,12]. DM typically presents as an acute or insidiously progressive proximal weakness that is accompanied or preceded by a characteristic skin rash



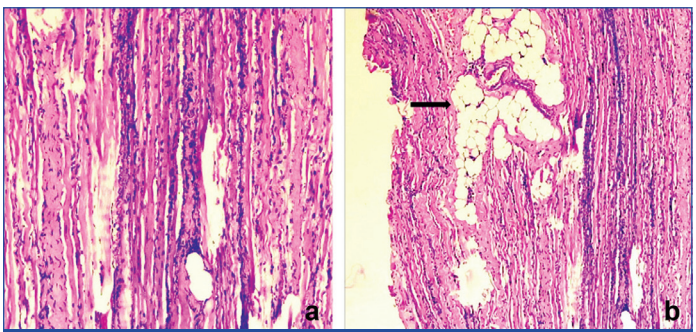
[Table/Fig-13]: a) Muscular dystrophy- Increased internalization of nuclei (black arrows) (Transverse section, H&E, X100); b) Muscular dystrophy- Fibrosis (Transverse section, Masson trichome, X100).

[13-15]. Patients complain of difficulty in getting up from a chair, climbing stairs, lifting things and combing hair. In this study, most common clinical feature for DM was swelling over limbs with rash. The earliest histological abnormality is the deposition of the C5b-9 Membrane Attack Complex (MAC) around the microvasculature [16,17] leading to abnormalities in both perimysial intermediate sized vessels and endomysial capillaries [18]. As a result, muscle biopsies demonstrate perifascicular atrophy, often without an inflammatory infiltrate. In this study, perifascicular atrophy was seen in three out of five cases (60% cases), lymphoplasmacytic infiltrate in perivascular and perimysial spaces seen in all the cases (100%). In this study, 14 out of 63 cases (22.22%) of PM were found which matched with the results of Owji M et al., and Hafner P et al., [Table/Fig-14a,b] [3,4].



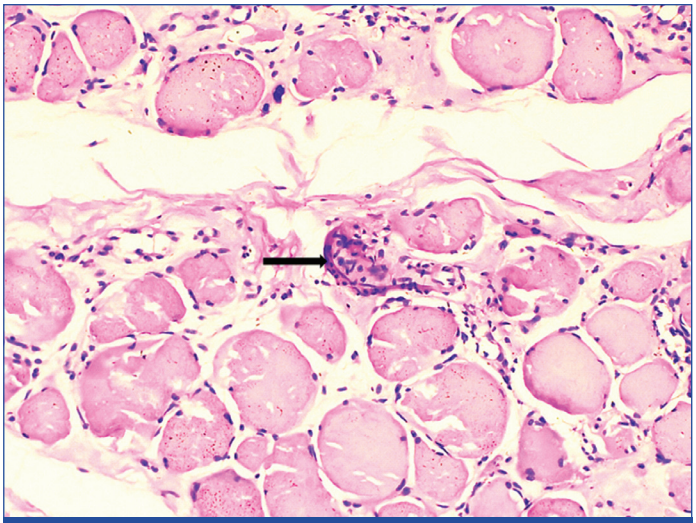
[Table/Fig-14]: a) Dermatomyositis-Perivascular and perimysial mononuclear inflammatory infiltrate (Transverse section, H&E, X100); b) Dermatomyositis-Perifascicular atrophy (black arrow) (Transverse section, H&E, X400).

PM presents with muscular and extramuscular organ involvement similar to DM, without rash [19-21]. The main muscle biopsy features are variability in fiber size, cellular invasion of non necrotic muscle fibres expressing Major Histocompatibility Complex (MHC)-1 antigens and scattered necrotic and regenerating fibres. Microscopically, changes noted in the present study were variability in fibre size seen in all cases, necrosis seen in about nine cases and degenerative/regenerative fibers observed in about 12 (85.71%) cases. Perivascular and perimysial inflammatory infiltrate was seen more commonly in cases of DM while inflammatory infiltrate was restricted to endomysium in PM and muscular dystrophy [Table/Fig-15a,b,16].



[Table/Fig-15]: a) Inflammatory myopathy- Inflammatory infiltrate in endomysium and perimysium (Longitudinal section, H&E, X40); b) Polymyositis- Adipose tissue infiltration- (black arrow) (Longitudinal section, H&E, x100).

We observed two cases (one male, one female) of hypothyroid myopathy which is a complication of uncontrolled or untreated hypothyroidism. In the present study, both muscle biopsies showed



[Table/Fig-16]: Polymyositis- Myophagocytosis (black arrow) (Transverse section, H&E, X400).

pale muscle fibers with loss of striations and increased separation between the muscle fibers due to mucinous depositions.

There are various forms of spinal muscular atrophy as Spinal Muscular Atrophy (SMA) type I, II, III and IV. Genetic studies have shown that SMA is caused by absence of the Survival Motor Neuron (SMN)1 gene, which should be located in the telomeric region of chromosome 5 [22-24]. There is no consensus on the age of onset of Type IV SMA. Russman BS reported that it emerges after 10 years of age, whereas Wang CH et al., stated that weakness normally emerges during the second or third decade of life, or at about 30 years of age [25,26]. This study included only one such case with patient's age of 35 years which is in concordance with Wang CH et al., [26]. Classically motor function involvement is mild. These patients are able to walk normally and have normal life expectancy [25,26]. But in this study, patient presented with progressive proximal limb weakness for which muscle biopsy was done. Muscle biopsy showed presence of atrophic muscle fibers and focal necrosis. But these findings were non specific and can be observed in other causes of denervation as well. CK may be normal or five times lower than normal [27]. This was in synchronisation with the normal levels of CK seen in the present study. Serum CK levels can differentiate neurogenic diseases (of which SMA is one) from myopathic diseases (such as dystrophies) in which muscle damage raises CPK levels. Considering clinical picture, muscle biopsy findings and laboratory results, genetic study was performed in present study cases, which showed SMN1 gene panel-homozygous gene deletion which confirmed the diagnosis of spinal muscular atrophy type IV.

HIV associated myopathies vary in severity and portray a wide spectrum from myalgia and asymptomatically increased CK to rhabdomyolysis. Single case which was diagnosed in the present study showed features of progressive proximal limb weakness along with increased CK levels. It can occur at any stage of HIV disease, and is characterised by slowly progressive, proximal and symmetric weakness [28]. Pathological characteristics include inflammatory infiltrates of T-cells and macrophages primarily in the endomysial parenchyma. Fibre necrosis may also be seen [29]. The lone case found in the present study, showed necrosis and lymphoplasmacytic inflammatory infiltrate in perivascular and perimysial spaces. The diagnostic criteria used to define PM in HIV negative patients are also useful in the diagnosis of HIV associated myopathy. These include objective muscle weakness, elevated serum CK levels, myopathic findings on EMG and a myopathic muscle biopsy [30]. The presence of all four criteria leads to a definitive diagnosis.

In this study, overall diagnostic accuracy of muscle biopsy was 74.60% which correlated with Constantinides V et al., (80.4%) [9]. Muscle biopsy is highly sensitive and specific test for neuromuscular disorders. In this study, about 19.04% of normal muscle biopsies were seen in clinically suspected muscle disorders. This could have

been due to several causes namely, biopsy of an unaffected group of muscle or improper site of muscle biopsy or unsuitable selection of patients by clinicians or an early stage of disease. As quoted by Cai C et al., few of the diseases show patchy involvement of the muscle which could be detected by generous sampling of the tissue [31]. Further, it was observed by Joyce N et al., that certain diseases characterised by deficiency of myoadenylate deaminase showed light microscopy changes only when sampled shortly after an episode of rhabdomyolysis [32]. Thus, not only the biopsied muscle and the timing play a role but also poor fixation, faulty tissue processing, improper staining and subjective manual errors while reporting also play a significant role.

Limitation(s)

Rarely, due to overlapping features or absence of histomorphological changes in the muscle, assigning a muscle biopsy to any of the classes of muscle diseases becomes quite a challenge. In such cases, advanced diagnostic modalities have a prime role to play. The limitation of the study was the tests like immunohistochemistry, molecular genetic testing and electron microscopy were not performed, therefore definite opinion could not be formed in some of the cases.

CONCLUSION(S)

Histomorphological pictures clubbed together with clinical symptoms, enzyme levels and EMG findings pave the way towards an appropriate diagnosis. Close liaison between pathologist and clinicians is essential and histopathological findings should only be interpreted considering clinical manifestations and laboratory findings. Hence, the basic test of muscle biopsy together with special stains, enzyme and immunohistochemistry offers a substantive diagnostic yield helping in further management and guidance to the patient and family.

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