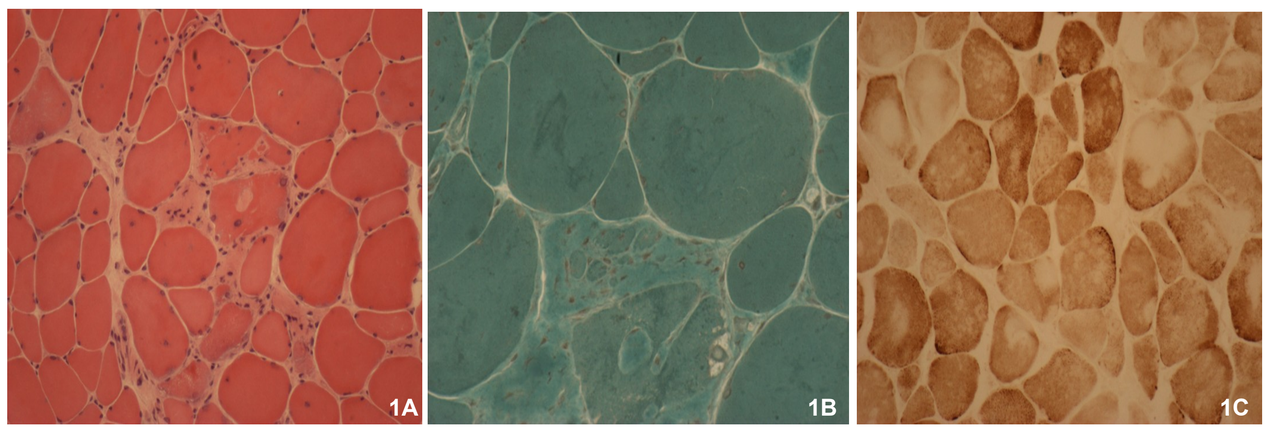
Dropped head syndrome as isolated manifestation of a myofibrillar myopathy

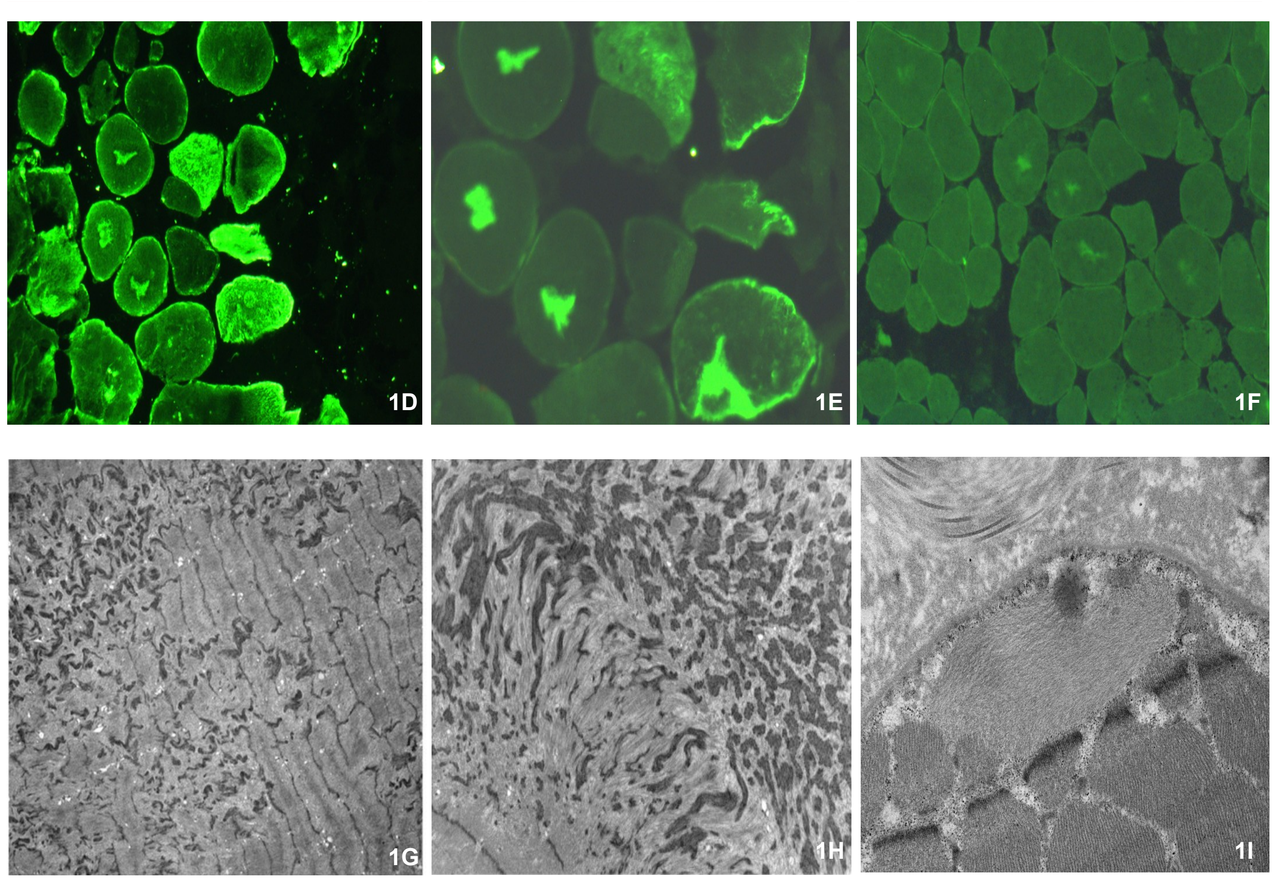
V. Vacchiano [1,2], M.L. Valentino [1,2], M. Columbaro [3], R. Liguori [1,2]

[1] IRCCS Institute of Neurological Sciences of Bologna, Bologna, Italy
[2] Department of Biomedical and NeuroMotor Sciences, University of Bologna, Bologna, Italy
[3] Laboratory of Musculoskeletal Cell Biology, IOR, Bologna, Italy

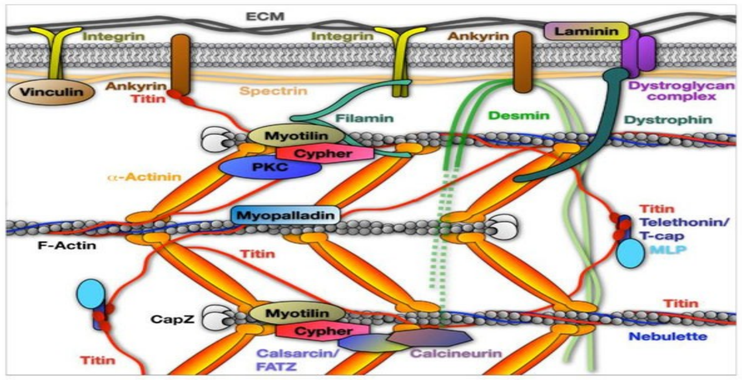
Myofibrillar myopathies (MFMs) are a heterogeneous group of hereditary neuromuscular disorders usually involving skeletal and/or cardiac muscle with variable age of onset and severity. Although the MFMs are associated with an increasing number of genes, they are characterized by typical histological and ultrastructural changes [1].

Case report: We observed a 62-year-old woman with a seven-month history of acute cervical pain associated with a progressive weakness of neck extensor muscles.
She was referred to us because a cervical spine MRI revealed a severe C3-C7 stenosis without myelopathy.
Her neurological examination showed weakness of neck extensor muscles (MRC 3/5) with head ptosis and bilateral atrophy of trapezius muscle.
Laboratory exams showed a slight CK increase (226 U/L); autoimmune screening including AchR and MUSK antibodies was negative.
EMG showed focal myopathic changes and denervation activity in the trapezius and paravertebral C8 muscles; repetitive nerve stimulation and ENG were normal.
ECG revealed a complete right bundle branch block and echocardiogram was normal. Muscle MRI of pelvis and inferior legs was normal.





Muscle biopsy of the left trapezius showed morphological changes suggestive of MFM.
Hematoxilin-Eosin staining showed myopathic changes with variability of fibers size, necrotic fibers, increased of central nuclei and amorphous material in the cytoplasm of many fibers (Fig.1A; 10x); Gomori Trichrome staining showed accumulation of dark blue material (Fig.1B;20x) and cytochrome c oxidase reaction revealed many fibers with areas devoided of enzyme activity (Fig.1C;10x). Immunohistochemistry showed focal areas of increased reactivity for desmin (Fig.1D;10x), αB crystallin (Fig.1E; 20x) and dystrophin (Fig.1F; 10x). The ultrastructural study detected myofibrillar disruption with streaming of the Z-disk (Fig.1G, 6000x; Fig.1H, 10.000x); subsarcolemmal accumulation of granulofilamentous material (Fig.1I; 75.000x)



Molecular analyses revealed the presence of a heterozygous sequence variation c.690 4823G>A in LDB3/ZASP gene corresponding to the mutation p.D117N.
The molecular analyses of DES, MYOT and CRYAB didn't show any mutation.

Discussion and conclusions

In our patient the muscle biopsy allowed the diagnosis of MFM. The only clinical manifestation of myopathy in this case was weakness of neck extensor muscles causing a dropped head syndrome. The genetic studies revealed an already known p.D117N mutation in ZASP gene. A focal and isolated involvement of paravertebral muscles is rarely reported in MFMs [2].
This mutation was originally found in one patient with dilated cardiomyopathy and also recently reported in a family with distal myopathy [1]. However, currently its pathogenic role is under discussion because it was identified in unaffected individuals belonging to bedouin families with dilated cardiomyopathy [3]. Our patient showed the characteristic morphological hallmark of MFM with atypical clinical presentation. Further studies are needed to confirm the pathogenic role of p.D117N mutation in ZASP gene and to define the genetic defect causing the MFM in our case.

1) Olivé M, Kley RA, Goldfarb LG. Myofibrillar myopathies: new developments. Curr Opin Neurol. 2013 Oct; 26(5):527-35.
2) Vattemi G, Neri M., Piffer S et al. Clinical, morphological and genetic studies in a cohort of 21 patients with myofibrillar myopathy. Acta Myologica 2011; XXX:121-126
3) Aviva Levitas, Yuval Konstantino, Emad Muhammad, et al. D117N in Cypher/ZASP may not be a causative mutation for dilated cardiomyopathy and ventricular arrhythmias. European Journal of Human Genetics 2016 ; 24: 666-671

Sin
XLVII CONGRESSO NAZIONALE
22-25 OTTOBRE 2016 – VENEZIA