

## **ULTRASTRUCTURAL CHANGES IN PERIPHERAL MUSCLE OF PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD).**

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In several systemic diseases as Diabetes Mellitus and Chronic Heart Failure, peripheral skeletal muscle is affected [1,2]. Several studies have demonstrated alterations and dysfunction in peripheral muscles of COPD patients, that contribute to the poor exercise performance and decreased quality of life in these patients [3,4]. Few reports have assessed the ultrastructural damage [5] and the presence of leukocytes in skeletal muscle in COPD [6]. The present study investigated the sub-cellular alterations in peripheral muscle of these patients. Muscle biopsy of vastus lateralis part of quadriceps muscle was taken and pulmonary resting function tests were performed in ten COPD patients and ten healthy subjects of similar age ( $66\pm 9$  and  $63\pm 5$  years respectively). COPD was defined as a post-bronchodilator forced vital capacity/forced expiratory volume in one second  $<0.7$ . Conventional transmission electron microscopy methods were used for the ultrastructural analysis of the muscle samples. Different degrees of muscle fiber atrophy were found in all patients, evidenced by widened subsarcolemmal and intermyofibrillar spaces (Fig.1), loss of striation and folding of sarcolemma (Fig. 3). In some of the patients there were fiber necrotic changes including the initial process of hypercontraction (Fig. 2). The mononuclear cell infiltrate was represented by macrophages (Fig. 2) mastocytes and neutrophils. Capillary alterations were present, such as occlusion (Fig. 3), widening of the basement membrane (Fig. 3), changes in electron density and caveolae distribution in endothelial cells and pericytes. In conclusion, fiber atrophy occurred in all studied patients. Capillary alterations were similar to those described in inflammatory and autoimmune diseases [8]. The presence of macrophages and neutrophils reinforces the hypothesis that inflammation plays a role in muscle dysfunction in COPD.

### **References**

- [1] S. H. Torres et al., J Endocrinol (2004) 181, 419.
- [2] H .R. Gosker, et al., Prog Respir Res (2002) 32, 18.
- [3] F. Maltais, et al., Clinics in Chest Medicine (2000) 21, 665.
- [4] A. G. N. Agustí, et al., Eur Respir J (2003) 21, 347
- [5] Orozco-Levi et al., Am J Respir Crit Care Med (2004) 169,A904
- [6] H.R. Gosker, et al., Eur Respir J (2003) 22, 280.
- [7] Finol et al. J Submicrosc Cytol Pathol (1994) 26, 245.

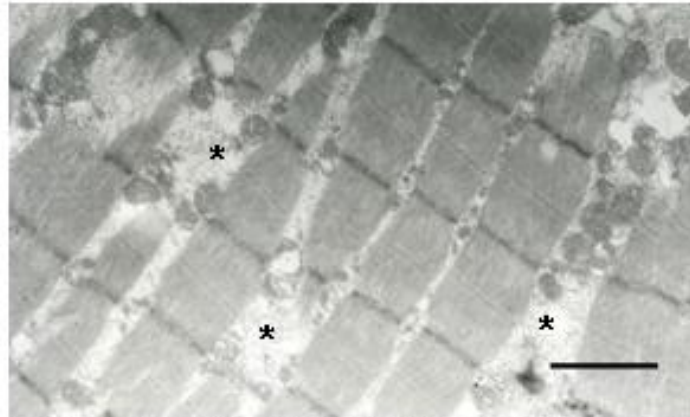


Figure 1.- Atrophied fiber showing widened intermyofibrillar spaces (asterisks). Bar = 1 $\mu$ m

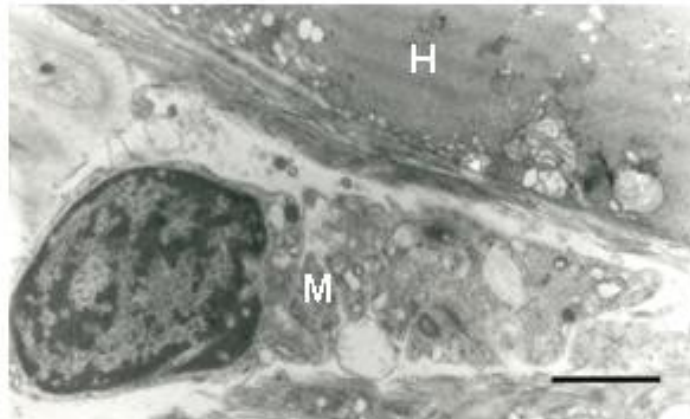


Figure 2.- In this section a macrophage (M) next to a fiber showing myofibrillar hypercontraction (H). Bar = 1 $\mu$ m

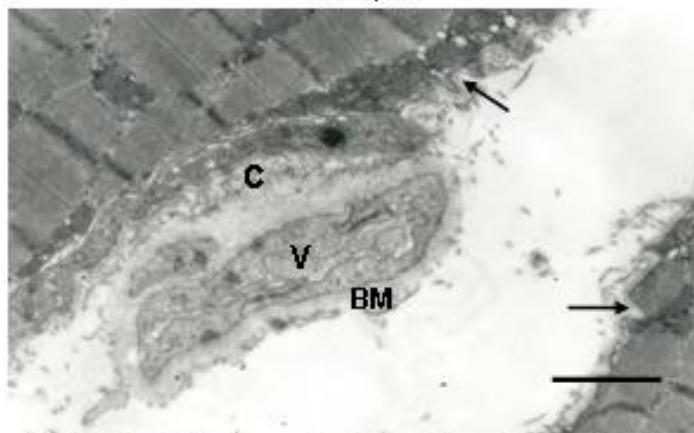


Figure 3.- An occluded capillary (V) is observed; notice the widened basement membrane (BM), foldings of sarcoplasmic membrane (arrows) and abundance of collagen fibers (C). Bar = 1 $\mu$ m