A158 EFFECTS OF IMMUNOSUPPRESSIVE TREATMENT ON LEUKOTRIENE PATHWAY IN POLYMYOSITIS AND DERMATOMYOSITIS

I Loell, L Alemo-Munters, C Ottosson, M Korotkova *Karolinska Institutet, Sweden*

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Background Polymyositis (PM) and dermatomyositis (DM) are characterised by infiltration of macrophages and T cells in skeletal muscle tissue. Immunosuppressive treatment has limited effects on the number of T cells in myositis, providing a basis for persistent immune reaction targeting muscle fibres. Leukotriene B₄ (LTB₄) is a powerful chemoattractant for myeloid leucocytes and activated T cells into inflamed tissue. LTB₄ is formed from arachidonic acid by 5-lipoxygenase (5-LO), 5-LO activating protein (FLAP), and leukotriene A₄ hydrolase. Enhanced expression of 5-LO mRNA has been demonstrated in muscle tissue from patients with PM/DM, suggesting a role for 5-LO in the pathogenesis of these diseases.

Aim To investigate the expression of 5-LO and FLAP in muscle biopsies from patients with PM or DM before and after conventional treatment.

Methods Muscle tissue biopsies were obtained from 24 patients with PM/DM and 6 healthy donors. For 17 of the patients, muscle biopsies were obtained before and after treatment with glucocorticoids and additional immunosuppressive drug for 8 months. Immunohistochemistry was employed to detect 5-LO and FLAP expression in muscle tissue. Double immunofluorescence staining was used to determine cellular localisation of these enzymes. Interstitial fluid of thigh

muscle was obtained by microdialysis from 10 patients and 4 healthy individuals at rest and in 8 patients after an acute bout of cycling. LTB4 levels were analysed in the microdialysis samples by enzyme immunoassay (EIA).

Results In healthy muscle, 5-LO was mainly expressed in vessels whereas FLAP expression was also seen in scattered mononuclear cells (MNCs). In patients, 5-LO and FLAP expression was detected around vessels, in scattered MNCs and MNCs in infiltrates. Patients had higher 5-LO but not FLAP expression than healthy controls. After treatment, FLAP but not 5-LO staining was lower in myositis muscle. Double staining showed 5-LO expression in CD163+ macrophages but not in T cells. No neutrophils were detected. Interstitial LTB4 levels in PM/DM patients did not differ from that in healthy controls at rest. After cycling, the patients had higher interstitial LTB4 levels (268 ± 153 pg/ml) than before cycling (134 ± 90 pg/ml; $p=0.02$).

Conclusion 5-LO but not FLAP expression was upregulated in muscle tissue from patients with PM/DM compared with healthy controls. In patients with PM/DM, LTB4 is released in skeletal muscle tissue at rest and levels are increased after acute cycling. Conventional treatment reduced FLAP but not 5-LO expression, which suggests that LTB4 could play a role in sustaining the local inflammation in PM and DM.