OSMOREGULATORY PATHWAYS ARE ACTIVATED IN POLYMYOSITIS: INCREASED EXPRESSION OF OSMOLYTE ACCUMULATORS IN MUSCLE FIBERS AND IMMUNE CELLS

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Background: Nuclear factor of activated T-cells 5 (NFAT5), the central regulator of cellular response to osmotic stress and inducer of pro-inflammatory pathways, is involved in inflammatory muscle disease. Design: We studied the expression of molecular NFAT5 targets involved in osmolyte accumulation, being aldose reductase (AR), taurine transporter (TauT) and sodium myo-inositol co-transporter (SMIT) in polymyositis (n=8) comparing with healthy muscle tissues (n=20) and using fluorescent immunolocalisation and western blotting. Results: In normal skeletal muscle, NFAT5 staining was present in myonuclei, and the sarcoplasm contained constitutive levels of AR. TauT and SMIT staining was, on the other hand, absent from fibers in normal muscle. In polymyositis, AR was increased in the atrophic fibers, TauT showed patchy sarcoplasmic staining mostly in CD56+ regenerating muscle fibers, and SMIT staining was membranous (variable in intensity and often discontinuous). The vast majority of inflammatory cells were AR and TauT negative, while many CD68+ and CD206+ type 2 macrophages and CD3+ T-cells were SMIT positive. Most CD68+ macrophages invading nonnecrotic muscle fibers were SMIT negative, while invading CD8+ cytotoxic T-cells were often SMIT positive. Quantitative western blotting could not detect TauT and SMIT in healthy muscle, but did detect the proteins in polymyositis samples. AR levels were significantly higher in polymyositis (0.83±0.06) than in control (0.52±0.10) and dermatomyositis (0.45±0.01) muscle samples. Conclusions: Osmolyte pathways are activated in polymyositis, indicating that osmoregulation may represent an important pathologic mechanism.