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Abstracts

Articles appearing in the May 2019 issue

Myalgia with the presence of pathologic EMG correlates with perimysial inflammatory infiltrates

Objective We aimed to define normal numbers of inflammatory cells in muscle biopsies and to identify the predictive value of isolated muscle pain and increased creatine kinase regarding the diagnosis of myositis.

Methods We analyzed muscle biopsies of 71 patients using immunostains for $CD3^+$, $CD4^+$, $CD8^+$, $CD68^+$, major histocompatibility complex Class I, perforin, and myeloid-related protein (MRP) 8. Patients were categorized as follows—group 1: myalgia without further clinical or laboratory abnormalities (n = 24); group 2: asymptomatic elevation of creatine kinase (hyperCKemia, n = 26); group 3: myalgia and pathologic EMG findings (n = 9); and group 4: otherwise healthy controls who had malignant hyperthermia susceptibility testing (n = 12).

Results In the normal muscle biopsy specimens from group 4, mean endomysial macrophage ($CD68^+$) density was 21.7 ± 5.6/mm^2, and perimysial density was 13.0 ± 5.6/mm^2. Numbers of T-lymphocytes ($CD3^+$) were 5 ± 3.5 endomysially and 2.2 ± 3.9/mm^2 perimysially. This was not different from groups 1 and 2. Only group 3 patients had increased mean numbers of perimysial macrophages (24.1 ± 6.3/mm^2; $p = 0.0005$), $CD3^+$ (7.6 ± 4.9/mm^2; $p = 0.0056$), and $CD8^+$ T-lymphocytes (5.4 ± 3.1/mm^2; $p = 0.0008$) and displayed the activation marker MRP8 in all cases. Although inflammatory cells were increased in the perimysium in group 3, histology did not fulfill the criteria for dermatomyositis, polymyositis, or inclusion body myositis.

Conclusions Normal muscle contains a considerable number of macrophages and T-lymphocytes. Muscle biopsy is likely to detect inflammatory changes in patients with myalgia or hyperCKemia only if pathologic EMG findings are present.

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Exosome-enriched fractions from MS B cells induce oligodendrocyte death

Objective To identify whether factors toxic to oligodendrocytes (OLs), released by B cells from patients with MS, are found in extracellular microvesicles enriched in exosomes.

Methods Conditioned medium (Sup) was obtained from cultures of blood B cells of patients with MS and normal controls (NCs). Exosome-enriched (Ex-En) fractions were prepared by solvent precipitation from Sup containing bovine serum and from serum-free Sup by ultracentrifugation (UC) or immunoprecipitation (IP) with antibodies to CD9. Ex-En fractions were diluted 1:4 with OL culture medium and screened for toxic effects on cultured rat OLs as measured by trypan blue uptake. Proteomic analysis was performed on Sup fractions.

Results MS B cell–derived Ex-En fractions prepared from Sup by solvent extraction, UC, or IP induced OL death, whereas corresponding Ex-En fractions from NC showed little toxicity. Proteomic analysis of Sup demonstrated enrichment of proteins characteristic of exosomes from both NC and MS B-cell Sup. Ontology enrichment analysis suggested differences in the types and cargo of exosomes from MS Sup compared with NC, with proteins related to cell surface, extracellular plasma membrane, and gliogenesis enriched in MS.

Conclusions Much of the in vitro toxicity of Sup from B cells of patients with relapsing-remitting MS is found in Ex-En fractions, as confirmed by 3 methods. Proteomic analysis of B-cell Sup indicates multiple differences between MS and NC.

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