PLASMA IP-10 LEVEL DISTINGUISHES INFLAMMATORY MYOPATHY

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Discrimination of idiopathic inflammatory myopathy (IIM) from other muscle diseases is at times difficult in clinical practice even after muscle biopsy. Plasma or serum cytokine levels have been reported to be changed in various muscle diseases, and thus we hypothesized that circulating cytokines could be a biomarker to distinguish IIM from other muscle diseases. We measured a variety of cytokines in plasma of patients with diverse muscle diseases and found that IP-10 (CXCL10) could be a potential biomarker.

Classification of evidence. This study provides Class III evidence that plasma IP-10 levels distinguish IIM from hereditary muscle diseases (HMD) (sensitivity 91%, specificity 90%).

Methods. We studied 100 patients with IIM (mean age 54.1 ± 23.2 years, 42 male and 58 female), including polymyositis (n = 19), dermatomyositis (n = 19), antisynthetase syndrome (n = 8), immune-mediated necrotizing myopathy (n = 17), and inclusion body myositis (IBM, n = 37). As non-IIM controls, we enrolled 50 patients with HMD (mean age 32.8 ± 20.2 years, 24 men and 26 women), including Duchenne muscular dystrophy/Becker muscular dystrophy (BMD, n = 6), limb-girdle muscular dystrophies (LGMD, n = 7: type 1B, n = 2; 2A, n = 1; 2B, n = 3; and 2L, n = 1), facioscapulohumeral muscular dystrophy (FSHD, n = 25), and GNE myopathy (n = 12). While patients with HMD did not receive any immunosuppressive therapy, we did not have full information in the patients with IIM. Diagnosis of IIM was made based upon findings on muscle pathology and autoantibody analyses and diagnosis of HMD was confirmed genetically or immunohistochemically. We chose subjects in a consecutive manner within each disease group.

We measured plasma levels of 27 cytokines (table e-1 on the Neurology® Web site at Neurology.org) with Bio-Plex Pro Human Cytokine Group I Panel 27-Plex in Bio-Plex 200 system (Bio-Rad, Hercules, CA) according to the manufacturer’s instructions. Means of duplicate measurements were used for analyses. Statistical comparisons were performed by Kruskal-Wallis test followed by Dunn multiple comparison post test. A p value of less than 0.01 was considered statistically significant. We performed Spearman rank correlation test to determine correlation between cytokine levels and age and receiver operating characteristic (ROC) analysis to assess the differential diagnostic potential of cytokine levels. All statistical analyses were performed using GraphPad Prism 5.0 (GraphPad Software, La Jolla, CA).

Standard protocol approvals, registrations, and patient consents. All the clinical information and materials used in the present study were obtained for diagnostic purposes and permitted for scientific use with written informed consent. All experiments in the study were approved by the ethical committee of the National Center of Neurology and Psychiatry.

Results. IP-10 and eotaxin showed statistically significant differences between every IIM and HMD group (table e-1). No significant differences were seen among subtypes of IIM. There was no significant correlation between the level of IP-10 or eotaxin and patient age (table e-2). ROC analysis revealed that IP-10 had a larger area under the curve than eotaxin (figure 1, figure e-1). Optimal accuracy of IP-10 as a differential diagnostic marker occurred at levels of 600–650 pg/mL, showing 91%. The cutoff level of 650 pg/mL gave 91% sensitivity and 90% specificity (figure 1). Even when HMD was limited to LGMD, FSHD, and BMD, which are more likely to be confused with IIM, the specificity was 91% (30/33). The sensitivity and specificity with optimal accuracy of each subset are described in table e-3.

Discussion. We demonstrated that plasma IP-10 level distinguishes IIM from HMD with high sensitivity and specificity. However, this study has a few limitations: (1) non-inflammatory acquired muscle diseases, such as toxic myopathy and endocrine myopathy, are not included; (2) it does not find a biomarker to differentiate IBM, which does not typically respond to immunosuppressive therapies, from other IIM; and (3) it lacks sufficient information about confounders
such as severity of the diseases, treatments, and concurrent inflammatory diseases. Validation of the IP-10 level as a biomarker should be performed prospectively in larger and independent cohorts with different quantification kits.

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