Serum miR-21 levels in patients with dermatomyositis

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There are only a few reports about the relationships between microRNAs (miRNAs) and polymyositis/dermatomyositis (PM/DM): Eisenberg et al. found that expression of several miRNAs are up- or down-regulated in the muscle tissues of PM/DM (1). First, we also determined the miRNA levels in muscle tissues of DM patients. Total miRNA were obtained from muscle samples of 4 DM patients and 4 healthy control subjects (2). Consistent with the previous report (1), miR-21 expression in the muscle tissues was significantly elevated in DM patients (Fig. 1a).

Accordingly, we tried to evaluate the possibility that serum levels of miR-21 can be a useful marker for the diagnosis and the evaluation of disease activity of DM. Serum samples were obtained from 30 DM patients (12 men and 18 women; mean age, 54.8 years). Control serum samples were also collected from 20 healthy volunteers, 10 clinically amyopathic DM (CADM) patients, 5 PM patients, 20 systemic lupus erythematosus (SLE) patients, and 10 systemic sclerosis (SSc) patients. Institutional review board approval and written informed consent were obtained before patients and healthy volunteers were entered into this study. By the real-time PCR using hsa-miR-21 primer and total miRNA purified from serum of healthy volunteer (2), the amplification curve of miR-21 was observed, and Ct values were increased by the serial dilution of the miRNA (Fig. 1b). Thus, using our method, hsa-miR-21 was likely to be detectable and quantitative in the serum.

Then, before miRNA isolation, serum was supplemented with synthetic non-human miRNA (C. elegans miR-39, Takara) as controls providing internal reference for normalisation of technical variations between samples (3, 4). Mean serum levels of miR-21 corrected for C. elegans miR-39 levels in the same samples were significantly higher only in DM patients than those in normal subjects (Fig. 1c, p=0.041). It has been reported that serum miR-21 levels are increased in various human neoplastic disorders (5-7). Our results indicate miR-21 expression is also increased in the muscles and sera of DM patients, and may be useful for the diagnosis of DM. miR-21 expression has been previously described to be up-regulated in T lymphocytes of SLE patients (6,8), whereas serum miR-21 levels in SLE patients were higher than those in normal subjects, but not statistically significant in our study. This discrepancy may be due to the small number of patients or the different expression pattern of miR-21 between lymphocytes and serum.

When the cut-off value was set at mean value+2SD of the healthy controls, there was no significant difference between patients with elevated serum miR-21 levels (n=12) and those with normal levels (n=18) in terms of the prevalence of Gottron's sign (80.0% vs. 86.7%), Heliotrope rash (83.3% vs. 66.7%), lung involvement (50.0% vs. 40.0%), or internal malignancies (33.3% vs. 18.8%). Serum creatine kinase levels were not significantly different between patients with and without elevated miR-21 levels (1130.3 vs. 2861.1 U/l). However, we found mean serum IgG levels were significantly higher in patients with elevated miR-21 levels than those without (1837.4 vs. 1283.6 mg/dl, p=0.0041 by Mann-Whitney U-test). Serum IgG level is thought to reflect the abnormal activation of immune system and regarded as one of the disease markers in DM. Thus, serum miR-21 may also be correlated with the disease activity of DM and be involved in the pathogenesis of this disease. Another possibility is that increased miR-21 expression in DM is linked to the muscle reconstruction. Clarifying the role of miRNAs in this disease may lead to further understanding of the disease and new therapeutic approaches. Larger studies are needed by measuring serum levels of miR-21 as well as other miRNAs in increased number of patients in the future.

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References


