Results

Mean serum G-CSF levels were significantly lower in AD cases compared to normal controls. In the AD group, G-CSF levels were significantly negatively associated with scores on the MMSE and significantly positively associated with scores on the CDR Global.

Significant interactions were observed between G-CSF and CRP, BDNF and thrombopoietin. When the sample was split upon BDNF and thrombopoietin levels, G-CSF was significantly associated with scores on the MMSE and CDR Global only among subjects in the middle tertile. However, when the subjects were stratified on CRP level, G-CSF was significant only among subjects grouped in the highest tertile.

Multivariate logistic regression analysis of G-CSF and MME scores among Alzheimer’s disease patients after stratification into tertiles on BDNF, CRP and thrombopoietin.

Multivariate logistic regression for MMSE among participants with Alzheimer’s disease.

Discussion

G-CSF levels were significantly lower among AD participants, relative to cognitively normal controls. These results are in agreement with Laske and colleagues, who observed lower plasma G-CSF levels in 50 subjects diagnosed with early Alzheimer’s disease relative to 50 cognitively intact controls (Laske et al., 2009). In contrast to Laske et al., we found that increased G-CSF was significantly associated with greater disease severity, as indicated by lower MMSE and higher GCSF levels.

Post-hoc analysis of interactions between G-CSF and other serum proteins suggested that the association between G-CSF and disease severity was mediated by inflammation.

G-CSF was associated with MMSE and CDR scores only among AD patients that had neither high nor low levels of BDNF or thrombopoietin, suggesting that the role for G-CSF was not related to dysregulation of neurotrophic factors and vascular function. In contrast, the association between G-CSF and disease severity was only apparent among AD patients with elevated serum CRP, an indicator of inflammatory activation.

The alteration of levels in inflammatory proteins and hematopoietic growth factors in the development and progression of AD points to a role for G-CSF in the pathophysiology of AD.

Conclusion

Granulocyte colony stimulating factor (G-CSF) promotes the survival, proliferation, differentiation and function of hematopoietic progenitors and mature neutrophils. Additionally, G-CSF may have a role in neuroprotection by increasing immunosuppressivity and suppressing apoptosis. Alzheimer’s disease (AD) is the most frequent form of senile dementia, and one of the most serious health problems in the world. Due to the role of G-CSF in a neurotrophic factor, we sought to determine if different levels of G-CSF were associated with different outcomes. We measured the serum levels of G-CSF and various other proteins in a group of 50 patients diagnosed with Alzheimer’s disease. The patients were grouped into tertiles based on their BDNF and thrombopoietin levels. Our results indicate that the alteration of levels in inflammatory proteins and hematopoietic growth factors in the development and progression of AD points to a role for G-CSF in the pathophysiology of AD.