Immunological Regulation in Bipolar Patients with Manic Episode (II)

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Abstract

Several studies suggest CMI is altered in bipolar patients with manic episode, although findings have been contradictory. The inconsistent results may due to the effect of age, sex, medications, and severity of manic symptoms. In this case-control study we investigate the bipolar patients in manic episode as well as in consequent remission regarding the plasma soluble CD4 (sCD4) and sCD8 concentration, the plasma IL-1 receptor anatagonist (IL-1RA) and clara cell protein 16 (CC16) level and the soluble transferrin receptor (sTfR) level. The plasma sCD4 level in manic episode is higher than in that of controls but did not reach statistical significance. Whereas, the sCD8 level in bipolar patients in manic episode as well as in remission is significantly higher (p<0.05) than in controls. The levels of IL-1RA both in bipolar patients in manic episode as well as in remission is significantly higher (p<0.05) as compared to controls. The mean levels of CC16 in bipolar patients in manic episode is

significantly lower than that of the remissions ($p<0.05$). The sTfR concentration in manic episode as well as in remission is significantly higher than controls ($p<0.05$). Basing on literature reviews, the increased levels of sCD8, but not sCD4 in manic episode suggests activation of cell-mediated immunity. The reduced CC16 production and increase production of IL-1RA of bipolar disorder in acute mania and consequent remission is similar to that of schizophrenia. An increase sTfR level is significantly higher than controls which was also observed in schizophrenia. Taken together, the activation of CMI in bipolar disorder is observed, the immune-inflammatory variables in acute manic is different than controls suggest there is a immune-modulation of bipolar disorder may vary from normal.

INTRODUCTION

Data suggested that activation of the monocytic and T-cell arms of cell-mediated immunity (CMI) play a role in the pathophysiology of schizophrenia. However, reports on the assessment of immunity in mania are limited and remain controversial.

Base on our previous study, increased lymphocyte proliferation and significantly increased plasma concentrations of sIL-2R but not sIL-6R in manic patients than in normal controls, suggested activation of CMI in mania patients. Since age, gender, and symptomatic severity have effects on immunity in patients with mood disorder, it is probable neither evaluating the immune parameters after a well-defined remission period nor comparing them with age- and sex-matched controls led to the inconsistent results.

The aim of the present study was to examine the plasma sCD4, sCD8, TfR, CC16 and IL-1RA concentrations in patients with mania and in normal controls.

MATERIALS AND METHODS

Subjects

Acute in-patients diagnosed as bipolar disorder, manic (DSM-IV) with YMRS scores $\geq$ 30, aged $\leq$ 45 years and free from acute infections or chronic diseases were recruited. During the index hospitalization, all the patients were treated with lithium and typical antipsychotics (haloperidol or chlorpromazine). Follow-up blood samples of patients were collected while in consequent remission (YMRS scores $\leq$ 12) free from any sign of depression. Age- and gender-matched healthy control subjects without any Axis I psychiatric disorder were recruited.

Plasma sCD4, sCD8, TfR, CC16, and IL-1RA level analysis

The plasma levels of sCD4, sCD8, TfR, CC16 and IL-1RA level were measured in duplicate using ELISA method.

RESULTS

The plasma sCD4 level in manic episode is higher than in that of controls but did not reach statistical significance. Whereas, the sCD8 level in bipolar patients in manic episode as well as in remission is significantly higher ($p<0.05$) than in controls. The levels of IL-1RA both in bipolar patients in manic episode as well as in remission is significantly higher ($p<0.05$) as compared to controls. The mean levels of CC16 in bipolar patients in manic episode is significantly lower than that of the remissions ($p<0.05$). The sTfR concentration in manic episode as well as in remission is significantly higher than controls ($p<0.05$).

CONCLUSION

Based on comparison between acute mania and consequent remission of bipolar individuals, a major finding of this study is that manic episode is accompanied by significantly elevated plasma sCD8, TfR, and IL-1RA levels. Since, increased plasma sCD8 and TfR levels are an unequivocal index of T cell activation. These results indicated that activation of cell-mediated immunity occurs in acute mania. Furthermore, the plasma sIL-1RA levels was significantly elevated in bipolar mania than in normal controls. These finding suggests that the activation of the monocytic arm of CMI may occur in this illness.

Unmedicated patients shown significantly increased sCD4, TfR and lower plasma CC16 than normal controls. Patients with medication shown significantly increased TfR and IL-1RA as compared to controls.

Taken together, in this study bipolar patients in acute mania are characterized by T lymphocyte and monocyte activation as evidenced by elevated plasma sCD8, TfR and IL-1RA levels. In patients with bipolar disorder, the immunomodulatory mechanism may vary from normals.

ACKNOWLEDGMENTS

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