Successful Lithium Carbonate Treatment for Steroid-induced Depression Following Bone Marrow Transplantation: a Case Report

Mizuho Ito1, Masanari Onose2, Tomoki Yamada2, Hideki Onishi3, Shin Fujisawa4 and Heiwa Kanamori4

1Department of Psychiatry, Kinko Hospital, Yokohama, 2Department of Psychiatry, Yokohama City University School of Medicine, 3Department of Psychiatry, Kanagawa Prefectural Cancer Center, Yokohama and 4First Department of Internal Medicine, Yokohama City University School of Medicine, Yokohama, Japan

Drug-induced mental disturbances are frequent in bone marrow transplantation (BMT) patients who require numerous kinds of drugs. Although steroid-induced mental disorder is common in BMT settings, its treatment has not been fully investigated. We encountered a patient with acute myeloid leukemia who developed depressive disorder induced by steroid given for graft-versus-host disease treatment. Lithium carbonate was effective for the treatment of depressive disorder without causing side effects such as renal dysfunction. This study demonstrates the effectiveness of lithium carbonate for the treatment of depressive disorder induced by steroids in BMT settings.

Key words: bone marrow transplantation – steroids – depression – lithium – adverse effect

INTRODUCTION

Mental disturbances such as adjustment disorder, mood disorder and delirium are frequent in patients who receive bone marrow transplantation (BMT) because of the physical and psychological stress (1). Sasaki et al. reported that mental disorders, diagnosed according to the Fourth Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (2) criteria, occurred in as many as 40% of BMT patients (1,3). Depressive state and depression are particularly common in such patients (4,5). Drug-induced mental disturbances are also frequent in BMT patients as they require many kinds of drugs. Specifically, steroids administered to treat graft-versus-host disease (GVHD) cause various mental disturbances such as mood disorder, delirium and hallucinatory paranoid state. The reported occurrence of steroid psychosis is 3–57% (6,7). Being female, taking more than 40 mg/day of prednisolone and long-term administration are considered as risk factors for steroid psychosis (6,8). The incidence of depression among patients with steroid psychosis is about 40% (6,8). Several reports indicate that tricyclic and tetracyclic antidepressants may exacerbate the symptoms and lithium carbonate is effective for the treatment of steroid-induced depression (9–12). However, these reports have mainly focused on patients with collagen disease. In BMT patients, treatment of steroid-induced depression with lithium carbonate has not previously been investigated, although mood disorder is common in BMT settings. In this paper, we report a case of depressive disorder induced by prednisolone for the treatment of GVHD. The patient was not controlled well by antidepressants, but lithium carbonate was found out to be effective for the treatment of her depressive symptoms.

CASE REPORT

A 37-year-old woman with acute myeloid leukemia (FAB M2) underwent HLA-unmatched BMT. She did not have past history or family history of mental disorders, drugs or alcohol abuse. Before BMT she had been treated with two courses of cytarabine, idarubicin and prednisolone and with one course of cytarabine and mitoxantrone hydrochloride.

At the time of transplantation, neurological examination was normal and depressive symptoms were not present. BMT was carried out following conditioning with total body irradiation of 3 Gy/day daily for four consecutive days (total 12 Gy), thiotepa 200 µg/m² once daily iv for two consecutive days and cyclophosphamide 2250 mg/m² once daily iv for two consecutive days. On day 22, she left the sterilized room.

Thirty days after BMT she developed diarrhea and skin eruption. On biopsy, she was diagnosed as having GVHD grade II.
and on day 42 prednisolone 50 mg/day was started. On day 46, depressive symptoms including depressed mood, agitation and suicidal ideation rapidly aggravated. We diagnosed this patient as having a major depressive episode caused by prednisolone according to DSM-IV criteria (2). Mianserin hydrochloride was started on day 46 and was gradually increased from 10 to 40 mg/day, with no response. On day 56, lithium carbonate 300 mg/day p.o. in divided doses was added to 40 mg/day of mianserin and prednisolone was reduced to 40 mg/day. Four days after starting lithium carbonate, her depressive symptoms dramatically improved and disappeared within 14 days. Prednisolone was decreased gradually to 15 mg/day p.o.

Thereafter, she remained stable and mianserin was reduced to 30 mg/day on day 95. On day 96, she developed right chest pain and eruption, which was diagnosed as herpes simplex to 10 mg/day iv. On day 96, she developed right chest pain and eruption, which was diagnosed as herpes simplex to 30 mg/day on day 95. On day 96, she developed right chest pain and eruption, which was diagnosed as herpes simplex to 15 mg/day p.o. per os because of nausea due to acyclovir, so the same dose (15 mg/day) of prednisolone was prescribed iv and lithium carbonate and mianserin were stopped. Thereafter, the patient showed depressed mood, sleeplessness and agitation, which were considered signs of relapse. On day 106, prednisolone was reduced to 10 mg/day, but depressive symptoms persisted. On day 125, she started to take lithium carbonate 200 mg/day p.o. with prednisolone 10 mg/day iv and her symptoms dramatically improved again within 1 week. She stopped taking prednisolone on day 172 and stopped lithium carbonate thereafter, but remained stable.

DISCUSSION

Drug-induced mental disorders are frequently encountered in BMT patients requiring various drugs. Steroids, specifically, are well known to cause mental disorders. We encountered a case of prednisolone-induced depression, which was successfully treated with lithium carbonate. This is the first reported case of steroid-induced depression successfully treated with lithium carbonate in a BMT setting.

In this case, the patient rapidly developed mental disorders such as depressed mood, agitation and suicidal ideation just after starting prednisolone. Steroid psychosis often occurs from a few days to 2 weeks after administration of this agent (6,8). Patients with steroid-induced psychosis often show mood disorders including being talkative, distractible, confused and hallucinating. Being female, taking more than 40 mg/day of prednisolone and long-term administration are considered to be the major risk factors for steroid psychosis (6,8).

In this case, two factors, namely being female and 50 mg/day administration of prednisolone, were present.

Treatment of steroid psychosis involves dosage reduction or discontinuation of prednisolone, but this usually cannot be done because of the severity of the underlying disease requiring prednisolone. In such cases, we have to treat the patient with antipsychotic drugs. Tricyclic and tetracyclic antidepressants have been reported to induce exacerbation of agitation (8–10), so we have to choose carefully when prescribing antipsychotic drugs. Lithium carbonate is effective for steroid-induced mood disorders, not only manic episodes but also depressive episodes (11). In this case, depressive disorder was dramatically improved shortly after starting lithium carbonate. Thereafter the patient showed depressive symptoms again when lithium was discontinued, but complete recovery was achieved after re-starting lithium. This case indicates that lithium carbonate is effective for steroid-induced depression in BMT settings.

We have used mianserin with lithium carbonate, and therefore we should consider the possibility that lithium augmented the action of the former. Lithium carbonate is sometimes administered with an antidepressant for treatment-resistant depression. In this case, however, we can consider that lithium carbonate worked not as an augmenter of mianserin action but as an antidepressant itself, because depression was not improved by mianserin alone but rather was quickly improved after starting lithium. This view is further supported by the recovery within a short time after re-administration of lithium.

If lithium worked via augmentation of mianserin action, recovery from depression would have taken longer.

The rapid antidepressant effect of lithium carbonate is caused by its action on serotonergic neurotransmission (10). This effect on this system requires less time than catecholaminergic neurotransmission and it seems that depression improved through activation of the serotonergic system activities by lithium. Therefore, selective serotonin re-uptake inhibitors other than lithium carbonate can be considered for steroid-induced depression. Future study on this aspect is to be encouraged.

Lithium is well known to cause various side-effects, including renal dysfunction and symptoms of lithium intoxication such as convulsions. While taking lithium, our patient did not show any signs of symptoms of liver or kidney dysfunction or lithium intoxication. Serum lithium levels were 0.4–0.6 mEq/l (normal 0.8–1.2 mEq/l). In BMT settings, immunosuppressive agents have a nephrotoxic effect and may cause renal dysfunction. It is necessary to monitor the serum lithium level and to evaluate any clinical signs or symptoms suggesting lithium intoxication. Lithium carbonate can be used for cancer patients by monitoring laboratory data many times. In many previous reports, lithium treatment was performed safely for steroid-induced depression in systemic lupus erythematosus patients who often have a risk of renal dysfunction (10,12).

The cases of steroid-induced depression previously reported have been mainly of patients with collagen disease. It is difficult to distinguish depressive episodes caused by steroids from those caused by central nervous system disorders in collagen diseases. In this case, however, we can assert that depression was caused by prednisolone and was improved by lithium carbonate. This study clearly indicates the effectiveness and presents the limitations of treating steroid-induced depression with lithium carbonate in BMT settings.
References


