Recurrent Cases of Corticosteroid-Induced Mood Disorder: Clinical Characteristics and Treatment

Ken Wada, M.D.; Norihito Yamada, M.D., Ph.D.; Hiroshi Suzuki, M.D., Ph.D.; Yomei Lee, M.D.; and Shigetoshi Kuroda, M.D., Ph.D.

Background: Corticosteroids often induce steroid psychosis, a collection of heterogeneous syndromes with different pathophysiologic mechanisms. To date, no study has focused specifically on recurrent corticosteroid-induced mood disorders and considered their long-term outcome and treatment strategies.

Method: Nine patients whose initial clinical presentation met DSM-IV criteria for a substance-induced mood disorder were identified by a review of medical records. Their clinical characteristics and treatments were examined.

Results: All 9 corticosteroid-treated patients had a clinical course of bipolar disorder. Seven patients initially developed a manic or hypomanic state with subacute onset ranging from 1 to 3 months. Six patients had manic episodes accompanied by psychotic features. The proportion of manic episodes relative to total mood episodes of the 9 patients was 65.6%, suggesting manic predominance. Seven patients showed mood episodes that had no direct relationship to corticosteroid therapy and were preceded by various psychosocial stressors. Four of 5 patients who received steroid pulse therapy rapidly became manic or hypomanic. Antidepressants as well as mood stabilizers were useful for treatment of the present 9 patients.

Conclusion: Recurrent cases of corticosteroid-induced mood disorder have interesting clinical features, such as subacute onset, manic predominance, frequent accompanying psychotic features, and similar recurrent episodes in association with psychosocial stressors and corticosteroid use. Management, including psychopharmacologic intervention, should be indicated by a consideration of the underlying illnesses and psychosocial stressors.

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Received April 27, 1999; accepted Nov. 2, 1999. *From the Department of Neuropsychiatry, Okayama University Medical School, Okayama, Japan.*

Reprint requests to: Ken Wada, M.D., Department of Neuropsychiatry, Okayama University Medical School, 2-5-1, Shikata-cho, Okayama, Japan.

It is well established that various psychiatric symptoms can develop in association with the administration of corticosteroids.[1–7] Collectively, these symptoms are conventionally known as steroid psychosis. The term *steroid psychosis* refers not only to overt psychoses, but also to deliria, mood disorders, and various other psychiatric syndromes. Therefore, steroid psychosis is not a specific clinical entity, but consists of heterogeneous syndromes with different pathophysiologic mechanisms. Although a number of previous studies have shown that psychiatric syndromes induced by corticosteroids involve a complex and variable constellation of symptoms,[1–5] clinical research on uniform cases is needed to clarify the underlying biological pathomechanisms. Moreover, established diagnostic criteria such as those of DSM-IV[8] have scarcely been used to evaluate psychiatric symptoms in previous studies of steroid psychosis.

Many patients who have systemic lupus erythematosus (SLE) or other autoimmune diseases experience multiple relapses and remissions. They often must receive intensive or long-term maintenance treatment with corticosteroids. Recurrence of steroid psychosis could therefore be found in clinical practice. However, few studies have examined long-term outcome and treatment strategies from the psychiatric point of view.[9–13]

Consequently, we focused on recurrent cases presenting as mood disorders, which are accepted to be the most frequent corticosteroid-induced psychiatric syndromes. We report the clinical characteristics and treatments of 9 cases of corticosteroid-induced mood disorder and review the literature to improve our understanding of those disorders.

METHOD

From 1990 to 1998, 1904 patients were referred to the Department of Neuropsychiatry at Okayama University Hospital (Japan) from other departments. Review of the records from our department revealed that 16 patients had first mood episodes, which were initially either manic or depressive, occurring in association with the administration of corticosteroid therapy. The patients' initial clinical presentation met DSM-IV[8] criteria for a substance-induced

mood disorder (*substance* corresponds to *corticosteroid* in this article). Of these patients, 9 had recurrent mood disorder on follow-up. Of the other 7 patients, we could not ascertain the recurrence for 1 woman because she had been transferred to another hospital after her hypomanic symptoms improved. From a review of the case notes and the consultant psychiatrists' evaluations, we were able to obtain the following information about each patient: age; sex; history of previous psychiatric illness; premorbid personality characteristics; medical indication for corticosteroid treatment; dose, duration, and route of corticosteroid administration (whether or not pulse therapy was employed); latencies of the onset of episodes; times of recurrence; characteristics of psychiatric symptoms; response to treatment; and outcome.

RESULTS

Table 1 summarizes the clinical findings from the case reports of 3 men and 6 women. Age at onset ranged from 18 to 68 years. All patients except patient 7, who had developed only manic episodes, had shown both manic and depressive episodes. The number of episodes ranged from 2 to 7. The duration of illness on follow-up ranged from 1 to 20 years. Except for patients 3 and 6, who had become mildly depressed at onset, all patients had initially developed a manic or hypomanic state. All 9 patients presented clinically with bipolar disorder in their longitudinal courses. Four patients, especially patients 1 and 5, had more manic than depressive episodes, and 4 had an equal number of manic and depressive episodes. It was evident that these patients were essentially manic-prone. Moreover, 6 of the 9 patients had manic episodes accompanied by psychotic features such as auditory hallucinations or persecutory delusions.

Two of the 8 patients who developed depressive episodes showed depressive stupor, and 3 attempted suicide by self-mutilation or intentional overuse of psychotropics. Although, in general, patients showing only mild depression are not always referred to psychiatrists, 6 of the 8 patients had depressive episodes that were diagnosed as severe. No patient developed a depressive episode with psychotic features.

No patient had had previous psychiatric episodes, and all had their first episode of mood disorder as a result of the treatment with corticosteroids. No patient had a family history of psychiatric disorders. Each patient's premorbid personality was different and no patient was prone to mania before the onset of the corticosteroid-induced mood disorder.

Patients showed subacute onset with latency of 1 to 3 months in their first mood episodes. However, among all episodes, 4 of the 5 patients (patients 2, 3, 6, 8, and 9) who received intravenous high-dose methylprednisolone rapidly became manic or hypomanic. In the longitudinal course, 7 patients showed mood episodes that had no relationship to either alterations in the dose or resumption of corticosteroids. Various psychosocial stressors, such as occupational difficulties or marital problems, preceded these mood episodes (Table 2). Seventeen of 21 manic episodes occurred after an increase in corticosteroid dose, which suggests that those episodes were corticosteroid induced. In contrast, only 3 of 11 depressive episodes were corticosteroid induced; the rest were stress related or treatment related, as in case 1 (see below). The proportion of manic episodes relative to total mood episodes was 65.6%, which shows manic predominance in the 9 subjects.

The patients had been pharmacologically treated with antipsychotics, mood stabilizers, and antidepressants. Intravenous clomipramine had been considerably effective for 2 patients with depressive stupor. No patients worsened after receiving antidepressants for their depressive symptoms. Carbamazepine was apparently effective for patient 2, and valproate was effective for patient 8. Particularly for patient 2, carbamazepine was considered to have prophylactic efficacy, because the patient has experienced no recurrence on maintenance treatment with carbamazepine, 600 mg/day, despite receiving 2 more courses of steroid pulse therapy. Except for patient 1, who developed a fluctuating course without complete interposed recovery and committed suicide, each episode of the other 8 patients had a relatively good outcome, with full remission after 1 to 3 months. All 9 cases are described below.

Case reports

Case 1. Ms. A, a 40-year-old woman, was admitted to the rheumatologic ward because of fever and muscle weakness. She had had no previous psychiatric episodes. She was diagnosed as having dermatomyositis and was treated with prednisolone, 60 mg/day. After 4 weeks, she became irritable and euphoric and was referred to our psychiatric department. When Ms. A was 42 years old, she was readmitted because of an exacerbation of the dermatomyositis. Prednisolone was given at 60 mg/day, and again she became manic. After the tapering of prednisolone, Ms. A gradually became depressed and was discharged in a mildly depressive state after 8 months' hospitalization. Her mood gradually improved without antidepressants.

When Ms. A was 44 years old, she was readmitted to the hospital and received betamethasone, 4 mg/day, because of the exacerbation of the dermatomyositis. After 4 weeks, she showed elevated mood, irritability, pressured speech, and aggressiveness and was referred to our psychiatric department again. Ms. A's mood improved with neuroleptic medication, but a mixed state followed for about 2 months, and thereafter she fell into a depressive state. Ms. A attempted suicide in a severely depressed mood 1 month after discharge and was admitted to our psychiatric ward. With a maintenance dose of betamethasone, 1 mg/day, Ms. A's symptoms of dermatomyositis were

Table 1. Clinical Characteristics of 9 Patients With Recurrent Corticosteroid-Induced Mood Disorder[a]

Patient	Sex	Age at Onset (y)	Underlying Illness/ Condition	No. of episodes/ Duration of Illness (y)	Polarity	Latency of Initial Onset (wk)	Psychotic Features	Pulse Therapy	Episodes Unrelated to Steroid Therapy
1	F	40	Dermatomyositis	7/5	M-M-M-D-M-D-M	4	No	No	Yes
2	F	18	MCNS	4/2	M-D-D-M	2	Yes	Yes	Yes
3	F	21	Polymyositis	3/2	D-M-D	4	No	Yes	Yes
4	F	23	Ulcerative colitis	2/1.5	M-D	4	Yes	No	Yes
5	F	28	SLE	6/20	M-M-M-M-M-D	Immediate	Yes	No	Yes
6	F	31	SLE	2/5	D-M	12	Yes	Yes	No
7	M	47	SLE	2/6	M-M	8	Yes	No	No
8	M	42	Kidney transplant	4/4	M-M-D-M	8	Yes	Yes	Yes
9	M	68	Membranous nephropathy	2/1	M-D	4	No	Yes	Yes

[a]Abbreviations: D = depressive episode, M = manic or hypomanic episode, MCNS = minimal-change nephrotic syndrome, SLE = systemic lupus erythematosus.

Table 2. Subclassification of Mood Episodes: Corticosteroid Induced or Non–Corticosteroid Induced

Type of Episode	No. of Episodes: Corticosteroid Induced	Non–Corticosteroid Induced	Total
Manic	17	4	21
Depressive	3	8	11
Total	20	12	32

stabilized. In spite of treatment with amitriptyline, 150 mg/day, or desipramine, 200 mg/day, she showed only slight improvement. Thereafter, her mood fluctuated between depression and mania, regardless of the betamethasone dose. Lithium administration was avoided because of hypothyroidism. Carbamazepine could not be continued owing to an urticarial rash. After 17 months' hospitalization, Ms. A was discharged home with partial remission of the mood disorder and received follow-up evaluation at another hospital. About 2 years later, she committed suicide.

Case 2. Ms. B, a 19-year-old woman who had a 1-year history of minimal-change nephrotic syndrome, was admitted to the nephrologic ward of our hospital. She had initially received pulse methylprednisolone treatment at 1 g/day in the previous year at another hospital. Ms. B had developed a manic episode with auditory hallucination and persecutory delusion 2 weeks after beginning pulse therapy. She had been treated with haloperidol and improved over the next 2 months. Meanwhile, she had a depressive episode without an increase in the dose of prednisolone. Before the episode, Ms. B began feeling sad about the ballooning of her face due to the corticosteroid.

On her first admission to our hospital, because of a relapse of the nephrotic syndrome, Ms. B was started on a regimen of oral methylprednisolone, 24 mg/day. She became gradually depressed and developed severe retardation and suicidal ideation after 4 weeks. Brain magnetic resonance imaging (MRI) results and electroencephalogram (EEG) were normal. She was referred to our psychiatric department and initially treated with setiptiline, a tetracyclic antidepressant with little anticholinergic action, at 6 mg/day. Tricyclic antidepressants were avoided because she had glaucoma. As soon as augmentation therapy with clonazepam, 3 mg/day, started, Ms. B showed dramatic improvement and was discharged home.

Although Ms. B remained well over the next 6 months, she afterward had another relapse of nephrotic syndrome. On her second admission to our hospital, pulse methylprednisolone, 500 mg/day, was started, and she rapidly developed euphoria, irritability, and increased motor activity. Phenothiazines caused excessive drowsiness, and valproate, 600 mg/day, could not relieve her irritability and dysphoria. Ms. B was transferred to our psychiatric ward, and carbamazepine, 600 mg/day, was started. This was effective for her manic symptoms. With this dose, Ms. B has continued to be mentally stable, despite receiving more pulse therapy for 2 subsequent relapses over the next 11 months.

Case 3. Ms. C, a 21-year-old woman, had been treated with prednisolone, 60 mg/day, for dermatomyositis 1 year before referral to our psychiatric department. She had had no previous psychiatric episodes. She gradually manifested irritability, poor concentration, diminished interest, and insomnia 4 weeks after admission. Although prednisolone was tapered and she was treated with sulpiride, a benzamide with mild antidepressant action, she never had complete remission of her depressive symptoms.

After 5 months, Ms. C was again admitted to the rheumatologic ward because of exacerbation of her dermatomyositis and received 2 courses of steroid pulse therapy. Two weeks after the second course of pulse therapy, receiving prednisolone at 50 mg/day, Ms. C became hypomanic and euphoric and was referred to our psychiatric department. Brain computed tomography (CT) scan and EEG showed no abnormality. She showed substantial improvement with neuroleptic medication and was followed up as an outpatient for mild mood lability. Her symptoms of dermatomyositis continued to be stable with a maintenance dose of prednisolone, 5 mg/day.

About 9 months later, Ms. C developed depressive stupor without any significant psychological stressor or

changes in prednisolone dose. She was admitted to our psychiatric ward and initially treated with intravenous clomipramine. She showed marked improvement within 2 weeks with combination treatment of clomipramine, 100 mg/day, and lithium carbonate, 300 mg/day. Since then, Ms. C has remained well on maintenance therapy with lithium carbonate.

Case 4. Ms. D, a 23-year-old woman, was admitted to the gastroenterologic ward for treatment of ulcerative colitis. She developed emotional lability, delusional mood, and increased motor and verbal activity 3 weeks after administration of betamethasone, 4 mg/day. Ms. D was referred to our psychiatric department and was diagnosed as having a hypomanic state with psychotic features. She improved with neuroleptic medication.

After 10 months, Ms. D became unable to speak and eat at home, and her family took her to the emergency unit of our department. She was mute and poorly responsive to questions. She showed no signs of neurologic disturbance, and betamethasone had been discontinued 10 months before. Ms. D was diagnosed as having depressive stupor and was treated with intravenous clomipramine. She became able to speak a little after finishing the infusion. All of Ms. D's symptoms quickly improved within 10 days. Intravenous clomipramine caused dizziness due to hypotension, and amoxapine, 150 mg/day, was prescribed instead after the sixth day. Brain MRI and EEG results were normal. A problem with her occupation was considered to have been a psychological stressor. Ms. D remained well and discontinued psychiatric medication after 11 months of maintenance therapy.

Case 5. Ms. E, a 47-year-old woman, had had SLE for 21 years, manifested by fever and arthritis, without involvement of the central nervous system (CNS). When she was 28 years old, she had a second relapse of SLE, and her dosage of prednisolone was increased. Ms. E was referred to our psychiatric department at that time because of a manic state characterized by pressured speech, flight of ideas, and severe aggressiveness. Haloperidol completely relieved her manic symptoms.

In the following 19 years, Ms. E had 2 manic episodes and 1 depressive episode in association with psychological stressors, such as overwork and marital problems, and 2 manic episodes in association with an increase in the dose of the corticosteroid. Only 1 manic episode with psychotic features developed during her clinical course. During her manic episodes, Ms. E always became markedly aggressive, compulsive, and sometimes confused. All episodes required psychiatric hospitalization. When she was depressed, she was treated with antidepressants, which did not cause manic change or deterioration. Lithium administration gave rise to polydipsia and polyuria. Ms. E showed improvement with neuroleptics in every episode and was functioning normally at work during remission. Her psychiatric symptoms were not correlated with the exacerbation of SLE and never improved with corticosteroid therapy.

Case 6. Ms. F, a 31-year-old woman, had SLE for 1 year. She had had no previous psychiatric episodes. At onset of SLE, she had brain infarction induced by CNS lupus and was treated with pulse methylprednisolone, 1 g/day. Her neurologic condition completely improved without any psychiatric symptoms. After 4 months, Ms. F received pulse therapy again, this time for peritonitis induced by SLE. During the maintenance treatment with prednisolone, she gradually became depressive. She manifested insomnia, irritability, agitation, and volitional inhibition and was referred to our psychiatric department. Ms. F's symptoms of SLE were inactive, and she had no signs of neurologic disturbance at that time. Brain CT scan showed no new lesions. Amitriptyline, 30 mg/day, relieved her depressive symptoms.

After 3 months, Ms. F was readmitted to the rheumatologic ward of our hospital because of another relapse of SLE. Prednisolone was increased to 30 mg/day. She showed irritability, insomnia, and persecutory delusion over 3 weeks. On referral to our department, she presented clinically with mutism, and haloperidol, 3 mg/day, was started. Although her symptoms were promptly stabilized, hypomanic state with euphoria, insomnia, and increased verbal activity emerged after discontinuation of haloperidol. With resumption of haloperidol, 1 mg/day, her mood promptly improved. Since then, she remained well on follow-up despite occasionally receiving prednisolone up to 15 mg/day for mild exacerbation of SLE.

Case 7. Mr. G, a 53-year-old man, had SLE for 6 years without involvement of the CNS. At onset of SLE, he was treated with prednisolone, 40 mg/day. After 2 months, Mr. G developed a manic state with grandiose delusions, increased motor activity, and abnormal behavior. He showed substantial improvement with haloperidol and remained well with a maintenance dose of prednisolone, 15 mg/day. Mr. G was readmitted to the nephrologic ward of our hospital because of exacerbation of lupus nephritis. Prednisolone was increased to 60 mg/day. He gradually showed increased motor and verbal activity, euphoria, and distractibility over 5 weeks. He was referred to our psychiatric department and was treated with zotepine, a thiepin derivative with antimanic action, at 25 mg/day. Brain MRI results were normal. Over the next month, Mr. G's mood improved markedly, and he was soon discharged home.

Case 8. Mr. H, a 42-year-old man, received a kidney transplant. After 3 weeks, he suffered from acute rejection and was treated with pulse methylprednisolone, 500 mg/day. Although his acute rejection was improved, he was referred to our psychiatric department because of a manic state that occurred 2 weeks after the beginning of pulse therapy. Increased motor and verbal activity, flight of ideas, and persecutory delusions were the prominent clinical features. Although Mr. H began to show gradual

improvement on haloperidol, 1.5 mg/day, and thioridazine, 25 mg/day, the acute rejection developed again. He was treated with another course of pulse methylprednisolone, 500 mg/day. He rapidly developed severe excitement and aggressive behavior with elevated mood and was involuntarily transferred to our psychiatric ward after sedation with intravenous diazepam. He showed substantial improvement with haloperidol and was discharged home 3 months later. During his stay at our ward, Mr. H had received 1 pulse therapy, but did not become manic.

Two months after discharge, he became depressed and attempted suicide related to worries about his company and his relationship with his wife. On readmission to our psychiatric ward, Mr. H gradually improved with valproate, 400 mg/day, and trazodone, 50 mg/day. Renal function was kept normal with methylprednisolone, 8 mg/day. Although he remained well during the 8 months after discontinuation of valproate, he transiently became hypomanic after his mother died. Mr. H promptly improved as soon as valproate was started again and remained well on follow-up.

Case 9. Mr. I, a 68-year-old man, was admitted to the nephrologic ward of our hospital for treatment of intractable nephrotic syndrome. He had received 2 courses of pulse methylprednisolone, 1 g/day, at another hospital. About 4 weeks after the beginning of the initial oral prednisolone treatment, Mr. I had gradually exhibited insomnia, pressured speech, and increased motor activity. These symptoms had worsened after the second pulse therapy.

At referral to our psychiatric department, Mr. I's symptoms included elevated mood, aggressiveness, and increased motor and verbal activity. Carbamazepine, 300 mg/day, and zotepine, 50 mg/day, were started, and his hypomanic symptoms gradually improved. His nephrotic syndrome was also brought under control with prednisolone, 20 mg/day. After discharge, his treatment was switched from carbamazepine, 300 mg/day, to valproate, 400 mg/day, because of dizziness. In the following 3 weeks, Mr. I complained of anorexia, anxiety, volitional inhibition, and depressed mood (which was worse in the morning) on prednisolone, 15 mg/day. Dothiepin, a tricyclic antidepressant with less anticholinergic action, was added at 50 mg/day, and his depression fully resolved over the next 6 weeks. Mr. I's condition continues to be stable on valproate, 400 mg/day.

DISCUSSION

Comparison With Previous Reports

To our knowledge, no previous report has focused only on corticosteroid-induced mood disorders diagnosed according to certain criteria. Therefore, we have reviewed the previous studies on steroid psychosis and compare these with our results.

Recurrence. It is widely accepted that affective symptoms are the most prominent clinical features in steroid psychosis.[2–7] Few studies have examined the recurrence of steroid psychosis in longitudinal follow-up. Although 1 or 2 of the 14 patients reported by Hall et al.[2] were probably recurrent, the authors did not describe the clinical features. Lewis and Smith[4] reported that 6 of 17 patients who had received 2 or more courses of steroid therapy had experienced recurrences of psychiatric symptoms. They mentioned only 1 case of mania and 1 case of delirium; the rest of the patients were not described in detail.

Given the different risks of recurrence between mood disorders and other psychiatric syndromes, it is necessary to prospectively investigate subjects categorized according to established clinical diagnostic criteria. Various risk factors for recurrence should be revealed with regard to therapeutic intervention.

Clinical characteristics of our patients. Interesting features of psychiatric symptomatology observed in our 9 patients included subacute onset, manic predominance, and frequent accompanying psychotic features.

Some previous reports[2,4] indicated acute onset, within several days to 2 weeks, probably because these studies included acute heterogeneous syndromes such as delirium. Naber et al.[7] reported that 13 hypomanic patients and 5 depressed patients fulfilled DSM-III-R criteria for an organic mood disorder among 50 ophthalmologic patients receiving corticosteroid treatment for 8 days. Since they did not follow up and assess psychiatric symptoms after the ninth day, transient alterations in mood that did not evolve into mood disorders may have occurred. Their results may, however, suggest that corticosteroid-induced mood disorder could be subclassified according to its latency of onset.

Depressive episodes appear to occur more frequently than manic episodes as a manifestation of corticosteroid-induced psychiatric syndromes.[4,5] Approximately 40% of patients in the literature were depressive, and 30% were manic or hypomanic. In primary bipolar disorders, both manic and depressive episodes are considered to occur with equal frequency over the longitudinal course.[14] Although it is known that depressive episodes are predominant in female patients,[14] no evidence has indicated manic predominance. In contrast, our 9 patients developed 21 manic episodes of a total of 32 mood episodes, which strongly indicates manic predominance in the clinical course. Even if we consider that the patients with recurrent mild depressive episodes are not always referred to psychiatrists, manic predominance would be the prominent clinical feature exhibited by recurrent patients of corticosteroid-induced mood disorder.

Goodwin and Jamison[14] estimated that among manic patients with psychotic features, 18% had auditory hallucinations, 47% had grandiose delusions, and 28% had persecutory delusions. In a previous report[4] on steroid psychosis, 56% of the depressed patients and 73% of the manic patients had had psychotic symptoms. Similarly, in

another review,[5] 51% of the patients who initially exhibited either hypomania or depression developed psychotic symptoms. Our findings also confirm the higher incidence of psychotic features (67%) than in primary mania, as is shown in these previous studies. However, no depressive episodes with psychotic features were seen in our severely depressed patients. Our results would account for manic predominance. It has been suggested that manic episodes are much more likely to occur with psychotic symptoms than depressive episodes in primary bipolar patients.[15] The frequent accompanying psychotic features are considered to be characteristic in recurrent patients of corticosteroid-induced mood disorder.[2–5] Only 1 of 7 patients who had single mood episodes in our series manifested psychotic features.

Why these clinical pictures appear is unknown. Although speculative, corticosteroid-induced mood disorder not only has the common pathomechanisms of primary bipolar disorders but also is associated with broader dysfunction in control of mood and cognition. In general, mania is considered a more severe pathologic condition than depression. The more severe discompensation of mood control in corticosteroid-induced mood disorder may contribute to manic predominance. Moreover, if this discompensation were to influence cognitive function, various psychotic features might easily appear.

Influence of psychosocial stressors. Seven of our 9 patients became manic or depressed without alterations in doses of corticosteroids. Significant psychosocial stressors preceded onset of episode in 4 patients. Some of these episodes could be distinguished from those closely associated with corticosteroid use, especially in patient 4. However, in patients 5 and 8, symptomatologically similar mood episodes occurred. Therefore, it is appropriate that our patients had their first mood episodes in association with corticosteroid treatment and showed recurrent courses due equally to the subsequent treatments and the psychosocial stressors. This finding indicates that the vulnerability to mood disorders caused by corticosteroid use is not specific to the subsequent corticosteroid challenge. A low maintenance dose of corticosteroid equivalent to prednisolone, 5 mg/day, influences the hypothalamic-pituitary-adrenal axis. It is quite plausible that intrinsic vulnerability to mood disorders is persistently maintained with relatively low doses of corticosteroids. Moreover, it is of interest to speculate that the vulnerability, once acquired, can be maintained for some time without persistent corticosteroid use in some subjects.

Influence of Steroid Pulse Therapy

Corticosteroid pulse therapy, represented by intravenous high-dose methylprednisolone, is commonly used in the hope that it will lead to more rapid effectiveness and/or less toxicity. To date, no studies have shown that psychiatric complications were observed more frequently with pulse therapy than with the usual oral administration.[16–18] However, in our series, 4 of 5 patients who received pulse therapy rapidly became manic or hypomanic. In another female patient, depressive symptoms gradually developed after pulse therapy. Rapid exacerbation of manic symptoms may indicate that high doses of corticosteroids, even if received in a short period, strongly induce psychological and behavioral changes in vulnerable subjects. Pulse therapy must be started carefully in patients with corticosteroid-induced mood disorder. However, we could not regard pulse therapy as a definite contraindication for these patients, because susceptibility to pulse therapy would be state dependent, as was seen in case 8, who did not exhibit manic symptoms after pulse therapy during admission to our psychiatric ward. Moreover, we can expect prophylactic effects with adequate pharmacotherapy, as was seen in case 2.

Pharmacotherapy

A few reports[9,10] suggest that lithium carbonate was effective for both mania and depression induced by corticosteroids. However, in clinical practice, quite a few diseases treated with corticosteroids, such as nephrotic syndromes or SLE, provoke renal dysfunction. Lithium carbonate should be carefully avoided. In these patients who are contraindicated to lithium therapy, we must choose the most beneficial mood stabilizer,[12,13,19] considering the underlying somatic dysfunction. It is strongly desirable to evaluate the effectiveness, including prophylaxis, of carbamazepine and valproate in controlled trials.

Hall et al.[2] observed exacerbations induced by tricyclic antidepressants in steroid psychosis and proposed to regard them as contraindicated. However, it appears that the 4 worsened subjects included in their study manifested some hypomanic or mixed symptoms. Accordingly, it is quite plausible that antidepressant therapy would have been inadequate in their study. Among the 8 patients who received antidepressants in our study, none experienced exacerbations. Moreover, intravenous clomipramine was obviously effective for 2 patients whose condition deteriorated into depressive stupor. The indication for antidepressants must be corroboratively reexamined in corticosteroid-induced mood disorder, because severe depressive episodes often occur in those individuals.

Viewpoint From Consultation-Liaison Psychiatry

In the management of corticosteroid-induced mood disorder, discontinuation of corticosteroids is ultimately desirable after the successful control of the underlying illness. Unfortunately, this goal is rarely achieved in clinical practice, and many patients must receive long-term corticosteroid therapy. These patients often experience various psychosocial difficulties and spend their lives under psychological stress, as well as suffering from recurrent courses of their illnesses. In fact, many recurrent episodes

occur in association with psychosocial stressors. As well as providing psychopharmacologic intervention, we have to cooperate closely with other physicians to prevent recurrence in these patients.

CONCLUSION

Recurrent cases of corticosteroid-induced mood disorder were characterized by subacute onset, manic predominance in longitudinal course, frequent accompanying psychotic features, and similar recurrent episodes in association with psychosocial stressors and corticosteroid use. Most episodes had a relatively good outcome, with full remission. Steroid pulse therapy must be carefully indicated because of the potential risk of mania. Mood stabilizers should be chosen according to the underlying illness. Antipsychotics and antidepressants are also useful when they are used appropriately. Continuous support by psychiatrists and their close cooperation with other physicians will contribute much to the quality of life of such patients. Further controlled prospective studies are strongly needed to throw some light on the pathomechanisms and treatments of corticosteroid-induced mood disorder.

Drug names: amitriptyline (Elavil and others), amoxapine (Asendin and others), carbamazepine (Tegretol and others), clomipramine (Anafranil and others), clonazepam (Klonopin and others), desipramine (Norpramin and others), diazepam (Valium and others), haloperidol (Haldol and others), methylprednisolone (Medrol and others), prednisolone (Prelone and others), thioridazine (Mellaril and others), trazodone (Desyrel and others).

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