Short report

State-dependent tardive dyskinesia in manic-depressive illness

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SUMMARY We report the occurrence of a drug-resistant tardive dyskinesia coexistent with Parkinsonism-like symptoms in a manic-depressive patient. The tardive dyskinesia completely disappeared during the manic phases and recurred after remission over the course of different mood-cycles.

Tardive dyskinesia is an extrapyramidal hyperkinetic syndrome which mainly affects the face, producing stereotyped and rhythmic movements of mouth, lips, tongue and jaws. These abnormal movements occur mainly following chronic neuroleptic drug treatment. The aetiology of this dyskinetic syndrome still is uncertain, the favoured hypothesis being the emergence of striatal dopamine-receptor supersensitivity after chronic dopamine-receptor blockade.¹⁻³ State-dependency of tardive dyskinesia in manic-depression has previously been reported by Ashcroft *et al*⁴ and Davies *et al*⁵ who indicated that abnormal movements deteriorated during mania and improved during depression. Cutler *et al*⁶ reported the reverse, namely two cases of tardive dyskinesia in manic-depression with dyskinetic symptoms recurring during depression and disappearing during mania. These observations are suggestive of an interaction between the biological changes associated with manic-depression and those mediating spontaneous or tardive dyskinesia. The present report is of a state-dependent tardive dyskinesia in a patient with manic-depressive illness: the tardive dyskinesia disappeared during the manic phases but reappeared in the euthymic interphases.

Case report

Mr S. was 40 years old when first seen by a psychiatrist. He had no prior history of psychiatric illness other than a brief episode of a tic-syndrome during childhood.

In 1976, following the death of his father, his wife noticed the emergence of periods of lassitude, alternating with periods of increased activity and nervousness. In February 1977, he developed a psychotic melancholic depressive syndrome, of acute onset, characterised by paranoid delusions, guilt feelings, self-accusations and visual hallucinations (devils and hell) threatening him with eternal condemnation for his sins. Neuroleptic treatment was started (haloperidol: 2.5 mg/day); a progressive improvement of the psychotic symptomatology followed but with no mood changes. A few days later the patient manifested a typical depressive syndrome with marked psychomotor retardation, clinophilia, guilt and hopelessness. Neuroleptic treatment was continued for three months (haloperidol: 5 mg/day), with slow improvement. The neuroleptics were replaced by a tricyclic antidepressant (trimipramine: 100 mg/day). On October 1977, the patient relapsed and presented a new psychotic episode characterised by mystical delusions, hyperactivity and insomnia. The neuroleptic treatment (haloperidol: 3 mg/day) was re-started and continued for 3 months, then was replaced by a benzodiazepine (bromazepam, dose unknown). A few months later, a new psychotic manic-like episode occurred and was successfully treated with haloperidol (3 mg/day). Neuroleptic treatment was continued up to 1979. In March 1979, a typical oro-bucco-lingual dyskinetic syndrome was first observed worsening after discontinuing neuroleptic treatment (fig). Various treatments were tried with unconvincing results (clonazepam pyridoxine, α -methyl dopa, amantadine, valproic acid). After initiating deanol (an acetylcholine precursor) the patient became agitated and the dyskinesia disappeared. The patient then developed an acute mania (insomnia, agitation and mystical delusions).

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Figure Time course of dyskinetic and manic symptoms, in relation to therapy.

Deanol was discontinued but the mania persisted necessitating hospitalisation. Haloperidol (3 mg/day) was initiated and the manic state remitted. The dyskinetic symptoms, however, reappeared with the clinical remission. Haloperidol was replaced by levo-mepromazine and in December 1979, lithium carbonate (750 mg/day) was added and continued thereafter. Severe tremor of an extrapyramidal nature were observed in the upper extremities. In May 1980, the patient developed a manic syndrome and the dyskinetic symptoms again completely disappeared. Fluphenazine was administered (intramuscularly 25 mg) and the psychotic state improved markedly but the dyskinesia reappeared with the clinical remission. Following clonazepam (2.5 mg/day) and thioridazine treatment (75 mg/day), the patient became hypomanic and the dyskinesia diminished. Clonazepam was withdrawn and a new manic state developed accompanied by a complete disappearance of the dyskinesia but not of the tremor. After increasing thioridazine, the mania improved and the dyskinesia reappeared.

In October 1981, the patient was admitted in our department in a normothymic state and treated with propranolol (up to 70 mg/day). The dyskinetic symptoms improved but propranolol had to be discontinued because of cardiovascular side-effects. A presynaptic dopamine depleting agent, tetrabenazine (up to 175 mg/day) produced a temporary amelioration of the dyskinesia, a worsening of the Parkinsonism-like symptoms and no mood changes. Finally, caeruleine (up to 0.03 µg/kg intramuscularly), a neuropeptide with antistereotypic effects in mice,⁷ had no effect on the dyskinetic nor on the Parkinsonism-like symptoms.

Discussion

The diagnosis of bipolar depression (rapid cyler) is consistent with the symptoms and episodic course of the illness. Despite lithium therapy, several manic-relapses occurred, as observed in rapid cyler patients, less responsive to lithium prophylaxis.⁸ After two years of neuroleptic treatment, the patient developed a dyskinetic syndrome. The most striking observation was the complete remission of the dyskinetic symptoms concomitant with a manic switch

and during the manic phases (to a lesser extent during hypo-mania), and its early reoccurrence in the euthymic interphases (fig). The sequence of the state-dependent tardive dyskinesia in our patient did not seem to be influenced by drug treatment and withdrawal, and was similar to the observations by Cutler *et al.*⁶ Our patient however presented tardive dyskinesia and Parkinsonism-like symptoms. Of these two coexistent extrapyramidal pathologies, only the tardive dyskinesia disappeared during the manic phases whereas the Parkinsonian symptoms remained unchanged.

If tardive dyskinesia results from the emergence of post-synaptic dopamine-receptor supersensitivity in the striatum, following prolonged neuroleptic treatment,¹⁻³ it is difficult to reconcile this state-dependent tardive dyskinesia with the current neurochemical hypotheses of affective disorders. Indeed, if we assume that mania is associated with a predominance of dopaminergic systems,⁹ we would hardly expect an amelioration of the dyskinesia during manic phases. If mania results from a relative hypoactivity of central cholinergic systems,¹⁰ an aggravation of the dyskinesia and a relief of the Parkinsonism-like symptoms would also be expected during mania. In this respect, it is interesting to notice that the first manic switch associated with a complete disappearance of dyskinesia was preceded by deanol treatment. The cyclical course of the dyskinesia observed in our patient is not consistent with a single biogenic amine hyper- and hypoactivity balance hypothesis of bipolar depression. Rather these rare occurrences of cyclical mood-dependent dyskinesia in bipolar rapid cyler patients suggest the presence of a common dopamine receptor instability in the courses of manic depression and tardive dyskinesia. Because of the reported high incidence of tardive dyskinesia induced by neuroleptics in depressed patients,¹¹ our data should also caution against the prolonged use of neuroleptics in patients suffering from affective illness.

References

- ¹ Baldessarini RJ. The pathophysiological basis of tardive dyskinesia. *Trends in Neuroscience* 1979;133-5.
- ² Marsden CD, Jenner P. The pathophysiology of extrapyramidal side-effects of neuroleptic drugs. *Psychol Med* 1980;10:55-72.
- ³ Klawans HL, Goetz CG, Perlak S. Tardive dyskinesia-review and update. *Am J Psychiatry* 1980;137(8):900-8.
- ⁴ Ashcroft G, Eccleston D, Murray LG, Glen IM. Modified amine hypothesis for the etiology of affective illness. *Lancet* 1972;ii:573-7.

- ⁵ Davies KL, Berger PA, Hollister LE. Tardive dyskinesia and depressive illness. *Psychopharmacology Com* 1976;**2**:125-30.
- ⁶ Cutler NR, Post RM, Rey AC, Bunney WE. Depression-dependent dyskinesias in two cases of manic-depressive illness. *N Engl J Med* 1980;**304**:1088-9.
- ⁷ Zetler G. Differential cataleptogenic and antistereotypic effects of caerulein and haloperidol. *Neuropharmacology* 1981;**20**:681-6.
- ⁸ Dunner DL, Fieve RR. Clinical factors in lithium carbonate prophylaxis failure. *Arch Gen Psychiatry* 1974;**30**:229-33.
- ⁹ Garver DL, Davis JM. Minireview: biogenic amine hypotheses of affective disorders. *Life Sci* 1979;**24**:383-94.
- ¹⁰ Janowsky DS, Davis JM, El-Youssef MK, Sekerke HJ. Cholinergic-adrenergic hypothesis of mania and depression. *Lancet* 1972;**ii**:632-5.
- ¹¹ Rush M, Diamond F, Alpert M. Depression as a risk factor in tardive dyskinesia. *Biol Psychiatry* 1982;**17**(3):387-92.