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# CASE REPORT

# Antidepressant Therapeutic Effect of Mianserin-Induced Generalized Tonic-Clonic Seizure in an Elderly Patient

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## SUMMARY

Generalized tonic-clinic seizures may appear as a side-effect of all antidepressant drugs, including mianserin. We present here a case of an 83-year-old woman whose major depressive episode (superimposed on mild dementia) completely resolved following a generalized tonic-clonic seizure. The improvement, which was maintained for 3 months, may be attributable to the drug-induced single convulsion. It would be of interest to know whether other psychiatrists have had similar experiences concerning an immediate antidepressant effect to a single tonic-clonic seizure (drug-induced or provoked by electroconvulsive therapy). If a subgroup of patients responsive to single generalized tonic-clonic seizure were to exist (especially among elderly patients), it would allow them to receive a minimal number of electroconvulsive therapy (ECT) sessions, decreasing the probability of the appearance of ECT side-effects.

KEY WORDS—convulsion; generalized tonic-clonic seizures; mianserin; antidepressant therapeutic effect; depression; elderly

The incidence of convulsions with most of the antidepressant drugs in common clinical use after oral administration of a therapeutic dose is 0.1–0.5%; mianserin is no more epileptogenic than the other tricyclic antidepressants (Edwards and Glen-Bott, 1983).

The production of a tonic-clonic type of generalized seizure is the mechanism behind the antidepressant therapeutic effect associated with electroconvulsive therapy (ECT) and pharmacoconvulsive therapy (Avery and Winokur, 1977; Weiner, 1985). However, there is no report of temporary or lasting antidepressant therapeutic effect due to generalized seizures induced by antidepressant drug treatment. We present here a case report of a major depressive episode remitting after a single generalized tonic-clonic seizure induced by mianserin treatment.

## CASE REPORT

Mrs T, an 83-year-old widowed lady, was referred to an ambulatory geriatric psychiatry unit because of a major depressive episode and because of symptoms suggesting cognitive decline. The depressive episode had begun 3 months earlier and the clinical picture was characterized by a depressive mood with occasional irritability, diminished interest and pleasure in almost all activities, decreased appetite, insomnia, diminished ability to concentrate and a

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sense of worthlessness and inappropriate guilt because of being a burden on her family—a sense that was severe, but not delusional. She had not had recurrent thoughts of death and suicide ideation. She was impaired in her capacity to feed herself, to dress herself and to maintain her personal hygiene. Two years before, she had begun to suffer from a slight memory impairment, but this impairment did not interfere significantly with her work, her social activities or her relationships with others.

On admission to the ambulatory geriatric psychiatry unit, the patient was psychiatrically evaluated, including a diagnostic work-up for dementia (Thompson, 1987). Her physical examination revealed a chronic obstructive lung disease, mild right hydronephrosis, mild to moderate left hydronephrosis, cholelithiasis, a left ovarian cyst, glaucoma of both eyes and a history of recurrent urinary tract infections. Review of medications showed that for a period of 3 years prior to the evaluation and afterwards, the patient was being treated with acetazolamide 250 mg twice a day and timolol maleate eye drops, one drop 0.25% solution in both eyes twice a day for her glaucoma, and also with acetylcysteine 200 mg twice a day. The above drugs are not implicated in causing cognitive decline and depressed mood except for timolol, which can cause depressed mood (Martindale, 1993c). However, because the patient had been treated with timolol eye drops without experiencing depressed mood for more than 3 years, the authors excluded timolol as a possible cause for depressed mood. There were no pathological findings in her laboratory tests including her serum levels of sodium, potassium, urea and creatinine. Her electrocardiogram, neurologic examination and electroencephalogram (EEG) also exhibited no pathological findings. A computerized tomographic scan showed mild brain atrophy, mild ventricular enlargement and two small calcifications with a diameter of less than 2 mm each. One calcification was localized in the posterior angle of the right lateral ventricle's body; the second calcification was localized in the periphery of the left frontal lobe cortex, near the falx cerebri. The two small calcifications showed no signs of mass effect. Chest X-ray revealed no evidence of significant pathological signs. When the patient's functional abilities were evaluated, she scored two points out of six on the Physical Self-Maintenance Scale (Lawton and Brody, 1969) and four points out of eight on the Instrumental Activities of Daily Living Scale (IADL; Lawton and Brody, 1969). Her Mini Mental State Examination (MMSE; Folstein *et al.*, 1975) score was 21/30. A neuropsychological examination demonstrated a mild decline in multiple cognitive functions, but also an impression that the degree of cognitive decline might be influenced by her depressive disorder. She scored 24 points on a 17-item Hamilton Depression Rating Scale (HDRS; Hamilton, 1960). She was evaluated separately by two psychiatrists, both of whom reported the existence of a differential diagnosis between: (1) mild dementia with depression and (2) pseudodementia as a manifestation of a major depressive episode. The above diagnoses were made according to DSM-III-R criteria (DSM-III-R; American Psychiatric Association, 1987).

Treatment was instituted for the depression, combining antidepressant medication and participation in the day care programme of the geriatric psychiatry ambulatory unit. Treatment with fluvoxamine was initiated with a gradual increase of dosage up to a maximum of 200 mg a day. Because of anxiety that had arisen at the beginning of treatment, the patient was also given oxazepam 20 mg a day. No therapeutic effect occurred within 4 weeks of treatment with fluvoxamine 200 mg a day. Her score on the HDRS at 4 weeks was 22. The fluvoxamine and oxazepam dosages were gradually reduced until they were completely withdrawn; treatment with mianserin was then prescribed. The dosage was gradually increased, but on the fifth day, with mianserin 45 mg a day, an episode of a generalized tonic-clonic seizure was observed by the day care staff and physician. She was given diazepam 10 mg iv and hospitalized in the geriatric department. Mianserin treatment was stopped. An EEG 24 hours after the convulsive episode was within normal limits. Treatment with phenytoin sodium was started orally. The patient was discharged with no antidepressant drug treatment, continued her participation in the day care programme and was monitored by the neurologist of the ambulatory geriatric psychiatry unit (including measurement of phenytoin levels that were in the appropriate range).

On psychiatric examination, there was immediate and significant improvement in all of the patient's depressive symptoms. The patient's score on the HDRS was five points. Two weeks after the convulsive episode, the patient's functional abilities were reevaluated. She was found to have significantly improved in her physical self-maintenance abilities, scoring five points out of six on the Physical Self-Maintenance Scale, while her IADL had improved slightly—she scored five points out of eight. However, her cognitive deficit remained the

same: she scored 22/30 on the MMSE. Three months after the convulsive episode, the patient was still free of symptoms of mood disturbance, though the mild dementia remained. It was concluded that the patient had suffered from dementia with depression, with the dementia most probably due to Alzheimer's disease.

## DISCUSSION

Major depression, especially in the elderly, often presents a dementia-like picture that is sometimes termed pseudodementia (Solomon, 1985; Wells, 1979) and this clinical entity needs to be distinguished from the disorder of dementia with depression (DSM-III-R; American Psychiatric Association, 1987).

However, in the present case, the depressive symptoms completely disappeared following a generalized tonic-clonic seizure, while the symptoms of dementia remained quite unchanged. This confirmed that the patient had suffered from dementia with depression.

Generalized convulsion of a tonic-clonic type may appear as a side-effect of all antidepressant drugs (De Jonghe and Swinkels, 1992) including mianserin. Convulsions induced by mianserin are uncommon events (Edwards and Glen-Bott, 1983). This side-effect occurs because antidepressant drugs decrease the seizure threshold (Hyman and Arana, 1991). The present patient, because of her cerebral lesions (two small calcifications and cerebral atrophy), had a predisposition to develop an epileptic seizure, but did not do so on fluvoxamine, perhaps because of a concomitant treatment with oxazepam. The patient had been treated with acetazolamide for her glaucoma for the past 3 years. This is used in some forms of epilepsy as an antiepileptic drug. Even though she had been treated with this drug, she developed a tonic-clonic type of generalized seizure. On the other hand, acetazolamide, like other antiepileptics, can in itself induce convulsion, raising the possibility that it was the combination of acetazolamide and mianserin that induced the seizure; however, the authors' assumption is that the convulsion was most probably caused by mianserin in this predisposed patient as indicated above. The clinical improvement in depressive symptoms may be attributable to the drug-induced single convulsion acting as if it were the therapeutic effect of one session of ECT.

The indications for ECT in the elderly are similar to those in a younger population. In the elderly, as in all groups of depressives, there are occasions when ECT should precede a therapeutic drug trial (Greenberg and Fink, 1992). Patients being treated for depression with ECT typically show some improvement after the first few sessions, with peak response between 5 and 10 (Weiner, 1985). Complete resolution of a depressive episode with a single convulsion when induced by ECT is extremely rare. In the present case, significant improvement in the depressed mood appeared after a single generalized convulsion due to mianserin treatment. The variety of cognitive effects of ECT range from brief postictal confusion (Daniel and Crovitz, 1986) to a period of anterograde and retrograde memory defects during illness and treatment; for most individuals these disturbances subside over the ensuing 6–8 weeks (Squire, 1986). Clinical experience suggests that geriatric patients develop more profound and longer-lasting memory problems than younger adults as a result of ECT (Alexopoulos, 1992).

In the present case, a single tonic-clonic type of generalized seizure due to drug treatment led to the complete disappearance of depressive symptoms, with the improvement being maintained at follow-up after 3 months. The possibility is raised whether a 'chance' or a drug-induced convulsion may have a different treatment effect (possibly more rapid) than a convulsion induced as part of ECT treatment. It would be of interest to know whether other psychiatrists have had similar experience concerning an immediate antidepressant effect to a single tonic-clonic seizure (drug-induced or provoked by ECT). If patients responsive to single generalized tonic-clonic seizure were to exist (especially among elderly patients), it would allow them to receive a minimal number of ECT sessions, decreasing the probability of the appearance of ECT side-effects.

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