Reversible Pathologic Jealousy (Othello Syndrome) Associated With Amantadine

Patrick McNamara; Raymon Durso, MD

Abstract

We describe a case of pathologic jealousy (Othello syndrome) in a patient with Parkinson disease, which abated after discontinuing amantadine. We indicate that early recognition and treatment of the syndrome in this disease may avert physical violence. We also believe that our report further suggests a link between this specific behavioral disorder and dopaminergic activity. (*J Geriatr Psychiatry Neurol* 1991;4:157–159).

Othello syndrome is an illness in which a delusion of infidelity of the spouse is the central dominating symptom.[1,2] In Shakespeare's play, Othello becomes psychotic after he discovers that he can be jealous. Once tapped, this jealousy grows to delusional proportions until it totally consumes him. As a consequence, Othello murders his wife in a jealous rage. Early diagnosis of this syndrome is crucial because homicide can occur in association with the disorder.[1]

Othello syndrome has been described in a number of different neuropsychiatric illnesses including manic-depressive illness, epilepsy, dementia, and alcoholism.[1–3] We now present its occurrence in a patient with Parkinson disease in whom the antiparkinsonian drug amantadine appears to have played an essential etiologic role. The striking observation in this case was the abrupt clearing of the delusional jealousy after withdrawal of this medication.

Case Report

This 74-year-old male was admitted to the Boston Veterans Administration Medical Center from the Parkinson/Movement Disorder Clinic with a 6-week history of delusional jealousy. He had a diagnosis of Parkinson disease for 6 years and had been treated with amantadine (100 mg twice daily) as his only antiparkinsonian medication for the prior 4½ years. Past medical history was significant for a suprapubic prostatectomy for benign prostatic hypertrophy 17 years earlier and hypertension for which he took hydrochlorothiazide 50 mg once daily. There was no significant past psychiatric history. His wife (a 68-year-old woman with no notable psychiatric or neurologic history) had brought the patient to the clinic before his regularly scheduled appointment because she had become increasingly fearful of her husband's threats. She stated that he had been accusing her of being unfaithful. Although the patient could not describe the man his wife was supposedly having an affair with, he believed that he constantly heard his wife talking with someone in another room. Whenever he tried to discover who the individual was, the person abruptly left "in order not to be discovered." "He [the supposed interloper] often escaped through the front door." Similarly, the patient claimed to have heard the man taking showers in the bathroom but again never could find him in the act. He reported that this individual arrived at the house every night in a different car so that he (the husband) would not get suspicious. At one point, the patient saw red lights out the front window of the house and a bright white spotlight out the back window. He believed this was a signal from the man

Received Jan 30, 1991. Received revised Feb 26, 1991. Accepted for publication Apr 11, 1991.

From the Departments of Neurology at Boston University School of Medicine and the Boston Veterans Administration Medical Center, Boston, MA.

Please address correspondence to Dr Raymon Durso, Director, Parkinson Clinic, Department of Neurology, Boston Veterans Administration Medical Center, 150 South Huntington Avenue, Boston, MA 02130.

to his wife but could not explain exactly what it meant.

The wife denied the patient's allegations and was shocked by his accusations. A daughter who lives near the couple supported the wife's position. These accusations became progressively intense, and the wife finally found them unbearable when they took on a quality of threatened physical violence (about 1 week prior to admission). She stated that no amount of evidence could convince the patient of the falsity of the accusations. When one of us (R.D.) questioned him in this regard he replied firmly "Look doc, I know what's going on, you don't!" The wife stated that the patient had no other specific delusions or hallucinations concerning any other part of their lives. She also related that he had "never been a jealous man" and that this behavioral change was totally unlike his usual personality. This assessment was obtained in extensive interviews by several hospital staff.

The patient was told to discontinue his amantadine, and hospitalization at the Boston Veterans Administration Medical Center was arranged for the following day. On admission, medical personnel noted that he was calm and not hallucinating, although the delusional jealousy persisted. Mental status examination revealed an alert and fully oriented elderly male with no evidence of an acute confusional state. He made one error in naming the last five presidents of the United States. Four of four objects were recalled with cuing. Digit span was 7 forward and 3 backward. Serial sevens were poorly performed. Speech was hypophonic but fluent. Naming, repetition, and reading were intact. There was no evidence of aphasia or agnosia. There was no right-left confusion or apraxia for facial, buccal, or appendicular tasks. Script was micrographic and designs were poorly drawn. A masklike facies was present. His motor examination revealed moderate bradykinesia and cogwheel rigidity of all four limbs. A mild pill-rolling tremor was present at rest in both upper extremities. Gait was characterized by a flexion posturing of the head and trunk with en bloc turning, a reduced stride, and extra steps on turns. Strength was intact in all four limbs. Cranial nerve, cerebellar, and sensory examinations were unremarkable. Deep tendon reflexes were symmetrical and normal in amplitude with flexor responses noted on plantar stimulation. Complete blood count and blood chemistries were unremarkable.

Over the next 3 days following admission, the patient's delusions concerning his wife quickly subsided. On the fourth day (5 days after discontinuing amantadine) the patient stated that "the man at home was a false . . . he disappeared out of my life." Two days later, he was astonished that he could believe his wife capable of infidelity. A repeat mental status examination at this point was essentially within normal limits, though digit span backwards was still poor (equal to 3).

He was begun on trihexyphenidyl, 2 mg twice daily, which he tolerated well, and he was discharged. On follow-up 1 month later, the patient remained free of any delusions. Over the last 4 years he has received small doses of trihexyphenidyl, carbidopa/levodopa, and bromocriptine. His most recent regimen (December 1990) was bromocriptine, 2.5 mg twice daily; carbidopa/levodopa, 25/100 mg twice daily; and trihexyphenidyl, 2 mg twice daily. He maintains a good antiparkinsonian effect from these medications without any return of delusions or hallucinations.

Discussion

Our patient presented with a relatively pure and classic case of delusional and morbid jealousy—Othello syndrome. By *DSM-III-R* diagnostic criteria, he would be characterized as having an organic delusional syndrome identical in symptomatology to a delusional disorder of the jealous type. Specific criteria for the latter are that (1) the delusion is of at least 1 month's duration, (2) hallucinations, if present, are not prominent, (3) apart from the delusion, behavior is not obviously odd or bizarre, and (4) the predominant theme of the delusion is that one's sexual partner is unfaithful. Further criteria for an organic delusional disorder require that the delusion not occur exclusively in the course of delirium. Our patient accordingly evidenced no signs of delirium or dementia, was free of auditory and visual hallucinations, and lacked any other delusions not related to his wife's supposed infidelity. This remarkably specific and circumscribed delusion intensified over a period of a month and a half before his wife decided to seek help. Interestingly, Enoch and Trethowan[1] report that the typical presentation includes sudden onset and 2 to 3 months of increasing suspicion often leading up to physical violence. As in our patient, the imagined lover is often unidentified and not even the simplest details concerning the interloper (eg, name and address) can be supplied.

The dramatic change in personality in the absence of a previous psychiatric history and with a lack of significant neurologic findings (other than those associated with his Parkinson disease) led to

the hypothesis that the delusional syndrome was related to amantadine. The latter is further supported by the rapid clearing of his jealousy after amantadine was discontinued. We believe that a spontaneous resolution was unlikely, since the delusion had become increasingly more intense over the 6 weeks prior to admission. We also assert that the delay between the initiation of amantadine and the development of this delusion (4½ years) is not unusual for drug-induced psychiatric complications in Parkinson disease. In fact, chronic (as opposed to short-term) dopaminergic therapy may be a prerequisite to the development of psychosis and hallucinations associated with treated Parkinson disease.[4] The basis of this hypothesis relates to the observation that chronic stimulation of dopamine receptors by dopamine or dopamine agonists leads to receptor hypersensitivity.[5,6] Rechallenge with amantadine in order to further prove an etiologic role for the drug was considered but decided against. Instrumental in this decision was his wife, who had been very frightened by the patient's threatened physical violence. In addition, the patient had obtained an acceptable response with other antiparkinsonian agents.

Amantadine hydrochloride (Symmetrel) was first used in the 1960s as an antiviral agent.[7] Initial reports of definite antiparkinsonian effects were given in 1969 by Schwab et al,[8] and the latter has since been repeatedly confirmed.[9] The capability of treating Parkinson disease signs and symptoms relates primarily to its ability to facilitate release and inhibit reuptake of dopamine from central nerve terminals.[10] We would thus propose that the delusional syndrome observed in our patient may have been related, in part, to amantadine's effect on central dopaminergic pathways. A role for dopamine in Othello syndrome is supported by Mooney[3] and Munro.[11] Both of these investigators have reported an excellent response in affected patients to dopamine antagonists (neuroleptics). It is clear, however, that amantadine's ability to induce pathologic jealousy in our patient was more complex than the simple enhancement of dopamine because this behavior has not recurred with use of other dopaminergic agents (ie, carbidopa/levodopa and bromocriptine).

We believe this report further emphasizes the link between neuropharmacology and even specific forms of behavior that might be encountered in treated Parkinson disease patients. To the extent that similar cases are recognized early in their course, our experience suggests that potential tragedy such as violent assault can be averted with appropriate medication adjustment, and the ultimate outcome can be excellent.

Acknowledgments

The authors are grateful to Dr Janice E. Knoefel for her review and suggestions in the preparation of this manuscript. We also thank Dr Paul Malloy, Sue E. Jolly, and Lisa Trepanier for their helpful and informative discussion of the case.

References

1. Enoch MD, Trethowan WH: *Uncommon Psychiatric Syndromes*, 2nd ed. Bristol, England, John Wright & Sons, 1979.
2. Cummings JL: Organic delusions: Phenomenology, anatomical correlations and review. *Br J Psychiatry* 1985;146:184–197.
3. Mooney HB: Pathologic jealousy and psychochemotherapy. *Br J Psychiatry* 1965;111:1023–1042.
4. Moskowvitz C, Moses H, Klawans HL: Levodopa-induced psychosis: A kindling phenomenon. *Am J Psychiatry* 1978;135:669–674.
5. Klawans HL, Margolin DI, Dana N, et al: Supersensitivity to *d*-amphetamine and apomorphine-induced stereotyped behavior induced by chronic *d*-amphetamine administration. *J Neurol Sci* 1975;25:283–289.
6. Klawans HL, Goetz C, Nausieda PA, et al: Levodopa-induced dopamine receptor hypersensitivity. *Ann Neurol* 1977;2:125–129.
7. Davies WL, Grunert RR, Haff RF, et al: Antiviral activity of *l*-adamantamine (amantadine). *Science* 1964;144:862–863.
8. Schwab RS, England AC, Poskanzer DC, Young RR: Amantadine in the treatment of Parkinson's disease. *JAMA* 1969;208:1168–1170.
9. Kulisevsky J, Tolosa E: Amantadine in Parkinson's disease, in Koller WC, Paulson G (eds): *Therapy of Parkinson's Disease*. New York, Marcel Dekker, 1990, pp 143–160.
10. Bianchine JR: Drugs for Parkinson's disease, spasticity and acute muscle spasms, in Gilman AG, Goodman LS, Rall TW, Murad F (eds): *The Pharmacologic Basis of Therapeutics*, 7th ed. New York, Macmillan, 1985, pp 473–490.
11. Munro A: Excellent response of pathologic jealousy to pimozide. *Can Med Assoc J* 1984;131:852–853.