and disturbed biological functions, and she was diagnosed with schizophreniform disorder. Past and family history revealed no psychiatric or neurological illness. Initially, she was treated with trifluoperazine (15mg/day) for 4 months, which was replaced with clozapine due to severe akathisia. The dose of clozapine was increased from 25mg to 100mg/day over a period of 2 weeks after performing hematological investigations, and she was maintained on the same dose for 4 months.

While being treated with clozapine, Mrs. F developed frequent and forceful blinking of her eyelids. She would blink her eyes about 40 times in a minute when exacerbated by bright light. An ophthalmological consultation was unremarkable for any eye pathology contributing to this presentation and the neurological exam did not reveal any abnormal movements, except for the blepharospasm. The patient had no prior personal or family history of blepharospasm or other movement disorders.

Five months later, clozapine was tapered and stopped, but Mrs. F continued to have blepharospasm even 4 weeks after discontinuing clozapine. Subsequently, clonazepam (1mg/day) was started and the blepharospasm disappeared a month after its initiation. Two years later, the patient had a second episode of psychotic illness and was again treated with clozapine, titrated up to 75mg/day. Five weeks later, she exhibited a similar form of blepharospasm, though it was not as severe. Again, clozapine was discontinued and Mrs. F had a complete resolution of the blepharospasm with clonazepam.

Comment

The reappearance of blepharospasm with the administration of clozapine strongly implicates this drug in this dystonic reaction. Blepharospasm is classified as a type of focal dystonia and has been reported to occur with atypical antipsychotics. In contrast to other atypicals, such as olanzapine, which have been anecdotally reported to cause tardive dystonia,[2] clozapine has been used in treating tardive dystonia, including blepharospasm.[3,4] However, in rare instances, clozapine has been reported to induce tardive dystonia as well.[5] In the above case, the patient developed cervical dystonia 2 years after clozapine was started. Given the rarity of reports of clozapine-induced tardive dystonia, our patient may have developed an idiosyncratic reaction to this drug. This is further supported by the observations that this patient did not develop tardive dystonia with trifluoperazine, which is a more potent D_2 receptor antagonist than clozapine, and that the proposed mechanism of drug-induced tardive dystonia is the sensitization of dopamine receptors following their blockade.[6] Another issue highlighted by this report and the existing literature is that clonazepam is an effective treatment of tardive dystonia,[3] and may be considered before more invasive procedures, such as botulinum toxin, are tried.

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References

1. Sienaert P, Peuskens J: Remission of tardive dystonia (blepharospasm) after ECT in a patient with treatment-refractory schizophrenia. J ECT 2005; 21:132–134
2. Charfi F, Cohen D, Houeto JL, et al: Tardive dystonia induced by atypical neuroleptics: a case report with olanzapine. J Child Adolesc Psychopharmacol 2004; 14:149–152
3. Shapleske J, Mickay AP, Mckenna PJ: Successful treatment of tardive dystonia with clozapine and clonazepam. Br J Psychiatry 1996; 168:516–518
4. Levin H, Reddy R: Clozapine in the treatment of neuroleptic-induced blepharospasm: a report of 4 cases. J Clin Psychiatry 2000; 61:140–143
5. Molho ES, Factor SA: Possible tardive dystonia resulting from clozapine therapy. Mov Disord 1999; 14:873–874
6. Trugman JM, Leadbetter R, Zalis ME, et al: Treatment of severe axial tardive dystonia with clozapine: case report and hypothesis. Mov Disord 1994; 9:441–446

Clozapine-Induced Cataplexy

SIR: Cataplexy is an abnormal state characterized by atonia and believed to represent dissociated REM (rapid eye movement) phenomena that intrude into wakefulness. Cataplexy-like phenomenon as a rare side effect of clozapine treatment was initially reported by Chiles et al.[1] in a series of four people with schizophrenia who were on variable doses of clozapine. Blum[2] also noted cataplexy during clozapine treatment along with hyperthermia and increased REM sleep. We report another patient presenting with this rare side effect of clozapine and attempt to explain the phenomenon with possible neurobiological mechanisms.

Case Report

A 29-year-old unmarried woman with unremarkable past, family and personal history presented with an episodic illness of 4 years duration suggestive of schizoaffective disorder, manic type. As she remained symptomatic even after adequate trials with various antipsychotics along with mood stabilizers, clozapine was introduced. She was on a regimen of sodium valproate, 1000mg/day, when clozapine was initiated and gradually hiked to 150mg/day. Though her symptoms

decreased significantly, she started complaining of a sudden onset of knee-buckling along with dropping objects, which was not associated with any emotional trigger, loss of awareness, or falling. She did not complain of sleep troubles at that time. The phenomenon started occurring in the first week after reaching 150mg/day and was taking place two to three times per day. A detailed neurological examination and laboratory work-up were unremarkable. Valproate serum levels were at 120 and 125μg/dl on two different occasions. A 32-channel 1-hour EEG (electroencephalogram) study revealed background slowing in 4.5–5 Hz theta range with no epileptiform abnormality. Clozapine was reduced to 125mg/day and cataplectic attacks decreased in frequency to one to two attacks on alternate days. Repeat EEG after a month was similar to the previous one. Increasing the dose of sodium valproate to 1200mg/day did not alter the frequency of such attacks. Because she continued to drop objects, administration of clozapine was stopped, followed by complete cessation of cataplexy attacks.

Comment

We can make three important observations from the case presentation. The example of cataplexy in our case was mild and probably a nonepileptic phenomenon. Such EEG descriptions were not previously included in Chiles' case series. Additionally, our patient did not have any sleep disorder. This corroborates with Chiles' description and the dissociation is supported by the recent finding that mechanisms for triggering cataplexy are different from those for REM sleep.[3]

The exact mechanism of drug-induced cataplexy is still unknown. Work on canine narcolepsy[3] suggests abnormality in the noradrenergic system, which influences dopamine D2/D3 receptors via a presynaptic mechanism, as key for generation of cataplexy. Another important mechanism is a lack of orexin-induced facilitation of motoneurons in cataplexy.[4] Clozapine is known for antagonism of noradrenergic α_1 and α_2 receptors and a recent study found that it can inhibit orexin A action.[5] Based on these recent neurobiological insights, we propose that clozapine's significant antiadrenergic effects coupled with inhibition of orexinergic transmission could possibly underlie the emergence of cataplexy.

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References

1. Chiles JA, Cohn S, McNaughten A: Dropping objects: possible mild cataplexy associated with clozapine. J Nerv Ment Dis 1990; 178:663–664
2. Blum A: Triad of hyperthermia, increased REM sleep, and cataplexy during clozapine treatment? J Clin Psychiatry 1990; 51:259–260
3. Nishino S, Arrigoni J, Valtier D, et al: Dopamine D_2 mechanisms in canine narcolepsy. J Neurosci 1991; 15:2666–2671
4. Yamuy J, Fung SJ, Xi M, et al: Hypocretinergic control of spinal cord motoneurons. J Neurosci 2004; 24:5336–5345
5. Monda M, Viggiano A, Viggiano A, et al: Clozapine blocks sympathetic and thermogenic reactions induced by orexin A in rat. Physiol Res 2004; 53:507–513

A Sibutramine-Induced Delusional Disorder Relapse

SIR: Sibutramine, an antiobesity drug, is a serotonin, norepinephrine, and, to a minor degree, dopamine reuptake inhibitor. Sibutramine has been associated with previous reports of psychosis,[1] hypomania and mania,[2,3] exacerbations of panic attacks,[4] depression, and suicidal tendencies.[5] Its abuse is currently under investigation. We report a patient who experienced a delusional disorder relapse shortly after being started on a regimen of sibutramine.

Case Report

A 50-year-old man presented with an acute paranoid state and behavioral alterations. He was diagnosed in 1987 as having a delusional disorder due to a paranoid and esoteric systematized delirium. Maintenance treatment with thioridazine (50mg/day) provided him with a mental state fit for social and work environments with only three similar relapses in 15 years. He was married, had one daughter, and worked in a company business.

On June 27, 2002, he was prescribed sibutramine, 9mg b.i.d., to treat obesity. Two days later, he began to feel anxious, with concentration and coordination difficulties mainly in vehicle conduction. The patient reduced the sibutramine dosage himself to 9mg/day. Over the next two weeks, his mental state continued to deteriorate. He presented with an acute florid delirious state associated with intense reference, suspiciousness, anxiety, and insomnia, requiring hospital admission. He denied any other psychiatric treatment, neurological disturbance, or substance abuse. Sibutramine treatment was discontinued and replaced by antipsychotic treatment. During the following 3 weeks, symptoms completely resolved. Diagnosis was a delusional disorder relapse without considering a potential sibutramine influence.

A few weeks later, sibutramine was reintroduced (9mg/day). Within days, he suffered another relapse with intense reference and