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Case Report

Psychiatry/Mental Health Section

A Case of SSRI Induced Irreversible Parkinsonism

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ABSTRACT

Serotonin specific reuptake inhibitors (SSRI) are widely used antidepressants for variety of clinical conditions and have found popularity. They are sometimes associated with extrapyramidal side effects including Parkinsonism. We report a case of generalized anxiety disorder on treatment with SSRI (fluoxetine / sertraline) who developed irreversible Parkinsonism. SSRI are known to cause reversible or irreversible motor disturbances through pathophysiological changes in basal ganglion motor system by altering the dopamine receptors postsynaptically. Clinician should keep risk benefit ratio in mind and change of antidepressant of different class may be considered. Case is reported to alert physicians to possibility of motor system damage while treating with SSRI.

Keywords: Drug induced parkinsonism, Epidemiology, Fluoxetine, Sertraline

CASE REPORT

A 29-year-old serviceman with no past or family history of any neurological illness was posted to Northern India. He manifested with tremors in his hands around Jan 2007 while doing military drills and weapon training. He was distressed and suffered loss of confidence. Subsequently, he also complained of nocturnal emissions and some odd sensation of ants crawling over his hands and feet. A psychosocial stressor was present in form of his wife undergoing three abortions in last four years of their marriage. He self reported to medical specialist and was evaluated to have digital tremors and warm moist palm. His thyroid status and CT scan brain were normal. Subsequently neuro-physician at higher centre evaluated him for postural tremors and undue anxiety and referred him to psychiatrist. Psychiatrist in Sep 2007 noted him to have tension, free floating anxiety, digital tremors, complaining of odd sensations in limbs, dizziness disturbed biodrives and inability to relax for more than six months and as per International Classification of Diseases 10 (ICD 10) used in services he was diagnosed and managed as a case of generalized anxiety disorder (GAD) with cap fluoxetine 20 mg once daily, clonazepam (0.5mg) thrice daily for short term and was placed under psychiatric surveillance with sheltered duties. During follow up individual was compliant with medications and was broadly asymptomatic till Sep 2009 excepting for having mild digital tremors and anxiety off and on. Individual had first relapse in Dec 2009 in the background of non compliance of medications for three months. He manifested with complaints of heaviness of head, tension, apprehension in chest and tremors. He was treated by psychiatrist with reinstitution of SSRI and discharged after one month of inpatient treatment on maintenance medication of tab sertraline 100 mg and propranolol 40 mg. Individual took medications for about three years but in Dec 2012 individual felt distressing tremors of whole body, apprehensive feeling in chest, generalized weakness, inability to sleep and difficulty to carry out day to day activities like brushing teeth, shaving and even had difficulty in signing cheques. He stopped all medication by himself as it didn't benefit him at all and reported to us in early April 2013 (35 years of age). His examination revealed facial flushing, crouched posture, intubation of head, bilateral tremors of hand and feet, blank staring looks, reduced psychomotor activity, quivering voice, reduced speech volume and tone, anxious cognition and subjective sense of uneasiness. He denied any depressive cognition or suicidal thoughts. He was managed with tab sertraline 50 mg twice daily, buspirone 5 mg thrice daily and clonazepam 1mg thrice daily and differential diagnosis of 1) GAD Relapse 2) GAD with thyroid dysfunction 3) GAD with alchohol withdrawal (due to easy availability of alcohol and peer pressure of drinking in soldiers) was entertained. Lab investigations including routine heamogram, Liver function test, Gamma-glutamyl transferase (GGT), USG abdomen, T3, T4, TSH and MRI brain were normal. He showed 20% improvement in form of reduction in facial flushing reduced subjective sense of distress, apprehension, weakness and improved biodrives within 10 days. However expressionless face, diminished speech prosody, persistence of tremors of hands and feet, reduced arm swing and rigidity persisted. His psychotropics were stopped. He was diagnosed as a case of GAD with Parkinsonism and sent for neurophysician evaluation who started patient on anti-parkinsonian drugs tab syndopa (110 mg) thrice daily, clonazepam (0.5 mg) thrice daily, inderal (40 mg) ½ twice daily with rapid improvement in his distressing motor symptoms. Revised diagnosis of Drug-induced Parkinsonism (DIP) with GAD was entertained. Patient was much improved in his facial expressions & was able to walk, shave and write in couple of days. After three month an attempt was made to taper off and stop his anti-parkinsonian drugs but there was reappearance of rigidity, tremors and bradykinesia. He was managed as a case of DIP and GAD on anti-parkinsonian drugs and mitrazapine 15mg once daily for five months. He was lost on follow up.

DISCUSSION

SSRI have relatively safe side-effect profile but are common offending agents among antidepressants to cause variety of movement disorders [1,2]. DIP can be induced by SSRI which can be reversible [3] or irreversible [4]. DIP is thought to rank second in order after Parkinson's disease (PD) in causing Parkinsonism, accounting for up to 20% of the PD cases [5]. The exact prevalence and incidence of DIP are unclear because it is frequently unrecognized or misdiagnosed as PD. A study from Bangalore in elderly home showed that 24% had parkinsonism, with PD being the commonest (71%) followed by DIP (2.5%) [6]. A 17 years study showed 20,855 adverse drug reactions, including 155 (0.7%) cases of drug-induced or worsened parkinsonism [7].

Earlier amongst SSRI fluoxetine was implicated in most cases of extrapyramidal symptoms (EPS) [1] subsequently sertraline [4,8],

citalopram [3], fluvoxamine [9] have also been implicated in DIP. Majority of cases are geriatric age group [3,4,9,10] females [3,9,10] who developed SSRI induced parkinsonism following short or long term exposure to SSRI. Review of case reports related to SSRI induced EPS revealed akathesia (45.1%) followed by dystonic reactions (28.2%), parkinsonism (14.1%) and tardive dyskinesia (11.3%). Elderly, female, pre-existing extrapyramidal disorder and other concurrent neuroleptic medications were considered risk factors [1]. There are two reports of sertraline-induced parkinsonism in elderly where parkinsonian symptoms did not resolve upon cessation of sertraline and patient had deteriorating course, eventually being diagnosed with PD [4,10]. Our patient on the other hand didn't share the risk factor of age, sex and developed parkinsonism induced by sertraline which warranted antiparkinsonian treatment. When dechallenged parkinsonism again reappeared. Recently escitalopram related pseudo-parkinsonism was reported in young male following short exposure of few weeks with full recovery [11]. Few Indian authors also reported pseudo-parkinsonism [12,13] in younger patients soon after starting fluoxetine however our patient differed from them in irreversibility of parkinsonism and longer duration of treatment with SSRI.

Most common causative agents of DIP are antipsychotics and antiemetics (domperidone, metoclopramide). Other drugs commonly associated are calcium channel blockers (flunarizine, cinnarizine and verapamil), Mood stabilizers (Valproate, Lithium) and others.

Extrapyramidal side effects of sertraline and other SSRI are thought to be secondary to the inhibitory effects of serotonin on dopamine neurotransmission within the basal ganglion system which may alter function in the striatum and induce a parkinsonian syndrome [8]. SSRI-induced parkinsonism may also represent a pre-existing vulnerability to future Parkinson's disease [9]. While one prospective study reported SSRI does not worsen Parkinson's disease [14]. Treatment of drug induced parkinsonism involves discontinuation of the offending drugs, which usually promotes remission of the parkinsonian syndrome within a short time, although parkinsonism may sometimes persist and require dopaminergic treatment as happened in our case. DIP is clinically indistinguishable from PD. Single-photon emission computed tomography (SPECT) imaging helps to determine whether DIP is entirely drug-induced or an exacerbation of subclinical PD [15].

Our patient was relatively young male he satisfied the clinical diagnostic criteria for DIP i.e the presence of Parkinsonism, no history of Parkinsonism before the use of the SSRI and onset of parkinsonian symptoms during use of the offending drug. He was on sertraline for about three years before developing DIP which was irreversible and warranted anti parkinsonian treatment to improve quality of his life. There was no known concomitant offending drug used beside SSRI. His PD was possibly unmasked by the sertraline.

CONCLUSION

SSRI are widely used agents in depression, generalized anxiety disorders, obsessive compulsive disorders, panic disorder, nocturnal enuresis and impulse control disorders. Clinicians should be careful if any motor symptoms appear or are reported in patients using SSRI as it can lead to diagnostic or treatment errors. This case report was an attempt to create an awareness of DIP as adverse reaction in patient taking SSRI so that timely recognition can prevent such adverse effects.

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