A RARE CASE OF NEUROLEPTIC INDUCED TARDIVE TICS RESPONDING TO CLOzapine - A CASE REPORT
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Abstract: The new generation of atypical antipsychotic agents has reduced concerns about tardive dyskinesia (TD), to some extent. Yet this disorder remains asignificant clinical problem for both patients and treating psychiatrists in few cases. Where we report a case 37 year old male with four and half year duration of psychotic illness, was on treatment with atypical antipsychotics presented with involuntary movements of neck and oro facial region which was diagnosed as tardive dyskinesia in the form of tardive tics. He was then started on clozapine one month back and the problem have decreased and patient is maintaining well with medications.

Keyword: tardive dyskinesia, tardive tics, risperidone, clonazapine

INTRODUCTION:
Neuroleptic induced tardive dyskinesia is the chronic form of drug induced movement disorder and is related to total lifetime of treatment, with cumulative incidence of 5% per year. In the past, tardive dyskinesia was used to describe the classical rhythmic oral-facial movements (1) but is now renamed as tardive stereotypies.

Tardive syndromes (TS) are a group of delayed-onset abnormal involuntary movement disorders induced by a dopamine receptor blocking agent. (2) Tardive dyskinesia also includes tardive chorea, tardive dystonia, tardive akathisia, tardive tics, tardive myoclonus and tardive tremors. A tic is a stereotyped repetitive involuntary movement or sound, frequently preceded by premonitory sensations or urges. (3) Tics often indicate the presence of a global brain developmental disorder in conditions like mental retardation, autism, and pervasive developmental disorder. Similarly, a variety of genetic and neurodegenerative conditions can cause tics, including Wilson disease, neuroacanthocytosis, neurodegeneration with brain iron accumulation, and Huntington disease. Tics can be a manifestation of neuroleptic drug-related tardive dyskinesia or withdrawal emergent syndrome.

Over age 65 years, the prevalence of TD was ve to six times greater than younger patients exposed to APDs. Moreover, rates of spontaneous remission decrease with increasing age. Other factors including female sex, brain damage or dementia, presence of a major affective disorder, longer duration of APD exposure, use of anticholinergic-antiparkinson drugs, and a history of acute EPS all have been tentatively associated with greater prevalence of TD. (4) For patients with mild to moderate TD, therapeutic efforts are primarily directed at minimizing neuroleptic exposure or, when possible, changing to atypical agents. Patients with moderate to severe forms of TD present greater challenges. These patients frequently require medication to suppress their dyskinesias. A variety of suppressive agents have been tried with limited success. No treatment strategy has emerged that is clearly superior or even successful in most patients.

CASE REPORT:
Thirty seven year old married male was brought to our OPD three years back with history of one and half years duration of psychotic illness characterized by suspicion over his wife’s fidelity, referential ideas, frequent change of job, quarrelsome at work place, anger outburst and sleep disturbance with the mental status examination revealing findings in support of the same psychotic features with intact cognitive functions and poor insight and so he was diagnosed as a case of schizophrenia, paranoid subtype. He also had a past history of head injury 20 years back following a fall, for which he was evaluated both clinically and radiologically. His neuroimaging studies were normal. He was started on atypical antipsychotics, olanzapine and his prescription was as follows: tablet olanzapine 5mg bd., tablet benzhexol 1 mg od., tablet diazepam 1 mg hs. Then after a month olanzapine was changed to risperidone 2 mg bd. and gradually titrated upto 6 mg. With continuous treatment his symptoms remitted in two years and he was maintained on risperidone 6 milligrams.

With three years of regular medications with risperidone, he developed abnormal, involuntary, repetitive and stereotypical movements of oro-facial region including forehead, eyebrows, lips, tongue and peri-oral area extending into the neck, that was lasting for four months. He presented with abnormal involuntary movements affecting the muscles of the face and neck, such as eye-blinking, head-jerking, mouth-grimacing throt-clearing, grunting and also complex motor tics of grooming behavior like combing hair. There was no history suggestive of obsessive compulsive disorder, seizure disorder and other neurological disorder. His neurological examination and other systems examination was normal. Then patient was evaluated to rule out other causes of involuntary movements, neurologist too opined that as drug induced dyskinesia and suggested investigations to rule out thyroid dysfunction, Wilson’s disease and neurological diseases.
The effect of clozapine on NMDA function is complex (8). Whereas haloperidol reduces NMDA activity (by phosphorylation through intracellular mechanisms), clozapine facilitates NMDA-receptor function (9). The precise mechanism of how clozapine enhances NMDA-receptor function is unknown. One possibility is that it acts through the glycine modulatory site on the NMDA receptor. Glycine and D-serine act as a coagonist at the NMDA receptor and both have been shown to be beneficial for the negative symptoms of schizophrenia, but not in the presence of clozapine. This facilitation of NMDA function by clozapine (which would be expected to normalize synaptic plasticity) provides indirect support for the synaptic plasticity hypothesis because of the lower rates of TD with clozapine, compared with other antipsychotics. Maladaptive NMDA-mediated synaptic plasticity (in the neocortex and/or the striatum) would provide the missing link on how dopaminergic hypersensitization and striatal interneuron dysfunction from chronic anti-psychotic exposure could lead to TD. One possible sequence of events is that chronic antipsychotic use produces D2-receptor hypersensitization on MSN (medium spiny neurons)interneurons and the feedback fast-spiking inter-neurons in the striatum. This produces secondary effects on the synaptic plasticity of the glutamatergic synapses on striatal interneurons, resulting in an imbalance of the direct and indirect pathway, which, in turn, produces abnormalities in the output to the sensorimotor cortex. In parallel, in the neocortex, chronic antipsychotic use also produces a maladaptive form of synaptic plasticity (e.g., loss of input specicity and impairment of synaptic depotentiation). This maladaptive synaptic plasticity in the neocortex, combined with abnormal basal ganglia output, causes impairments in sensori-motor integration, thereby producing triggering of motor programs and the abnormal movements (10). However, clozapine has an affinity for both dopamine and muscarinic receptors, and risperidone have very little, if any, muscarinic affinity. It is possible that the cholinergic characteristics of clozapine, not the serotonergic, are responsible for its "atypical" features. If this is the case, then risperidone is more similar to "typical" neuroleptics and is able to induce tardive dyskinesia. The response to clozapine used for treatment of tardive tics in this patient can be explained pharmacologically.

REFERENCES: