Olanzapine-induced Respiratory Dyskinesia: A Case Report of a Rarely Recognized Antipsychotic Adverse Effect

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Abstract
Respiratory dyskinesia (RD) is a rarely-recognized side effect of antipsychotic medication. There are only few reports of respiratory dyskinesia in patients with tardive dyskinesia (TD), and almost all came from developed countries. Reported here is a case of a 58-year old lady who developed tardive dyskinesia while on typical antipsychotics and subsequently respiratory dyskinesia while on olanzapine. The diagnosis of respiratory dyskinesia was missed initially by the psychiatrists when the symptoms were mild and later by other specialists even when the presentation was classical. It is recommended that patients on antipsychotics, especially those with TD should be regularly examined for RD and when any clinician is managing a patient on an antipsychotic with respiratory problems, the possibility of RD should be considered.

Keywords: respiratory dyskinesia, olanzapine, rarely-recognized.

Introduction
Tardive dyskinesia (TD) is a neurological syndrome characterized by an involuntary, repetitive, purposeless movement of the body especially the tongue, lips, face, trunk, and extremities that occur in patients treated with long-term anti-dopaminergic medications, though other agents such as anticholinergics, toxins, and substances of abuse have been noted to cause it in vulnerable individuals.

Some conditions have been described as variants of tardive dyskinesia such as: akathisia, pseudoakathisia, orofacial and limb dyskinesia[1]; dystonia and tics[2]; as well as respiratory dyskinesia and rabbit syndrome[3].

Respiratory dyskinesia (RD) is a common but under-recognized (or easily misdiagnosed) side effect of chronic neuroleptic administration known to occur almost exclusively in association with other tardive effects of antipsychotics, such as tardive dyskinesia and tardive akathisia[4]. It usually manifests as irregular respiration, dyspnoea, grunting or gasping, and abnormal chest or oesophageal movements[5].

RD may mimic other respiratory or cardiac disorders and it is often overlooked or misdiagnosed[6] and authors who have written much on tardive dyskinesia often failed to discuss this respiratory variant or dismissed it as a rare phenomenon[5].
Though few cases of RD were reported many years ago, none of such reports was from Nigeria, notwithstanding that many of our patients develop tardive dyskinesia in the course of their treatment and the condition has continued to exist with clinicians often missing the diagnosis.

Case Report
Mrs K.K. is a 58-year-old headmistress who has been coping with schizophrenia since after her third child birth 28 years ago (then she was 30). She first received different types of typical antipsychotics including depot neuroleptics at various times. About 10 years ago, she was confirmed to have tardive dyskinesia and she was switched over to clozapine—a drug she tolerated (though the dyskinetic movements did not completely relieve) till early 2017 when she threatened to stop the drug because of excessive sedation and embarrassing hypersalivation.

The clozapine was replaced with olanzapine, 5mg every night. The salivation ceased and her sleep normalized. However, 3 months later, she complained of not sleeping adequately and the dosage was increased to 10 mg every night. A week after this increase, she complained that she was experiencing shortness of breath and slight increased subjective restlessness. But there was no associated orthopnoea, paroxysmal nocturnal dyspnoea, cyanosis, peripheral oedema, or worsening of the dyskinetic features like chewing movements and the breathing discomfort was not there while at sleep. She was referred to the respiratory unit where she was evaluated but no clear abnormality was detected. She was counseled and told to continue with her medications (olanzapine 10 mg nocte and vitamin E, 1000 iu daily).

In August 2017, she travelled to her village in a near-by state for an annual home-coming of the women and two days later, she was noticed to be hyperventilating, grunting, and overtly restless, pacing from one place to the other within the house. She was not a known asthmatic and had not had any chronic cough. She was afraid she might die and as her anxiety heightened, the breathing difficulty was noticed to worsen. She was rushed to a specialist hospital in the state where she received expert thorough evaluation from a pulmonologist, a cardiologist, and an otorhinolaryngologist with adequate laboratory work-up. A provisional diagnosis of ‘unspecified obstructive airway disease’ was made and a trial of steroids and bronchodilators, among others, was undertaken while she maintained her antipsychotic drugs (on insistence of the husband who told the doctors that she had been on antipsychotics for many years and each time she attempted stopping them, her speech and behaviour changed). However, no progress was observed as the dyspnoea and breathing difficulty persisted.

Eventually, the husband called on phone and narrated her experiences as she travelled to the village. We communicated the managing doctors to stop the olanzapine and every other drug, which they did. The following day, she herself called and reported that she was much better. She was discharged then.

A note from the doctor that managed her in the specialist hospital captured: ‘She was dypsnoeic and reported an inner feeling of restlessness in respiration. We observed that she was unable to breathe leisurely in a relaxed manner and she kept gasping for air for quite some time’.

A week later, she was recommenced on olanzapine, starting from a low dose of 2.5mg nocte, to be gradually titrated upwards. The respiratory difficulties re-emerged few hours later. She was then switched over to aripiprazole, 5mg daily—a drug she has remained stable on for over six months before this documentation.

Discussion
Respiratory dyskinesia is a common but under-recognized side effect of chronic neuroleptic administration[5]. It manifests as irregular respiration, dyspnoea, grunting or gasping, and abnormal chest or oesophageal movements and occurs almost exclusively in association with
other tardive effects of antipsychotics, such as tardive dyskinesia and tardive akathisia. The dyspnoea is often momentarily suppressed when the patient takes a quick, full breath to relieve the perceived restlessness and exacerbated when the patient keeps the respiration still[7].

The cause of respiratory dyskinesia in people with antipsychotic-related tardive dyskinesia is not very clear. Our patient when she travelled to the village presented with features that an average doctor would think the problem is of primary cardiac or respiratory origin, just like the doctors that attended to her there. Similar experience has been documented 40 years ago by Weiner and colleagues who, because of the ages and nature of the complaints of three of their patients with neuroleptic-induced tardive dyskinesias, originally thought the patients had cardiac and pulmonary disorders[8]. We ourselves also did not think of olanzapine-related respiratory distress when she first complained of shortness of breath probably because it was mild. These go a long way to support the report that RD could be easily missed or misdiagnosed [5,6].

Our patient manifested both subjective and objective restlessness as earlier observed in all the five patients reported from Japan[7]. The withdrawal of olanzapine led to an immediate restoration of respiration. When she was re-challenged with olanzapine, even at a lower dose than before, the respiratory problem re-emerged. This is similar to our earlier observation with antipsychotics[9].

We are convinced that our patient’s respiratory problem was related to olanzapine medication for the following reasons:

1) She had been on antipsychotics for many years and had also developed tardive dyskinesia for several years without any obvious respiratory discomfort.
2) Respiratory manifestations started shortly after she was commenced on olanzapine.
3) The withdrawal of olanzapine led to an immediate relief and normalization of respiration.
4) A re-administration of olanzapine caused a recurrence of respiratory discomfort, which also relieved on a subsequent withdrawal of the drug.

Conclusion
Respiratory dyskinesia is a distressing clinical condition often not recognized by doctors, including mental health experts. Clinicians who prescribe antipsychotics should be aware of this condition while treating such patients. Other specialists who come across patients on antipsychotics with breathing difficulties should also have this condition as a differential. It is advised that regular examination of patients on antipsychotics for any evidence of dyskinetic movements including respiratory musculature should be a routine as early diagnosis would lead to a better outcome and save the patient from unnecessary consultations and expenses.

Acknowledgement
I appreciate the patient and her husband for consenting to the publication of this case. I am also grateful to the doctors that managed her when she travelled out of our state for adhering to my advice that patient be put off all drugs and also for writing a comprehensive report to me on their observations and actions during the short period of their care.

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