



## Clomipramine Induced Torticollis: A Case Report

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### ABSTRACT

Torticollis caused by clomipramine: a case report Drug-induced torticollis is a movement disorder that occurs most often with neuroleptics, though there are many drugs in its etiology. The exact mechanism of antidepressant-associated extrapyramidal side effects (EPS) is not known. However, hypotheses including inhibition of dopaminergic function in the nigrostriatal pathway, impaired balance between dopaminergic, serotonergic, noradrenergic or cholinergic activity, and serotonergic inhibition of dopaminergic functions in the striatum leading to extrapyramidal side effects have been suggested. The number of cases with torticollis during clomipramine use is low. We wish to draw attention to this rare side effect of clomipramine and to contribute to the literature by presenting a case of torticollis on the 5th day of clomipramine treatment in a 22-year-old male patient<sup>1</sup>.

### INTRODUCTION

**T**orticollis, also known as wry neck, is a painful dystonic condition defined by an abnormal asymmetrical head or neck position, which may be due to a variety of causes. It sets on suddenly and is uncomfortably painful for the patient. The condition is more frequently seen in young persons. The spasms in the neck can present as opisthotonus. Mainly there are three types of torticollis which include spasmodic, congenital and iatrogenic. The most common form of torticollis is spasmodic torticollis which begins in adulthood and has no underlying cause. There may however be some genetic susceptibility to spasmodic torticollis such as a mutation in GNAL or THAP1 genes. Spasms in the ocular muscles can turn the eyes sidewise or upwards (oculogyric crisis). The tongue may be enlarged and extend outwards in a laryngospasm or jaw dystonia. While the physiopathological mechanisms have not yet been fully explained, it is assumed that an imbalance between the striatal dopaminergic and cholinergic systems due to a sudden and extreme blockage of the dopamine receptor is responsible for this presentation. Drug-induced torticollis mostly originates from substances blocking dopamine activation, especially those blocking dopamine D2 receptors in

the caudate, putamen, and globus pallidus<sup>2,3</sup>. Other drugs causing torticollis are those changing the balance between serotonin and dopamine or dopamine and acetylcholine in the basal ganglia<sup>4</sup>. Clomipramine is a tertiary amine tricyclic antidepressant with specific D2 antagonist activity and strong serotonin reuptake inhibitor properties. The most important side effects reported are vertigo, hypokinesia, headache, irritability, constipation, increased appetite, nausea, dryness of the mouth, increased perspiration, and cardiac side effects. Other potential side effects are convulsions and an increased disposition for convulsions<sup>5</sup>. By contrast, our paper presents a patient developing torticollis with clomipramine.

### CASE HISTORY

A 22 years old male patient was admitted in psychiatry department with abnormal positioning of neck. patient did not have any other medical co-morbidities. Around 1 year back he was using MDMA and Alcohol and had visited a polyclinic with chief complaints of decreased sleep, disturbed thoughts, rigidity, tremor, palpitation and was diagnosed with depression with psychotic symptoms. After 2 months he restarted the use of MDMA and Alcohol. On that occasion he was taken to a

polyclinic, and he was prescribed with atomoxetine 10mg OD, clozapine 25mg HS, lorazepam 1mg BD, diazepam + imipramine HS, rabeprazole + domperidone OD for 1 month. There was no relief of symptoms and hence the second month he was prescribed with fluoxetine 50mg HS, lorazepam 1mg BD, aripiprazole 5mg HS, clozapine 25mg BD. Following on the third month he was prescribed with clomipramine 25mg BD, clozapine 25mg HS, Aripiprazole 5mg HS, Lorazepam 1mg BD. On 4<sup>th</sup> day he was hospitalized, due to abnormal posturing of neck. During hospitalization haematology, blood biochemistry {Na, K, Ca, Mg, Creatinine, Urea etc.....} lipid profile tests were normal. An emergency reassessment did not reveal any pathologic findings. It was assumed that the patient had developed clomipramine induced Torticollis or opisthotonus. Clomipramine treatment was discontinued and promethazine 25mg IV was administered. Within 1 hour reduction in the patient complaints of neck spasm was observed. The ADR were assessed according to Naranjo's adverse drug reaction probability scale, which measures to what degree the adverse drug effect is likely related to drug rather than caused by other factors. Our patient scored a total of 8 points on the scale, which corresponds to a highly probable relation. The patient treatment was set to tablet trihexyphenidyl 2mg OD, tablet promethazine 25mg BD, tablet lorazepam 2mg BD, tablet propranolol 20 mg + clonazepam 0.25mg BD, tablet olanzapine 2.5mg HS and tablet pantoprazole + domperidone BD. As the spastic complaints decreased with promethazine 25mg, it was continued and the complaints were resolved after 1 week. General complaints also decreased quickly with the above treatment. On the 8<sup>th</sup> day of hospitalization the patient was discharged with a medication plan to continue same medication for 10 days. During the follow up examination no recurrence of spasms were observed.

## DISCUSSION

Torticollis can be triggered by various causes, with drug-related adverse effects being the most common cause. Torticollis has been linked to the following drug classes: neuroleptics, antiemetics, tricyclic antidepressants, monoamine oxidase inhibitors (MAO inhibitors), selective serotonin reuptake inhibitors (SSRIs), serotonin antagonist and reuptake inhibitors (SARIs), serotonin-noradrenaline reuptake inhibitors (SNRIs), and antiepileptic drugs (phenytoin, carbamazepine, diazepam). Typical antipsychotics have a chance of developing a torticollis ranging from 2.3 to 60%, while atypical antipsychotics have a risk of 2 to 3%.<sup>2</sup> Torticollis has also been linked to antidepressants, however not as much as to antipsychotics. According to a case series, the SSRI group implied a greater risk in comparison to other antidepressants. High blood levels of SSRIs such as paroxetine and fluvoxamine have been linked to an increased risk of torticollis. The pathophysiologic mechanisms for drug induced movements disorders are poorly understood. Blockade of dopamine (D2) receptors in the basal ganglia and dopaminergic tracts has been implicated in neuroleptic-induced EPS. It seems likely that SSRI-induced EPS results from interaction between serotonergic and dopaminergic pathways.<sup>5</sup> A reviewed study on extrapyramidal side effects of cyclic antidepressants and found that 26% of TCA users experienced akathisia, 17% had dystonia, 52% had reversible dyskinesia, 4% had neuroleptic malignant syndrome.

To a lesser extent, TCAs also block dopamine reuptake pumps in addition to serotonin and noradrenaline reuptake pumps. Certain TCAs, including clomipramine, are stronger serotonin

reuptake pump inhibitors; others (desipramine, maprotiline, nortriptyline, and propranolol) are more selective for noradrenaline than for serotonin. Nevertheless, the majority of TCAs inhibit both noradrenaline reuptake and serotonin. Although earlier sources typically claim that extrapyramidal adverse effects from TCA usage are uncommon, more current research and case studies indicate that these side effects are common but frequently go unrecognized due to inadequate awareness. Acute dystonia with atypical antipsychotic agents, although relatively rare, has been reported with other atypical agents, including with clozapine. Their 5-HT<sub>2A</sub> antagonism, as a group, likely explains their low potential for extrapyramidal side effects.<sup>6</sup> A 25-year-old female patient with a depressive episode of 2 months duration characterized by low mood, lack of interest, ideas of hopelessness, and anhedonia. Oxcarbazepine 300 mg once daily was started and unpredictable mood fluctuations. After two days of treatment Sertraline 50 mg once daily was started while continuing oxcarbazepine 300 mg/day. Within 2 days of starting treatment, she began to experience involuntary opening of jaw lasting for about 23 min each time suggestive of mandibular dystonia. These episodes would recur multiple times daily. Tablet sertraline was stopped quickly while continuing oxcarbazepine. This was followed by immediate and complete resolution of dystonia were reported in 2019.<sup>7</sup>

Acute focal dystonia, which starts rapidly within the first 7 days (typically 96 hours) after medication treatment (with antipsychotics, antidepressants and other drugs). Muscle spasms produce abnormal postures with pain and fever have also been reported.<sup>8</sup> Wang et al. also reported a patient with major depression and acute dystonia in two separate episodes after the patient suddenly stopped taking bupropion. The first episode occurred when the drug was suddenly switched from bupropion to duloxetine. In both instances, the symptoms, which included trismus, dysphagia, and torticollis, resolved after the reintroduction of bupropion or the injection of biperiden.<sup>9</sup>

As far as we could see, there are a small number of reports about incidents with clomipramine use. Ninety percent of cases of torticollis occur within the first three days of drug use. TCAs are a group of antidepressants frequently used in the treatment of a number of psychiatric diseases. By presenting a case with torticollis, a rarely seen side effect of these drugs, we want to draw the attention to this TCAs side effect and contribute to the literature.

## CONCLUSION

Clomipramine can cause unpredictable acute dystonic reactions such as torticollis. And they can be life threatening and should be detected early. The extrapyramidal side effects should be monitored in patients on clomipramine since a single dose can cause these symptoms. The case highlights a torticollis reaction following the administration of clomipramine.

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