Cases Journal

Case Report

Social phobia following maprotiline: the first case report
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Abstract

Introduction: It has long been recognized that anxiety symptoms and syndromes may be caused by medication and/or substance of abuse. The aim of this report is to present a patient who experienced social phobia following maprotiline, an adverse drug reaction which has not been reported previously with this agent.

Case presentation: A 27 year-old male patient was suffering from dysthymia for 6 years. He received different kinds of pharmacotherapy including TCAs, SSRIs, MAOIs. Due to his poor response, augmenting therapy with liothyronine and lithium and also cognitive therapy have been tried for him. Since he did not respond well to these treatments, maprotiline was administered for him 50 mg daily. His psychological problems improved with maprotiline, however he experienced social phobia that has not experienced yet.

Conclusion: This could underlie the precipitation of social phobia after maprotiline. However there is a need for further studies.

Introduction

It has long been recognized that anxiety symptoms and syndromes may be caused by medications and/or substance abuse. Many medications are capable of engendering anxiety disorder including anesthetics, analgesics, antidepressants (Tricyclics, SSRIs, bupropion), antihistamines, antimicrobials, bronchodilators, calcium-blocking agents, cholinergic-blocking agents, digitalis, estrogens, ethosuximide, hydralazine, insulin, levodopa, muscle relaxants, narcoleptics, non-steroidal anti inflammatory drugs, procarbazine, sedatives, steroids, sympathomimetics, theophylline and thyroid preparations. In addition, withdrawal from CNS depressant drugs, aspirin intolerance, drug intoxication and caffeinism also have been proposed as the causes for social phobia [1].

Maprotiline is a tetra cyclic antidepressant agent which has been approved for the treatment of depression and anxiety associated with depression [2]. The aim of this report is to present a patient who experienced social phobia following maprotiline administration, an adverse drug reaction which has not been reported yet with this agent. He complained from low energy on fatigue, low self steam, feeling of hopelessness and poor concentration. These symptoms were continuously. He has never been with out the symptoms more than 2 month at a time.

Case Presentation

A 27 year-old male patient (was suffering from dysthymia for 6 years). He did not have any anxiety disorder, mood
disorder, substance use disorder, and personality disorder ago. However, he had a family history of mood disorder, in one of his first degree relatives his brother was suffer-
ings from dysthymia.

He has been taken various treatments including pharma-
cotherapy and psychotherapy and biological therapy. He
has adequate courses of amitriptyline, nortriptyline, clo-
 mipramine, fluoxetine, trazodone, sertraline, and trany-
cypromine augmented by liothyronine, lithium and
cognitive therapy for six month. In spite of all of these
therapies, his condition did not improve.

Finally, he received maprotiline 50 mg daily. His condi-
tion improved by maprotiline, significantly. Wide range
of social phobia symptoms including flushing, tachycar-
dia and tremulousness occurred when he was talking to
other peoples. In other words he had a marked and per-
sistent fear of more social or performance situation in
which he is exposed to unfamilies people or to possible
scrutiny by other. These symptoms were disappeared fol-
lowing dosage reduction to 25 mg maprotiline daily.

Discussion
As well as we know, there is not any report regarding the
social phobia following maprotiline administration.
Maprotiline is a tetra cyclic antidepressant drug with
actions and uses similar to those of tricyclic antidepres-
sants. It is a selective inhibitor of the neither reuptake of
nor epinephrine [3].

Adverse effects with maprotiline are broadly similar to
those with tricyclic antidepressants, but antimuscarinic
effects are less frequent. Skin rashes seem more common
with maprotiline than with tricyclic antidepressants. Sei-
zures have occurred in patients with no prior history of
such disorders as well as in those with a history of epilepsy
and the risk are increased if high doses of maprotiline are
employed. It should not be used in patients with epilepsy
or a lowered seizure threshold [4].

It is postulated that nor epinephrine may has an impor-
tant role in the path physiology of social phobia [5].

Patients with performance phobias may release more
norepinephrin or epinephrine, both centrally and periph-
erally, than do non phobic person or such patients may be
sensitive to a normal level of adrenergic stimulation[6].

The locus ceruleus area in the brainstem is the major
source of nor epinephrine, and its stimulation produces
arousal and symptoms of anxiety. Over activity of
noradrenergic neurons may underlie some cases of anxiety,
and elevated concentrations of nor epinephrine and
its major metabolite, 3-methoxy-4-hydroxy phenyl glycol
(MHPG), have been found in the plasma and cerebrospi-
nal fluid of anxious patients. Administration of yohim-
bine, an antagonist of the presynaptic α-2 adrenergic auto
receptor, increases nor epinephrine release in the locus
ceruleus and produces anxiety in humans. Drugs that
decrease noradrenergic function can possess anxiolytic
effects. Clonidin, a presynaptic α-2 adrenergic agonist that
decreases noradrenergic activity, reduces anxiety symp-
toms and has also been effective in the treatment of alco-
hol and opiate withdrawal syndromes characterized by
symptoms of anxiety [7]. Facilitation of gamma-amino
butyric acid (GABA) by benzodiazepines also reduces
noradrenergic activity. (Considering the pharmacody-
namic action of maprotiline and the above mentioned
evidences regarding the role of nor epinephrine in the
path physiology of social phobia, it would be reasonable
to explain this adverse reaction to the over activity of the
sympathetic pathways).

However School avoidance, social phobia and separation
anxiety have been reported as potential consequences of
neuroleptic treatment of patients with Tourette’s disorder.

Mikkelsen and colleagues reported a series of case reports
including 15 children and adults who experienced anxiety
and work avoidance with haloperidol happened weeks to
months after beginning of treatment. The mean doses
were 2.5 mg/day. The phobic syndrome was not associ-
ated with akathisia, and disappeared completely in all
patients with the discontinuation of the drug [8]. Pimoz-
ide has also been reported to produce school phobia and
separation anxiety [9].

Conclusion
Clinicians should be alert to social phobia as a possible
adverse reaction of maprotiline, and on the basis of this
reported case, we suggest that this reaction could be
-treated successfully with dosage reduction.

Patients’ Perspective
I am suffering from low energy on fatigue, low self steam,
feeling of hopelessness and poor concentration continu-
ously. When I am talking to other peoples, I feel flushing
and palpitation. In other words I have a marked and per-
sistent fear of more social or performance situation in
which I am exposed to unfamiliar people.

Abbreviations
SSRIs: selective serotonin reuptake inhibitor; CNS: central
nervous system; MHPG: 3-methoxy-4-hydroxy phenyl
glycol; GABA: gamma-amino butyric acid; TCAs: tricyclic
antidepressants.

Consent
Written informed consent was obtained from the patient
for publication of this case report and accompanying
images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

**Competing interests**
The authors declare that they have no competing interests.

**Authors' contributions**
SHH was attending, corresponding author and the major contributor in writing the manuscript. ES was pharmacologist and as a contributor in writing the manuscript too.

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