

Atomoxetine and Methylphenidate induced Psychosis in Patient with Moderate ASD: A Case Report

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Introduction

There is significant evidence that patients with concomitant Autism Spectrum Disorder (ASD) and ADHD are at increased risk for psychosis at baseline.¹ This risk can be further exacerbated by medical interventions, with an estimated 1 in 660 patients experiencing psychosis after initiating a stimulant medication for ADHD.² Less is known about the effect of non-stimulant medication including atomoxetine on developing psychosis. Here we present a case of a patient who exhibited psychotic behaviors after starting Atomoxetine following a failed trial of methylphenidate.

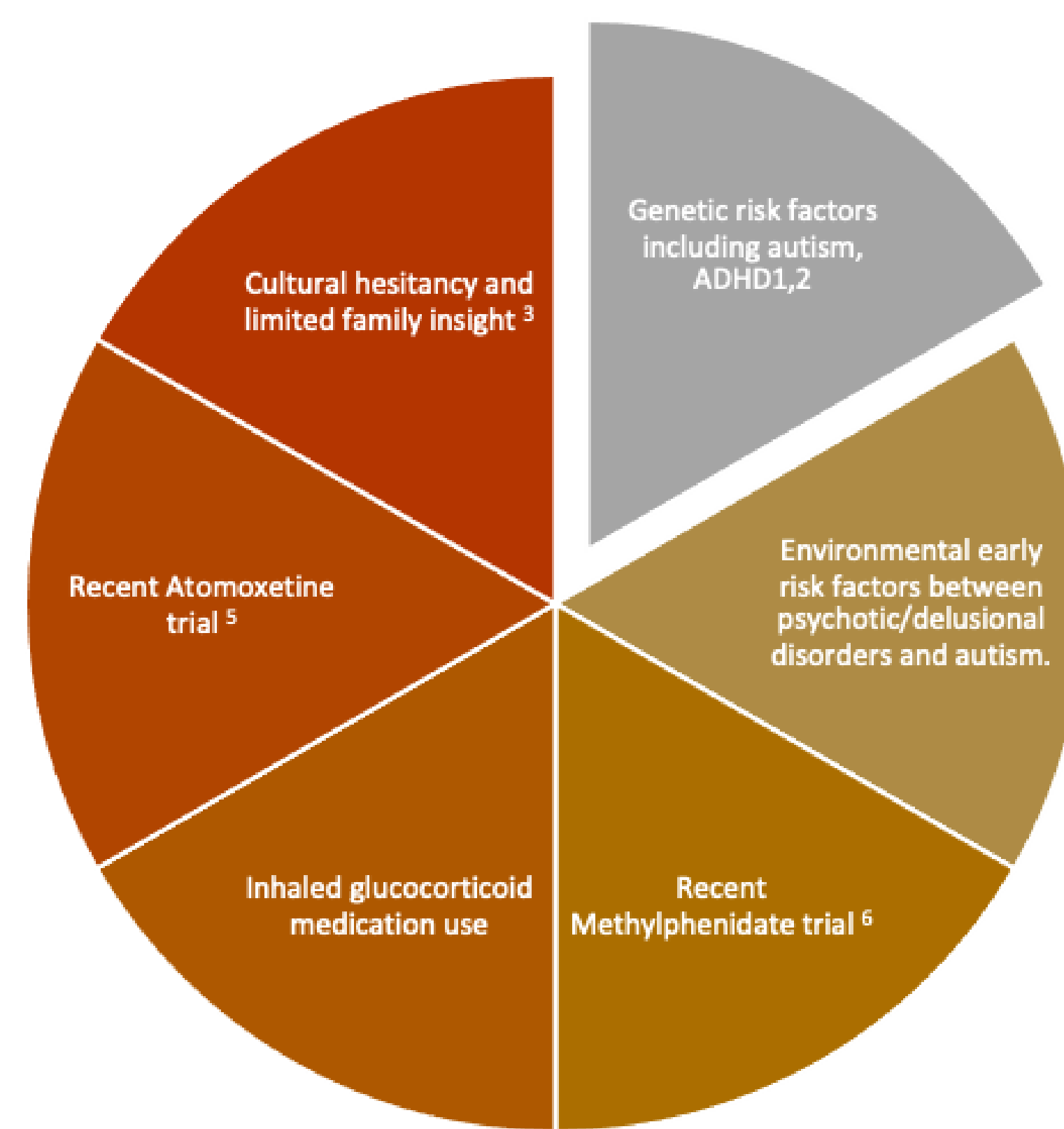
Case

- 16 y/o M high-functioning autism, ADHD, and Asthma presented to CT Children's after exhibiting psychotic behaviors and was admitted to Mount Sinai CAPS unit in early October.
- On Atomoxetine 25 mg for two weeks under management by child psychiatrist for ADHD with last dose one day prior to admission
- Previously failed methylphenidate 18mg trial with titration to 36mg due to adverse reaction with mood changes in August under management by pediatrician
- Hx of prior methylphenidate trial at 18 mg and 27 mg in 4th/5th grade that resulted in changes in mental status, and headaches
- Recent hx of COVID-19 infection two weeks prior. Did not use any oral ICS for his asthma at that time

Presentation

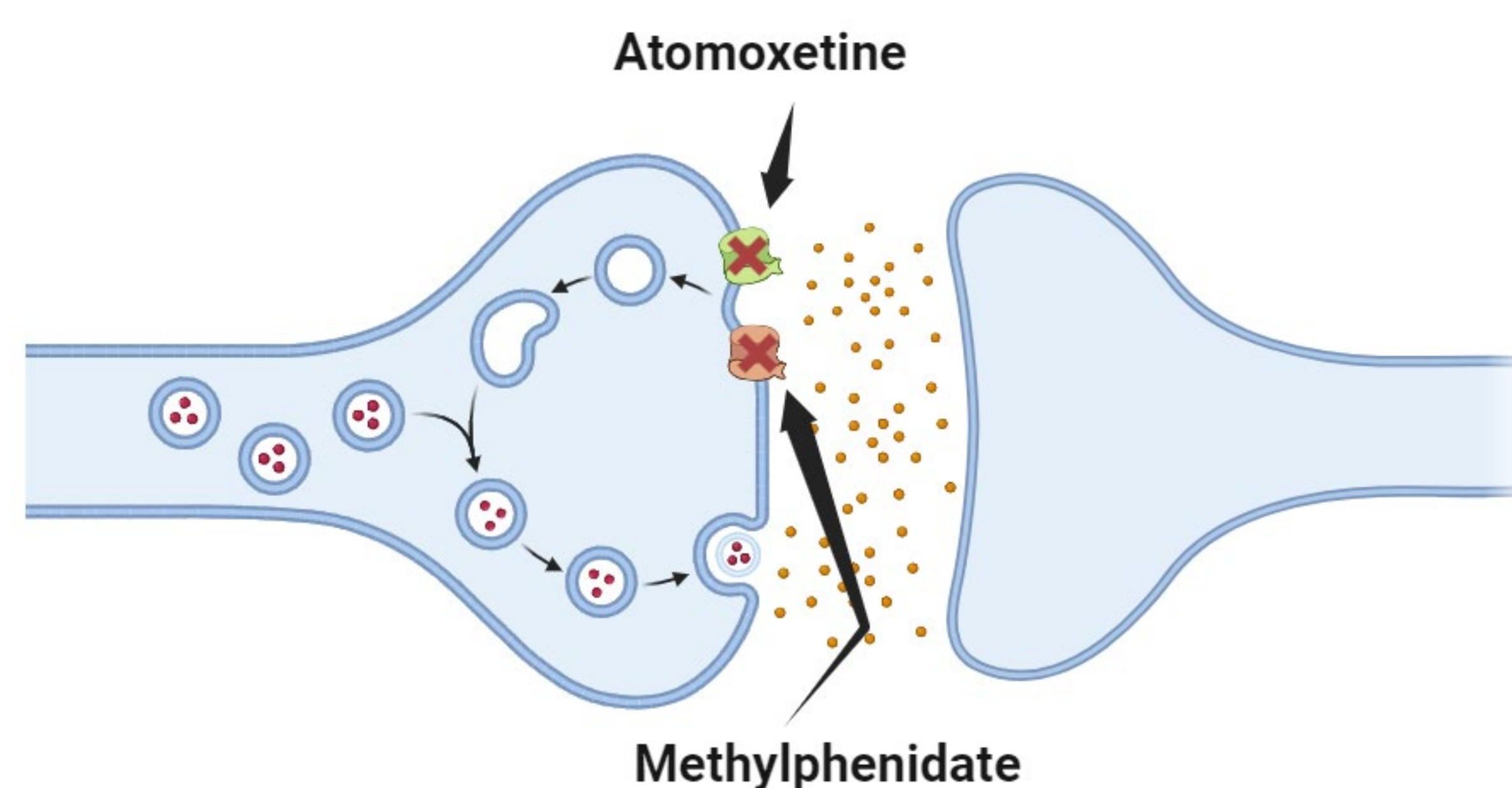
- Patient presented with labile affect, fragmented speech, significant thought blocking, endorsing visual hallucinations, appeared to be responding to internal auditory stimuli and acutely delirious. He was AAOx3. In discussing SI, he endorsed feelings of not being able to be safe by himself on the unit and was placed on a 1:1 observation.
- Patient's family was unwilling to consent to starting medication to address psychotic symptoms due to mistrust of medications after the onset of his psychotic symptoms.
- Patient was observed on unit with no pharmacological interventions. His thought process slowly seemed to improve

Risk Factors



ADHD Pharmacology

- **Atomoxetine**
 - Inhibits the presynaptic norepinephrine (NE) transporter (NET), preventing the reuptake of NE throughout the brain along with inhibiting the reuptake of dopamine (DA) in specific brain regions such as the prefrontal cortex (PFC).
 - It is mainly metabolized by the highly polymorphic drug metabolizing enzyme cytochrome P450 2D6 (CYP2D6).
- **Methylphenidate**
 - Inhibits presynaptic NET and dopamine transporter (DAT) preventing the reuptake of NE and DA predominantly in the striatum and prefrontal cortex.
- There have been several case reports in the literature describing psychosis induced by atomoxetine and/or methylphenidate^{5, 6}
- Excess dopaminergic activity in the mesolimbic pathway disposes to psychosis.



Management

- Identification and management of psychosis in Autism and ADHD in pediatric patients is complex and necessitates a multi-disciplinary and collaborative approach.
- Prior adverse reaction and risk factors requires slow and carefully monitored medication induction and titration.
- A family centered approaches incorporating psychoeducation, supportive therapy, and focus on functional outcomes, symptom reduction and social integration is paramount
- Cultural sensitivity plays important role in addressing denial and driving family engagement and treatment adherence in patient care.
- Collaboration between PCP, School Therapists and Psychiatrists is instrumental for patient and family education on benefits of carefully monitored psychopharmacologic interventions for concomitant ASD, ADHD and Psychosis.
- Early Psychosis Intervention Program and Applied Behavioral Analysis to facilitate improvement of social, communication and learning skills.

Discussion

- This 16 year old male had genetic and physiologic risk factors to psychosis due to concomitant ASD.
- Comorbid ADHD in this patient required initiation of methylphenidate and atomoxetine for attentive symptoms.
- The mechanisms of methylphenidate and atomoxetine involve dopaminergic signaling, increasing the likelihood of acute psychosis and given this patient's vulnerability to psychosis he should have underwent a very slow titration of dopaminergic medications.
- Parental education is essential to identification of psychosis in the pediatric patient and prompt discontinuation of offending medications.
- Cultural sensitivity by the provider is imperative to creating a therapeutic alliance between the patient and their family especially in the context of mental health and adverse reactions to medications

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