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Article

Case Report of a Rare Asenapine Induced Tachycardia in a Bipolar Affective Disorder Patient with Underlying Glucose-6Phosphate Deficiency

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***Abstract*— Mr. R is a 29-year-old single male with underlying Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency since childhood. He presented with elated mood for 10days prior. He had 1 prior admission because of increased agitation and being aggressive towards his family doctor. G6PD has been linked with an increased risk of developing Bipolar Affective Disorder. Asenapine is a new antipsychotic on the market, which could be used as a mood stabilizer. It has a proven benefit in treating bipolar affective disorder. This case report highlights a very rare side effect of Asenapine induced tachycardia.**

***Keywords*— Asenapine, Bipolar, Tachycardia.**

I. INTRODUCTION

Bipolar Affective Disorder (BPAD) is a severe, recurrent affective disorder associated with considerable morbidity and mortality[1]. The lifetime prevalence rates of BPAD are estimated to be between 1-5% in the general population. The median lifetime prevalence as per a review conducted by Wittchen HU was found to be 1.3% (range: 0.6 – 3.3)[2]. Of this, the lifetime prevalence of Bipolar Disorder Type 2 as per the Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (DSM-IV) specifically was found to be between (0.5-3.0)% of the general population[3].

A large part of morbidity arises from the impact BPAD has on social and professional functioning as well as the chronicity the disease process can take. Mortality is largely contributed to suicide and other unnatural causes. Muller-Oerlinghausen B et al states that the mortality rate in BPAD is 2-3 times higher than the general population with 10-20% of those with BPAD committing suicide and about 33% attempting suicide at least once[4]. As a result of the recurrence, chronicity and high risk of suicide in BPAD, long-term prophylactic treatment is indicated early in the course of the condition.

Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency, the most common enzyme disorder worldwide, affects approximately 400 million people globally with differing variations of severity. It is an X-linked inherited disorder, which shows a higher prevalence in persons of African, Asian, Mediterranean and Middle-Eastern descent, as well as North and South America and northern European countries. It is estimated that gene frequencies are estimated to be between 5-25% in these regions[5].

Individuals with G6PD deficiency can remain asymptomatic, while others present with a range of clinical conditions including haemolytic anaemia (acute and chronic), and neonatal hyperbilirubinaemia leading to increased risk of neonatal jaundice and kernicterus (which can cause permanent neurological damage or death). However, the disease is rarely fatal.

G6PD Deficiency has been found in presentations of psychotic illnesses such as catatonic schizophrenia, acute mania and bipolar disorders[6]. However, the exact role G6PD Deficiency plays in the development and severity of such disorders is not well understood. In an effort to better understand the association between G6PD deficiency and bipolar/bipolar schizoaffective disorders; Bocchetta A et al conducted 2 studies in Sardinia, Italy. It holds a relatively high prevalence of G6PD deficiency (10-15%). Both studies were conducted on patients attending the outpatient psychiatric or lithium clinics. In the study published in 1994, they reported that in 408 patients who presented with bipolar II disorder or bipolar schizoaffective disorder, there was a disproportionately higher incidence of G6PD deficiency (38%), especially in males (47)[7].

II. CASE REPORT

Mr. R, a 29 year old single Sardinian male, presented to his GP with a 10-day history of elated mood, flight of ideas, over-spending, anxiety and insomnia.

This is on a background of G6PD since childhood and being previously diagnosed with Adjustment reaction with predominant depressive symptoms. He required hospitalization twice in the last 6 years.

With regards to this index episode, the patient described being over-friendly and elated. He was overly generous, giving away money to homeless people excessively. He also reported an increase in spending; buying 32 cameras online which he had no use for. On top of this, he also reported early insomnia, being highly energetic and experienced racing thoughts. He would talk more than usual and would pick up fights with work colleagues and friends as he experienced increased irritability towards other people.

He had a prior hospitalization in 2011 for low mood, insomnia and suicidal ideation. He was prescribed sertraline 50mg daily and zopiclone 3.75mg in the short term, but did not adhere to medications.

There were positive mental illness histories in the family. His father was diagnosed with Bipolar Affective Disorder Type 1. Two sisters have a history of Major Depressive Disorder. On mental status examination, he was talkative with pressured and increased rate of speech. His mood was both subjectively and objectively elated. The affect was euphoric and reactive. He had over-expansive ideas. He stated that he could be the boss of his company just because he is brighter than anyone else around.

He was diagnosed with Bipolar Affective Disorder Type 2 and was commenced on Olanzapine 5mg initially, but had limited response to treatment. He was subsequently started on Aripiprazole 10mg nocte orally, but it was discontinued as he had developed akathisia.

Mr. R was then prescribed Asenapine 5mg twice daily sublingually. He reported intermittent palpitations on the initial commencement of Asenapine. Towards his second dose, he had to attend the Emergency Department as he was having symptomatic tachycardia. He experienced severe palpitations with dyspnoea, dizziness and chest tightness. In the emergency department, he had an electrocardiogram, which showed an elevated sinus heart rate of 130 beats per minute. His other vitals were normal, albeit with a slight increase in blood pressure of 138/97. He was reviewed by the medical team and after excluding other medical causes he was diagnosed with Asenapine induced tachycardia.

As a result, asenapine was stopped and he was started on another psychotropic, Quetiapine. He gradually improved over the subsequent 2 weeks and was subsequently discharged to the outpatients department.

III. DISCUSSION

Asenapine is an atypical antipsychotic, approved by the US Food and Drug Administration (FDA) in 2009 for sublingual administration for acute treatment of schizophrenia in adults and mania/mixed episodes with bipolar I disorder in adults. The Canadian Network for Mood and Anxiety Treatments (CANMAT) recommends the use of asenapine as first line or adjunctive therapy in the treatment of acute mania and third-line treatment in the maintenance therapy of bipolar disorder[8].

Asenapine has a receptor-binding profile similar to other atypical antipsychotics, with antagonism at serotonin (5-HT_{2A}, 5-HT_{2B}, 5-HT_{2C}, 5-HT_{5A}, 5-HT_6, 5-HT_7), dopamine (D_2, D_3), histamine (H_1, H_2) and noradrenergic (α_{1A}, α_{2A}, α_{2B}, α_{2C}) receptors. However, it has no notable activity at muscarinic acetylcholine receptors. Similar to other atypical antipsychotics, it has predominance for occupancy at 5-HT_{2A} over D_2 receptors.

Studies have been published documenting the efficacy, safety and tolerability of Asenapine[9]. In a double blind 40-week study between asenapine and olanzapine, McIntyre RS et al identified similar efficacy and adverse effect profiles to olanzapine but with a lower risk of weight gain[9]. The most frequently reported side effects with asenapine were parkinsonism, tremor and constipation. Uncommon side effects reported are sedation, irritability, dizziness, oral hypoesthesia and dyskinesia[9].

Reports of ECG changes have been reported in multiple studies at a low rate. In a study by McIntyre RS et al, of 488 patients (183 treated with asenapine), there were 3 patients who experienced clinically significant ECG changes (asenapine=2, olanzapine=1)[9]. With asenapine, there was 1 case of supraventricular tachycardia, and 1 of QTc prolongation. In the 40-week study, McIntyre RS et al report the incidence of 1 case of non-specific ST-T change and right bundle branch block out of 76 patients randomized to asenapine (total N=218)[9].

In a randomized-controlled trial conducted by Potkin SG et al in the treatment of schizophrenia, with doses of asenapine of 5mg twice daily (similar to that prescribed for bipolar disorders), of 121 patients there were 2 cases of sinus tachycardia (RD 0.01, 95% CI -0.11 to 0.12)[10].

These studies indicate the possibility of the occurrence of tachycardia or bradycardia with asenapine although rare can present with serious complications. The reported rate is 1 in 1000 cases, in which it could also be associated with sinus bradycardia, bundle branch block and Qtc prolongation[11],[12].

IV. CONCLUSIONS

As asenapine is fairly new on the market, extra caution should be used as it does come with its on adverse effect profile. As there had been rare reported cases of anaphylactic reaction to asenapine, it is best to educate patients about the potential side effects and advised to attend the nearest medical centre for any complications. The associated tachycardia side effect is extremely rare, but hyper vigilance is advised upon prescribing.

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