

# Solifenacin-induced acute psychosis: a case report

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## ABSTRACT

Solifenacin is a muscarinic receptor antagonist that has been used to treat overactive bladder since 2004. It has a great affinity for the detrusor M3 receptor, which must be stimulated for bladder muscle contraction, and demonstrates the most selective profile to the bladder of the muscarinic receptor subtypes. It is thought that urinary antimuscarinic agents, due to their passage to the central nervous system and lipophilic properties, may cause central nervous system symptoms in some rare cases. A case report of a 42-year-old male patient who had an acute psychotic attack as a result of solifenacin treatment for overactive bladder is presented in this article.

## INTRODUCTION

Overactive bladder (OAB) is defined as urinary urgency, usually accompanied by increased daytime frequency and/or nocturia, with urinary incontinence (OAB-wet) or without (OAB-dry), in the absence of urinary tract infection or another detectable disease.<sup>1</sup> In a population-based survey of 16 776 men and women aged >40 years conducted in six countries, the prevalence of OAB in Europe was estimated to be 15.6% in men and 17.4% in women, with an overall prevalence of 16.6%.<sup>2</sup> Antimuscarinic medications are currently the mainstay of treatment for OAB. They differ in their pharmacological profiles, including muscarinic receptor affinity and other modes of action, and also differ in their pharmacokinetic properties, such as lipid solubility and half-life. Systemic adverse effects are common in treatments due to the extensive involvement of muscarinic receptors in the autonomic nervous system and the passage of some agents to the central nervous system. Five muscarinic receptor subtypes (M1 to M5) have been identified, with M2 and M3 being the most prevalent in the detrusor. Although M2 is one of the most expressed subtypes, the M3 subtype is more functionally significant in bladder contractions.<sup>3 4</sup> Solifenacin demonstrated a highly bladder-selective profile in preclinical studies when compared with other antimuscarinic agents.<sup>5</sup> Common side effects of solifenacin that lead to discontinuation of treatment have been reported as dry mouth,

blurred vision, constipation and headache. In one study, it was stated that headache, confusion, cognitive impairment, disorientation, agitation, dysarthria and changes in consciousness might be observed due to the high penetration of solifenacin, which is not a P-glycoprotein substrate. Such agents can increase the dopamine level in the synaptic gap.<sup>6</sup>

In the literature, although there was no case of psychotic disorder due to solifenacin use, it was reported that a man in his 80s was prescribed solifenacin for the diagnosis of OAB whose clinical manifestation that began with anxiety progressed to delirium. The delirium manifestation improved with the discontinuation of the treatment.<sup>7</sup> This article presents a case report of a 42-year-old male patient who had an acute psychotic attack due to solifenacin treatment for OAB.

## CASE HISTORY

A 42-year-old married man, a high school graduate, working in the private sector, belonging to middle upper socioeconomic status and living with his family presented at the psychiatry emergency department with his relatives because of psychiatric complaints. The patient himself and his family had no known history of psychiatric illness. In addition, the patient had no other known medical disease. He was recently diagnosed with OAB due to lower urinary tract symptoms, with predominant storage symptoms such as urinary urgency, increased urinary frequency, pass urine that is difficult to defer and involuntary loss of urine. Fifteen days ago, he was initiated on solifenacin at a dose of 5 mg/day by the urologist. He was advised to apply for a follow-up examination 4 weeks after he started taking medication. Because symptoms persisted despite taking the prescribed dose, on the fifth day of his treatment, the patient doubled his daily dose without consulting his doctor. Although his psychiatric complaints started right after he increased the medicine



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dosage, he continued to use the medicine at a dose of 10 mg/day.

Initially, there were complaints of restlessness, irritability and sleep disturbance, along with excessive suspiciousness. A few days later, these complaints were accompanied by self-talking, leaving home without informing anyone, and severe, tenaciously held, systematised paranoid thoughts that his wife would hurt him and his family was pursuing him. The family discontinued solifenacin treatment given that the patient could not cooperate in applying to the hospital and getting psychiatric help.

Approximately 7 days after the treatment was discontinued, the patient presented to the psychiatry emergency service with his relatives of his own will. In his mental state examination and his anamnesis, his level of consciousness and awareness were intact, his mood and affect were irritable and his thought content included paranoid thoughts about his colleagues. There were no hallucinations. Goal orientation, abstract thinking, attention, memory functions and test judgement were intact; the insight about the current situation and the recommended treatment was partial. There was no active homicidal or suicidal thinking. According to a history obtained from the patient's family, his condition was closely observed by family members throughout 1 week. His thought that he would be harmed if he left home decreased over time. The neurological examination, blood tests, cranial CT and diffusion MRI of the patient consulted in the neurology department revealed no abnormalities. The urology department was consulted about the patient's current condition and how to proceed with the treatment in future. They were advised to wait until the patient's psychiatric symptoms subsided, after which he would be re-evaluated to determine the right treatment and that it would be more appropriate to follow up without using anticholinergic drugs during this time.

The patient did not have active homicidal or suicidal ideation. He refused to be treated in an inpatient psychiatric clinic. Consequently, he was discharged after obtaining both his consent and the consent of his family members, and communicating with them about the need for oral medication (outpatient) and follow-up. Olanzapine 10 mg/day treatment was initiated. After the second week of the treatment, the patient's delusions completely regressed, his mood changed in the direction of euthymia and he gained a complete insight about his disease and treatment. In the following course, the dose of olanzapine was reduced to 5 mg/day due to sedation side effects. As no psychotic findings were noted during the follow-up period, the treatment was continued with olanzapine at a dose of 5 mg/day.

## DISCUSSION

Anticholinergic agents can increase the dopamine level in the synaptic gap, and confusion, cognitive impairment, disorientation, agitation, dysarthria and changes in consciousness may accompany the typical psychotic

symptoms in psychotic disorders associated with anticholinergic drug use.<sup>8</sup> They also act as potent indirect dopamine agonists by blocking the presynaptic uptake of dopamine and causing its release from presynaptic terminals.<sup>9</sup> Adverse effects associated with the use of antimuscarinic drugs relate to the central nervous system which are frequently mentioned in the literature. In a meta-analysis published in 2011, these side effects were listed as dizziness, sleepiness, vertigo, insomnia, restlessness, weakness, confusion and cognitive dysfunction. The most common side effects were stated as dizziness and sleepiness.<sup>10</sup> The presence of the receptors on the drugs used in the treatment of OAB affects the central nervous system; the presence of factors that affect the deterioration of the blood-brain barrier, especially in older adults, leads to variability in terms of side effects with pharmacodynamic and pharmacokinetic differences.<sup>11</sup>

In a comparison of studies performed with different antimuscarinic agents, no significant difference was found in terms of central side effects, and it was stated that anticholinergic side effects may be observed due to the high rate of oral oxybutynin treatment crossing the blood-brain barrier.<sup>12</sup> A single dose of solifenacin, oxybutynin and placebo was investigated in another randomised, double-blind study that investigated attention, information processing, processing memory, episodic memory and mood changes; oxybutynin was shown to cause impairment in various cognitive areas.<sup>13</sup> This study also noted that cognitive impairment related to antimuscarinic use may increase with age, accumulation of anticholinergic effects of other drugs used, Parkinson's disease, cerebrovascular diseases, multiple sclerosis and schizophrenia.

When evaluated together with the literature, in our case, the discontinuation of solifenacin treatment the regression of symptoms in the second week after the initiation of antipsychotic treatment, the absence of organicity that may cause psychosis and the lack of need for high antipsychotic doses in outpatient clinic visits suggest that the psychotic attack was associated with solifenacin.

Solifenacin is a frequently used agent in the treatment of OAB. Although it is known that it may have central nervous system and psychiatric side effects with its introduction to the market in 2004, data on this subject are limited. To our knowledge, this is the first case of psychosis associated with solifenacin reported in our country. Although psychosis is very rare with solifenacin treatment, it should be kept in mind that if an acute psychotic attack occurs while under solifenacin treatment, the disorder may be related to this treatment. In addition to the necessity of selecting agents with known lower central effects for treatment, it would be highly beneficial to inform patients about acute psychiatric conditions that may occur due to this treatment and how to manage these conditions.

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