Psychiatria Danubina, 2025 Vol. 37, No. 3, pp 377-379 https://doi.org/10.24869/psyd.2025.377 *Case Report*

Suspected post-injection delirium/sedation syndrome following aripiprazole long-acting injection

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INTRODUCTION

We highlight the occurrence of a group of symptoms most probably resulting from an application of aripiprazole long-acting injection (ALAI). There is only limited literature on aripiprazole exposure and overdose (Christensen et al., 2018). To our knowledge, in the literature, there are no known cases of possible post-injection delirium/sedation syndrome following aripiprazole long-acting injection. Our case report was presented as a poster at the 37th ECNP Congress (Gabersek et al., 2024).

CASE PRESENTATION

A 43-year-old Caucasian woman diagnosed with paranoid schizophrenia and major depressive disorder had been hospitalised multiple times in a psychiatric clinic in the past and has been regularly treated as an outpatient at the psychiatric outpatient care centre. She also had a history of drug addiction, with abstinence having lasted for six years. The infection with hepatitis C in 2015 has been in remission since 2017. The patient has a diagnosis of celiac disease from the early age.

The patient was receiving regular once-monthly application of ALAI since 2015, in the dose of 400 mg. Since 2019 the interval of applications of ALAI has been shortened to 3-3.5 weeks on the patient's request, because she experienced restlessness and anxiety symptoms in the last week prior to the next application.

On 23 September 2022, the patient received her regular application of ALAI, according to the manufacturer's instructions (RxList, 2015). In the early morning on that day, she had consumed her regular dose of sertraline 150 mg. After the application, the patient left the outpatient care centre, accompanied by her mother.

Four weeks later, at the next regular medical presentation, the patient reported retrospectively about the symptoms, which started appearing approximately 30 minutes after the last application of ALAI and lasted for about 24 hours. The patient described, she had suddenly felt warm and had been sweating excessively. She experienced hearing loss in both ears, and immediately after that she lost consciousness and fell to the ground. According to her mother, she was unconscious for a few seconds and was not reacting to her mother's calls or her tapping her face. Then she stood up, her skin being pale, she started sweating excessively, she felt a headache at the back of her head and had blurred vision. Approximately one hour later she felt very cold but was not shaking. The whole afternoon and the evening she could not think clearly, had trouble concentrating and was feeling restless. In the evening she was unable to fall asleep for many hours. During that afternoon, the evening and the next morning she noticed a few slight nosebleeds.

The patient's mother reported retrospectively about similar symptoms. At the time of the symptoms the patient did not contact any medical professional. In the medical follow up the patient's mental status was normal and by psychiatrist's impression there were no deviations in her somatic and neurological status. The laboratory analysis on 21 November 2022 and 12 January 2023, including complete blood count, electrolytes, hepatic and renal panel, thyroid function, prolactin level, vitamin B12, folic acid levels and urine analysis, was normal. Aspartate aminotransferase was slightly above the normal range at 0.53 mckat/L. The vital signs and electrocardiogram were normal.

After the described symptoms the therapy with ALAI was converted to oral aripiprazole in the daily dose of 25 mg. During the subsequent three-year course of outpatient psychiatric treatment, no psychological or physical sequelae related to the described event were observed in the patient.

DISCUSSION

No cases of overdose associated with adverse effects were reported in clinical studies with ALAI. Special care should be taken to prevent accidental injection of this drug

into a blood vessel. The potentially medically significant signs and symptoms of intoxication observed included lethargy, increased blood pressure, somnolence, tachycardia, nausea, vomiting and diarrhoea. The potentially medically serious signs and symptoms reported included somnolence, transient loss of consciousness and extrapyramidal symptoms (European Medicines Agency, 2018).

Aripiprazole may cause orthostatic hypotension due to its α_1 adrenergic receptor antagonism (Takahashi et al. 2021). Orthostatic hypotension, postural dizziness and syncope were reported in placebo-controlled trials on adult patients (Torgovnick et al., 2008). A review of literature showed there is only limited literature on epistaxis as a side effect of aripiprazole. A few risperidone-related cases of epistaxis in adult and children are described. Binici & Güney (2017) describes two children who had epistaxis during aripiprazole and risperidone treatment. They also describe possible mechanism of aripiprazole that could explain this adverse effect (thrombocytopenia and 5HT2A antagonism).

Supportive therapy, maintenance of airway patency, oxygenation and ventilation, and symptom management are key in the treatment of overdose. Close medical supervision and monitoring should be continued until the patient has fully recovered (European Medicines Agency, 2018).

CONCLUSION

This report has some major limitation. The first one is that the data are only based on the reporting of symptoms retrospectively by the patient and her mother, so the symptoms have not been evaluated by medical professionals and the medical follow up was delayed.

Another limitation is that, according to our findings, a group of symptoms that could speak in favour of a possible post-injection syndrome after ALAI application has been described for the first time. So far, the post-injection syndrome has only been described for olanzapine pamoate, the incidence of which is approximately 0.07% of all injections applied and in approximately 1.4 % of patients (Jakovljević, 2014; Uzun S et al., 2017). Only one case report has been published (Mirza et al., 2018) about possible post-injection syndrome when using paliperidone palmitate (10 days after second application).

To conclude, we believe it is important to report this case since it draws attention to an important possible complication after the application of ALAI. It is our hope that our case report will encourage observation and further research in the area.

Ethical Considerations: Does this study include human subjects? YES

Authors confirmed the compliance with all relevant ethical regulations.

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