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Aripiprazole causing false positive urine amphetamine drug screen in an adult patient with bipolar disorder

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ABSTRACT

There has been only a few reports regarding aripiprazole causing false positive urine amphetamine drug screens, exclusively on children accidently ingesting aripiprazole.
Herein, we present the first reported case of a 40 year old woman affected by Bipolar I Disorder, treated with aripirazole at therapeutic oral dose ranging from 15 mg/day to 30 mg/day, in the context of a depressive episode with mixed and psychotic features, showing a false positive urine amphetamine drug screen. We document the relationship between aripiprazole-dose, plasma concentration and amphetamines values in toxicologic urine examinations over time. Awareness of potential false positive urine amphetamine drug screens during aripiprazole treatment can condition therapeutic choices and prevent legal implications.

1. Introduction

Urine drug screening (UDS) is commonly used to identify the presence of certain substances. The most frequently used UDSs are the immunoassay techniques because of their low cost, simple use and rapidity of results. Unfortunately, due to the lack of specificity, false positive results can occur and many medications showing a cross reaction with the immunoassay used in UDS have been reported in literature [1]. The majority of these false positives results stem from a similarity in the structure of the parent medication or one of its metabolites to the tested drug [2]. The best practice following a positive UDS involves confirmation with the mass spectrometry (MS) technique, such as gas chromatography–mass spectrometry (GS-MC) or liquid chromatography-tandem mass spectrometry: MS testing, however, is limited or not available in many hospitals [3]. An ample list of cross-reacting medications, including a variety of antidepressants and antipsychotics, can be found in literature. Of the selective serotonin reuptake inhibitors, sertraline has been reported to cause false-positive results for benzodiazepines and lysergic acid diethylamide (LSD), and fluoxetine has been reported to cause false-positive results for LSD and amphetamines. Of the tricyclic antidepressants (TCA), amitriptyline, desipramine, doxepin, and imipramine have been reported to cause false-positive results for LSD, and desipramine and doxepin have additionally been reported to cause false-positive results for amphetamines. Of the second-generation antipsychotics, risperidone has been reported to cause false-positive LSD results; quetiapine, false-positive methadone and TCA results. The first generation antipsychotics chlorpromazine and haloperidol, may cause false-positive LSD results [1].

In particular, amphetamine immunoassays are the most commonly associated with false-positive results screening tests available, due to the difficulty of developing specific antibodies able to detect amphetamines, their isomers and other amphetamine-type compounds, as well as other metabolically produced amine-containing compounds [4,5].

Aripiprazole is an atypical antipsychotic approved for the treatment of specific psychiatric disorders due to its peculiar activity of 5HT2 antagonism and partial dopamine agonism [6]. There is an emerging use of aripiprazole in substance use disorders, for example in treating psychotic symptoms of patients diagnosed with amphetamine-induced psychotic disorder, in particular negative psychotic symptoms [7]. Some recent studies suggested a possible efficacy of aripiprazole in the context of dual disorders, lowering both desire for and the use of cocaine [8] and alcohol [9] in comorbid schizophrenic subjects; moreover, it has been demonstrated also the effectiveness of aripiprazole on obsessive-compulsive specific component of craving in alcohol dependence [10].

To our knowledge, only two cases of aripiprazole causing false positive urine amphetamine in drug screen have been reported, consisting of two infants: a 16 month-old girl after accidental ingestion of

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aripiprazole to 45 mg and a 20-month old girl with an ingestion of aripirazole at unknown dosage [11].

2. Methods

This was a case report. Informed consent was obtained from the patient.

3. Case report

A 40 year old woman diagnosed with Bipolar I Disorder was hospitalized for acute psychotic mixed episode in our psychiatric department.

When the patient was hospitalized at the beginning of January, blood analyses were performed and were unremarkable, including electrolytes, liver, thyroid and kidney functions and UDS was negative. A regimen of aripirazole was started and increased up to a dosage of 20 mg/day with clinical improvement. The patient was discharged after two weeks and continued clinical observation and therapies in a Day Hospital setting.

Another hospitalization was deemed necessary after few weeks, due to relapse of psychotic symptoms. At week 1 we increased aripirazole dosage up to 30 mg/day and urine drug screen and aripirazole plasma concentration were performed.

UDS tested positive only for amphetamines, revealing 789 μg/L, while aripiprazole blood concentration was 452.5 ng/mL, above therapeutic range (150–350 ng/mg). The patient had no prior history of illicit drugs abuse before and she assured doctors of no drug use in the recent past. Such an information was cross-checked also with other family members.

Hence, we reduced aripiprazole to 20 mg/day and optimised mood-stabilizing therapy with valproic acid, obtaining initial response of psychotic symptoms.

Compliance to psychopharmacological therapy and prevention of substance use were monitored by repeated checks of aripirazole plasma concentration and UDS during week 2, 3 and 4 (see Fig. 1).

In week 2 a blood aripirazole dosage of 320 ng/mL and a 499 μg/L dosage of urinary amphetamine were found with an aripiprazole daily dose of 20 mg/day.

During week 3, aripirazole dosage was further reduced to 15 mg/day and then stopped on week 4 to replace it with another atypical antipsychotic (olanzapine).

Week 3 screening tests showed aripirazole blood levels of 256 ng/mL and urinary amphetamine levels of 333μg/L, week 4 tests scored respectively 106.2 ng/mL and <100 μg/L (see Fig. 1, Table 1).

The patient being hospitalized leads to a fair amount of certainty that no substance had been used, hence the finding of a concentration close to amphetamine cutoff levels may be related to cross reaction.

4. Discussion

To our knowledge, the present report is the first to document potential false-positive UDSs in an adult female patient taking oral aripirazole. After searching Pubmed and Embase for published case reports and case series implying an association between aripirazole and amphetamine urinary levels only two case reports of accidental aripiprazole ingestion in infants were identified to support the hypothesis that the false positive amphetamine results were secondary to aripiprazole.

We can infer that the observed values of amphetamines were not related to the assumption of any illicit drug, as they were still detectable in urine for a long time after the first 72 h following the hospitalization, showing, indeed, a proportional trend to the dosage of aripiprazole (Fig. 1).

Clinicians should be aware of all the psychotropic agents that could have a potential cross-reaction with illicit drugs in order to avoid misinterpretation of data and subsequent misleading clinical and therapeutic decisions.

Hence, in this report, we want to focus the attention on the possible cross-reaction of aripiprazole with amphetamines, since this can lead to a relevant issue, given its wide use in psychiatric disorders, especially in dual disorders.

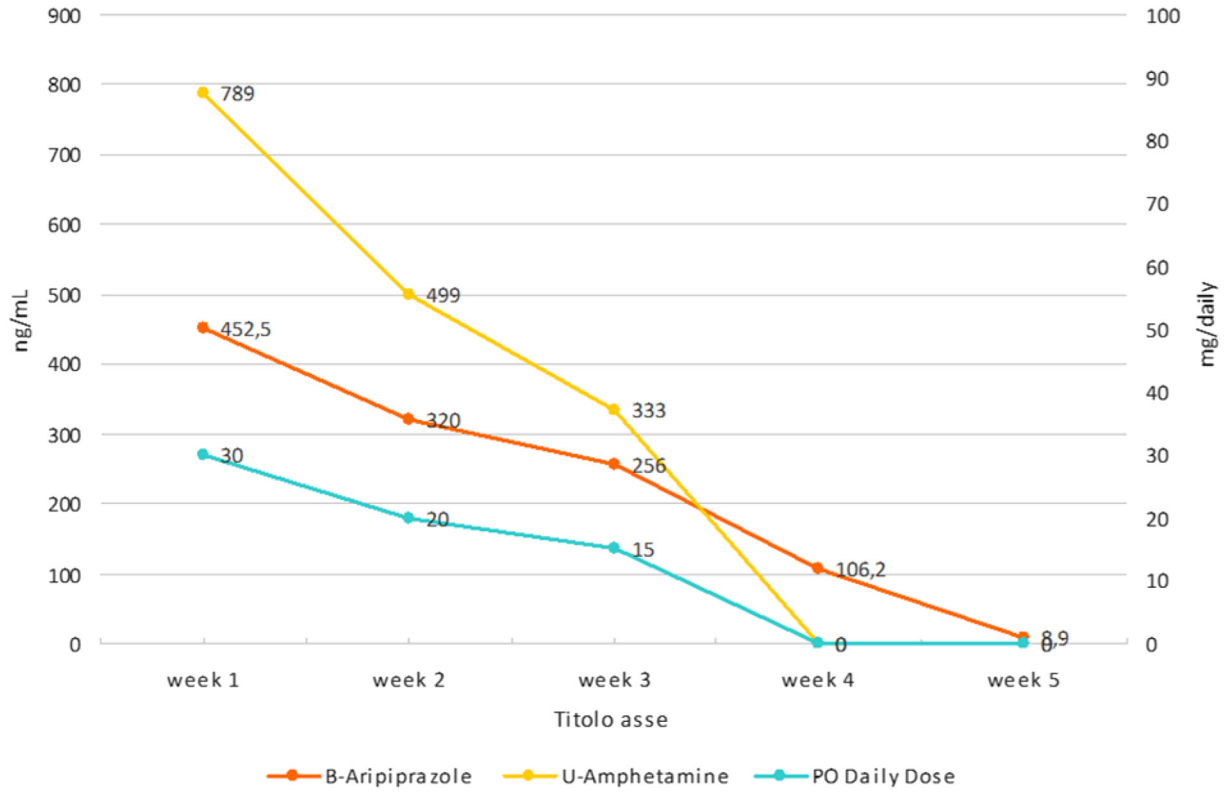

Fig. 1. Relationship between Aripirazole dosage, plasma concentration and Amphetamine urinary values.

Table 1
Aripiprazole dosage, blood concentration and urinary values.

	Week 1	Week 2	Week 3	Week 4	Week 5
PO daily dose	30	20	15	0	0
B-Aripiprazole (Aripiprazole blood concentration)	452,5	320	256	106,2	8,9
U-Amphetamine (urinary amphetamine concentration)	789	499	333	0	0

Ultimately, further insight in the field can concur to optimize patient care, since positive UDSs can have a profound impact in the patient's life, with serious social, familiar and legal implications and consequences.

Declaration of competing interest

Drs. V. Caricasole, I. Di Bernardo, G. Cirnigliaro, E. Piccoli report no financial relationships with commercial interests.

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