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Case report: Albendazole associated psychosis

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Abstract

Introduction: The association of psychosis with albendazole monotherapy has not been established in current literature.

Case Report: We present the first reported case of acute psychosis associated with albendazole. Upon cessation of the agent and the introduction of aripiprazole, the patient's psychosis remitted, and the patient did not present for acute treatment in the months to follow.

Discussion/Conclusion: The temporal relationship and laboratory data support albendazole's role in leading to the aforementioned toxicity. Such reactions, although rare, can drastically impact patient care and may warrant increased provider consideration when choosing to prescribe albendazole.

Keywords: albendazole, psychosis, toxicity, case report

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Introduction

Albendazole is a benzimidazole broad-spectrum anthelmintic agent that is used worldwide to treat infections with nematodes, cestodes, and some tremadoes.[1,2] Dosing duration varies from a single dose to daily dosing for up to 6 months, dependent upon the indication. Common daily dosing ranges from 400 to 800 mg given in single or divided doses.[1]

Due to its penetration of central nervous system, albendazole is used for treating parasitic infections of the brain, including neurocysticercosis, and neurologic adverse reactions (ie seizures, headaches) have been reported.[3] Whether these side effects are secondary to drug therapy versus parasitic infection is unknown.[4] However, there have been no reports of albendazole monotherapy leading to psychosis in the current literature.[5,6]

To our knowledge, this is the first case of albendazole monotherapy, although at a supratherapeutic dose, that has been associated with psychosis.

Case Report

In October 2018, a 39-year-old female with a pertinent history of major depressive disorder, borderline personality disorder, type-2 diabetes mellitus, and polysubstance use disorder was brought to the emergency department with altered mental status. Patient was disorganized, responding to internal stimuli, laughing inappropriately, and reporting visual hallucinations of her father. Patient scored 58 on the Brief Psychiatric Rating Scale, indicating markedly ill disease. Of note, no history of depression with

psychotic features or previous psychosis associated with borderline personality disorder was noted in the chart. Patient was noted to be covered in scabs, which she attributed to "worms," despite active picking. Emergency medicine providers noted no signs of active infection. To eradicate this delusional infestation, the patient reported purchasing a supply of albendazole from an online manufacturer in the Ukraine and taking a dose of albendazole 1000 mg by mouth (PO) once daily for 20 consecutive days prior to admission, which she self-discontinued 2 days prior to admission. Patient reported taking this dose as the bottle had specified a dose of albendazole 500 mg PO daily for canines, and "I wanted to make sure I had a higher dose than what you'd give a dog." Patient's husband confirmed the above and the current presentation as an acute change from baseline (although, he did report infrequent, benign delusions in the past). Husband denied any other substance use and acknowledged that the above symptoms began "a few days" following albendazole initiation.

Patient denied any previous psychiatric hospitalizations but was noted to have a history of multiple suicide attempts by overdose. Patient denied any active suicidal or homicidal ideation. Upon admission, current medications included fluoxetine 40 mg PO once daily, gabapentin 300 mg PO 3 times daily for pain, alprazolam 2 mg PO twice daily, metformin 500 mg PO twice daily, and simvastatin 20 mg PO at bedtime. Appropriate adherence to medication was confirmed by review of refill history and no medication changes had been noted in recent months. Patient reported smoking "a little over one pack per day" of cigarettes and denied recent alcohol consumption.

As seen in the Table, pertinent laboratory tests and monitoring upon admission included elevated liver enzymes and a prolonged QTc of 690 ms. More specifically, the patient's electrocardiogram upon admission was read as normal sinus rhythm with a QRS of 74 ms and a QTc of 690 ms, potentially secondary to albendazole or fluoxetine therapy.[7,8] The most recent routine QTc value was reported as 442 ms (4/2014). A confirmatory blood drug test using gas chromatography resulted as negative for all substances besides alprazolam. Confirmatory test was comprehensive and tested for pertinent substances, including barbiturates, benzodiazepines other than alprazolam, cannabinoids, cocaine, ethanol, muscle relaxants, opiates/opioids (including methadone but excluding buprenorphine and fentanyl), phencyclidine, and stimulants. Upon psychiatric admission, the patient's albendazole was discontinued and aripiprazole 10 mg PO at bedtime was started. Aripiprazole was chosen over other antipsychotics because of its decreased risk of causing a prolonged QTc interval.[8] Fluoxetine therapy was held because of the prolonged QTc.

TABLE: Pertinent labs throughout patient hospital stay

Variable Tested	Hospital Day 1	2	3	4
Sodium, mmol/L	144	141		
Potassium, mmol/L	3.6	3.8		
Serum chloride, mmol/L	104	101		
Glucose, mg/dL	315	260	221	245
Calcium, mg/dL	10	9.9		
Aspartate aminotransferase, U/L	75	92		
Alanine transaminase, U/L	112	122		
Magnesium, mg/dL	2			
International normalized ratio, units			0.97	
Prothrombin time, sec			12.7	
QTc, ms	690		464	

On hospital day 3, the patient appeared clearer, was no longer responding to internal stimuli, denied any hallucinations, and appeared more organized. A repeat electrocardiogram also showed improvement (QTc = 462 ms). On hospital day 4, the Brief Psychiatric Rating Scale score was 21 (36% reduction since admission), and the patient was discharged home with aripiprazole 10 mg PO at bedtime, gabapentin 300 mg PO 3 times daily, metformin 500 mg PO twice daily, and simvastatin 20 mg PO at bedtime. Follow up was arranged for further outpatient evaluation of antidepressant therapy and appropriateness of aripiprazole continuation due to symptomatic resolution. Upon follow up within 1 month, the patient was restarted on fluoxetine 40 mg PO daily and aripiprazole was tapered off. Per chart review, fluoxetine was restarted to target the patient's history of major depressive episodes (although active symptomatology was not noted). Aripiprazole was weaned off due to the patient's outpatient provider deciding that the psychotic symptoms were most likely secondary to albendazole versus an organic process. No repeat episodes of psychosis were noted in the approximately 10 months to follow this case. No further electrocardiograms were conducted to further evaluate the long-term resolution prolonged QTc interval.

Confirmatory testing against an authentic albendazole standard via Fisher Scientific with high performance-liquid chromatography-mass spectrometry was conducted to validate the contents of the patient-provided sample. The resulting peaks from both products at 254 nm were identical, as shown in the Figure, confirming the presence of albendazole in the patient sample. Concentration data from the ultraviolet analysis suggested that the sample contained approximately twice the amount of albendazole that was indicated on the label, indicating even higher supratherapeutic doses of albendazole 2000 mg PO daily (patient specific dose of 22.3 mg/kg/d). The ultraviolet

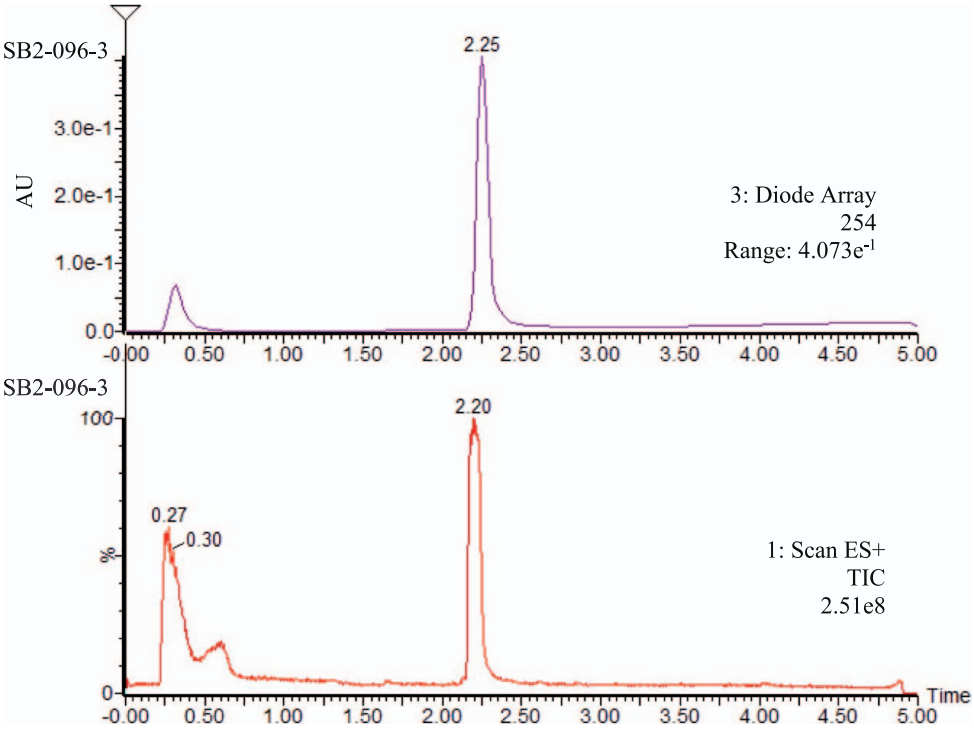

FIGURE: Comparison of albendazole standard (upper image; 1 mg/mL) and patient-provided sample (lower image; 1 mg/mL) at 254 nm

analysis also indicated that the sample contained about 3 to 5% impurities. However, all impurities were structural analogues of albendazole. (The complete ultraviolet report is available upon request.)

Discussion

Although current literature[5,6] reports rare cases of psychosis associated with albendazole-ivermectin combination therapy, no evidence exists that relates albendazole monotherapy with this symptomatology. This association is supported by the temporal relationship between the initiation of albendazole and the onset of symptoms. This link is further supported by symptomatic improvement following albendazole discontinuation. Per patient report, albendazole therapy was self-discontinued approximately 2 days prior to admission. Based off the terminal half-life of albendazole's active metabolite, albendazole sulphoxide, of 8 to 17 hours, the drug undergoes complete clearance in approximately 40 to 85 hours in healthy individuals.[9-11] However, our patient's resolution of symptoms occurred about 5 days following cessation. As the reported half-life of albendazole sulphoxide was studied in healthy individuals at recommended doses/durations of therapy without elevated liver enzymes, a prolonged half-life is possible for our case. Further, as mentioned above, in the 10 months that followed, recurrence of the psychotic symptoms did not occur despite the tapering of the aripiprazole.

Proposed mechanisms for albendazole's association with psychosis stem from the limited evidence of benzimidazole compounds acting as ligands at the dopamine and/or serotonergic receptors.[12] Theoretically, this case suggests that when albendazole is given at supratherapeutic doses, the medication may serve as an agonist at dopamine and or/serotonin receptors, leading to psychotic symptoms. Overall, the Naranjo score resulted at 3, indicating a possible association between albendazole and psychosis.[13]

This report is limited by the small percentage of impurities found in the albendazole sample; however, as they only made up about 3% to 5% of the overall sample, the possibility that the patient's psychosis was secondary to the impurities is very unlikely. Further cases and research are necessary to establish a definite causational link between albendazole and psychosis.

Conclusion

This case is the first to associate albendazole monotherapy, although at supratherapeutic doses, with psychosis. Evidence from this report suggests that providers should monitor for signs and symptoms of psychosis if choosing to prescribe albendazole therapy.

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