Hypothermia induced by *Aripiprazole* in the psychogeriatric patient

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BACKGROUND

Healthcare providers commonly prescribe antipsychotic drugs for various purposes, including managing, preventing, or treating conditions such as psychosis, substance withdrawal, delirium, and agitation (Grover, 2018). **It's essential to be aware that while hypothermia associated with antipsychotic drugs is relatively rare, hypothermia can still pose a significant risk to patients**.

Early diagnosis of hypothermia and the prompt implementation of appropriate treatment measures are crucial in preventing potentially life-threatening outcomes (Kamp et al., 2021). Therefore, **healthcare professionals must exercise vigilance and monitor patients closely when prescribing antipsychotic medications** to ensure their safety and well-being.

RESEARCH QUESTION

In the psychogeriatric patient, does Aripiprazole contribute to incidences of life-threatening hypothermia?

Aripiprazole (*ABILIFY*)

MOA: Atypical antipsychotic that partially agonizes dopamine D2 and serotonin 5-HT1A receptors, antagonizes serotonin 5-HT2A receptors

Indications: Schizophrenia, Bipolar I disorder, Major Depressive Disorder

Serious Reactions: Neuroleptic Malignant Syndrome, Tardive Dyskinesia, Orthostatic Hypotension, Convulsions, Stroke

Black Box Warning:
- Increased mortality risk in elderly pts on antipsychotic treatment for dementia-related psychosis; most deaths due to cardiovascular or infectious events
- Not approved for depression in peds pts due to increased suicidality risk in this age group.

Table 1. Drug Information on ABILIFY (Otsuka America Pharmaceutical, 2019)

METHODS

Question formulated based on interest in selected case.

Key Terms: "*Antipsychotic drugs"; "Geriartric"; "Hypothermia", "Aripiprazole", "Thermoregulation"*

Databases Used:
- PubMed
- University of Maryland Eastern Shore Frederick Douglass Library.

Three relevant articles were selected based on a systematic reviews and retrospective studies investigating the incidences of hypothermia due to antipsychotic medications.

A written informed consent was obtained from the patient for
publication of this case report. A copy of the written consent is
available for review upon request

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CASE DESCRIPTION

Patient: A 62 y.o female who resides at Caroline nursing facility at Denton, MD with a medical hx significant for schizoaffective disorder, developmental delay, hypothyroidism, paroxysmal a-fib not on anticoagulation, HLD, frequent UTI, dysphagia, venous stasis, obesity, bedbound status-frequent admissions for presentation of hypoglycemia, hypotension, and hypothermia – found to be septic at times without a source of sepsis.

C/C: "Sent from group home for low temp per staff was 93 F. Enroute EMS report temp of 97.7 and patient has no complaints"

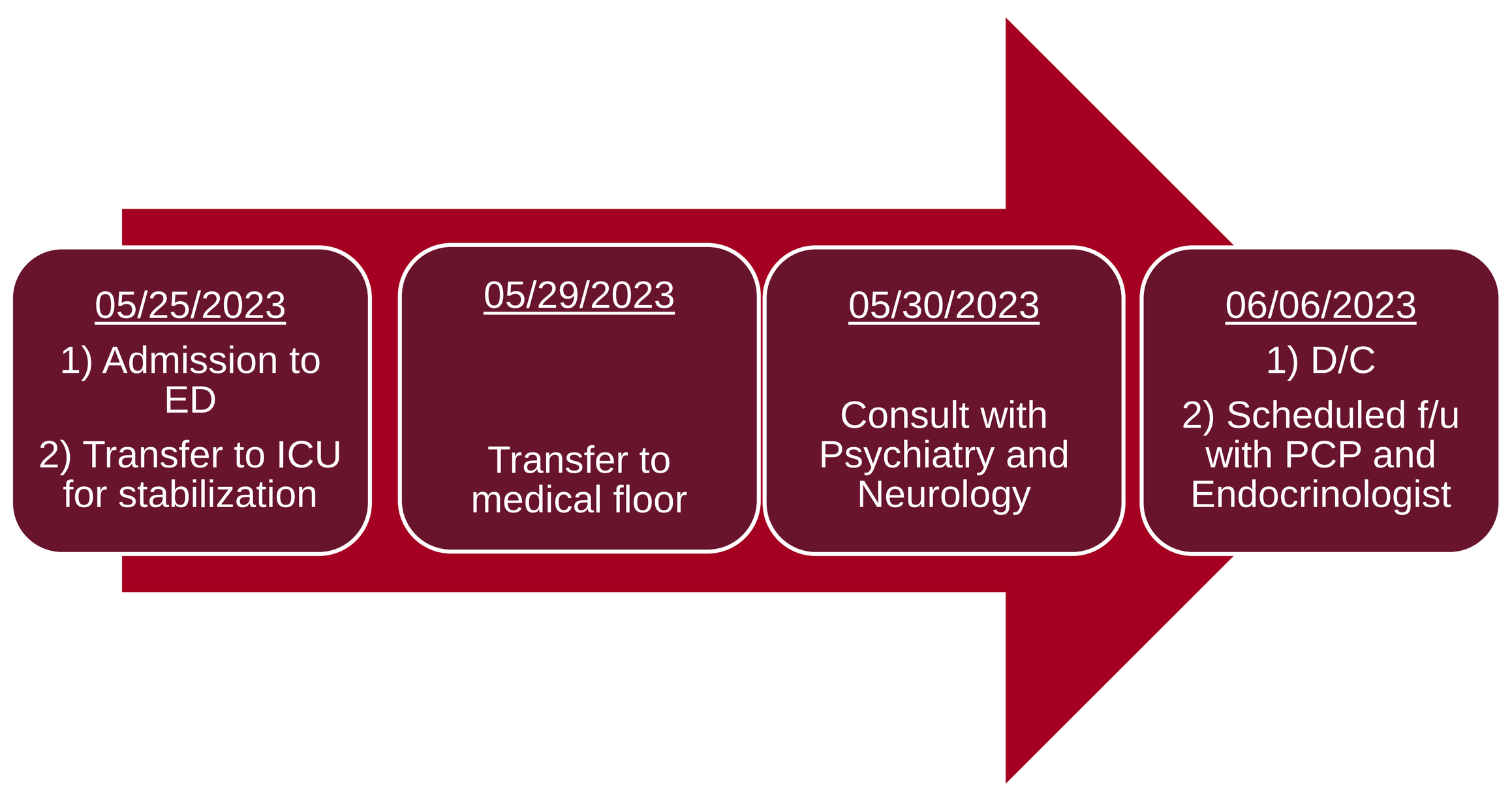


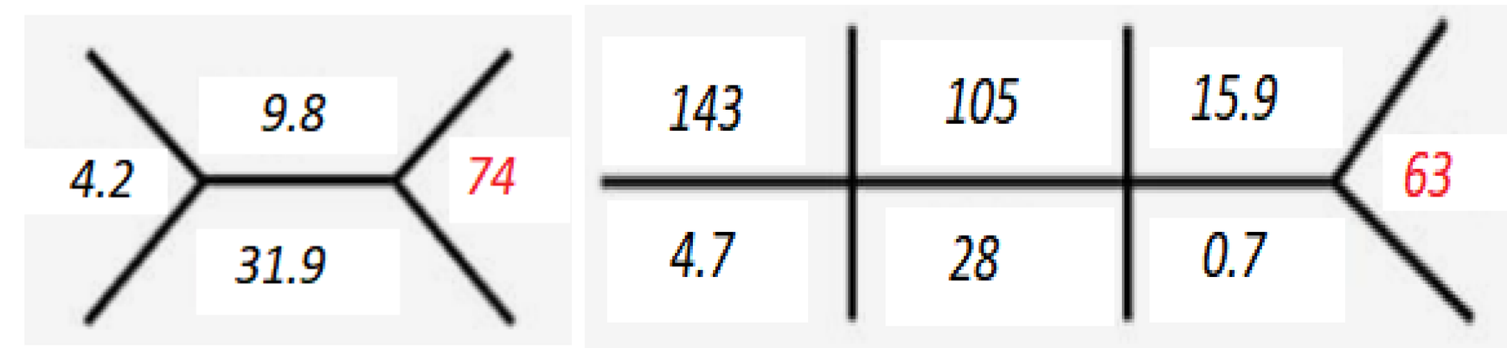
Figure 1. Chronological description of episode of care

RESULTS

05/25/2023

Pt arrives to the ED from nursing home due to hypothermia. Vitals on arrival are BP 134/96 HR 60 RR 20 **T 90.3 F** → Pt placed on Bair hugger to increase body core temperature. Repeat vitals **BP 65/33 HR 40** RR 12 **T 94.8 F.** Pt is lethargic, unresponsive to questions**.**

Labs
UA – Moderate Leukocyte Esterase with moderate blood
eGFR – 98
Viral Swabs (COVID, RSV, Flu A and B) – NEG
EKG – NSR without ST-abnormalities
TSH – 1.9 (WNL)
Free T4 – 1.29 (WNL)
Blood Cultures 2X – NEG



Imaging
CXR – Bilateral Alveolar Pulmonary Perihilar Infiltrates, no pleural effusions
CT Abdomen/Pelvis – Cholelithiasis with gallbladder distension, no evidence of obstruction or appendicitis
CT Brain – No Acute Abnormalities
MRI Brain – No Acute Abnormalities

Plan:
1) Transfer to ICU for continued care
2) Treatment
Bair-hugger to restore Body core temperature (BCT).
Dextrose Drip for hypoglycemia
IV Fluid Bolus for hypotension
Zosyn + Vancomycin for concerns of Aspiration Pneumonia as seen in CXR.
Discontinue Aripiprazole – as was done in the past for similar presentation of patient..

05/29/2023

Outcomes: BCT, blood glucose, and blood pressure slowly corrected with the above interventions. Pt became more interactive, able to state her name. Can be seen coloring books.
Vitals before transfer to Medical Floor
BP 124/68 HR 68 RR 18 T 98.2 F

05/30/2023 - Consults

Consult Neurology – Unable to appreciate neurological issue contributing to symptoms.
Consult Psychiatry – Medications likely contributing to pt's presentation; likely culprit includes Aripiprazole OR Keppra – **Neurology not concerned about Keppra toxicity**.
Keppra Levels – 59 mg/L (Ref 12-46 mg/L)
Consult Surgery – Pt not a candidate for surgery (Cholecystectomy).
Consult Palliative care to discuss goals of treatment.

06/06/2023

Patient was discharged back to nursing facility with planned follow-up with PCP and Endocrinologist (Not documented on patient's chart)

Significant Events:

Pt did start having visual hallucinations while off the Aripiprazole – dose was titrated to therapeutic dose by psychiatry prior to D/C. Was visibly tearful in bed, however, non-verbal as to why – likely secondary to underlying depression. Did say that she did not want to return to nursing facility.

DISCUSSION

A study conducted by Ajayi and Holroyd (2017) found that intolerance to APDs can occur suddenly, especially in the geriatric population. Although the patient had been on Aripiprazole for many years before her presentation, it is possible that she suddenly developed an intolerance to this drug. A systematic review by Zonnenberg et al. (2017) found that Hypothermia can occur within 2-14 days of initiating an antipsychotic treatment or a dose increase.

In patients experiencing delirious symptoms, aphasia, bradycardia, and nonspecific fatigue, it is vital to consider hypothermic thermoregulatory failure due to APD administration (Kreuzer et al. 2012). For this reason, the discontinuation of Aripiprazole was appropriate in the care of this patient. However, since all possible contributing factors to the Hypothermia were addressed simultaneously (including infection vs. medication etiology), it is difficult to assess which factor was most significant. It would be ideal to address each contributing element in future studies. Given the patient's diminishing condition upon presentation, all the interventions were necessary.

The patient's family expressed frustration because, until now, there has not been an actual explanation for what has been contributing to her recurrent symptoms. Previous studies, as well as the findings in this case report, are highly suggestive that her Hypothermia was likely secondary to an intolerance to her APD. However, this is difficult to conclude with great certainty due to possible contributing factors present in this case, including her response to a UTI, pneumonia, and levetiracetam toxicity.

CONCLUSION

1 - Healthcare providers should engage in regular body temperature monitoring of patients who initiate (or increase the dose of) APDs especially in the presence of multiple risk factors. Providers should have an increased index of suspicion for antipsychotic medications as hypothermia inducers, even in cases where patients have used them for an extensive period without such effects prior, especially in the geriatric population. More studies are needed to assess the relative risk of Hypothermia associated with individual APDs.

2 - Implication for medical literature:
This case report contributes to evidence of APD-induced hypothermia. Furthermore, it alerts healthcare providers of the rare side effect of antipsychotic medications, which calls for closer monitoring of patients who are started on these medications.

3 - Limitations to this case report include:
- The patient had multiple comorbidities that may be contributing to Hypothermia.
- All possible contributing factors were addressed at once (versus individually) – it was difficult to assess which factor was most significant (Infection vs Drug Induced)
- No long-term follow-up documented.
- Low reliability due to multiple factors being addressed all at one – difficult to assess true cause of hypothermia.

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