A Case of Risperidone-Associated Hyperthermia

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Introduction

We report an elderly stroke rehabilitation patient with polypharmacy who developed recurrent unexplained fever that resolved completely after discontinuation of risperidone.

Case Report

A 75-year-old female with three prior cerebrovascular accidents and a history of hypertension, cognitive disorder, neuralgia, and seizure was admitted for rehabilitation following a subcortical Intracranial hemorrhage in the right putamen. She was on Levetiracetam, Carbamazepine, Pregabalin, Amitriptyline, and Clonazepam. Risperidone was added for delirium. Initial Korean Modified Barthel Index (K-MBI) score was 32, indicating severe functional dependence. Early during rehabilitation, the patient exhibited high fever unresponsive to antipyretic therapy accompanied by mild elevation of CRP. Despite the absence of significant subjective symptoms and unremarkable chest and abdominal CT findings, empirical broad-spectrum antibiotic therapy was initiated to cover a possible occult infection.

After antibiotic cessation, fever > 38°C recurred in a three-day cyclical pattern, reported after exertion and unresponsive to antipyretics. Extensive re-evaluation (labs, cultures, PCRs, EKG, echocardiogram, chest and abdominopelvic CTs) identified no infectious source, with normal procalcitonin and all cultures negative.

Risperidone-associated hyperthermia was suspected, so we discontinued Risperidone and Amitriptyline, and halved Clonazepam stepwise, without applying antibiotics. Fever resolved completely, and the patient was discharged home ambulating under supervison and a K-MBI score of 86.

Discussion

This case involved an elderly stroke rehabilitation patient with polypharmacy who developed recurrent hyperthermia, prompting an extensive infectious workup. Bacterial infection was unlikely given consistently normal procalcitonin and negative cultures. Central neurogenic fever was also unlikely, as fever resolved completely upon risperidone discontinuation. Neuro-leptic malignant syndrome was excluded by the absence of muscle rigidity, autonomic instability, and creatine kinase elevation.

Risperidone-associated hyperthermia is explained as failed heat dissipation rather than an elevated hypothalamic set point, consistent with unreliable antipyretic response. Risperidone's dopamine D2 antagonism and serotonin 5-HT2A blockade may disrupt hypothalamic thermoregulation. Contributing factors likely included central impairment of heat-loss pathways; increased anticholinergic burden from combined psychotropics reducing diaphoresis and evaporative cooling; sedation diminishing behavioral thermoregulation; and peripheral vasoconstriction limiting convective heat loss.

This case supports that risperidone may evoke fever via neurotransmitter-mediated hypothalamic dys-regulation, compounded by sedation, autonomic impairment, and reduced evaporative heat loss. Early recognition and withdrawal are essential, as discontinuation reverses thermoregulatory dysfunction.

References
- Drug-associated non-pyrogenic hyperthermia: a narrative review
- Antipsychotic Medication-Induced Hyperthermia Leading to Cerebrovascular Accident: A Case Report

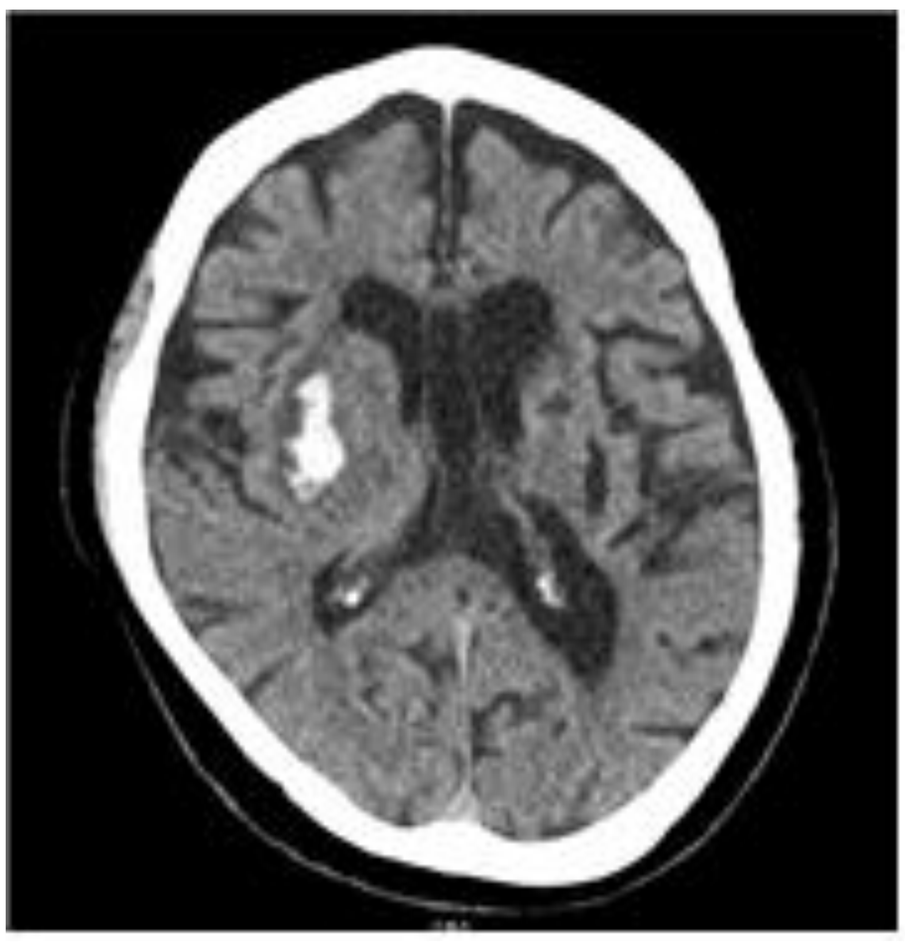

Figure 1. CT Brain without enhance (HD#1) : Acute ICH in right BG

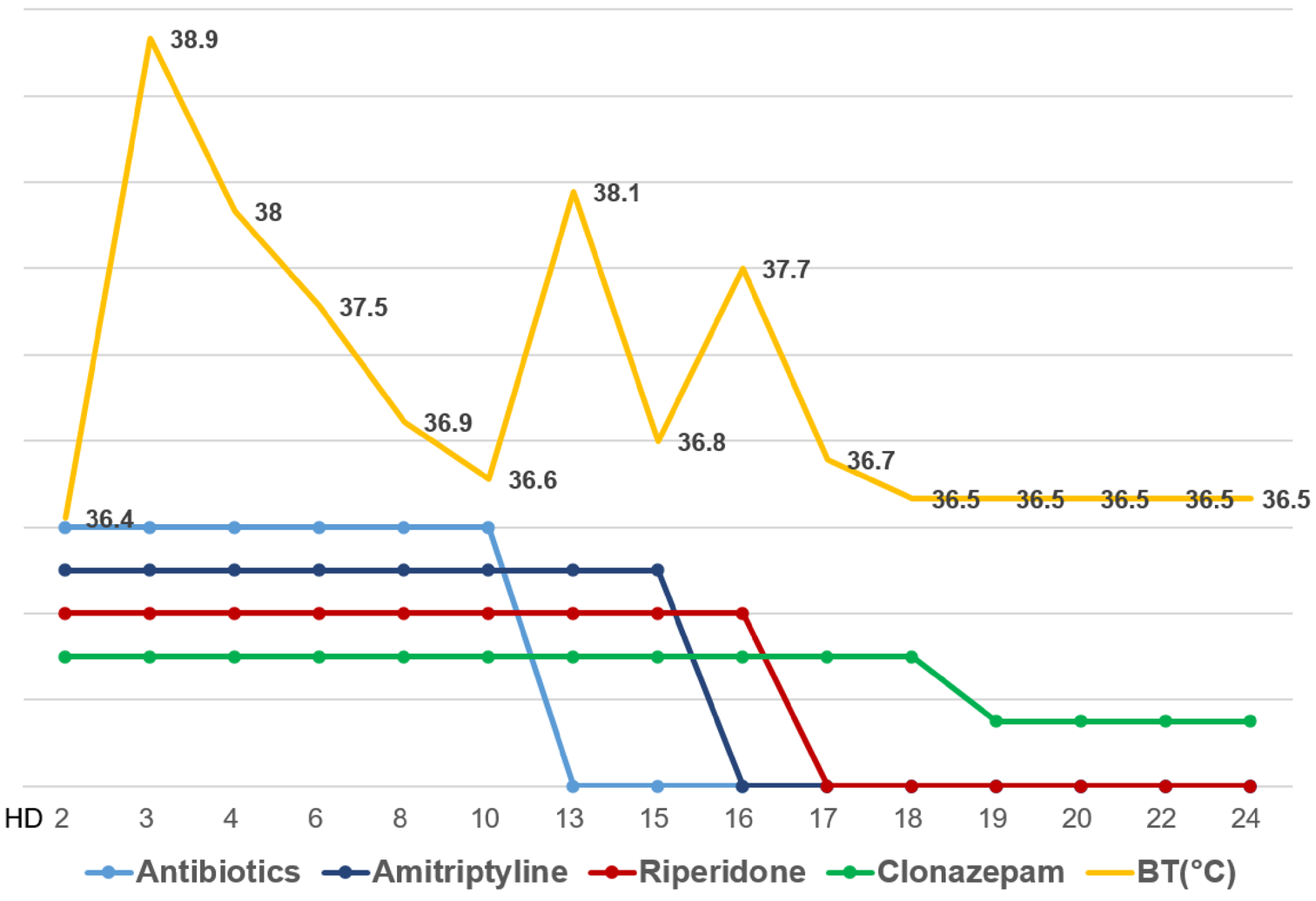

Figure 2. Temporal Relationship between body temperature and medication use