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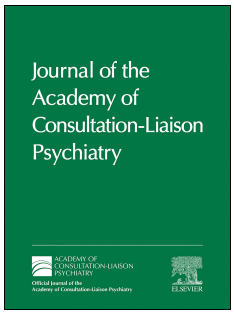

Acute Parkinsonism in a Man with Acute Cholecystitis

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Title: Acute Parkinsonism in a Man with Acute Cholecystitis

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To the Editor,

Acute illness can significantly alter drug metabolism through overt organ dysfunction and by cytokine-mediated inhibition of hepatic enzymes, a mechanism well documented with clozapine.[1] However, less is known about other hepatically metabolized antipsychotics for which routine drug level monitoring is uncommon. This case describes acute parkinsonism in a patient with both acute liver dysfunction and baseline renal disease in the absence of recent dose increase. It highlights the importance of considering altered pharmacokinetics in the setting of acute illness and chronic organ dysfunction, where impaired metabolism and clearance may lead to delayed or unexpected toxicity.

Case

A 64-year-old man with bipolar I disorder and CKD III presented to the Emergency Department with one week of progressive ambulatory dysfunction. His bipolar disorder was well managed on risperidone 3 mg nightly and valproic acid 1000 mg nightly for the past several years, and he denied any changes to his medications in over 2 months. In the week prior to his presentation, the patient developed a shuffling gait, urinary incontinence, memory impairment, and tremors. He had previously been fully independent.

On exam, the patient was oriented to self and date but not to place or circumstance. He had a resting tremor in his jaw, cogwheel rigidity in all extremities, and dysdiadochokinesia in both hands. Finger-to-nose testing was intact, and asterixis was absent. He did not feel safe to walk. Head CT revealed no acute pathology or ventricular enlargement. Laboratory results showed AST 375 and ALT 431, alkaline phosphatase 285, PT 15.7 (all normal 3 months earlier), creatinine 1.40 (baseline ~1.31) and GFR 54 (baseline ~59). Valproate levels were 24 total, 9 free. Ammonia was normal. Abdominal ultrasound revealed an enlarged liver with multiple gallstones and gallbladder wall thickening, concerning for acute cholecystitis.

Risperidone and valproate were held for suspected drug-induced parkinsonism and acute liver injury. The patient was admitted to surgery and underwent laparoscopic cholecystectomy. His liver function tests normalized within 2 days post-op, during which the patient's motor and cognitive function rapidly improved. He did not develop any manic, depressive, or psychotic symptoms during hospitalization. He was fully ambulatory and without rigidity or tremor on post-op day 3. Risperidone was restarted at 2 mg nightly and valproate at 500 mg nightly. The patient was discharged home and did not require any physical or occupational therapy services.

Discussion

This case highlights the importance of considering altered pharmacokinetics of psychiatric medications during acute illness. Acute organ dysfunction likely altered risperidone pharmacokinetics, leading to medication accumulation and reversible medication toxicity.

Risperidone undergoes hepatic metabolism to active metabolites that are primarily renally cleared.[2] Impairment of either hepatic metabolism or renal excretion can therefore increase exposure to risperidone and its active metabolites. In addition to overt organ failure, systemic

inflammation and cytokine release can impact cytochrome P450 enzymes and meaningfully reduce hepatic drug metabolism.[3]

In this patient, an acute deterioration in liver function superimposed upon chronic renal impairment most plausibly led to the accumulation of risperidone or its active metabolites. Both motor (rigidity, bradykinesia) and nonmotor (incontinence, confusion) symptoms of parkinsonism subsequently developed.[4] Alternative explanations were considered and deemed less likely. Neuroimaging showed no structural causes such as normal pressure hydrocephalus or valproate-associated cerebral pseudoatrophy. Valproate-induced parkinsonism has been described in case reports, but the vast majority of cases reviewed showed notably higher serum levels than those observed in this patient.[5] The absence of asterixis and normal ammonia pointed away from hepatic encephalopathy. Acute delirium can present with motor symptoms, though these are generally nonfocal. Although establishing direct causality in individual cases has limitations, the patient's rapid improvement following risperidone discontinuation and normalization of liver function supports a reversible, medication-related effect despite no history of recent dose changes.

Ultimately, this case underscores the value of integrating medical and psychiatric knowledge in assessing new neuropsychiatric symptoms. Though routine monitoring of most antipsychotic drug levels is not standard practice, this case could suggest a potential role for individualized drug monitoring in the medically complex psychiatric patient.

Conflict of Interest/Disclosure Statement:
The author has no conflicts of interest to disclose.

Consent Statement:
Written informed consent was obtained from the patient for publication of this case report. All identifying information has been removed to protect patient confidentiality.

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Declaration of Interest Statement

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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