Young adult woman with altered mental status and mirror-writing following long-term use of montelukast

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Introduction
Montelukast is an oral leukotriene receptor antagonist used primarily for asthma and exercise-induced bronchoconstriction since 1998. It was linked to neuropsychiatric events that are more common in children. A black box warning was issued in 2020 by the FDA (1). These include anxiety, depression, aggressiveness, agitation, attention, memory impairment, sleep disorders, seizures, paresthesias, hypoesthesias and suicidal ideation (2). We report a case of a woman who presented with altered mental status and mirror writing following long-term use of montelukast.

Case Presentation
A young adult woman presented with altered mental status from home. Medical history significant for severe persistent asthma, motor vehicle accident complicated by traumatic brain injury at an early age, migraine and panic disorder. Per the mother, daughter looked confused, unable to recognize family members and unable to perform activities of daily living. Denied any headache, neck pain, nausea, vomiting, fever or chills. On ICS/LABA, montelukast, benralizumab, topiramate, eletriptan and sertraline. She had been intermittently on montelukast for 9 years and unclear adherence with previous reports of difficulty focusing, vivid dreams, insomnia, nightmares and “bad thoughts”.

Presented afibrile, tachycardic to 110. On physical exam, appeared tearful, in no apparent distress, oriented only to self, unable to recognize mother, followed commands. Laboratory analysis showed no anemia, no electrolyte derangements, euglycemia and normocapnia. Chest x-ray was normal. CT head without contrast reported no acute or chronic abnormalities. Neurology was consulted for altered mental status.

Workup included prompting the patient to draw a clock to understand cognition and constructional ability, where it was noticed that she mirrored several numbers (figure 1). The written test showed inversion of some letters and mirroring of others (figure 2).

When prompted to read, she would read backwards, right to left. MOCA test showed mild to moderate cognitive impairment. Neurology had concern for episodic seizures and required further infectious work up. Brain MRI reported no acute or chronic abnormalities. Short term EEG reported staring episodes, reported as normal without focal or epileptiform abnormalities. 24-hour video EEG report was normal in awake/drowsy/asleep phases without areas of focal slowing, persistent asymmetry or epileptiform discharges. Lumbar puncture showed clear colorless fluid, normal opening pressure, high protein 65.8 mg/dl, glucose 68mg/dl, no microorganisms (virus, bacteria, fungi) and negative cultures.

Treatment was supportive, montelukast was stopped and had frequent reorientation with family support bedside.

Patient improved through the 10 days of in-hospital stay and was discharged to follow up with neurology.

Discussion
This case illustrates a potentially new side effect of montelukast, presenting as fluctuating mental status with mirror writing. Literature review shows multiple case reports and case series of neuropsychiatric events associated with montelukast, where most of the adverse effects resolved within days to weeks after stopping the drug, however, none report mirrored writing (3-5).

Learning Objectives
- Altered mental status has a broad differential, therefore, important to keep in mind adverse drug reactions (ADR).
- Montelukast has a black box warning due to its association with neuropsychiatric events that are more common in children.
- The Naranjo ADR scale may be utilized to estimate the probability of an ADR.

References
2. Ekhart C, van Hunsel F, Sellick V, de Vries T. Neuropsychiatric reactions with the use of montelukast. BMJ. 2022;376:e067554