Cyproheptadine withdrawal with features of serotonin toxicity
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Case Report:
An 8 yo male without previous psychiatric history had been taking cyproheptadine 8 mg PO BID for headaches for 2 months. The medication was abruptly discontinued when his local pharmacy ran out of its supply.
He presented to the ED three times over the ensuing 72 hours exhibiting worsening symptoms of agitation and restlessness with some signs of autonomic instability (sweating, tachycardia).
He required escalating need for chemical and ultimately physical restraints at each visit. (See Table)
His symptoms reversed significantly with reintroduction of cyproheptadine at doses similar to his previous dosing regimen.
At the time of 3rd hospital discharge, a plan was made to initiate a prolonged cyproheptadine taper starting at his original dosing of 8 mg PO BID.

Discussion/Conclusion:
Cyproheptadine is a histamine blocker and 5-HT receptor antagonist frequently used to treat mild to moderate serotonin syndrome.
Adverse effects such as sedation and increased appetite are well described.
Anticholinergic toxicity has been reported both in overdose and in therapeutic use.
There is sparse literature describing adverse effects upon discontinuation of chronically administered cyproheptadine.
This case describes a withdrawal syndrome exhibiting features of serotonin toxicity (mental status changes, neuromuscular hyperactivity, autonomic instability).
We postulate that our patient became hypersensitized to 5-HT in the setting of chronic 5-HT antagonism and that abrupt removal of the antagonist resulted in functional serotonin overstimulation.

Background:
Cyproheptadine is an antihistamine with serotonin (5-HT) antagonist properties that is used to treat serotonin syndrome.
Sparse literature describes its use for pediatric migraine headaches.1,2
We describe a case of abrupt discontinuation of high-dose cyproheptadine that resulted in features of serotonin toxicity.

Visit #1 (36 hours)
Visit #2 (48 hours)
Visit #3 (72 hours)

<table>
<thead>
<tr>
<th>Exam</th>
<th>Visit 1</th>
<th>Visit 2</th>
<th>Visit 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Agitated, diaphoretic</td>
<td>Tachycardia (110s), psychomotor agitation with no tremor or clonus</td>
<td>Inconsolable, agitated, and undirectable</td>
</tr>
<tr>
<td>Laboratory values</td>
<td>n/a</td>
<td>Basic labwork unremarkable; UDS (+) for benzos</td>
<td>n/a</td>
</tr>
<tr>
<td>Treatment</td>
<td>Lorazepam 1 mg PO</td>
<td>Midazolam 2 mg IV</td>
<td>5-point restraints</td>
</tr>
<tr>
<td></td>
<td>Lorazepam 2 mg IV</td>
<td>cyproheptadine 4 mg PO</td>
<td>olanzapine 5 mg IM</td>
</tr>
<tr>
<td>Disposition</td>
<td>Discharged home</td>
<td>Admitted to observation unit overnight</td>
<td>Admitted to observation unit overnight</td>
</tr>
</tbody>
</table>

References: