PALLIATIVE CARE CASE OF THE MONTH

"Identifying and Managing Drug Induced Akathisia"

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Case: A 47-year-old man was admitted to the hospital with a gastric perforation secondary to metastatic and unresectable gastric cancer. The patient's course was complicated by anxiety and nausea. The patient was treated with several medications for these symptoms, including sertraline, ondansetron, and olanzapine, all without relief. As a result, metoclopramide was utilized for nausea. The patient's nausea did not improve, and both the patient and his bedside nurse noted that his anxiety had worsened significantly. Metoclopramide was discontinued, and his anxiety improved. His nausea remained severe, and he subsequently developed hiccups refractory to treatment with gabapentin and baclofen, after which his nausea worsened further. As a result, he was initiated on Thorazine 25 mg TID. He again noted that his anxiety worsened; he said, "I want to crawl out of my skin," and he was pacing in his room. The constellation of his symptoms and adverse response to anti-dopaminergic agents raised the question of akathisia.

Discussion:

What is akathisia?

The term akathisia derives from the Greek, meaning "inability to sit." Akathisia is a subjective feeling of restlessness and an inability to remain still. Akathisia was initially identified as a distinct movement disorder and a symptom in patients with Parkinson's disease. However, acute akathisia is more commonly drug-induced, particularly with first-generation antipsychotics[1] It can also be associated with second-generation antipsychotics, antiemetics, SSRIs, venlafaxine, and TCAs.[2]

What is the relevance of drug-induced akathisia to general medicine/palliative care?

General medicine providers and palliative medicine providers frequently encounter patients on medications that can cause akathisia and, more importantly, frequently initiate medications that can cause acute akathisia. Two studies in cancer patients referred to psychiatry for any cause found a prevalence of akathisia of 4.8% and 4.7%. [3,4] A systematic review of studies of delirium managed with antipsychotics reported akathisia rates of up to 28.5%.[5]

Which medications are most frequently implicated in akathisia?

- First-generation antipsychotics (one systematic review indicated 25% incidence in patients treated for schizophrenia with haloperidol)
- Second-generation antipsychotics (the same systematic review indicated 9% incidence in patients treated for schizophrenia with olanzapine and 5% incidence in patients treated with quetiapine)[6]
- Metoclopramide (one study suggested a 17% incidence in ED patients receiving metoclopramide)[7]
- Prochlorperazine (one study indicated 44% of patients experienced akathisia)[8]

Diagnosing akathisia

Akathisia is challenging to diagnose because the symptoms are nonspecific and overlap with other conditions. The differential diagnosis for an internal sense of restlessness includes generalized anxiety disorder, delirium, tardive dyskinesia, withdrawal syndromes (including opiate withdrawal), and restless leg syndrome.[9,10] The core features of akathisia are a combination of a subjective feeling of inner restlessness, tension, an urge to move, or an inability to remain still, along with objective evidence of limb or trunk movements while stationary, shifting while sitting or standing, or pacing.[11] Contributing to difficulty diagnosing the condition is the fact that patients may not describe their symptoms as restlessness, may lack objective signs of restlessness, or may have less severe symptoms.[12] The history is critical to differentiate akathisia from other similar conditions, with a history of previous anxiety disorder with similar symptoms and recent discontinuation of opiates suggesting an alternate diagnosis. Symptoms such as inattention or disorganized thought would suggest a diagnosis such as delirium and predominantly lower extremity symptoms without an internal sense of restlessness would be more consistent with restless legs syndrome.[13] The Barnes Akathisia Rating Scale is a validated scale that can be utilized to document the likelihood and severity of akathisia and consists of both objective observations and the patient's subjective report of symptoms.[14] Ultimately, akathisia should be suspected in a patient who develops restlessness, motor hyperactivity, or worsened anxiety after starting a dopamine antagonist including anti-emetics and antipsychotics for hyperactive delirium.

Management of akathisia

The mainstay of treatment for akathisia is discontinuing the offending medication. If it is not possible to discontinue the offending agent or symptoms are severe, several medications have been used to treat akathisia. There is not consensus on the optimal pharmacologic treatment for drug-induced akathisia. The most evidence exists for propranolol, but it may take days to have an effect and has obvious cardiovascular side-effects. The recommended initial dose is 10 mg PO twice daily. Other – potentially faster acting - treatments with mixed evidence include diphenhydramine, benztropine, or benzodiazepines.[15] A small RCT from Turkey demonstrated that both IV diphenhydramine (20 mg) and IV midazolam (2 mg) were effective in treating akathisia. While midazolam led to significantly faster symptom resolution, it also led to significantly more sedation.[16] There is also evidence that mirtazapine can be utilized to minimize symptoms.[17]

If an anti-dopaminergic medication is necessary, second generation antipsychotics have lower rates of akathisia with quetiapine, clozapine and olanzapine being reported as having the lowest rates of akathisia within the class.

Case Conclusion:

Thorazine was discontinued and he was administered 25 mg IV diphenhydramine, with improvement in what he described as anxiety. Anti-dopaminergic medications were avoided for the remainder of his hospitalization and the patient did not have recurrence of his symptoms

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