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CLINICAL VIGNETTE

Resolution of Recurrent Headaches and Nausea Resistant to Standard Treatment with a Tricyclic Antidepressant

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Introduction

The International Classification of Headache Disorders, 3rd edition, identifies two etiologies of recurrent gastrointestinal disturbances that may be associated with migraines, cyclic vomiting syndrome and abdominal migraine.[1] We describe a case of a woman who presented to primary care with refractory episodic nausea and vomiting that resolved with low-dose amitriptyline. She had previously undergone an extensive workup and multiple therapeutic trials that failed to identify a cause or effective treatment for her symptoms.

Case presentation

A 34-year-old female presented with 2 days of acute worsening of chronic nausea, accompanied by myalgias, malaise, and a brief increase in tactile temperature. The patient first experienced acute, severe nausea and 9 months previously which persisted for several weeks. Unremitting nausea returned about 5 months later. During this time the patient had multiple consultations with gastroenterologists. A workup that included esophagogastroduodenoscopy and colonoscopy was non-contributory, showing only mild gastritis and no indication of infection with H. Pylori. Her nausea was not improved by ranitidine or esomeprazole, each given for several weeks. Treatment with dicyclomine for presumptive diagnosis of irritable bowel syndrome provided only some relief from occasional abdominal cramping. A therapeutic trial of antibiotics for C. Difficile similarly provided no relief of symptoms. During this time she found prochlorperazine to be ineffective, and experienced only minimal improvement with oral ondansetron. Consequently, she relied on ginger and doxylamine for symptom management, but the persistent nausea had a significantly negative impact on quality of life and work productivity. At the time of presentation, the only treatment which provided several hours of complete symptom relief was 8 mg of parenteral ondansetron.

The patient denied emesis, diarrhea, blood per rectum, headache, early satiety, or abdominal bloating. She had no personal or family history of inflammatory bowel disease diabetes mellitus, and denied use of dietary supplements, illicit drugs, or new medications prior to the initial onset of symptoms or subsequently. Physical exam was unremarkable, including abdominal exam which revealed normoactive bowel sound without tenderness, palpable masses, hepatosplenomegaly, or hernias. A complete blood count and metabolic panel were within normal limits. An initial trial of 25 mg of amitriptyline given for the possibility of nausea as a migraine equivalent began to relieve symptoms within several days and obviated the need for any other medications. One year later the patient reported only occasional and mild nausea which responded within 2 days of resuming amitriptyline.

Discussion

The central nervous, autonomic nervous, and endocrine systems as well as gastric dysrhythmias and psychology all play a role in the development of nausea. These complex systems explain nausea's various presentations and managements.[2] The vomiting mechanism is controlled by the brainstem. The medullary area postrema receives afferent information from the gastrointestinal tract via sympathetic and vagal impulses, other peripheral inputs, and humoral factors, and sends information via the nucleus of the solitary tract to initiate the vomiting response.[3] The conscious perception of nausea, however, is highly complex and thought to be mediated by multiple higher brain regions including areas of the cerebral cortex and subcortical nuclei, with multiple inputs which include projections from the aforementioned brainstem center, vestibular nuclei, and other brain regions and humoral factors.[4] Both nausea and vomiting are mediated by serotonin, dopamine, histamine, and acetylcholine, which are the basis of two common treatment categories: centrally acting antiemetics (suppression of nausea and prevention of vomiting) and prokinetics (modulate gastrointestinal motility).[5]

The use of tricyclic antidepressants (TCAs) as anti-emetics is an uncommon and less understood therapy, but their beneficial effect is thought to be due to the inhibition of serotonin transporter and norepinephrine transporter.[6] These transporters are both present in the central and enteric nervous systems and in the gut mucosa.[7-9] Retrospective studies show symptom reduction in cyclical vomiting syndrome patients, but because there is a lack of prospective studies, their use is reserved for refractory symptoms.[10] In a retrospective study of 37 patients with chronic functional nausea, 51% patients had a complete response and an additional 33% had symptom reduction with

low dose TCAs.[11] Abdominal migraine is a disorder that presents predominantly in children and rarely in adults, and can mimic or may be related to cyclic vomiting syndrome. This condition may respond to TCAs at doses that have little or no antidepressant effect.[12]

Conclusion

A therapeutic trial of tricyclic antidepressant is a reasonable consideration in patients who have recurrent headaches that have not responded to typical interventions. Prospective studies may further help to elucidate their benefit.

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