CASE REPORT

PSYCHO-PHARMACOLOGIC APPROACH FOR CHRONIC CYCLICAL VOMITING SYNDROME: A CASE REPORT

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Abstract

Objective: **In this case report, a middle aged lady presenting with persistent vomiting of 12 years duration, not responding to conventional management and showing dramatic response to combinations of low dose Imipramine and Trifluperazine is discussed.** ***Method:*** **In our case, a middle aged lady presenting with chronic, recurrent episodes of severe vomiting for approximately 12 years with poor treatment outcome was evaluated and treated with low dose imipramine and Trifluperazine, which was found to be highly effective.** ***Results:*** **Low dose Trifluperazine and imipramine is effective in the treatment of cyclic vomiting syndrome.** ***Conclusion:*** **Cyclic Vomiting Syndrome is often missed and appropriate psychiatric intervention gives a better outcome.** ***ASEAN Journal of Psychiatry, Vol. 14 (2): July – December 2013: XX XX.***

Keywords: Cyclical Vomiting Syndrome, Imipramine, Trifluperazine

Introduction

Essential criteriae of Cyclical Vomiting Syndrome (CVS) consist of recurrent, severe, discrete episodes of vomiting of unknown cause lasting from hours to days with inter-episodic normal health [1]. It is self-limiting and follows a stereotypic pattern [1]. Associated signs and symptoms can be nausea, abdominal pain, headache, motion sickness, photophobia, phonophobia, lethargy, fever, pallor, dehydration, excess salivation, or social withdrawal [1]. Samuel Gee had first described Cyclical Vomiting Syndrome in English literature [2].

This condition is diagnosed most often in children but can affect people of any age [1]. It has been reported in children as young as 6 months of age and in adult as old as 73 years. Prevalence ranges from 4 to 2000 per 100,000 children. Although relatively rare in adults, recent studies suggest this condition could be as common as in children [2, 3]. Most of the clinical characteristics of the CVS are similar irrespective of age of onset.

Case Report

A 45-year-old lady with history of recurrent episodes of vomiting for twelve years was referred to Department of Psychiatry from Department of Medicine for the management of recurrent episodes of vomiting which did not improve with conventional treatment. All routine blood investigations, upper G.I endoscopy, Ultrasonogram of abdomen were within normal limits. All the organic causes of vomiting were ruled out by the Department of Medicine before referring the patient for

psychiatric consultation. There was no past history of any syndromal psychiatric illness. During the past 12 years after onset of vomiting episodes, there were mild depressive and anxiety symptoms accompanied by sleep disturbances, which used to subside with improvement of vomiting episode.

Patient's recurrent vomiting episodes began at 33 years of age and each episode used to last for 5 to 15 days, repeating at an interval of one to one and half months. The frequency of vomiting was 10 to 25 times per day. Most of the time, vomiting episodes were preceded by 8-10 days prodrome of loss of appetite and apprehension for upcoming vomiting episode but did not correlate with food intake.

For the last 6 months prior to psychiatric consultation, the vomiting episodes were precipitated by psychosocial stressors and most of the episodes of vomiting in past six months prior to hospitalization had temporal correlation with stressors, like disputes between patients and her husband or in-laws. She used to cry after such disputes and at times would not eat anything the whole day after the dispute. Earlier episodes were mostly spontaneous (independent of stressors). Six months prior to hospitalization, she used to react to stressor in similar way and the vomiting episodes were not temporally related to stressors. During such episodes of vomiting, she would generally have low mood and decreased sleep. Vomitus used to be scanty in amount, watery, sometimes bilious, and non-projectile. There was no history of significant weight loss during the course of illness. There was history of hyperemesis gravidarum in all three pregnancies. She had undergone hysterectomy 6 months before the onset of illness. There was no history of diabetes, hypertension, chronic headache or any significant medical, surgical or psychiatric illness. There was no family history of migraine or chronic fatigue syndrome. The patient was a married housewife of rural background. There was no past history of obvious psychosocial stressor.

At the time of admission, general physical examination revealed no evidence of systemic illness or GI disorders. Neurological & mental status examinations were unremarkable except for low mood of mild degree. Routine hemogram, Ultrasonography of abdomen, Upper Gastrointestinal endoscopy, and CT scan brain were within normal limits.

During the whole course of illness, except for the initial 6 months, she always remained on medications prescribed by various general physicians but frequency and duration of episodes mostly remained unaffected. There were minimal documented side effects with these medications.

Her treatment records were available since 2008. She was treated with antipsychotics such as Risperidone up to 4mg/day, Olanzapine up to 20mg/day, antidepressants (Amitriptyline up to 75mg/day, Mirtazapine up to 15mg/day, Fluoxetine 40mg/day), anticholoinergic (Procyclidine up to 5mg/day, antacids-prokinetic agents (Pantoprazole, Ranitidine, Domperidone), and multivitamins at different periods of time by different physicians who diagnosed her to be suffering from gastritis (H. Pylori infection, idiopathic gastritits), Premenstrual dysphoria, Psychogenic vomiting, and somatoform disorder. She was never treated with any structured psychotherapy modality. Prior to admission in our psychiatric ward, she was hospitalized several times and was managed with injectable Proton Pump Inhibitors, anti-emetics, antibiotics (cephalosporin & amikacin), anti-H. Pylori treatment regime and Thioridazine in low doses, intravenous fluids and extensive laboratory, endoscopic & radiological evaluations were done.

In the psychiatric ward, she was treated with low dose tricyclic antidepressant Imipramine (50 mg in divided doses) which later increased to 75mg/day along with fixed dose combination of Trifluperazine (2.5mg) and Trihexyphenidyl (1mg) twice daily. She was also given low dose benzodiazepine (Diazepam 5mg/day, in divided doses).

Her vomiting stopped completely from the first day itself as opposed to gradual reduction in earlier episodes and this improvement was

sustained for the subsequent 4 months in the follow-up. Quality of improvement was substantially better this time in terms of subjective well-being and absence of residual morning nausea and vomiting which used to persist in the apparently asymptomatic interval episode. She was able to accept all kinds of foods as opposed to gradual acceptance in earlier episodes. She was evaluated by physicians, gastro-enterologists and no local erosive lesions or ulcers or strictures were reported in the throat area.

She was diagnosed to be suffering from CVS as she fulfilled all the essential criteria of recurrent, severe, discrete episodes of vomiting with varying intervals of normal health in between, duration of vomiting episodes lasting from hours to days, and with no apparent cause of vomiting i.e. negative laboratory, radiographic and endoscopic findings. Her episodes of vomiting were of self-limiting nature and followed a stereotypic pattern. Only her most of the recent episodes had temporal correlation with stressor, otherwise her episodes of vomiting were independent of stressors.

Discussion

Although pathogenesis of CVS is unknown, several brain-gut mechanisms have been proposed but migraine related mechanisms seem most appropriate as neurologic symptoms like headache, photophobia, phonophobia and vertigo is often found. There is significantly high prevalence of migraine headaches in family members of CVS patients [2,4]. Mitochondrial DNA (mtDNA) mutations may be involved in the pathogenesis of CVS as is evident by greater prevalence of migraine on maternal side [4]. Sympathetic hyper-responsivity and autonomic dysfunction also appear to contribute to pathogenesis of CVS. The stress response (physical & psychological) leading to increased levels of ACTH and cortisol, heightened neuronal excitability, mitochondrial energy deficits, and hormonal state (menstrual periods) can potentially induce CVS [4].

The chemoreceptor trigger zone at the base of the fourth ventricle which is the vomiting centre has numerous dopamine D_2 receptors, serotonin 5-HT_3 receptors, opioid receptors, acetylcholine receptors, and receptors for substance P [5, 6]. Stimulation of different receptors are involved in different pathways leading to emesis, in the final common pathway substance P appears involved [5, 6]. Boles et al, in their study on 385 subjects with CVS, compared the efficacy of Coenzyme Q10 and amitriptyline. Co-Q serves as the electron shuttle between complexes 1 or 2 and complex 3 of the mitochondrial respiratory chain, thus essential for energy metabolism are being increasingly used for the treatment of a wide variety of conditions, including migraine, primary inborn errors of mitochondrial dysfunction and so on [7, 8]. Amitriptyline was found to be slightly more efficacious but tolerability was significantly more for Co-Q. As per case report of Mi-Sunet al [9], Topiramate via its anti-migraine effects by suppressing neuronal excitation was found to be effective in increasing symptom-free intervals.

Thus, probable reason for the combination prescribed being highly effective is the synergistic anti-emetic effect via their multiple modes of action like anti-cholinergic (Imipramine & Trihexyphenidyl), antihistaminic (Tricyclic antidepressant (TCA)), anxiolytic (Diazepam), anti-dopaminergic (Trifluperazine), and substance- P blockade (Imipramine). Another effective treatment alternative can be combination of flupenthixol and melitracen. This combination also carries the ability to act on multiple receptors involved in cyclical vomiting syndrome as mentioned above.

Although combination of TCA and anti-dopaminergic drugs (Olanzapine) had already been tried it was not of much help. Probably the dose of TCA was suboptimal (Amitriptyline 25mg OD for 2 months) and may be anti-dopaminergic routes are less implicated in the case of CVS. Thus, deploying multiple anti-emetic strategies is likely to be effective in the management of CVS. Although in literature TCA has been described only for prophylactic purposes but in this case, it proved to be effective in terminating the episode itself. Speed and completeness of response in this case along with nil side-effects reported suggest that this

combination may be further considered in similar cases.

Chronic, unexplained vomiting not responding to conventional pharmaco-therapy needs psychiatric evaluation. Cyclic vomiting syndrome has a lot of psychiatric significance. Psychiatric comorbidities like anxiety, panic, and depressive symptoms amounting to subsyndromal to syndromal level are seen in patients with CVS [2]. Sympathetic over-sensitivity, stress and psychological vulnerability are common to both CVS and Hyperemesis Gravidarum. Continuous interplay of biological factors (sympathetic oversensitivity), psychological factor (individual's psychological vulnerability) and social factors (family related stress) may be responsible for causation of Hyperemesis Gravidarum and CVS in our patient. This patient had poor coping skills to handle stress such as crying or not eating and which seemed to be worsened during the course of illness as evidenced by having an episode of vomiting following psychosocial stressors in the last six months. It could be due to the chronic illness (CVS), which had added to the burden of stress.

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