CASE REPORT

Acute episode of cyclic vomiting syndrome preceded by arterial hypertension – Case presentation and review

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ABSTRACT

Cyclic vomiting syndrome (CVS) is a functional disorder with recurrent episodes of vomiting. Between these episodes patients recover to well-being. Lack of awareness often leads to a delay in making the diagnosis. The diagnosis is based on a typical medical history and exclusion of other causes. We present a case report of a middle-aged patient who had recurrent episodes of vomiting for 12 years coinciding with hypertension. After excluding other causes, CVS was diagnosed. The episodes of acute vomiting were stopped by administration of antiemetic and sedative drugs and urapidil reduced the hypertension. Treatment with sedatives stops vomiting caused by the emetic centre of the central nervous system.

KEYWORDS

Cyclic vomiting syndrome, CVS, vomiting, hypertension, amitriptyline, smoking

INTRODUCTION

Cyclic vomiting syndrome (CVS) is a functional disorder, which comprises recurrent and stereotypical episodes of nausea and vomiting, lasting for hours or even days[1-17] and intervals of well-being with absence of symptoms between the vomiting episodes, lasting days to months.[1-7,9-15,17,18]

CVS is a rare disease that can occur in all age groups, but has its onset predominantly in childhood.[1,5,8, 11-15] Adults typically develop CVS in middle age.[1,5,9,19,20] Prevalence is about 2% in childhood and the disease is less frequent in adults.[2,3,7,10,14,18,21]

CVS comprises four phases.[1,5,14,15] Phase I is defined as the symptom- and nausea-free interval between episodes of vomiting and nausea.[5,6,15] If symptoms of CVS occur as prodromes with nausea and indisposition these indicate the next phase.[3,5,15,17,22] Increasing nausea and the start of vomiting characterise phase III, often accompanied by abdominal pain.[1,5,14,15] Vomiting episodes are in most cases stereotypical in manner and duration. The vomiting episodes occur on average 6-12 times per year and last several hours to 7 days.[1-14,21,23-25] The frequency of vomiting in patients with CVS can reach 20 times per hour.[5,7,14] As soon as the vomiting stops, the recovery period (phase IV) begins, which individually lasts between minutes to days. After phase IV, CVS returns to the symptom-free phase I.[5,15,17,25]

Frequently reported triggers of CVS vomiting episodes are stress, tiredness, infections, asthmatic attacks, hypoglycaemia or hyperglycaemia, and even chocolate or cheese.[1,4,5,7-10,14]

Little is known about the pathogenesis of CVS.[4, 7-11,13-16,21,23] It has been suggested that CVS is a functional disorder with strong associations towards migraine.[2,5,7-9,11,13-15] Moreover, familial clustering of CVS has been reported.[8,16]

To date, there is no specific test to diagnose CVS.[9,15,17] The diagnosis of CVS requires a typical accurate anamnestic report, fulfilment of specific diagnosis criteria and most importantly the exclusion of other disorders that are associated with recurrent vomiting.[12,15,16] The ROME III diagnosis criteria of 2006 comprise recurrent, self-limiting, stereotypical episodes of high-intensity vomiting lasting less than seven days without an organic cause.[1,5,10,13-15,17] The frequency of vomiting episodes must exceed two episodes in the last year.[13-15]

Typical symptoms of CVS as nausea, vomiting and abdominal pain are highly unspecific and can also occur

in many other diseases. Therefore, and because of a lack of awareness, making the correct diagnosis of CVS is often delayed for months or even years.[1,4,5,14,17,18,26,27]

Important differential diagnoses of acute or recurrent vomiting of CVS are gastroenteritis, gastroesophageal reflux, gastric and duodenal ulcers, appendicitis, cholecystitis, pancreatitis, hepatitis and other infections, porphyria and other metabolic disease, pyelonephritis, medication side effects, drug use, endometriosis, abdominal angina, gastric stenosis, neurological disease, gastroparesis or vestibular factors.[5,14,15,17,23]

To date, neither treatment of acute vomiting episodes nor prophylaxis of CVS is evidence based.[11,15]

Symptomatic acute treatment comprises antiemetic medications (e.g. ondansetron, granisetron, dimenhydrinate), sedatives (e.g. lorazepam) and antimigraine therapy (e.g. sumatriptan, zolmitriptan).[1,2,4,7,8,10-14,21,23,24,28] Moreover hypovolaemia should be corrected and use of proton-pump inhibitor has been recommended.[4,5,7,10,14,17] Hypovolaemia is associated with a risk of collapse as well as thromboembolic events.

Prophylactic treatment consists of avoidance of triggering factors for vomiting episodes with sufficient sleep, physical exercise and adequate nutrition.[13,18] A medical prophylactic therapy of CVS is worth considering, especially if the frequency of vomiting episodes exceeds once a month.[1,4,7,18] Prophylactic treatment with amitriptyline and propranolol has been the best studied and the efficacy of both medications has been proven.[1-5,7,9-14,17,19,20,29] Amitriptyline at a dose of 5-25 mg per day currently represents the standard prophylactic treatment of CVS.[2,7] Beside these two drugs, a large number of other drugs have been tested for prophylaxis of CVS, with varying degrees of success.[1,2,4,7,10-12,14,19,21,24,30,31]

The prognosis of CVS is good. Diet, trigger factor avoidance and medical prophylaxis are beneficial in most CVS patients.[5,15]

CASE REPORT

A 56-year-old woman presented to our emergency department with hypertensive crisis and nausea. The patient's blood pressure was elevated up to 205/140 mmHg. Restlessness was another symptom.

She reported having recurrent episodes of vomiting for 12 years. These vomiting episodes occurred up to twice a week and lasted about 12-16 hours with more than two vomiting attacks per hour. The vomiting attacks were almost stereotypical and between them she fully recovered to a sense of well-being. During and before vomiting episodes, she did not have headaches. The symptom-free intervals varied in duration between days and several months. She reported that hypertensive blood pressure was common during the vomiting episodes. In the intervals free from symptoms, her blood pressure was normal to low with systolic blood pressure values of 100-120 mmHg. Arterial hypertension was not known.

On several occasions she had been under the care of a physician due to vomiting attacks, but mostly without success. Several examinations were performed to find the cause of the patient's recurrent episodes of vomiting. She underwent multiple endoscopies and ultrasounds, which showed no pathological findings. The last oesophago-gastro-duodenoscopy was performed about three months ago. Moreover, she was examined by a neurologist, who performed a cranial computer tomogram which was again without pathological findings. Antiepileptic drugs and antidepressants such as topiramate and desipramine were unable to prevent the recurrence of the episodes of vomiting. As a result, the recurrent vomiting led to a significant psychological strain with social alienation and conflicts in her professional and private life. The patient denied drug abuse such as cannabis or cocaine.

During the hypertensive crisis on the day of admission, the patient took her husband's antihypertensive drugs (nifedipine and clonidine) which did not sufficiently lower her blood pressure. Physical examination demonstrated a good general condition and no pathological findings. The blood pressure was elevated up to 225/105 mmHg. We admitted the patient with the tentative diagnosis of hypertensive crisis within the context of arterial hypertension and CVS.

We started antihypertensive therapy with urapidil for acute treatment of her hypertensive crisis and ramipril and thiazide for long-term antihypertensive therapy. In this way, her blood pressure could be reduced towards the normal range. Standard ECG and 24-hour ECG showed no pathological findings. The 24-hour blood pressure examination showed a good blood pressure profile under the started antihypertensive treatment. The highest systolic blood pressure was 145 mmHg. We detected a non-dipper finding associated with the patient's restlessness in the night hours. Transthoracic echocardiography showed a normal left ventricular ejection fraction, concentric hypertrophy of the left ventricular myocardial muscle and no pathological valve findings.

During the hospital stay her blood pressure was well adjusted in the first two days. Then, the blood pressure increased once again and the patient reported increasing nausea. Her heart rate was also accelerated. Although we started to treat the patient's nausea with dimenhydrinate, her restlessness with oral lorazepam and the hypertensive crisis with oral nifedipine, the patient soon developed recurrent vomiting associated with increasing restlessness and persistent hypertensive crisis.

Abdominal ultrasonography showed a status post cholecystectomy with normal width of the bile duct and

no further pathological findings. Laboratory examinations, including hepatitis screening, were without pathological findings. Especially the inflammation markers were in the normal range.

We diagnosed an acute episode of CVS combined with a hypertensive crisis. Antiemetic treatment did not decrease the frequency of the vomiting attacks. The blood pressure increased once again up to 230/120 mmHg. Intravenous sedation was started with lorazepam to interrupt the vomiting episode. Furthermore, hypovolaemia was corrected by intravenous administration of isotonic NaCl fluid, and pantoprazole was injected intravenously to prevent gastric or oesophageal lesions. We administered urapidil intravenously to reduce the blood pressure in the context of a hypertensive crisis.

The vomiting episode was interrupted when the patient was sedated. The blood pressure dropped due to cessation of the vomiting and intravenously administered urapidil. The patient fully recovered after eight hours of sleep.

Therefore, we confirmed our tentative diagnosis of CVS with a concomitant hypertensive crisis. Moreover we concluded that the hypertensive crisis might have triggered the vomiting episode. The diagnosis of CVS and the suggested trigger was explained to the patient. We recommended identification and avoidance of triggering factors for the vomiting episodes as well as consideration of a pharmaceutical prophylaxis with amitriptyline or propranolol.

DISCUSSION

Our case report presents a typical history of a CVS patient. The patient had been under the care of physicians several times due to vomiting attacks without finding the correct diagnosis. Making the correct diagnosis of CVS was delayed for more than ten years, although extensive examinations were performed by physicians, gastroenterologists and neurologists. Without a correct diagnosis, treatment was symptomatic and ineffective. Because of the highly unspecific symptoms of nausea, vomiting and abdominal pain, it is not uncommon that patients with undiagnosed CVS undergo surgery for suspected appendicitis or acute cholecystitis. Treatment with sedatives stops the vomiting caused by the emetic centre of central nervous system.

It is important that physicians become more aware of CVS. CVS should be recognised and identified early in the course of disease and adequate treatment for the acute phase and prophylaxis should be started, if necessary.

During a CVS episode, concomitant hypertensive crisis and tachycardia are recognised in about 20% of all CVS patients.[5] In this context, hypertensive crisis and tachycardia occur at the beginning of the vomiting episode and are primarily caused by stress during the episodes of vomiting.

The 56-year-old woman in our case report presented with hypertensive blood pressure values both during the vomiting phase of CVS, but also before the prodromes with nausea had started. Therefore, we suggest that the hypertensive crisis was not only a concomitant symptom of an acute vomiting episode in CVS, but may also be a triggering factor for CVS vomiting episodes. It is well known that gastrointestinal symptoms can occur with severe hypertensive crisis.[32] It could be hypothesised that these patients with an elevated blood pressure and tachycardia response in an acute episode of vomiting have a higher sympathetic level than those CVS patients without this response. These patients seem to be more prone and receptive to sympathetic triggers with an earlier response. Interestingly, in our patient, we found typical echocardiographic signs of a hypertensive heart disease with left ventricular hypertrophy, without a known history of arterial hypertension. Therefore, arterial hypertension could have been present – unnoticed – for a longer period of time.[33] We diagnosed arterial hypertension and started antihypertensive treatment.

Of peculiar interest in the treatment of hypertensive crises related to CVS is the fact that antihypertensive treatment of the hypertensive crises during the vomiting episode with intravenous urapidil was successful, while nifedipine therapy was not. Nifedipine is an antihypertensive drug with a peripheral effect on the vascular system, while urapidil acts on the peripheral postsynaptic α-receptors as well as on the central serotonin receptors.

In irritable bowel syndrome, serotonin (5-HT) has been described as an important neurotransmitter and paracrine signalling molecule in the gastrointestinal tract.[34] 5-HT is released from enterochromaffin cells, which initiate peristaltic, secretory, vasodilatory, vagal and nociceptive reflexes.[34] The enteric nervous system is a semiautonomous effector system connected to the central autonomic nervous system.[34] Activation of parasympathetic and sympathetic nerve systems modulates the enteric nervous system via afferent and efferent communications.[34] Bidirectional brain–gastrointestinal tract interactions involve 5-HT pathways.[34] 5-HT is one of the major signalling molecules in the central nervous system with influence on diverse systems and physiological functions, including mood, appetite, nausea, sleep, memory and the learning process and homeostasis.[34] 5-HT modulators have been successfully used to treat many disorders including anxiety, migraine, nausea, chronic pain and hypertension.[34] Therefore, 5-HT could be the pathomechanistic link between arterial hypertension and CVS vomiting episodes.

Avoidance of CVS trigger factors is primarily beneficial in the prophylaxis of further CVS vomiting episodes[5,15] and

may also be beneficial in reducing the severity of vomiting and nausea in the acute vomiting phase, but in most cases a vomiting episode cannot be terminated exclusively by trigger avoidance, which is also the case with an acute migraine attack. Therefore the treatment of hypertensive crisis within a CVS vomiting episode should be helpful and supportive but not be crucial to terminate an acute CVS vomiting episode.

CONCLUSION

These described facts lead to the hypothesis that sympathetic activation and 5-HT modulation have an impact on the vomiting episodes of CVS in some CVS patients.

CONFLICTS OF INTEREST

None.

DISCLOSURES

None.

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