First Case Report: Dramatic Response of Depersonalization Derealization Disorder to an Eradication Therapy of Helicobacter Pylori Infection

Hasan S. Alamri, MD*

ABSTRACT

Depersonalization and derealization are common dissociative symptoms in the general population and are frequently temporary. Depersonalization derealization disorder (DDD) is a diagnosis for which there is little evidence of successful treatments, and no approved pharmaceutical treatments are currently available. We present the case of a young guy who presented with symptoms that were consistent with DDD. SSRIs, tricyclic antidepressants, antipsychotics, and antiepileptic medicines all failed to work for him. After receiving eradication medication for H. pylori infection, his condition dramatically improved. Given that we don't know the etiology of DDD and currently there aren't any approved treatments for it, we need to understand more about the link between H. pylori infection and its treatment and DDD.

Keywords: Depersonalization, Derealization, Helicobacter pylori, Concomitant therapy

INTRODUCTION

Dissociative symptoms, such as depersonalization and derealization, are very widespread in the general population. Depersonalization is defined as "experiences of unreality, detachment, or being an outside observer with respect to one's thoughts, feelings, sensations, body, or actions (e.g., perceptual alterations, distorted sense of time, unreal or absent self, emotional and/or physical numbing)" by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). "Experiences of unreality or detachment with respect to surrounds (e.g., humans or objects are experienced as unreal, dreamy, hazy, lifeless, or visually distorted)" is how derealization is characterized[1]. Furthermore, reality testing is unaffected, and these depersonalizations and derealization symptoms are not better described by another mental disease or physical condition, and the symptoms cause severe functional and social impairment. According to Sierra and David (2011), the key experiential components of the disease include abnormal physical experience, emotional numbing, anomalous subjective memory, and derealization[2]. Depersonalization/derealization Disorder (DDD) is diagnosed when symptoms of depersonalization and/or derealization become recurring or persistent[1].

In a systematic study, prevalence rates for clinically relevant DDD symptoms were reported to be 1.2-2.4 percent in the community and 30-82 percent in clinical samples[3]. DDD is also frequently found as a comorbidity, particularly in depression and anxiety[4]. The majority of DDD experiences are fleeting and fade away when situational conditions subside. DDD, on the other hand, can last for days, weeks, or months, recur, or be permanent in a significant number of patients[3]. Adolescence is the age of onset, and an earlier onset is linked to greater severity and a worse prognosis[4-6].

In cross-sectional research on the genesis of DDD, harm-avoidant temperament was found to be related with DDD[7]. Another cross-sectional investigation comparing healthy controls to 49 DDD patients found that emotional abuse was linked to the severity of DDD but not to the severity of other forms of childhood maltreatment[8]. A prospective cohort study discovered that teacher-estimated childhood anxiety 20 years prior was the single risk factor for significant adult depersonalization at the age of 36. Environmental risk variables such as socioeconomic status, parental death or divorce, and self-reported accidents were not shown to predict DDD later in life[9]. DDD symptoms are considered a hard-wired response to severe stress from an evolutionary perspective, which is perpetuated by personality factors such as low self-regulation capacities (e.g., low self-esteem, low affect tolerance, low self-cohesion) according to various disease models of DDD[10-12]. Seizures, migraines, brain injuries, and illegal drug usage can all bring about depersonalization and derealization symptoms[6]. There is currently no licensed drug for the treatment of DDD, and no randomized controlled trial on the psychotherapeutic treatment of DDD has been conducted[3].

Helicobacter pylori (H. pylori) is a spiral-shaped, non-spore forming, gram-negative bacterium that lives on the epithelium of the human stomach, with prevalence ranging from 50 to 90 percent depending on economic development[13,14]. Peptic ulcers, atrophic gastritis, gastric cancer, and MALT lymphoma are all possible complications of H. pylori infection[15]. It's also linked to unexplained iron deficiency anemia, idiopathic thrombocytopenic purpura, vitamin B12 insufficiency, and early signs of atherosclerosis, stroke, Alzheimer's, and Parkinson's disease[15]. The majority of people infected with H. pylori don't have any symptoms. Infection with H. pylori can cause gastroduodenal inflammation in children, which can cause epigastric pain, nausea, vomiting, and gastrointestinal (GI) bleeding[16]. The Taipei Global Consensus in 2020 stressed the importance of H. pylori eradication in achieving the aim of lowering or eliminating gastric cancer fatalities[17]. A variety of H. pylori therapies have been developed, including triple therapies containing a proton pump inhibitor (PPI), amoxicillin and clarithromycin, metronidazole, a fluoroquinolone, or rifabutin. Another H. pylori treatment is a four-drug regimen that includes a proton pump inhibitor (PPI), amoxicillin, clarithromycin, and metronidazole. Depending on how they're given, they're referred to as sequential, concurrent, hybrid, or reverse hybrid therapies.

In this report, the case of an adult male patient with DDD symptoms who responded successfully to therapy with the four-drug regimen for H. pylori is presented.

* Department of Internal Medicine
College of Medicine, King Khalid University
Abha, Kingdom of Saudi Arabia.
E-mail: hsalamri@kku.edu.sa

PATIENT CASE

Ali, a 25-year-old Saudi man, is a university student who is free of chronic illnesses. He had a three-month major depressive episode four years ago before getting treatment. Feelings of sadness, a lack of enjoyment, a lack of energy, poor focus, a loss of appetite, and sleep disturbances were among the symptoms. As the severity of his condition worsened, he had ideas about wishing for death, but no thoughts of self-harm. In addition to the foregoing symptoms, he also had a bizarre feeling that the environment around him was not real, and that there was a barrier of fog separating him from what was around him, which he summed up by saying, "I feel as if I am in a dream and not in reality."

Ali went to a psychiatric clinic after three months of suffering and was diagnosed with major depressive disorder. He was administered the antidepressant Sertraline as well as Bromazepam pills for sleep disturbances. Ali's condition began to improve after two weeks of treatment, and after six weeks on a daily dose of 200 mg of Sertraline, almost all of his depression symptoms had vanished. The only symptom that remained was the strange feeling about the surroundings, and the psychiatrist recommended that he continue the treatment for a longer period in the hopes that these symptoms would vanish. Ali was still experiencing the bizarre sensation that the external world was unreal and that he was in a dream three months after starting sertraline. Depersonalization Derealization disorder was diagnosed, and he was referred to a neurology facility for a second opinion. The appropriate physical examination was performed in the neurology clinic, and everything was found to be normal. The necessary medical tests were ordered, including a complete blood count, blood chemistry, hormones, and vitamin levels, as well as an electroencephalogram (EEG) and magnetic resonance imaging (MRI) of the brain, all of which came back normal. As a result, the patient received the same diagnosis. Ali's DDD was treated with a variety of drugs for almost a year, but there was no change. Clomipramine, Sulpride, Risperidone, and Carbamazepine are some of these medications. Table 1 indicates the dose and duration of each treatment. After a year of failed treatment attempts, the patient was advised that there was no treatment that could help him, and he was referred to a psychotherapy facility to help him cope with his unusual feelings. Despite the fact that his depression symptoms had not returned, Ali was recommended to continue taking sertraline 100 mg daily because quitting treatment while still suffering from DDD could result in a relapse of major depressive disorder. Ali's social and academic levels were clearly impacted by his DDD, as he became less mixed with others due to his observation that the symptoms of the illness worsened when he was around others, and his academic level was also negatively impacted due to the difficulty of concentration and comprehension coupled with the constant feeling that the world around him is unreal.

Table 1: Medications which were used for treatment of DDD

Name	Daily dose	Duration in days
Clomipramine	200 mg	30
Sulpride	450 mg	30
Risperidone	4 mg	42
Carbamazepine	800 mg	42

Ali was checked in the gastrointestinal clinic 14 months ago after experiencing epigastric pain, nausea, vomiting, bloating, indigestion, and weight loss for several weeks. A breath test revealed the presence of high levels of H. pylori bacteria, and an upper endoscopy of the stomach and duodenum revealed gastritis. Biopsies were collected from the stomach and duodenum walls, which confirmed the presence of high levels of H. pylori bacteria. Ali was started on three antibiotics (Amoxicillin, Clarithromycin, and Metronidazole) as well as one proton pump inhibitor (Omeprazole), with a two-week treatment planned. Table 2 indicates the dose and duration of each treatment. Ali employed this treatment to get rid of H. pylori infection and treat gastritis, which had already occurred by the end of the second week, but the effect of this course of treatment on DDD surprised him. The symptoms of DDD were noticeably eased at the end of the first week of treatment, and by the end of the second week, the symptoms had almost vanished, and Ali's awareness of the outer world around him had returned to normal. For the last year, Ali's DDD has been limited to two episodes, each lasting one to two hours and very lightly, which indicates a significant improvement in his condition, as he was suffering from DDD symptoms severely and continuously, day and night for many years. The current treatment strategy is to progressively reduce Ali's sertraline dose until it is no longer needed, and to monitor him for the following two years to ensure that the symptoms of depression or DDD do not reappear.

Table 2: Medications which were used for treatment of H. pylori infection

Name	Daily dose	Duration in days
Amoxicillin	1000 mg every 12 hours	14
Clarithromycin	500 mg every 12 hours	14
Metronidazole	500 mg every 12 hours	14
Omeprazole	40 mg every 12 hours	14

DISCUSSION

The current case study suggests that H. pylori eradication therapy may be beneficial in the treatment of DDD. Ours is the first case study to show that H. pylori treatments can aid in the treatment of DDD. Because the etiology of DDD is uncertain and there are a limited number of clinical investigations on DDD, pinpointing the reason for the patient's improvement after getting H. Pylori drugs is difficult. The question is whether this improvement is due to the therapeutic eradication of H. Pylori, the direct effect of antibiotic drugs, or both. There have been no studies linking the elimination of H. Pylori infection and antibiotic exposure to the treatment of DDD. However, based on what we know about how the gut and the brain interact, we can make some guesses about what's going on.

The gut-brain axis, which regulates nerve signals and neuropsychiatric traits like mood, memory, and cognition, has recently been discovered to have a key role in mental diseases. Disruption of the gut-brain axis and intestinal flora may have a role in the etiology of mental diseases, according to recent data[18]. H. pylori infection has been shown to influence the gut microbiota in recent investigations[19,20]. However, the actual interaction between H. pylori and the gut microbiota is not fully understood, and the research indicates mixed outcomes. H. pylori infection is linked to a disruption to the gut microbiota homeostasis (dysbiosis) and altered gastric microbiota, both of which have been linked to the etiology of gastric disorders[21,22]. However, it is unclear whether H. pylori infection promotes the growth of unwanted microbes or, conversely, whether a changed microbiota promotes H. pylori colonization. It's highly likely that the invading H. pylori stimulates the growth of some microorganisms and vice versa in a complex interplay. Dysbiosis may encourage alterations in the stomach mucosa that favor H. pylori colonization[19]. The gut microbiota of H. pylori-negative children had a larger relative abundance of gammaproteobacteria, betaproteobacteria, bacteroidia, and clostridia classes, as well as a higher bacterial richness and diversity, according to a study in children[23]. Another study reported a contrasting result whereas children infected with H. pylori had a higher number of gut microbiota, including Proteobacteria, Clostridium, Firmicutes, and Prevotella, than

children who did not have the illness[24]. It's unclear if these variations are the primary cause of H. pylori infection or whether they're the result of changes in the inflammatory and metabolic settings. To completely understand these relationships and their implications on linked disorders, more research linking the gut microbiota-host-H. pylori interactions is needed.

Several population studies have looked into the direct etiological connection between neuropsychiatric symptoms and H. pylori infection in the general population[25,26], but its significance in the pathophysiology of mental diseases has been discounted. H. pylori secretes a cytotoxin known as vacuolating cytotoxin A (VacA), which has direct cytotoxic and pro-inflammatory effects and can induce abnormalities indirectly by disturbing the brain-gut axis, such as cognitive and memory impairment, anxiety, and depressive-like behaviors[27]. Furthermore, H. pylori can induce axonal/neuronal damage, neurotoxicity, increased free radical production, and changes in neuropeptide expression, such as vasoactive intestinal peptide (VIP) and c-fos[28]. Furthermore, it has been demonstrated that eliminating H. pylori reduces motor and sensory symptoms linked with neuropsychiatric diseases[29,30].

Short antibiotic exposure reduced and corrected chronic unpredictable mild stress-induced anxiety-like and depression-like behavior in rats, according to behavioral tests[31]. Selective Serotonin Reuptake inhibitors (SSRIs) with quadruple H. pylori eradication therapy improved the psychological symptoms of several depressed patients after two weeks[32]. Antipsychotics combined with quadruple therapy greatly improved therapeutic efficacy and effectively reduced the recurrence rate in H. pylori-caused peptic ulcer patients with anxiety and depression, according to another clinical observation[33].

In this paper, we provide evidence in support of H. pylori infection as an environmental cofactor in psychiatric disorders and potential anti-H. pylori therapeutic implications. Based on our current case report, a supporting hypothesis concerning the possible link between H. pylori infection and DDD might be established. As a result, extensive research is needed to understand the therapeutic implications of H. pylori interactions with the gut-brain axis and their role in mental illness. Such research will help understand the pathophysiology of H. pylori infection and provide novel therapeutic approaches for the management of DDD.

CONCLUSION

To the best of our knowledge, this is the first case report of H. pylori eradication-based antibiotic therapy and DDD improvement. The majority of DDD therapy tactics concentrated on antidepressants; however, recent research in the gut-brain axis, microorganisms (such as H. pylori), and mental diseases may allow these less researched areas to emerge more fully, contributing in the development of novel DDD management strategies. This study will aid researchers in identifying essential components of the brain-gut axis in the context of DDD and H. pylori eradication by antibiotic treatment, as well as encourage more in-depth research, particularly in the context of H. pylori eradication therapy in the treatment of DDD.

Authorship Contribution: All authors share equal effort contribution towards (1) substantial contributions to conception and design, acquisition, analysis and interpretation of data; (2) drafting the article and revising it critically for important intellectual content; and (3) final approval of the manuscript version to be published. Yes.

Potential Conflict of Interest: None.

Competing Interest: None.

Acceptance Date: 13 June 2022

REFERENCES

1. American Psychiatric Association, Spitzer R (ed). Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Washington, DC. Am Psych Assoc 2013;302-6.
2. Sierra M, David AS. Depersonalization: A selective impairment of self-awareness. Conscious Cogn 2011;20(1):99-108.
3. Hunter EC, Sierra M, David AS. The epidemiology of depersonalisation and derealisation. A systematic review. Soc Psychiatry Psychiatr Epidemiol 2004;39(1):9-18.
4. Baker D, Hunter E, Lawrence E, et al. Depersonalisation disorder: clinical features of 204 cases. Br J Psychiatry 2003;182(5):428-33.
5. Simeon D. Depersonalisation disorder: a contemporary overview. CNS Drugs 2004;18(6):343-54.
6. Simeon D, Guralnik O, Knutelska M, et al. Personality factors associated with dissociation: temperament, defenses, and cognitive schemata. Am J Psychiatry 2002;159(3):489-91.
7. Simeon D, Guralnik O, Schmeidler J, et al. The role of childhood interpersonal trauma in depersonalization disorder. Am J Psychiatry 2001;158(7):1027-33.
8. Lee WE, Kwok CH, Hunter EC, et al. Prevalence and childhood antecedents of depersonalization syndrome in a UK birth cohort. Soc Psychiatry Psychiatr Epidemiol 2012;47(2):253-61.
9. Simeon D. Depersonalization/Derealization Disorder. In Gabbard's Treatments of Psychiatric Disorders. 5th edition. Edited by Gabbard GO. Washington, DC. Am Psych Publishing Inc 2014;459-69.
10. Sierra M. Depersonalization: A New Look at a Neglected Syndrome. Cambridge: Cambridge University Press. 2009.
11. Michal M, Kaufhold J, Overbeck G, et al. Narcissistic regulation of the self and interpersonal problems in depersonalized patients. Psychopathology 2006;39(4):192-8.
12. Sadock BJ, Sadock VA, Ruiz P. Kaplan & Sadock's Comprehensive Textbook of Psychiatry, Vol. 1. 9th ed. Philadelphia, PA: Wolters Kluwer Health Lippincott Williams & Wilkins. 2009;1:1995-8.
13. Khoder G, Muhammad JS, Mahmoud I, et al. Prevalence of Helicobacter pylori and its associated factors among healthy asymptomatic residents in the United Arab Emirates. Pathogens 2019;8(2):44.
14. Hooi JK, Lai WY, Ng WK, et al. Global prevalence of Helicobacter pylori infection: systematic review and meta-analysis. Gastroenterology 2017;153(2):420-9.
15. Malfertheiner P, Megraud F, O'Morain CA, et al. Management of Helicobacter pylori infection-the Maastricht V/Florence consensus report. Gut 2017;66(1):6-30.
16. Jones NL, Koletzko S, Goodman K, et al. Joint ESPGHAN/ NASPGHAN Guidelines for the Management of Helicobacter pylori in Children and Adolescents (Update 2016). J Pediatr Gastroenterol Nutr 2017;64(6):991-1003.
17. Liou JM, Malfertheiner P, Lee YC, et al. Asian Pacific Alliance on Helicobacter and Microbiota (APAHAM). Screening and eradication of Helicobacter pylori for gastric cancer prevention: the Taipei global consensus. Gut 2020;69(12):2093-112.
18. Hao WZ, Li XJ, Zhang PW, et al. A review of antibiotics, depression, and the gut microbiome. Psychiatry Res 2020;284:112691.
19. Sheh A, Fox JG. The role of the gastrointestinal microbiome in Helicobacter pylori pathogenesis. Gut Microbes 2013;4(6):505-31.

20. Schulz C, Schutte K, Koch N, et al. The active bacterial assemblages of the upper GI tract in individuals with and without Helicobacter infection. Gut 2018;67(2):216-25.
21. Coker OO, Dai Z, Nie Y, et al. Mucosal microbiome dysbiosis in gastric carcinogenesis. Gut 2018;67(6):1024-32.
22. Ferreira RM, Pereira-Marques J, Pinto-Ribeiro I, et al. Gastric microbial community profiling reveals a dysbiotic cancer-associated microbiota. Gut 2018;67(2):226-36.
23. Llorca L, Perez-Perez G, Urruzuno P, et al. Characterization of the Gastric Microbiota in a Pediatric Population According to Helicobacter pylori Status. Pediatr Infec Dis J 2017;36(2):173-8.
24. Benavides-Ward A, Vasquez-Achaya F, Silva-Caso W, et al. Helicobacter pylori and its relationship with variations of gut microbiota in asymptomatic children between 6 and 12 years. BMC Research Notes 2018;11(1):468.
25. Gu Y, Zheng L, Kumari S, et al. The relationship between Helicobacter pylori infection and depressive symptoms in the general population in China: The TCLSIH cohort study. Helicobacter 2019;24(5):e12632.
26. Carabotti M, Scirocco A, Maselli MA, et al. The gut-brain axis: interactions between enteric microbiota, central and enteric nervous systems. Ann Gastroenterol 2015;28(2):203-9.
27. Chauhan N, Tay ACY, Marshall BJ, et al. Helicobacter pylori VacA, a distinct toxin exerts diverse functionalities in numerous cells: An overview. Helicobacter 2019;24(1):e12544.
28. Budzyński J, Kłopocka M. Brain-gut axis in the pathogenesis of Helicobacter pylori infection. World J Gastroenterol. 2014;20(18):5212-25.
29. Gorlé N, Bauwens E, Haesebrouck F, et al. Helicobacter and the Potential Role in Neurological Disorders: There Is More Than Helicobacter pylori. Front Immunol 2021;11:584165.
30. Martinez MC. Famotidine in the management of schizophrenia. Ann Pharmacother 1999;33(6):742-7.
31. Meng C, Feng S, Hao Z, et al. Antibiotics exposure attenuates chronic unpredictable mild stress-induced anxiety-like and depression-like behavior. Psychoneuroendocrinology 2022;136:105620.
32. Zainaldeen HA, Al-Faraj HMA. Helicobacter pylori associated gastritis among Bahraini children presenting with abdominal pain. J Bahrain Med Soc 2010;22(2):52-4.
33. Wang Z, Hu B, Ding B. Clinical observation on effect of flupentixol and melitracen combined with quadruple therapy on peptic ulcer patients with anxiety and depression. Chinese J Gastroenter 2015;20(6):366-8.