Case Report

Irritable bowel syndrome: an avenue for therapeutic restoration of peripheral nerve imbalance

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Abstract: The bowel is a tightly regulated and controlled system that can easily be disrupted by changes in the intestinal microbiome, neurotransmitters, motility or ion balance. Despite numerous proposed pathophysiological mechanisms, much remains unknown regarding irritable bowel syndrome (IBS). In particular, there is a scarcity of research describing IBS secondary to peripheral nerve dysfunction outside of diabetic populations. Recent research surrounding the mesentery has redefined our understanding of the bowel microenvironment. The function of the mesentery in bowel pathology is a novel area of interest and has potential as a pharmacological target. Serotonin is a key neurotransmitter in the interaction between mesentery and bowel, with serotonergic neurons comprising 2% of the mesenteric neurons. This relationship makes serotonin a potential target to regulate bowel functioning among IBS patients. This article outlines a case of treatment-resistant IBS that was effectively managed by targeting an underlying peripheral neuropathy. This case highlights the link between peripheral nerve dysfunction and IBS. It also outlines a potential avenue of therapeutic management for those with refractory symptoms.

Keywords: Irritable bowel syndrome (IBS); peripheral nervous system diseases; mesentery

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Introduction

Irritable bowel syndrome (IBS) is a multi-faceted disease characterized by bowel instability, bloating and abdominal pain (1). It is a common diagnosis, with an estimated prevalence of up to 20% in the western world (2). There is no clear pathogenesis for IBS and diagnosis is made based on the exclusion of an organic cause (1). Varying subtypes of IBS have been described based on the predominance of constipation, diarrhea or a mixed presentation (1). The gastrointestinal symptoms of IBS significantly impact everyday functioning, with some reports indicating that it is the second-leading cause of workplace absenteeism in the United States (3). It is also a leading cause of referral to gastroenterology (4).

As the pathophysiology of IBS is not well understood, multiple theories have been established (5). Visceral hypersensitivity, alterations in fecal microflora, intestinal inflammation and psychogenic illness are just some of the mechanisms that have been proposed (5). Strong associations between IBS and anxiety disorders exist (2). Psychosocial markers of anxiety and insomnia are independent risk factors for the development of IBS symptoms (6). Recently, research has indicated that the enteric nervous system may play a role in the pathobiology of IBS (6,7). For example, IBS secondary to somatization has been well-described (6). Further support for a role of the enteric nervous system stems from reports of diabetic neuropathy relating to gastroparesis and IBS symptoms. In diabetes mellitus, autonomic dysfunction of the enteric nervous system can lead to disordered motility and osmotic diarrhea (8).

The bowel is a complex muscular structure essential for water reabsorption, nutrient absorption and excretion of

waste. Proper functioning of the bowel is dependent on peristalsis, which propels faeces towards the rectum. The microenvironment of the bowel is tightly controlled and can easily be disrupted by changes in neurotransmitters, motility, ion balance and to the intestinal microbiome (1). Mechanical support is provided by the mesentery, which suspends the bowel, facilitating nerve, blood and lymphatic supply (9). Our understanding of the bowel has been redefined due to current research regarding the mesentery (9). The function of the mesentery in bowel pathology is a novel area of interest and has potential as a pharmacological target (10).

There is a scarcity of research describing IBS secondary to peripheral nerve dysfunction outside of the diabetic population. This report outlines the case of a non-diabetic patient with IBS refractory to traditional therapies. IBS symptoms were effectively managed by targeting and restoring peripheral nerve imbalance. We present the following case in accordance with the CARE reporting checklist available at http://dx.doi.org/10.21037/map-19-228.

Case presentation

This case study presents a 66-year-old Caucasian woman who presented with persistent and severe diarrhoea. For two-and-a-half years she experienced severe bowel dysmotility and nausea. Bowel movements were accompanied by daily abdominal pain and were a cause of severe functional impairment. Additionally, she experienced significant weight loss during this period. On examination, she was found to have peripheral neuropathy.

Significant negative findings included lack of constipation, indigestion and flatulence. Her bowel symptoms were refractory to typical therapeutic management including diphenoxylate and domperidone. Colonoscopic investigations were unremarkable. Her thyroid function demonstrated a normal TSH with a high T4 at 26 µg/dL. Exocrine pancreatic dysfunction, carcinoid tumour and pheochromocytoma were ruled out by 24-hour urine collection and computerized abdominal tomography (CT).

The patient had a relatively healthy lifestyle. She was physically active; either cycling or walking most days and did not smoke. She consumed a single unit of alcohol per week. Her diet was moderate with good variety and avoidance of red meat, sugar and butter. However, she reported a poor sleep pattern, averaging five hours per night. She also reported feelings of exhaustion and anxiety.

Following consultation, she was started on a range of medications aimed at relieving her bowel symptoms. When these failed to lead to an improvement in symptoms she was commence on the following regimen; Amitriptyline 10 mg, nocte; Duloxetine 30 mg, mane; Methimazole 5 mg, od; and Pancrelipase 10,000 units, tds.

This patient returned after 3 months for a follow-up appointment, at which time her bowel symptoms had settled. She reported complete cessation of any diarrhoea and abdominal pain. The above described treatment regimen was continued.

Written informed consent was obtained from the patient for publication of this case report. All the data for this paper had informed consent from the patient involved.

Discussion

This report describes a patient with neuropathic IBS experiencing persistent bowel dysfunction. Her symptoms were resistant to first-line IBS treatments including dietary changes and pharmaceutical management. Her symptoms responded extremely well to a second-line regimen consisting of low dose Amitriptyline and duloxetine.

Serotonin (5-HT) is a key mediator of the brain-gut relationship. It is secreted by Enterochromaffin (EC) cells of the bowel in response to enteric nerve stimulation (11). Intestinal microbes influence the production of serotonin from EC cells, with reports stating that 90% of serotonin production in the body is mediated by these gut microbes (12). Serotonin also plays a large role in the control of the mesentery, with 2% of the mesenteric neurons consisting of serotonergic neurons (13). Proper functioning of the mesentery is required as it plays an important role in the support and innervation of the gut, thus impacting gut motility. This relationship makes gut serotonin balance and the mesentery potential targets to regulate bowel function among IBS patients (13).

Restoration of the gut microbiome is one possible treatment option for those with IBS. This would include dietary changes that promote healthy microbiota (11). Improvement of the gut microenvironment impacts the EC cell interface which regulates mesenteric serotonin levels and impacts control of bowel motility. In some individuals, dietary changes alone may not be sufficient to restore serotonin balance in the gut (11). For these individuals, pharmaceutical intervention is warranted. Medications that target serotonin reuptake at the post-synaptic cleft have been used to restore this serotonin imbalance. These medications include low dose tricyclic antidepressants

(TCAs) and low dose serotonin-norepinephrine reuptake Inhibitors (SNRIs). The mechanism by which these medications improve IBS symptoms is through restoration of circadian rhythm to neurons in the mesentery and bowel, which help improve peristaltic function (11). TCAs have been demonstrated to be effective for the treatment of IBS, there is less research supporting the use of SNRIs (14,15).

Peripheral nerve dysfunction is a known complication of poorly controlled diabetes. Common sites of peripheral neuropathy in these patients are vagal and sympathetic nerve dysfunction (16). Diabetic gastroenteropathy typically takes the form of gastroparesis, but IBS has also been described (16). The cause of the peripheral nerve dysfunction in diabetes endocrine dysfunction (i.e., where the bowel loses its normal peristaltic rhythm), is still unknown (9,16). Novel research postulates disruption of the cells of Cajal, found in the intestinal wall, as a possible mechanism for diabetic enteropathy (9). Endocrinologists have targeted peripheral neuropathy in diabetic patients with IBS through the use of low dose TCAs and low dose gabapentin with promising results. Less research is available on peripheral neuropathy in non-diabetic populations.

This case further supports the link between IBS and peripheral nerve dysfunction. The use of anti-depressant agents to regulate gut serotonin levels and control bowel functioning may be effective in this subset of IBS patients. Further research is needed to establish an optimal treatment regimen for the management of neuropathic IBS.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at http://dx.doi.org/10.21037/map-19-228

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Written informed consent was obtained from the patient for publication of this case report. All the data for this paper had informed consent from the patient involved.

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