Chapter

Faecal Incontinence and Autoimmune Diseases

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Abstract

Anal and rectal continence depend on many factors such as such as consistency of stool, integrity of neuromuscular sphincter complex, rectal capacity, sensation of defecation, higher cerebral function, and mobility. Any disturbance to these parameters may lead to various degrees of faecal incontinence. Continence may also be affected by immunological disorders that cause vasculitis as well as gastrointestinal mucosal and smooth muscle damage due to the formation of autoantibodies and immune complexes in autoimmune disease. A thorough knowledge of the gastrointestinal manifestations of autoimmune disease is important in order to be able to manage patients' symptoms optimally.

Keywords: autoimmunity, immune tolerance, inflammasomes, cytokines, faecal incontinence

1. Introduction

Faecal incontinence is characterized by inability to control bowel motions, causing the unexpected leakage of flatus and feces per rectum [1]. It may adversely affect the quality of one's life. Faecal incontinence may be precipitated by conditions such as diarrhea, constipation, pelvic muscle damage, nerve damage, and vaginal delivery. Faecal continence depends on many factors; for example, consistency of faecal substance, neuromuscular sphincter complex, rectal capacity, and sensation of defecation [2]. Other causes of faecal incontinence include immunological disorders that cause muscle damage due to formation of autoantibodies in autoimmune diseases [3, 4].

2. What is autoimmunity?

Autoimmunity is a disorder of the immune system. It is characterised by the absence of immune tolerance (tolerance is the absence of an immune response in an immunologically competent person), be it central tolerance in the thymus or peripheral tolerance through Treg cell CD4+ and CD25+ (T regularity). It is due to a defect in immune regulatory and signaling mechanisms; genetic factors like single-gene defects or gene mutation can also cause an immune dysregulation and autoimmunity [5].

3. Causes of autoimmunity

3.1 Epigenetic alterations

Epigenetic alterations like DNA methylation, histone modification, and microRNAs alter the transcription and activity of genes that are involved in autoimmune responses and disease pathogenesis. These lead to aberrant epigenetic modifications in CD4 T helper cells' function through deregulations in several transcriptional genes like Ifng, Cd70, Tnf, Dnmt3a, and Foxp3 that determine T cell identity. Adding to this, epigenetics target regulatory genes like Tim-3, cereblon, protein kinase C theta, octamer transcription factor 1, basic leucine zipper transcription factor ATF-like, p70 kinase, and lactate dehydrogenase A that influence T cell activation, differentiation, and metabolism [6].

3.2 Genetic mutation in inflammasome

Inflammasomes are multi-protein complexes that consist of NOD-like receptor (NLR) and AIM-like receptor (ALR) and apoptosis-associated speck-like protein that contains a CARD and caspase-1. The active caspase-1 cleaves pro-IL-1β and pro-IL-18 to IL-1β and IL-18, resulting in inflammation. Genetic mutations in inflammasomes result in autoimmune diseases. NOD-like receptor family, pyrin domain containing 1 (NLRP1) haplotypes contributes to susceptibility to autoimmune disease and single nucleotide polymorphisms (SNPs) that alter the susceptibility and severity of autoimmune disease. IL-1β and IL-18 maintain Th17 responses and endothelial cell damage, which potentiate autoimmune diseases. Autoimmunity is mediated in part by innocent bystander cells, augmented by inflammasomes [7].

3.3 HLA-associated autoimmune diseases

Autoimmune diseases have associations with particular HLA alleles through displaying the autoantigens targeted by self-reactive T cells that escape thymic deletion because most HLA alleles are capable of presenting self-antigens even in healthy individuals [8].

3.4 Cytokines pathway

Cytokine and cytokine receptor genetic polymorphisms have been associated with many different autoimmune diseases like *IL23R* and IL-23 that augment the pro-inflammatory action of Th17 cells that leads to tissue damage, and anti-cytokine therapy can be nicely used as a target to treat autoimmune diseases [9–11].

4. Mechanism of autoimmunity

The mechanism of autoimmune reactions is due to an imbalance between two immune responses, effector and regulatory, that develop through stages of initiation and propagation, and often show phases of resolution or remissions and exacerbations or flares. The mechanism of autoimmunity is defective elimination and/or control of self-reactive lymphocytes. A major goal of treatment is reestablishing the normal balance between effector and regulatory immune responses [12] (**Figure 1**).

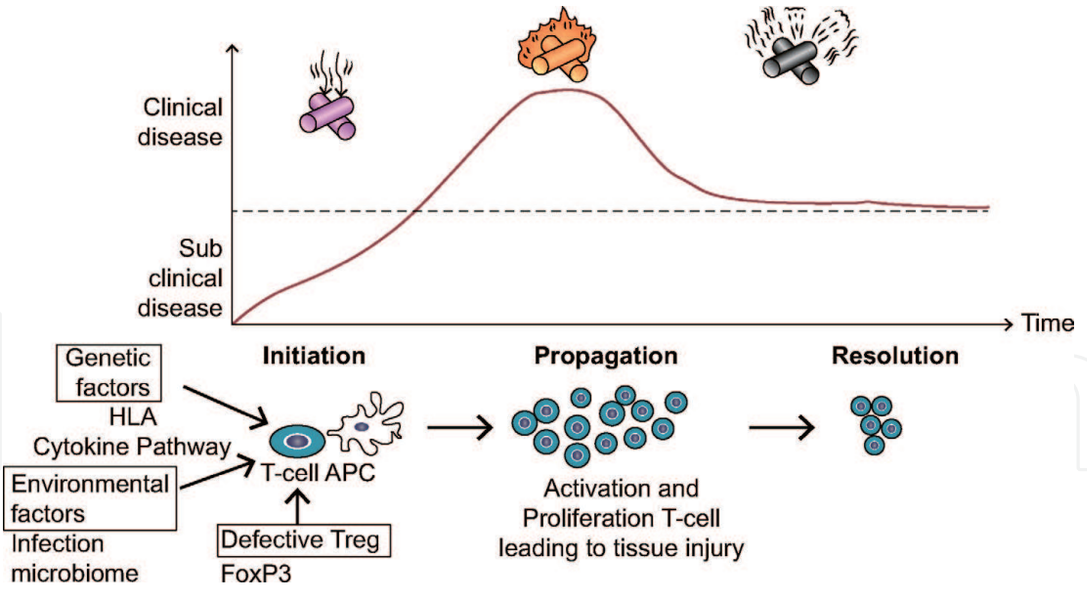

Figure 1.
Mechanism of autoimmunity.

5. Gastrointestinal manifestations in systemic autoimmune diseases

The systemic autoimmune diseases include different diseases like collagen vascular diseases, systemic vasculitides, Wegener granulomatosis, and Churg-Strauss syndrome that involve any part of gastrointestinal tract, hepatobiliary system, and pancreas. Patients with these diseases had different gastrointestinal symptoms like oral ulcers, dysphagia, gastroesophageal reflux diseases, abdominal pain, constipation, diarrhea, faecal incontinence, pseudo-obstruction, perforation of GIT tract, and bleeding [13].

5.1 Effects of autoimmune diseases on the gastrointestinal tract

Some autoimmune diseases are characterized by autoreactive T cells attacking body's own tissues. One of the manifestations of these diseases is gastrointestinal manifestation, which is either the initial presentation or the complications of the disease.

5.1.1 Systemic lupus erythematosus

Systemic lupus erythematosus (SLE) is an autoimmune disease of unknown etiology, characterized by deposition of autoantibodies and immune complexes in tissues (type III hypersensitivity). Gastrointestinal manifestations of SLE are due to primary gastrointestinal disorders, complications of therapy, and SLE itself. Any part of the gastrointestinal tract may become involved in SLE. Many GI conditions can be mimicked by SLE [14]. Lupus enteritis, a distinct subset of SLE, is defined as either vasculitis or inflammation of the small bowel. The clinical manifestations include decreased salivation, buccal mucosal ulcers, dysphagia, oesophageal ulceration, gastric ulceration, pseudo-obstruction, and faecal incontinence [15–17].

5.1.2 Rheumatoid arthritis

It is also a type III hyper sensitivity reaction due to deposition of immune complexes in the synovium of small interphalangeal joints of hands. Gastrointestinal

manifestations are common and variable. It involves the esophagus resulting in decreased peristalsis, decreased lower esophageal sphincter tone, hiatal hernia, and esophageal ulcer. It may also result in peptic ulcer and chronic atrophic gastritis. Colonic inflammation such as collagenous colitis with secondary amyloidosis may also occur, leading to diarrhea and faecal incontinence [18].

5.1.3 Sjogren's syndrome

Sjögren syndrome is a common autoimmune disease due to B cell activation and invasion of T and B lymphocytes to affected exocrine glands. This disease affects the gastrointestinal tract resulting in dry mouth, difficulty in swallowing, esophageal atrophy, epigastric pain, dyspepsia, chronic atrophic gastritis, chronic pancreatitis, jejunitis, sigmoiditis, and inflammatory bowel disease [19, 20].

5.1.4 Progressive systemic sclerosis (scleroderma)

It is one of the connective tissue diseases of unknown etiology that affects females more than males. It is characterized by vasculopathy, tissue fibrosis, and autoimmunity. It causes overproduction of collagen due to autoimmune dysfunction that leads to fibrosis of many visceral organs. The immune system attacks the kinetochore of the chromosomes that leads to genetic malformation of nearby genes. Patients experience gastrointestinal tract symptoms like thinning of the lips, tightening of the perioral skin, impaired taste sensation, atrophy of the mucous membrane and tongue papilla, dysphagia and dyspepsia, gastroesophageal reflux, peptic esophagitis, Barrett's metaplasia, gastric antral vascular ectasia (GAVE) or watermelon stomach, and dysmotility of small intestine leading to chronic pseudo-obstruction. As scleroderma progresses, it may lead to decreased motility of the intestine and to progressive fibrosis and scarring of the small intestine leading to bacterial overgrowth and malabsorption of nutrients and growth in stagnant intestinal fluid. Large intestine and colon will be involved, causing pseudo-obstruction or ischemic colitis [21, 22]. Anorectal involvement causes faecal incontinence and rectal prolapse. Gastrointestinal tract involvement greatly affects morbidity and mortality in this disease and therapy aims to relieve these symptoms [23, 24].

5.1.5 Polyarteritis nodosa

The gastrointestinal manifestations of systemic vasculitis that results from mesenteric ischemia are vague nonspecific abdominal pain, hematemesis, melena, hematochezia, jejunal ulceration, and perforation. Liver may be involved with acalculous cholecystitis, appendicitis, pancreatitis, and biliary strictures [25–27].

5.1.6 Kawasaki disease

This is a syndrome that is characterized by oral mucosal changes, fever, lymphadenopathy, and polyarteritis in addition to gastrointestinal symptoms like abdominal pain, vomiting, diarrhea, small bowel obstruction, jaundice, and paralytic ileus [28].

5.1.7 Inflammatory muscle disorders: polymyositis and dermatomyositis

These are systemic autoimmune diseases characterized by inflammation of striated and smooth muscle of the body. Patients had a progressive weakness of

proximal striated muscles and skin rash with dermatomyositis. The whole gastrointestinal tract may be affected but the proximal esophagus is more common affected. Gastric and esophageal emptying and peristalsis are affected in many patients, so they complain of dysphagia, aspiration, nasal regurgitation, early satiety, bloating, reduced gastrointestinal motility, hiatal hernia, gastroesophageal reflux disease (GERD), stricture, dilated atonic esophagus associated with delayed gastric emptying, and intestinal mucosal thickening. In addition to that, there are colonic pseudodiverticulosis and pneumatosis coli. Neurological dysfunction and diminished smooth muscle contractility due to muscle atrophy and fibrosis lead to bowel wall oedema, ulceration, and perforation [29].

5.1.8 Giant cell arteritis

This is a granulomatous inflammation of the arteries, particularly cranial and temporal, leading to narrowing the lumen of the arteries. The main symptoms are headache and fever. Blindness may occur suddenly. There are associations with intestinal manifestations like bowel ischemia and gangrene, acute pancreatitis, liver granulomas, lymphocytic infiltration, and dilated bile canaliculi. The erythrocyte sedimentation rate is high [30, 31].

5.1.9 Henoch-Schönlein purpura

This is an IgA-mediated immune complex deposit resulting in systemic vasculitis in small vessels. Gastrointestinal signs and symptoms are common such as periumbilical pain with nausea and vomiting. Sometimes ulceration of the mucosa of the second part of the duodenum and less commonly in the colon and rectum may occur [32].

5.1.10 Takayasu arteritis

This is a chronic vasculitis of unknown etiology. The inflammatory processes cause thickening, narrowing, and eventual occlusion of the walls of the affected arteries. Patients usually experience gastrointestinal symptoms such as abdominal pain, nausea, diarrhea, and hemorrhage due to the involvement of the descending abdominal aorta [33].

5.1.11 Cogan's syndrome

This is a chronic inflammatory disorder characterized by interstitial keratitis, audiovestibular system involvement, aortitis, mesenteric vasculitis, weight loss, fever, lymphadenopathy, hepatosplenomegaly, abdominal pain, nausea, and vomiting [34].

5.1.12 Churg-Strauss syndrome

This is an allergic angiitis that occurs mostly in asthmatic patients, and is associated with granulomatous necrotizing vasculitis. Patients have eosinophilia, fever, and allergic rhinitis. Sometimes gastrointestinal involvement occurs in about 50% of patients, leading to eosinophilic gastroenteritis associated with abdominal pain, bloody diarrhea due to multiple ulcers, nausea, and vomiting. Perforation of the small intestine and colon may commonly occur. Necrotizing granulomatous vasculitis of the mesenteric artery leads to mucosal ischemia [35].

5.1.13 Wegener granulomatosis

This is a systemic autoimmune disease characterized by granulomatous vasculitis of the upper and lower respiratory tracts leading to infection, glomerulonephritis, and small-vessel necrotizing vasculitis with granuloma formation. Gastrointestinal manifestations of Wegener granulomatosis are oropharyngeal mucosal lesions, gingivitis, ulcer of gastric mucosa, small intestinal perforation, colonic ulceration, non-healing perianal ulcers, cholecystitis, recurrent acute pancreatitis, and splenic necrosis [25].

5.1.14 Antiphospholipid antibody syndrome

This is a disorder characterized by recurrent vascular thrombosis, abortion, and thrombocytopenia due to increased antiphospholipid antibodies. The gastrointestinal manifestations of antiphospholipid antibody syndrome lead to vasculopathy and tissue ischemia. Antiphospholipid antibodies in SLE patients are associated with Budd-Chiari syndrome, with patients presenting with abdominal pain, ascites, and hepatic failure [36–38].

5.1.15 Spondyloarthropathies

These are a group of interconnected chronic inflammatory rheumatic diseases including ankylosing spondylitis, arthritis associated with inflammatory bowel disease and reactive arthritis. The spondyloarthropathies are associated with the HLA-B27 gene. About 36% of patients have reactive arthritis secondary to a dysenteric infection were positive for HLA-B27. Subclinical gut inflammation, ulcerative colitis, and Crohn's disease are frequent types of idiopathic IBD that are associated with arthritis or spondylitis [39–43].

5.1.16 Behçet's disease

This is a widespread autoimmune vasculitis of unknown origin occurring in all ages resulting in a damage to blood vessels in all the body. Patients usually had uveitis with oral and genital ulcers. Clinical manifestations also include vascular, neurological, articular, renal, and gastrointestinal manifestations. Gastrointestinal Behçet's disease symptoms are similar to those caused by inflammatory bowel diseases, and include nausea, abdominal pain, and bloody diarrhea. In addition, ulceration in the mouth, gastrointestinal tract, or genitalia may occur, the ulcers typically being painful, shallow and round with discrete borders. Segmental mucosal ulceration in the ileocecal and colonic area leads to perforation and bloody diarrhea [44].

6. Mechanisms of how autoimmune disorders cause faecal incontinence

The precise cause and mechanism how autoimmune diseases cause faecal incontinence are unknown, but multiple factors are probably involved. These factors include deterioration and destruction of collagen framework by the effect of autoantibodies, resulting in inflammation, reduced compliance of rectal muscles with consequent urgency, and urge faecal incontinence. Diarrhea is one of GIT manifestation of autoimmune connective tissue diseases, and this in itself may lead to incontinence even in the presence of normal sphincters.

7. Conclusion

Continence usually requires normal functioning of both the muscles of the lower digestive tract and pelvic floor, and the nervous system. There are many causes of faecal incontinence. In this chapter, we have discussed the various autoimmune disorders and their involvement in the disruption of the continence mechanism. Further studies are necessary in this field, focusing on targeted therapies to minimize the effect of these diseases on the gastrointestinal tract.

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