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Chapter

Effect of Autoimmunity in Fecal Incompetence

Batool Mutar Mahdi

Abstract

Fecal incontinence is an embarrassing social problem to the patients affecting patients' work and social ordinary life. It affects both sexes characterized by inability to control bowel motions causing leaking stool or flatus unexpectedly from the rectum and anus, and in severe cases, it causes a complete loss of bowel control. The causes are severe diarrhea, constipation, muscle and nerve damage that is caused by aging, vaginal delivery, episiotomy or forceps delivery. Anal and rectal continence depends on many aspects like consistency of stool, neuromuscular sphincter complex, rectal capacity, sensation of defecation and ability to move and reach a toilet. Another cause is immunological disorders that cause muscle damage due to formation of autoantibodies in autoimmune diseases or in association with gastrointestinal manifestation of autoimmune diseases like multiple scleroses and other autoimmune diseases. Simply, it can be diagnosed by routine digital rectal examination that has good sensitivity and poor specificity in discriminating small from severe anal sphincter defects.

Keywords: autoimmunity, tolerance, fecal

1. Introduction

Fecal incontinence is an embarrassing social problem to the patients affecting patients' quality of life. It affects both sexes (males and females) characterized by inability to control bowel motions causing leaking stool unexpectedly from the rectum while passing gases and sometimes a complete loss of bowel control [1]. This condition caused by diarrhea, constipation, muscle damage and nerve damage that caused either by aging or vaginal delivery. Thus fecal continence depends on many factors like consistency of fecal substance, neuromuscular sphincter complex, rectal capacity, sensation of defecation and ability to move and reach a toilet [2]. Another cause is immunological disorders that cause muscle damage due to formation of autoantibodies in autoimmune diseases [3]. Simply it can be diagnosed by routine digital rectal examination that had good sensitivity and poor specificity in discriminating small from severe global anal sphincter defects [4].

2. What is autoimmunity?

Autoimmunity is a disorder of the immune system characterized by absence of immune tolerance (Tolerance is absence of immune response in immune

competence person) whether central tolerance in the thymus or peripheral through Treg cell CD4 + CD25 + (T regulatory). It is due to a defect in immune regulatory and signaling mechanisms, genetic factors like single-gene defects or gene mutation can cause an immune dysregulation and autoimmunity [5].

3. Causes of autoimmunity

It was caused by interaction of environmental that augment activation of self-reactive lymphocytes which escaped control in the thymus and are react against self-constituents antigens and genetic factors that mentioned below:

3.1 Epigenetic alteration

Epigenetic alterations like DNA methylation, histone modification, and microRNAs that alter the transcription and activity of genes that are involved in autoimmune responses and diseases pathogenesis. These leads 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 that, 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 inflammasomes

Inflammasomes can be defined as multi-protein complexes consisting of NOD-like receptor (NLR)/an AIM-like receptor (ALR), 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 alters 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 disease

Autoimmune diseases had an 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 augments the proinflammatory action of Th17 cells that leads to tissue damage and anticytokines therapy can be nicely used as 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**).

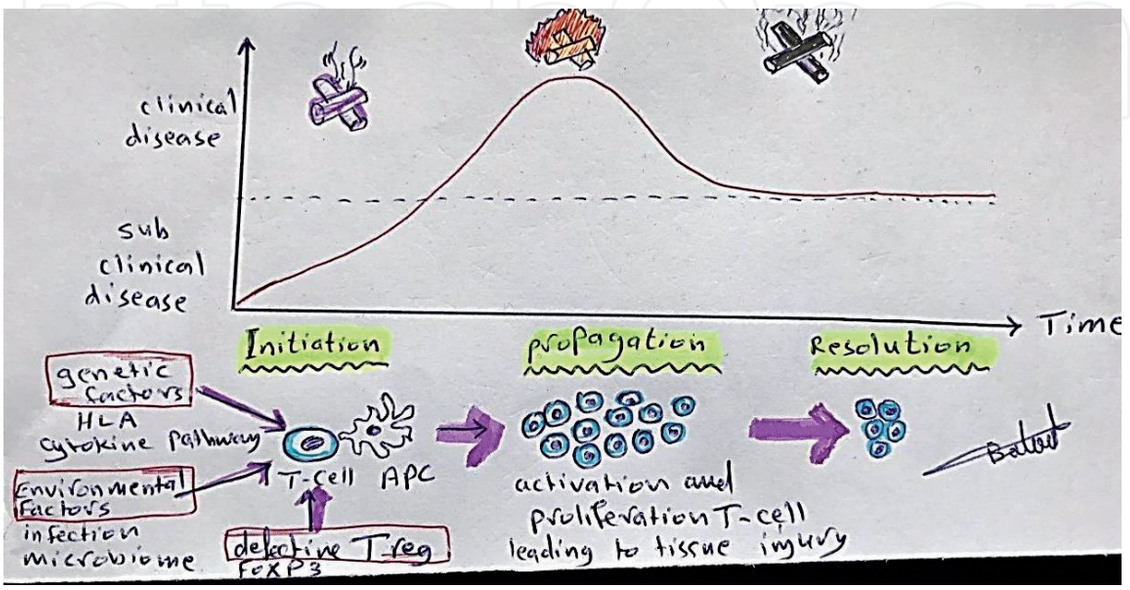

Figure 1.
Mechanism of autoimmunity.

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, fecal incontinence, pseudo-obstruction, perforation of GIT tract and bleeding [13].

5.1 Effects of autoimmune diseases on the gastrointestinal tract

Autoimmune disease characterized by autoreactive T cells attacking body's own tissues. Gastrointestinal manifestations are either initial presentation or late 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 defines as alimentary tract lesions in SLE. The manifestations include oral mucosal ulcers and decreased salivation occurring in the hard palate, buccal mucosa, dysphagia, esophageal ulceration, gastric ulceration, pseudo-obstruction and fecal incompetence [15–17].

5.1.2 Rheumatoid arthritis

It is also type III hyper sensitivity reaction due to deposition of immune complexes in the synovium of small interphalangeal joints of the hands. Gastrointestinal manifestations are common and variable. It involved esophagus that decreased peristalsis, decreased lower esophageal sphincter tone, hiatal hernia, esophageal ulcer, peptic ulcer, chronic atrophic gastritis, colonic inflammation like collagenous colitis and fecal incompetence with secondary amyloidosis may occur [18].

5.1.3 Sjogren's syndrome

Sjogren's syndrome is a common autoimmune disease due to B cell activation and invasion of T and B lymphocytes to affected exocrine glands. This disease affect the gastrointestinal tract like 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 disease 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 lead to genetic malformation of nearby genes. Patients had 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, dysmotility of small intestine may cause chronic pseudo-obstruction. As scleroderma progresses leads to decreased motility of the intestine and leads 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 fecal incontinence and rectal prolapse. GIT involvement greatly affects morbidity and mortality in this disease and therapy aim to relieve these symptoms [23, 24].

5.1.5 Polyarteritis nodosa

The gastrointestinal manifestations of systemic vasculitis that results from mesenteric ischemia are vague non specific abdominal pain, hematemesis, melena, hematochezia, jejunal ulceration and perforation. Liver may be involved with acalculous cholecystitis, appendicitis, pancreatitis and biliary strictures [25–27, 36].

5.1.6 Kawasaki disease

It is a syndrome that characterized by oral mucosal changes, exanthem, enanthem, 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

This is a systemic autoimmune diseases characterized by inflammation of striated and smooth muscle of the body. Patients had a progressive weakness of proximal striated muscles, 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 is 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 pseudodiverticula, pneumatosis, and constipation. Neurological dysfunction and diminished smooth muscle contractility due to muscle atrophy, fibrosis and inflammation leading to wall edema, ulceration and perforation [29].

5.1.8 Giant cell arteritis

It is a granulomatous inflammation of the arteries particularly cranial and temporal leads to narrowing the lumen of the arteries. The main symptoms are headache, fever, increased erythrocyte sedimentation rate and blindness occurring suddenly associated with intestinal manifestation like gangrene, acute pancreatitis, liver granulomas, lymphocytic infiltration, dilated bile canaliculi, and hepatocellular [30, 31].

5.1.9 Henoch-Schönlein purpura

It is an IgA mediated immune complex deposits resulting in systemic vasculitis in small vessels. Gastrointestinal signs and symptoms are common presenting symptom like periumbilical pain with nausea and vomiting. Some times ulceration of the mucosa of the second part of the duodenum and less in colon and rectum [32].

5.1.10 Takayasu arteritis

It is a chronic vasculitis of unknown etiology. The inflammatory processes cause thickening, narrowing, and occluding of the walls of the affected arteries. Patients usually complaining from gastrointestinal symptoms due to the involvement of the descending abdominal aorta like abdominal pain, nausea, diarrhea and hemorrhage [33].

5.1.11 Cogan's syndrome

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

5.1.12 Churg-Strauss syndrome

It is an allergic angiitis occurs mostly in asthmatic patients associated with granulomatous necrotizing vasculitis. Patients had eosinophilia, fever, and allergic rhinitis and 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 commonly occurs. Necrotizing granulomatous vasculitis of the mesenteric artery leads to mucosal ischemia [35].

5.1.13 Wegener granulomatosis

It is a systemic autoimmune disease characterized by granulomatous vasculitis of the upper and lower respiratory tracts 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, 36].

5.1.14 Antiphospholipid antibody syndrome

It is a disorder characterized by recurrent vascular thrombosis, abortion and thrombocytopenia, increased antiphospholipid antibodies. The gastrointestinal manifestations of antiphospholipid antibody syndrome leads to vasculopathy and tissue ischemia. Antiphospholipid antibodies in SLE patients are associated with Budd-Chiari syndrome presenting with abdominal pain, ascites and hepatic failure [37–39].

5.1.15 Spondyloarthropathies

They 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 had 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 [40–44].

5.1.16 Behçet's disease

It 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. Regarding gastrointestinal Behçet's disease symptoms which is difficult to differentiate it from inflammatory diseases are nausea, abdominal pain, bloody diarrhea, ulceration in mouth, gastrointestinal tract or genetal which is painful, shallow, round with discrete borders. Segmental mucosal ulceration in the ileocecal and colonic area leads to perforation and bloody diarrhea [45].

6. Conclusions

It had been found that fecal incompetence which is due to muscle damage that make anal sphincter difficult to hold stool properly after birth, episiotomy or

forceps. Other cause is nerve damage that due to nerve injury that affect sense stool in the rectum or anus which is due to childbirth, spinal cord injury, stroke, diabetes and multiple sclerosis that cause nerve damage. It can also be occur either due to autoimmune diseases or due to administration of medications like certain immunomodulators or immunosuppressive drugs.

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