Gastrointestinal Manifestations of Systemic Diseases in Critically Ill

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ABSTRACT

Systemic disorders can have gastrointestinal (GI) manifestations which are characterized by nausea, vomiting, diarrhea, constipation, abdominal pain, jaundice, and abnormal liver function tests. These gastrointestinal symptoms can be signs of various immunologic, infectious, and endocrine diseases. Gastrointestinal manifestations can be the first signs and symptoms for which the patient can be admitted in a critical care unit. In this article, we will discuss the GI manifestations of various topical diseases, endocrine diseases, and immunological diseases which are the major bulk of patients in intensive care unit (ICU).

Keywords: Acute liver failure, Acute pancreatitis, COVID-19, Dengue.

Indian Journal of Critical Care Medicine (2020): 10.5005/jp-journals-10071-23610

GASTROINTESTINAL MANIFESTATIONS OF TROPICAL DISEASES

Malaria

Gastrointestinal (GI) manifestations are common in malaria. Gastrointestinal manifestations are more common in pediatric patient than adults. These include dyspepsia, vomiting, diarrhea, hepatitis, gastrointestinal bleed, abdominal pain, subacute intestinal obstruction such as presentation and acute abdomen. There are few case reports of perforated duodenal ulcer.

Mild jaundice is common in malaria. Sometimes severe jaundice may occur in P. falciparum infection due to hemolysis, hepatocyte injury, and cholestasis. Liver manifestations are more common in adults than children. Hypoglycemia is a common complication of severe malaria. It occurs due to diminished hepatic gluconeogenesis, depletion of liver glycogen stores, increase in the consumption of glucose by the host (and, to a much less extent, the parasite), and quinine-induced hyperinsulinemia. Hypoglycemia is more common in children and pregnant women.

Leptospirosis

Leptospirosis may present with wide variety of GI and non-GI complications. GI manifestations are nausea, vomiting, abdominal pain, acalculous cholecystitis, enteritis, pancreatitis, peritonitis, and liver failure. Liver failure in leptospirosis is characterized by increased bilirubin level with normal level of aminotransferases.

Enteric Fever

Various GI manifestations of enteric fever are loss of appetite and weight loss, coated tongue, abdominal pain, pea soup diarrhea, and marked constipation. Dread GI complications are intestinal hemorrhage and perforation. Terminal ileum is most commonly affected followed by the ileocecal valve, the ascending colon, and the transverse colon. Left side colon is least affected. In colonoscopy, multiple variable-sized punched out ulcers with elevated margin are found. Intestinal perforation generally occurs more frequently among adults than children and is associated with high mortality rates. Typhoid intestinal perforation usually occurs during the third week of febrile illness and is due to necrosis of the Peyer’s patches in the antimesenteric bowel wall.

Dengue

Gastrointestinal symptoms are common in dengue patient. More than half of patients presented with nausea, vomiting, and abdominal pain. Some patients also presented with diarrhea. Few patients also develop gastrointestinal bleed. Hepatomegaly found around 18% of patients. Abnormal LFT is characterized by transaminitis in around 90% of cases. However, transaminitis is mild to moderate. Few patients develop fulminant liver failure due to hepatitis or focal necrosis of liver causing hepatic encephalopathy and death.

GASTROINTESTINAL MANIFESTATIONS OF COVID-19

Unexpected pneumonia-like symptoms was found in Wuhan, China, in December 2019. Subsequently, it was labeled as SARS CoV-2 which resulted widespread pandemic. Incubation period ranged from 2 to 11 days. Usual symptoms are fever, cough, headache, and shortness of breath. Some atypical symptoms are anosmia and loss of taste. Many patients presented gastrointestinal manifestations like nausea, vomiting, abdominal pain, and diarrhea. Some studies have also found the presence of COVID-19 viruses in

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anorectal swabs and in stool samples, despite negative in upper respiratory tract samples. Different studies demonstrated the presence of angiotensin-converting enzyme 2 receptor (ACE2) in gastrointestinal epithelial cells which might facilitate the evidence of this possible route for COVID-19 infection. ACE 2 receptors are expressed in glandular cells of gastric, duodenal, and rectal epithelial supporting entry of COVID-19 into host cells.

Up to 60% patients develop liver impairment characterized by transaminitis, elevated bilirubin, low serum albumin, and elevated alkaline.

**Gastrointestinal Manifestations of Endocrine Disease**

Gastrointestinal Manifestations in Diabetic Ketoacidosis

In all, 50–75% of patients with diabetic ketoacidosis (DKA) presented with gastrointestinal symptoms such as nausea, vomiting, abdominal pain, and abdominal distention. The mechanism of gastrointestinal symptoms is due to central neurogenic response the ketoacidosis, gastric atony, generalized ileus, increased level of counter regulatory hormones such as glucagon and catecholamines, gastritis, or pancreatitis. These symptoms resolve with fluid therapy and insulin.

Combination of clinical history, physical examination, and laboratory examination is required for differential diagnosis of DKA from cholecystitis, acute pancreatitis, and mesenteric vascular insufficiency. Nausea, vomiting, and abdominal pain associated with DKA are acute in onset in contrast to intermittent abdominal pain over days to weeks in intra-abdominal disorder. On physical examination, there is generalized abdominal pain in DKA in contrast to localized abdominal pain in intra-abdominal disorder.

Laboratory evaluation in DKA is required to differentiate it from atypical presentation of myocardial infarction, intestinal perforation, gastric atony, generalized ileus, and obstruction. These include ECG, CBC, abdominal films, serum enzymes such as serum amylase, lipase, alkaline phosphatase, SGOT, SGPT, CPK, glucose, electrolytes, urea, and creatinine. In DKA, there is increase in leukocyte count with toxic granulation because of increase in stress hormone. Hematocrit also increases because of severe dehydration. Forty to 79% of DKA patients have increased serum amylase levels. In the absence of any symptoms, the level of serum amylase can be increased to more than three times of normal value. But the serum level of lipase is normal or slightly increased.

There is derangement in SGOT, SGPT, LDH, and other enzymes in DKA. In an observational study, Knight et al. found that 33% of patients had mild to marked elevations in hepatic enzymes. Abdominal pain, nausea, vomiting occurring secondary to acidosis resolve within 12–24 hours. If the pain persist for more than 12–24 hours additional etiology should be sought.

**Gastrointestinal Manifestations in Thyroid Disorder**

In all, 30–50% of hyperthyroid patients have gastrointestinal symptoms. Gastrointestinal symptoms range from frequent bowel movements, diarrhea, chronic dyspeptic symptoms such as epigastric pain and fullness, nausea, and vomiting. Sometimes intractable vomiting is also reported in hyperthyroidism. There is gastrointestinal motor dysfunction manifested as altered intestinal motility and decreased intestinal transit time in hyperthyroidism. The mechanism behind gastrointestinal manifestations is not clear, but one of the proposed hypotheses is due to direct effect of hormone on central nervous system.

Dysphagia is a rare manifestation of hyperthyroidism which is due to direct compression of thyroid on esophagus and myopathy of striated muscles of pharynx and esophagus. Dysphagia resolves on correction of hyperthyroidism.

In 27–37% of patients, there is increase in SGOT and SGPT. In 64% of patients, there is increase in alkaline phosphatase because of high turnover in bones. Sometimes, there is mild increase in gamma glutamyl transferase and bilirubin levels. Few case reports of fulminant hepatic failure have been described in hyperthyroidism. Long-term untreated hyperthyroidism can lead to cirrhosis.

Graves’ disease patients are at increased risk of coeliac disease and ulcerative colitis. Some case reports of primary biliary cirrhosis reported in graves’ disease.

Severe hypothyroidism may lead to disturbance in esophageal peristalsis. There is reduced velocity and amplitude of esophageal peristalsis and decrease in lower esophageal sphincter pressure which all contribute to dysphagia. Other gastrointestinal manifestations are decreased appetite, but there is weight gain because of decreased metabolism and water retention. There is reduction in peristalsis and constipation. Although rare in severe hypothyroidism, there may be severe ileus and pseudo-obstruction. Sometimes, there is diarrhea in severe hypothyroidism due to bacterial overgrowth syndrome. Severe upper gastrointestinal bleeding refractory to usual treatment also reported in severe hypothyroidism.

Mechanism for gastrointestinal dysfunctions are multifactorial with possible explanations being alteration in hormone receptors, neuromuscular disorder, and myopathy. Thyroid hormone deficiency may influence transepithelial flux by inhibiting Cl−/HCO3− anion exchange which have effect on intestinal motility.

In 50% of patients with hypothyroidism, there is some degree of mild liver abnormality, despite normal histological findings. Myxoedema ascites is found in some long-standing case of hypothyroidism which is characterized by serum to ascites albumin gradient more than 1.1 g/dl with high protein content. Hypothyroidism patients are also at high risk of Crohn’s disease, pernicious anemia, and primary biliary cirrhosis.

**Gastrointestinal Manifestations in Autoimmune Disorders**

**Inflammatory Bowel Diseases**

Ulcerative colitis and Crohn disease are autoimmune diseases together called as inflammatory bowel disease. They are characterized by widespread intestinal inflammation and ulceration. They are admitted to intensive care unit (ICU) with presentation like lower gastrointestinal bleeding, intestinal perforation leading to severe abdominal sepsis, and septic shock.

**Antiphospholipid Syndrome**

Antiphospholipid syndrome (APS) may be associated with systemic lupus erythematosus or as an isolated finding. Since gastrointestinal tract is highly vascular and rich in capillary, it is highly vulnerable to be affected by autoimmune disease. There is widespread vascular thrombosis in antiphospholipid syndrome due to procoagulant effect of autoantibodies. Catastrophic antiphospholipid syndrome
may manifest as ischemia involving esophagus, stomach, small intestine, and colon resulting in gastrointestinal bleeding, abdominal pain, and esophageal necrosis with perforation. Thrombosis of hepatic and portal vein may result Budd-Chiari syndrome, hepatic veno-occlusive disease, hepatic infarction, portal hypertension, and cirrhosis.

**Systemic Lupus Erythematosus**

Up to 40% of patients with systemic lupus erythematosus (SLE) have gastrointestinal manifestations. These manifestations may be due to vasculitis or due to side effects of medications used for treatment. Dysphagia is the most common gastrointestinal manifestation which may be due to gastrointestinal motility disorder, gastroesophageal reflux disease, or due to infection by candida, CMV, and herpes simplex virus. Some case reports of intestinal pseudo-obstruction reported in SLE which is characterized by abdominal pain, distention, and bloating. Mechanism behind pseudo-obstruction is unknown, but possible explanations are due to immune complex deposition in smooth muscles of intestine and due to vasculitis induced chronic ischemia. Other gastrointestinal manifestations are protein losing enteropathy, autoimmune hepatitis, lupus hepatitis, acute pancreatitis, mesenteric vessel vasculitis, and peritonitis which may lead to admission in ICU.

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