Cases report.

Gastrointestinal perforation in COVID-19 patients – case series and review of literature.

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Abstract :

Severe acute respiratory syndrome coronavirus -2 (SARS-CoV 2) involving respiratory tract started in 2019 at Wuhan , China but spread to almost all parts of world to the extent that it was declared pandemic by WHO. As more and more number of cases are detected, the involvement of systems other than respiratory was observed and nearly 5 to 50 % patients have abdominal symptoms like pain and diarrhea. During course of treatment, few patients developed rare complication of gastrointestinal perforation. Three cases ( two with colonic perforation and one with gastric perforation) of gastrointestinal perforation in COVID-19 positive patient are reported in article with review of literature regarding various hypothesis of intestinal perforation in these patients.

Keywords : COVID-19 , gastrointestinal perforation, Severe acute respiratory syndrome coronavirus -2 (SARS-CoV 2) , Tecilizumab

Introduction :

Severe acute respiratory syndrome coronavirus -2 (SARS-CoV 2) caused coronavirus disease and it had affected 5 crore world’s population with 14 lakh deaths. Since the virus primarily affected respiratory systems, initial phase of symptomatology revolved round respiratory symptoms like dry cough, fever etc. due to involvement of lungs. But as the time passed, varied symptoms were increasingly noted either in addition to respiratory symptoms or in isolation like loss of smell and taste, myalgia, pain abdomen, diarrhea. Lately, gastrointestinal symptoms with acute abdomen was observed in few patients and diagnosis of gastrointestinal perforation were made.

As more and more studies poured in regarding nature of Severe acute respiratory syndrome coronavirus -2 (SARS-CoV 2), theories were postulated regarding pathogenesis of perforation. Presence of ACE 2 receptors in stomach, duodenum and rectum, thromboembolic phenomenon leading to ischemia of gut, neuroinvasive propensity of virus causing dilatation of gut, increase intraluminal pressure due to constipation and finally rare side effect of Tecilizumab used for COVID-19 cases treatment were considered as causes for gastrointestinal tract perforation.

We are presentling case report of three cases presenting as perforation during the course of COVID-19 disease along with review of literature regarding causes of such perforation.

Case – 1.

A 60 years old female was admitted with symptoms of dry cough, fever and myalgia and tested positive for COVID-19 RT-PCR. She was known case of hypothyroidism ( on 75 microgram thyroxine per day). She was treated with steroids and Rivaroxaban and sent for home isolation after 7 days. On 4th day of her discharge, she complained of pain abdomen and distension. Examination revealed distension with guarding and rigidity all over abdomen. Besides other investigation, COVID-19 RT-PCR was repeated which was positive. D-Dimer was 953 ng/ml, LDH- 735 U/L, PT was 30.6 with 2.56 INR. IL-6, Ferritin and other investigations were within normal limit. CT thorax was suggestive of multifocal areas of consolidation in bilateral peripheral lung fields – typical of COVID-19 with severity score of 17/25 (Fig 1). X-Ray chest showed bilateral consolidation with gas under diaphragm (Fig. 2).

Exploratory laparotomy revealed faeco-purulent collection of 2 litres with dense adhesion and 1 cm size perforation over the anterior wall of upper one-third of rectum. Surrounding rectal wall was odematous. Repair of perforation with decompressing transverse loop colostomy was done. Patient was treated in ICU with antibiotics, fluconazole, low molecular weight heparin. Repeated RT-PCR for COVID-19 was negative on 6th post-operative day. She was discharged from hospital on 11th post-opeative day.

Case – 2.

A 24 year female was admitted in Department of Obstetric with full term pregnancy and labour pains. She was subjected to emergency Lower segment caesarean section. On fifth post-operative day she complained of severe pain abdomen, vomiting and distension of abdomen. Patient had tachycardia with abdominal distension and obliteration of liver dullness. Being immediate post-partum period, guarding and rigidity was not appreciated due to lax abdominal wall. CT chest revealed atypical viral pneumonitis (Fig.3). X-Ray was showing massive pneumoperitoneum (Fig. 4) and COVID-19 RT-PCR was positive. D-Dimer was 3000 ng/ml, IL6 – 127 AND LDH was 800 u/ML Patient was subjected to emergency exploratory laparotomy. There was 1.5 L of faeco-purulent fluid in peritoneal cavity with adhesion and a 1.5 cm size perforation on anterior wall of caecum and odema of caecal wall. Primary closure with decompressing loop ileostomy was done. Oxygenation supplementation ,higher generation antibiotics with low molecular weight heparin and steroid were given. Patient recovered and discharged with ileostomy.

Case – 3.

A 21 year old male patient presented in surgical emergency with history of pain, fever, cough, vomiting and distension of abdomen. Clinical examination revealed distended abdomen with guarding and rigidity along with pyrexia. No previous history of drug intake or acid peptic disease was present. X-Ray flat plate abdomen revealed gas under diaphragm. COVID-19 RT-PCR was positive. Other routine investigations were normal except INR of 2.14. D-Dimer, IL 6 and LDH were marginally raised. Emergency exploratory laparotomy was done and there was inflamed thick omentum with 2 L of bile stained purulent fluid. 0.5 cm size perforation was seen on anterior wall of the stomach at pre-pyloric region. Closure of perforation with Graham’s patch and LMWH, antibiotics, corticosteroids and oxygen supplementation were administered. Patient was discharged on 11th post-operative day.

Discussion:

Severe acute respiratory syndrome coronavirus -2 (SARS-CoV 2) cause novel coronavirus disease. Although it started in Wuhan, China in 2019, now it had spread to all other parts of world becoming a pandemic. India is second most affected country across the world (nearly one billion cases) with a mortality of about 1.5 %. Since it primarily affect respiratory system, symptoms such a fever, dry cough, dyspnea, and respiratory illness represent the most common manifestation [1].

Since the virus and illness is relatively new, symptomatology is not very well understood and as the number of cases are increasing, various new symptoms like loss of smell and taste etc. have also been reported. Approximately 5 to 50% of the cases have gastrointestinal symptoms [2] like pain abdomen, diarrhea, and vomiting [3]. Detection of COVID-19 virus in stool [4] and a potential faecaloral transmission route has been suggested [5].

Various mechanism by which gastrointestinal tract is affected in COVID-19 have been postulated. High expression of the angiotensin converting enzyme (ACE) 2 receptor in epithelium of stomach, duodenum and rectum [6] with SARS-CoV 2 binding to these receptor in order to gain entrance to host cell [7] is the key mechanism of involvement of gastrointestinal tract.

Studies have stated that critically ill patients with COVID-19 are more likely to have a hypercoagulable state, with the manifestation of intravascular coagulation due to local damage [8,9]. This may lead to ischemia of the entire gut with colonic perforation as a part of septic and thromboembolic phenomenon caused by viral infection directly and indirectly.

SARS-CoV 2 RNA was mainly detected in cytoplasm of gastrointestinal epithelial cells indicating infection and replication of virus in these cells leading to local damage [10].

Since the neuroinvasive propensity has been demonstrated as a common feature of coronavirus, a neuronal injury should be regarded as a possible pathogenetic mechanism [11]. This causes imbalance of the autonomic innervation of the colon, altered colonic motility and dilatation of colon.

Critically ill ICU patients due to COVID-19 are mostly kept nil orally and can also have stress related mucosal damage with ulceration. These patients become significantly constipated contributing to increased intraluminal pressure [12]. Colonic dilatation and increase intraluminal pressure can precipitate perforation of gastrointestinal tract particularly stomach, duodenum and colon. Study have demonstrated the detectable presence or coronavirus RNA in stools of infected patients [10,13]. Perforation in COVID-19 patients have been reported in various studies [2,14]. Combination of factors like mucosal damage, ulceration, overdistension of bowel and increased intraluminal pressure contribute to perforation of bowel.

Tecilizumab , a monoclonal IL-6 receptor antibody, is used in rheumatoid arthritis and its use was identified as a risk factor associated with lower intestinal perforation, which had been reported as rare but serious complication in clinical trial of this drug [15]. The mechanism of intestinal perforation in patients receiving Tecilizumab is not fully understood, but prior diverticulitis has been noted as a risk factor [15]. Since there is no elevation of C-Reactive protein in these patients there is some delay in diagnosis of perforation. Tecilizumab is also used in treatment of cytokine release syndrome associated with severe COVID-19 [16]. Other author have also warned about the possibility of risk of intestinal perforation while using Tecilizumab in COVID-19 patients[17]. However, in the cases reported in this study, Tecilizumab was not used in any patient for COVID-19 treatment.

Diagnosis of gastrointestinal perforation can easily be made by history of pain, distension of abdomen, guarding and rigidity and radiographic evidence of pneumoperitoneum. In a clinically stable patient, CT abdomen is more sensitive investigation along with CT chest to predict outcome post-surgery. Early operative intervention carries better prognosis. Delay in diagnosis of gastrointestinal perforation is associated with poor prognosis due to compromised respiratory status, septicemia, oedema of gut precluding optimum closure of gut and high incidence of thromboembolic phenomenon. However, in cases diagnosed later with poor general condition, drainage of peritoneal cavity at the bedside with non-operative conservative management can be attempted although with guarded prognosis.

Declarations :

Authors’ Contribution:

Deepak Verma – Participate in surgical treatment and writing the article

Sarthak Sharma – Carry out treatment and Record keeping and data acquisition.

Lalit Kishore Garg – Checked the article and supervised the patient’s care

Aishwarya Tinaikar – Follow the patient in outcome point.

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Conflicts of Interests:

The authors declared that there is no conflicts of interest to disclose.

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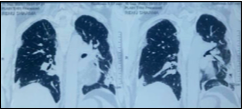
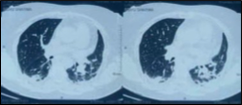
 

Figure 1. Chest CT scan of case 1 showing patchy consolidation of COVID-19 (Score 17/25)



Figure 2. X-Ray Flat plate abdomen in erect posture showing gas under diaphragm (Case 1.)



Figure 3. CT scan chest showing atypical viral pneumonitis (COVID-19) of case 2



Figure 4. Presence of gas under diaphragm case 2.

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