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Mesenteric Panniculitis among Clinically Proven Covid-19 Patients: A Case Series

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Abstract: COVID-19 initially considered a respiratory tract pathogen, but it can present with various clinical features with multiple organ dysfunctions, among which gastrointestinal manifestations such as nausea, diarrhea, vomiting, and mild abdominal pain have been reported. Omental panniculitis have been reported as rare presentations of COVID-19. Due to the increased advent of imaging studies among patients presented with acute abdominal pain, Omental/mesenteric panniculitis are not uncommon finding during the pandemic. This atypical presentation may lead to difficulties in establishing the diagnosis in a timely manner; furthermore, they may lead to unnecessary investigations and surgical intervention. We presented four cases with acute abdominal pain, necessitating surgical assessment and evaluation, from the western part of Odisha state of India during the 2nd wave(β-variant) of COVID-19 pandemic(September-October,2021),diagnosed as cases of clinically proven COVID-19 by clinical, biochemical markers, serological and imaging studies and all cases managed conservatively and did not require surgical management.

Keywords: Acute abdomen, Omental panniculitis, Mesenteric Panniculitis, COVID-19, SARS-CoV-2.

INTRODUCTION:

SARS-CoV-2(COVID-19) has caused global health crisis. Initially considered a respiratory tract pathogen, it can cause multiple organ involvement and a wide variety of complications during infection. Venous and arterial thromboembolism has been described; however, there is limited published data available regarding mesenteric thrombosis by COVID-19. Arterial thrombosis reported so far include stroke, acute limb ischemia, acute coronary syndrome and Acute Mesenteric Ischemia (AMI). AMI can occur as a presenting feature or a late complication of COVID-19 and presenting symptoms were nausea, vomiting, abdominal pain, diarrhea, fever, cough, shortness of breath, eructation, pain in throat. AMI is a rare abdominal emergency and is associated with high rates of morbidity and mortality. The diagnosis of AMI was made by contrast enhanced computed tomography (CT) imaging. Prompt diagnosis requires a high index of suspicion and early CT imaging. The exact pathological mechanism leading to the complication of AMI in COVID-19 is not well understood at present.[1]

The mesentery is a fold of tissue within the peritoneum is a continuous organ that extends from the duodenojejunal flexure to the mesorectum that supports and attaches the small and large intestine to the walls of the abdomen.The mesentery contains fat, blood vessels, lymphatic tissue, lymphatic vessels and other forms of connective tissue. Mesenteric panniculitis (MP)/Omental panniculitis is characterized by acute inflammation, degeneration and necrosis of the fatty tissue and due to chronic inflammation leads to scarring and fibrosis of fatty tissue within the mesentery. The portion of the mesentery that is adjacent to the small intestine is most often affected in MP. MP has been associated with a variety of other conditions, including infection, neoplasms, autoimmunity, vasculitis, and abdominal trauma. Clinical symptoms of mesenteric panniculitis are highly variable. Some individuals have few or no noticeable symptoms; others may be greatly affected by a variety of complaints including abdominal pain, nausea/vomiting, bloating, early satiety, loss of appetite and diarrhea or constipation. The most common symptom of mesenteric panniculitis is abdominal pain. The pain is generally located in the middle portion of the abdomen but can be present in other areas of the abdomen or pelvis as well. In some patients a tender mass may be detected in the middle portion of the abdomen. Abdominal pain, are due to the mass-like effect of mesenteric inflammation, and potentially involvement of adjacent structures including the small intestine. Some affected individuals may develop complications such as small bowel obstruction or acute abdomen. Systemic symptoms, especially fatigue, commonly occur in patients with mesenteric panniculitis. The second group of symptoms that can occur in the presence of chronic inflammation and may include weight loss, fever and fatigue. Abdominal distension from chylous ascites has also been described. Theories have been proposed to explain this disorder, including post inflammatory reactions to acute inflammation or infection, or ischemia to the mesentery. Due to its variable clinical presentation and rarity, the diagnosis of mesenteric panniculitis is often delayed. Affected individuals may have non-specific laboratory abnormalities such as anemia, raised inflammation markers such as ESR,C-reactive protein(CRP),ferritin and LDH.Imaging studies such as Ultrasonography, CT scanning or MRI reveals characteristic findings in the abdominal or pelvic mesentery. These imaging reveals characteristic thickening and necrosis of mesenteric fat and sometimes with lymph node enlargement. Mild cases are referred to a “misty mesentery” sign. Because MP is not an invasive disorder, blood vessels within the mesentery appear to be spared from the inflammatory mass. This is referred to as the “halo sign” is highly characteristic of mesenteric panniculitis. There are five diagnostic signs that have been felt to be specific for mesenteric

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panniculitis include the presence of a well-defined "mass effect" on neighboring structures (sign 1) constituted by mesenteric fat tissue of inhomogeneous higher attenuation than adjacent retroperitoneal or mesocolonic fat (sign 2) and containing small soft tissue nodes (sign 3). It may typically be surrounded by a hypo-attenuated fatty tissue "halo sign" (sign 4) and a hyper-attenuating pseudo-capsule may also surround the entity (sign 5).[2]

Pathophysiologically MP belongs to a continuum of disorders of the mesentery and peritoneum referred to as "sclerosing mesenteritis". Sclerosing mesenteritis is characterized by inflammation and variable amounts of fibrosis and fat necrosis of the mesentery.Pathologically, Sclerosing mesenteritis can be evolve in three stages. The first stage is mesenteric lipodystrophy in which a layer of foamy macrophages replaces the mesenteric fat. The second stage is an infiltrate of plasma cells, polymorphonuclear leukocytes, and foamy macrophages. The final stage is retractile mesenteritis, which is characterized by collagen deposition, fat necrosis, and fibrosis that leads to tissue retraction. MP can be diagnosed on CT imaging after exclusion of many other possible causes of a misty mesentery including disorders that result in mesenteric edema, lymphedema, hemorrhage, and infiltration with inflammatory or neoplastic cells. CT imaging findings of Mesenteric Panniculitis: - are mass like area of heterogeneously increased fat attenuation that may displace local bowel loops, but typically does not displace the surrounding mesenteric vascular structures. Ultrasound may show a well-defined hyperechoic mass with small central hypoechoic areas or a heterogeneous but predominantly hyperechoic mass. On MRI, a mesenteric mass is seen with intermediate signal intensity on T1- weighted images and with slightly higher signal intensity on T2-weighted images.[3]

STRATEGIES OF DIAGNOSIS OF COVID-19-INDUCED OMENTAL PANNICULITIS:

During the second wave of COVID-19 pandemic, patients presented with gastrointestinal manifestations mimicking acute abdomen having RAT and RT-PCR test negative reports, were diagnosed to be cases of COVID-19-induced omental panniculitis, with CT/MRI/Ultrasonography study of abdomen findings suggesting of Omental panniculitis, if they met ≥ one of the following diagnostic criteria, such as elevated inflammatory markers i.e. serum LDH, CRP, Ferritin, elevated D-dimer levels and decreased lymphocyte, eosinophils and platelet counts, adopted for clinical diagnosis of COVID-19 infection [4] along with supportive X-ray chest/HRCT findings . Furthermore, COVID-19 specific serologic antibodies tests for Total Antibody (TAb), IgM, and IgG were done at appropriate follow up time to confirm the recent COVID-19 exposure. Morbidity and mortality outcome were noted during the follow up.

Case presentations from the VIMSAR,Burla, western part of Odisha state of India during September - October, 2021, in the 2nd wave (β-variant) of COVID-19 pandemic.

Case No.1.

A 70 years old female presented with history of diffuse abdominal pain mostly central, with loss of appetite, fever, general weakness, mild dry cough since 15 days. On examination her BP was 120/80mmHg, PR-84/min, Temperature-100^{0}F. On investigations,TLC-5700/cmm, N-82%, L-15%, E-2%, B-0%, ESR-115mm, CRP-99mg/ml, serum Ferritin-96ng/ml,LDH-414U/L,FBS-93mg%, Urea-18mg%, creatinine-0.71mg%, Na^+-139mEq/L, serum K^+-3.9mEq/L, ,Hb-10gm%. Chest x-ray PA view showed Rt. lower lobe groundglass opacities. USG study of abdomen showed thickened heterogeneous omentum (16-20mm), with probe tenderness and mild amount of anechoic collection in the peritoneal cavity. COVID-19 specific antibody tested Total antibody (TAb) positive with 32.2 OD ratio and IgG positive > 20 OD ratio (>1 positive) suggested recent exposure. She was symptomatically treated with oral Cefuroxime 500mg BD, Famotidine 40mg TID, and Indomethacin slow release formulation 75 mg OD and Drotaverine 80 mg TID for pain abdomen. Bromehexine (8mg/ml) 2 tsf thrice daily for cough. Her fever and cough subsided on fifth day and pain abdomen lessened to some extent and on 13th days follow-up investigations,TLC-5,400/µL,N-88%,L-9%,M-1%,ESR-100mm,CRP-91.39mg/L,LDH-625U/L, serum Ferritin-142ng/ml,Hb-10.2gm%.Chest x-ray showed right lower lobe consolidation. USG study showed gross ascites with thickened omentum and right side moderate pleural effusion with right lower lobe consolidation. She was put on injection Artesunate 240mg IV bolus BD X5 days, injection Ceftazidime 1gm IV TID, Ornidazole 500 mg orally twice daily, Deflazacort 6 mg TID x 5 days, Indomethacin SR 75mg OD orally. On 24th day her serum LDH-507U/L, Ferritine-143ng/ml,ESR-85mm,CRP-23.92mg/L. Repeat USG study showed moderate ascites, omentum thickened and in the right thorax moderate pleural effusion with lower lobe collapse consolidation and mild effusion in left thorax. Patient feeling better with slight loss of appetite and recovered gradually fully over one month.

Case No. 2.

A 32 years old male after received 1st dose of Covasheild vaccine one week back, presented with fever, cough, diffuse pain abdomen and loss of appetite, with occasional vomiting since 14 days. On investigations serum LDH was >1240U/L, Ferritin 1000g/ml,CRP-232mg/ml,ESR-150mm.USG study showed hepatitis and thickened peritoneum with moderate ascites. Upper GI endoscopy showed oesophagitis and antral gastritis. Chest x-ray showed groundglass opacities in right lower lobes more than left side. COVID-19 specific Total antibody (TAb) was positive with 16.5 OD ratio (> 1 positive) and IgG was positive with 10 OD ratio (>1 positive), suggested recent exposure to COVID-19 infection. The patient refused hospitalization and lost for follow up.

Case 3.

A 55 years old male presented with epigastria and diffuse lower abdominal pain, loss of appetite, general weakness since 8 days. O/E his BP was 130/80mmHg, PR-88/min, RR-20/min, and SpO2 98 %, afebrile. On investigations, TLC-11800/µL, N-84%, L-13%, E-2%, M-1%, ESR-80mm, CRP-274.01mg/L, LDH-938U/L, Hb-12.0gm/dl, HbA1c-8.40%, FBS-138mg/dl, Urea-38mg/dl, Creatinine-1.21mg/dl, Na^+-131mEq/L, K^+-3.1mEq/L, serum Lipase-20U/L, Amylase-40U/L. Chest x-ray showed patchy opacities in the right lower zone. Ultrasonography of abdomen revealed decreased peristaltic with mild dilatation (2.5-2.9cm) fluid filled bowel loops with thickened echogenic mesentery noted extending to pelvic cavity with minimal echogenic fluid collection. Upper GI endoscopy showed esophagitis

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and antral gastritis. He was diagnosed to be a case of type 2DM with clinical COVID-19 presented with severe omental panniculitis, oesophagitis with antral gastritis. He was treated symptomatically with oral Famotidine (40mg) tid , Sucralfate 1 tsf 6 hourly, oral potassium solution, Cefuroxime (250mg) twice daily, Indomethacin-SR(75mg) daily. Teneligliptin 20mg,Pioglitazone 15mg OD, Drotavarine 80mg tid, Deflazacort 6mg tid x 5 days. He was slightly better than before after 6 days and he had no epigastric pain, but had persisting lower abdominal pain with loss of appetite and general weakness. On investigations on 6th day, FBS was 238mg/dl, LDH-365U/L,CRP-238mg/L,ESR-107mm,Hb-11.2gm/dl,TLC-12000/µL,N-86%,E-2%,L-11%,M-1%, B-0%. After 6 days his epigastric pain subsided, but his lower abdominal pain remained almost same but to a lesser extent than before, for which he was admitted to hospital on 12th day and treated with empirical IV antibiotics, PPI and IV bolus Artesunate(240mg) for 3 days and his pain abdomen subsided after 2 days. On 13th day routine investigations, TLC-12.87X10^3/µL,N-70%,L-15.1%,M-12.8%,E-1.5%,RBS-157mg/dl,Urea-50.6mg/dl,Creatinine-1.2mg/dl, serum protein-5.56gm/dl, Albumin-2.22gm/dl. Total cholesterol was 101.5mg/dl,HDL-16.3mg/dl,LDL-48.8mg/dl,VLDL-27mg/dl,TG-134mg/dl,ESR-70mm,TPC-23.6X103/µL,Hb-7.5gm/dl,FBS-120mg/dl,CRP-200MG/l,Ferritin-243ng/ml,D-dimer-0.5mg/L,LDH-487U/L.Total bilirubin-0.51mg/dl, direct-0.22mg/dl, AST-18.7U/L, ALP-104U/L. Repeat USG study of abdomen showed RIF mesenteritis with adherent bowel loops, mild hepatomegally with fatty changes and left non-obstructive nephrolithiasis. Patient discharged on 14th day.

Case. 4.

A 24 years old male presented to OPD with chief complains of epigastric pain and diffuse tender severe central abdominal pain for 1 month, aggravated by food intake, associated with occasional vomiting. He was a chronic alcoholic. On investigations,TLC-6700/µL,N-71%, E-4%,L-24%,M-1%,B-0%,CRP-1.01mg/L,LDH-511 U/L, serum Amylase-41 U/L, Lipase-36 U/L,Hb-11.8gm/dl,ESR-80mm. On USG study there was focal thickening of greater omentum which was probe tender. Upper GI endoscopy showed grade-4 GERD with hiatus hernia, erosive distal gastritis and duodenitis. Chest X-ray showed patchy opacities in the right lower lobe. He was treated with oral PPI and Sucralfate and antiemetic. On 2nd visit after 1 month, he reported that epigastric pain subsided within five days of symptomatic treatment and central abdominal pain subsided after 15 days and his serum LDH was 473 U/L, ESR-25mm.

DISCUSSION:

SARS-CoV-2 infection can present with various clinical features, among which gastrointestinal manifestations such as nausea, diarrhea, vomiting, and mild abdominal pain have been reported. Recognition of rare presentations of SARS-CoV-2 infection has increased over time. Severe abdominal pain can be the presenting feature of COVID-19. Abdominal CT scan with mid to lower cuts of the chest is of additional value as it can also detect the involvement of lower lobes of lung by COVID-19. Omental panniculitis can present with an acute abdomen necessitating surgical assessment and on evaluation, later they turn out to be SARS-CoV-2 positive and do not require surgical management. The cause of abdominal pain may be due to nonocclusive mild undiagnosed mesenteric ischemia caused by microthrombus formation, hinted by severe abdominal pain and disproportionately mild abdominal tenderness or due to appendagitis. Ashraf et.al reported three cases of MP admitted to hospital with a picture that mimicked an acute abdomen, necessitating surgical assessment and on evaluation all cases turned out to be SARS-CoV-2 positive and did not require surgical management.[5]

Gastrointestinal (GI) symptoms are highly prevalent in COVID-19 ranging from 17.6% to 53%. The proposed mechanism for GI symptoms involves SARS-CoV-2 virus binding to the host cell's ACE2 receptor, commonly found in gastrointestinal tract epithelial cells. Most initial presentations were GI bleeding; gastroenteritis and pancreatitis associated with COVID-19 infection which resolve by 3 months follow up. Malnutrition is the most persistent GI sequelae without resolution at 3-6 months follow. GI symptoms of malnutrition, weight loss, and anorexia may persist for several months after COVID-19 infection and may require further medical attention, while GI bleeding, gastroenteritis, and pancreatitis are likely to resolve after initial presentation. Upper endoscopy were gastric and duodenal ulcers, gastritis, duodenitis and by Lower endoscopy Angioectasias, Rectosigmoid ulcers, Diverticulitis, Hemorrhoids were found.[6]

Chiara et al noticed the occurrence of the misty mesentery sign in the upper abdomen of COVID-19 patients who underwent chest computed tomography. Fifteen (13.3%) out of the 113 patients matching the inclusion criteria showed an area of high density within the mesenteric fat associated with enlarged lymph nodes. Patients with misty mesentery showed significantly higher CRP values (117.5±95 vs 56±65mg/L, and assume that misty mesentery sign was associated with the hyperinflammation due to COVID-19.[7]

Human adipose tissue from multiple depots is permissive to SARS-CoV-2 infection and that infection elicits an inflammatory response, including the secretion of known inflammatory mediators of severe COVID-19.Two cellular targets identify for SARS-CoV-2 infection in adipose tissue: mature adipocytes and adipose tissue macrophages. Adipose tissue macrophage infection is largely restricted to a highly inflammatory subpopulation of macrophages, present at baseline that is further activated in response to SARS-CoV-2 infection. Preadipocytes, while not infected, adopt a proinflammatory phenotype. It was demonstrate that SARS-CoV-2 RNA is detectable in adipocytes in COVID-19 autopsy cases and is associated with an inflammatory infiltrate. These findings indicate that adipose tissue supports SARS-CoV-2 infection and pathogenic inflammation and may explain the link between obesity and severe COVID-19.[8]

Clinical presentation, radiologic findings, and disease course in COVID-19 cases are affected by severity of the cytokine-mediated inflammation. Circulating cytokines can impact multiple other organ systems, causing secondary diseases and complications. ACE2 receptors are also found in the brain, heart, arterial and venous endothelial cells, kidneys, liver, gastrointestinal tract, and gallbladder. This offers the potential for SARS-Cov-2 to impact multiple organ systems, leading to atypical COVID- 19 clinical presentations and the need for a wider range of radiologic imaging. Highlighting that COVID-19 should be approached as a multisystem disease secondary to its affinity for ACE2 receptors across multiple organ systems,

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cytokine-mediated inflammation, and patient co-morbid disease(s). ACE2 receptors are found throughout the gastrointestinal tract, with greatest functional role in the small bowel and colon.[9]

CONCLUSIONS:

Clinicians should be aware of gastrointestinal presentation symptom of acute abdominal pain which may be due to mesenteric panniculitis and should have a low threshold to diagnose amid the current pandemic. Mesenteric/Omental panniculitis is now not uncommon clinical presentations, leading to improper investigations and management that may be invasive. Omental panniculitis can be diagnosed by thorough clinical evaluation, raised inflammatory biochemical markers, and imaging study of chest and abdomen for findings suggestive of mesenteric panniculitis among patients presented with acute abdominal in the current ongoing COVID-19 pandemic. They can be managed conservatively without surgical intervention.

Conflict of interest**:**-Nil

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