Mucormycosis of Colon: Report of Two Cases in COVID-19

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Abstract:- Mucormycosis is a rare infection in Gastroenterology practise and usually affects patients with organ transplant or immunosuppression. Faciomaxillary mucormycosis was significantly observed in the COVID-19 pandemic, but GI mucormycosis was rarely noticed. We present two cases of colonic mucormycosis who had manifestation of colonic bleed and perforation.

Keywords:- GI bleed, Perforation, Steroids, Diabetes, Black fungus, Colitis.

I. INTRODUCTION

Mucormycosis is a rare and devastating fungal infection of humans. It is an ubiquitous fungus that belongs to class zygomycetes and order Mucorales(1). Mucomycosis usually occurs in patients who are being treated with immunosuppresants or having underlying conditions like solid organ transplant, hematological malignancy, diabetes mellitus or immunocompetent individuals with major trauma or burns. The second wave of COVID 19 infection seems to have predisposed individuals for this fatal infection and large numbers have been reported from various parts of India. Nearly 11,000 cases have been reported throughout the country and the predominant presentation has been rhino-orbito-cerebral and to a lesser extent pulmonary. Gastrointestinal (GI) mucormycosis has not been frequently reported in this COVID pandemic.

In December 2019, first case of severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) infection was identified in Wuhan, China (2,3). This disease (COVID-19) has spread throughout the world in a short span and presented as first wave in India - March 2020 & second wave from March 2021. SARS-COV-2 is transmitted through respiratory droplets, aerosol & close contact (4,5). Faeco-oral spread has also been suggested (6). The treatment of COVID-19 is symptomatic, with antivirals, steroids, anticoagulants & oxygen. Patients with COVID 19 may be predisposed to opportunistic infections like mucormycosis in view of associated comorbid conditions, diabetes, steroids and lymphocytopenia. We report two cases of mucormycosis affecting colon in COVID-19 patients who had a fatal outcome.

II. CASE REPORT 1

A 54 year old man with COVID-19 was referred for lower GI bleed. Earlier he was admitted at another hospital for hypoxia. He was treated with Remdesivir, antibiotics, steroids, convalescent plasma and oxygen. There was gradual improvement over a period of 15 days. Later he developed large volume bleeding per rectum with hypotension and breathlessness. He was resuscitated with fluids, blood transfusion and referred to our center. Colonoscopy revealed circumferential ulceration and necrosis with blackish pigmentation in caecum (Figure 1). KOH stain revealed broad, aseptate ribbon like hyaline hyphae with wide angle branching at irregular intervals suggestive of mucormycosis (Figure 2). Liposomal Amphotectin B was adminstered intravenously and semi emergent surgery was performed: Ileocaecal & proximal ascending colon was resected along with the ulcerated area. Biopsy confirmed mycormycosis. Post operatively patient required high F1O2, worsening of hypotension and ultimately succumbed to disease.



Fig 1 Colonoscopy Showing Circumferential Ulceration and Necrosis with Blackish Pigmentation in the Caecum

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> Operative Specimen & Microscopic Images



Fig 2 Gross hemicolectomy specimen shows ulcerated brownish black colored lesion at ileocecal region(Image A). Microscopic examination: hematoxylin and eosin stained slides show infarctoid necrosis of bowel wall(Image B and C) along with vascular invasion by fungus. (Image D). On high power examination fungus was characterized by broad aseptate thick walled hyphe as highlighted on GMS stain for fungus. (Image E).

III. CASE REPORT 2

A 58 year old male with diabetes, hypertension & chronic smoking with COVID-19 LRTI and treated elsewhere with ventilatory support, tracheostomy and subsequently ECMO support for 38 days, was referred to our center for lung transplantation. Workup revealed pancytopenia, CT chest showed COVID sequlae and CT abdomen revealed sigmoid colon perforation with faecal peritonitis. Emergency laparotomy, sigmoid resection and descending end colostomy was done. Patient developed MODS, thrombocytopenia, liver failure, AKI and coagulopathy. He was treated with broad spectrum antibiotics and Anidulafungin. Patient continued to deteriorate & succumbed to refractory hypotension. Histopathology of the resected specimen showed evidence of mucormycosis (Fig 3).



Fig 3 Infarctoid Necrosis with Vascular Invasion Adjacent to Perforated Ulcer

IV. DISCUSSION

The outbreak of COVID-19 spread rapidly and became pandemic. India experienced two waves of infection, first in 2020 and second in early 2021. During the second wave, several reports of mucormycosis, mainly involving the Rhino-orbital area were noticed. Gastrointestinal mucormycosis was rarely reported.(7).

The Stomach is the most common site of GI mucormycosis followed by colon, small intestine & esophagus. The symptoms of GI mycormycosis include fever, nausea, abdominal pain, GI bleed and perforation. High level of suspicion is needed to make early diagnosis. Endoscopy usually reveals large ulceration with necrosis and dark greenish black pigmentation. Diagnosis is confirmed by KOH stain from secretions or tissue, histopathology and/or PCR from tissue. Culture requires 2-3 weeks. Liposomal Amphotericin B is the drug of choice and needs to be given for 3 weeks at a dose of 5mg/kg/day(8). Sequential treatment may have to be continued with posaconazole. Apart from medical therapy aggressive surgical treatment needs to be considered. Despite combined treatment, prognosis is usually poor (9).

This report documents colonic mucormycosis in severe COVID patients with prolonged hospital stay and who experienced a variety of therapies. (like antivirals, steroids, plasma and ventilatory support). Mucormycosis in the first patient, manifested with lower GI bleed and in the second, with colonic perforation. Diagnostic and therapeutic procedures are likely to be delayed in view of critical nature of underlying disease and associated respiratory and multi organ support systems.

COVID-19 seems to be a predisposing factor for mucormycosis. COVID patients with severe disease usually have a high level of inflammatory cytokines like IL-2, IL-6, TNF and associated depletion of lymphocytes including CD4 and CD8. Underlying disorders like diabetes, cardiac disease, steroids cause an increased susceptibility to the opportunistic infection (10).

GI mucormycosis is a disease with poor outcome. Clinical suspicion has to be very high in subjects with severe COVID disease. Endoscopy and/or colonoscopy needs to be performed in subjects with GI bleed, abdominal pain or related symptoms without delay and tissue needs to be obtained for KOH stain, histopathology and PCR. Early treatment with amphotericin and surgery may be helpful in salvaging a few cases. Delay in diagnosis and treatment is usually fatal.

V. CONCLUSION

GI mucormycois is a rare disease and should be considered in patients with lower GI bleed. Prompt attention needs to be given for early diagnosis and appropriate treatment. More studies and information is needed to evaluate the reason for the predisposition of mucormycosis in COVID-19 patients.

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REFERENCES

- [1]. Adhikari S, Gautam AR, Paudyal B, Sigdel KR, Basnyat B. Case report: gastric mucormycosis- a rare but important differential diagnosis of upper gastrointestinal bleeding in an area of Helicobacter pylori endemicity. Wellcome Open Res 2019;4:5
- [2]. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382:1708-1720
- [3]. Rothan HA, Byrareddy SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. J Autoimmun 2020;109:1024 33
- [4]. Zhao Y, Zhong S-P, Li F, Liu G-Q, Wang X-F, Liu Z-J. Analysis of clinical characteristics and risk factors of gastrointestinal symptoms of COVID-19 patients in Xinyang, Henan province. *Chinese J Digest* 40: E011–E011, 2020. doi:10.3760/cma.j.issn.0254-1432. 2020.0011.
- [5]. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, Zhao X, Huang B, Shi W, Lu R, Niu P, Zhan F, Ma X, Wang D, Xu W, Wu G, Gao GF, Tan W, China Novel Coronavirus I, Research T; China Novel Coronavirus Investigating and Research Team. A novel coronavirus frompatients with pneumonia in China, 2019. *N Engl J Med* 382: 727–733, 2020. doi:10.1056/NEJMoa 2001017.
- [6]. Yeo C, Kaushal S, Yeo D. Enteric involvement of coronaviruses: is faecal-oral transmission of SARS-CoV-2 possible? *Lancet Gastroenterol Hepatol* 5: 335–337, 2020. doi:10.1016/S2468-1253 (20)30048-0.
- [7]. Epifanio Silvino do Monte Junior, Marcos Eduardo Lera dos Santos, Igor Braga Ribeiro, Gustavo de Oliveira Luz, Elisa Ryoka Baba, Bruno Salomão Hirsch, Mateus Pereira Funari and Eduardo Guimarães Hourneaux de Moura. Rare and Fatal Gastrointestinal Mucormycosis (Zygomycosis) in a COVID-19 Patient: A Case Report lin Endosc 2020;53:746-749 https://doi.org/10.5946/ce.2020.180
- [8]. Spellberg B, Walsh TJ, Kontoyiannis DP, Edwards J, Jr., Ibrahim AS. Recent advances in the management of mucormycosis: from bench to bedside. Clin Infect Dis 2009;48:1743-1751.
- [9]. Roden MM, Zaoutis TE, Buchanan WL, et al. Epidemiology and outcome of zygomycosis: a review of 929 reported cases. Clin Infect Dis 2005;41:634-653.
- [10]. Song G, Liang G, Liu W. Fungal co-infections associated with global COVID-19 pandemic: a clinical and diagnostic perspective from China. Mycopathologia 2020;185:599-606.