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Post Covid Gastrointestinal (GI) Mixed MYCOTIC Infection in a Patient with Severe Liver Fibrosis

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ABSTRACT:
In this case report, we describe a rare and uncommon Gastrointestinal (GI) Mucormycosis and mixed mycotic infection as a squeale of COVID-19, which should be considered in a post COVID-19 patient with history of diabetes and use of corticosteroids presenting with GI symptoms. A combined team investigated the patient, Colonoscopy guided biopsy and histopathological examination was followed by special staining and culture. A final diagnosis of GI mixed mycotic infection was made, and patient was treated accordingly. Hence, it is prudent to assess the risk factors, type of invasive mycosis, spectrum of coinfections, diagnostic modalities, and their limitations and above all a need for standardized as well as individualized treatment in COVID-19 patients for the upcoming complications.

Keywords:
COVID -19, MIXED MYCOTIC INFECTIONS, MUCORMYCOSIS GIT, POST COVID SYNDROME

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Key Messages:
Profound immunosuppression in COVID-19patients due to imbalance between pro and anti-inflammatory cytokines and an overexuberant viral replication causes immunologic collapse of the host protective/ defence system.
High index of suspicion should be exercised in all Post COVID-19cases, presenting with pain in abdomen and GI bleed to ensure a prompt treatment to cure this deadly disease. Hence, it is prudent to assess the risk factors, type of invasive mycosis, spectrum of coinfections, diagnostic modalities, and their limitations and above all a need for standardized as well as individualized treatment in these patients.Persistent post-COVID syndrome (PPCS) includes persistent immunosuppression as well as pulmonary, cardiac, and vascular fibrosis further leading to increased mortality and a worsened quality of life.

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I. Introduction

Pandemic of COVID-19after China reported the first case in December 2019. As of April 19, 2021, over 141 million cases of COVID-19were reported globally causing more than 3 million deaths.[1] A multitude of complications have emerged, many being reported and a lot many are still in discovery mode. Profound immunosuppression in COVID-19patients due to imbalance between pro and anti-inflammatory cytokines and an overexuberant viral replication causes immunologic collapse of the host protective/ defence system.

Mucormycosis and Mixed Mycotic Infections (MMI) are identified as an emerging complication in post covid patients, who are typically immunocompromised and have comorbidities like Diabetes Mellitus. It is rarely seen in healthy individuals.[2] Mortality rate due to GI Mucor mycosis can be very

high[3].Persistent post-COVID syndrome (PPCS) includes persistent immunosuppression as well as pulmonary, cardiac, and vascular fibrosis further leading to increased mortality and a worsened quality of life.

II. Case History

A 53-year Indian male with a history of diabetes (DM), hypertension (HTN) and covid-19 positive status for 20 days presented to emergency department with complaints of shortness of breath, pain in abdomen and blood in stools since past 3 days, for which he was treated with antibiotics,
low molecular weight heparin, insulin mixtrad and oral hypoglycemic agents (OHA), along withinjection Dexamethasone 6mg for 7 days.

On admission in our center, his SPO2 was 93% at room air, and patient appeared to be inmoderate distress. He was already under OHA and insulin for uncontrolledtype 2 DM and HTN. Initial evaluation was done by a combined team to assess hiscondition and an HRCT Chest showed a CT severity score of 14/25, consistent with changes ofcovid pneumonitis. The investigation showed Hb 13.5 gm/dl, Total leucocyte count 9.93 k/ul, Absolute neutrophil count: 9030/mm^3, Absolute lymphocyte count: 370/mm^3, Neutrophil Lymphocyte ratio (NLR): 24.59, Platelet: 65,000/ul, Erythrocyte sedimentation rate: 41 mm/hr., Serum Ferritin: 1060.5 ng/ml, D-dimer: 1483 FEU ng/ml, C- Reactive Protein: 53.5 mg/L, SGOT/SGPT: 178/586 U/L, Alkaline phosphate: 176U/L and Gamma glutamyl transferase: 297U/L, Glycated hemoglobin (HbA1C): 9.4%. Urine and blood culture showed no growth after 48 hours of incubation. Stool for occult blood was positive. Rest other parameters were within normal limit.

Radiological findings (Figure 1): Contrast CT scan of whole abdomen revealed chronic liver disease with hepatosplenomegaly with Portal hypertension. Concentric thickening of proximal ascending colon with mild fat stranding was noted with a possibility of Infective/ Inflammatory etiology. Ultrasound guided **liver elastography** revealed average liver stiffness of 23-49 KPa and maximum liver stiffness of 44.84 KPa, made an impression of severe liver fibrosis. **Colonoscopy (Figure 2)** showed a large ulcer with clot at transverse colon, guided biopsy was taken from the same site.

Histopathological examination (Figure 3) revealed mostly necrotic slough without any viable mucosal lining. Amidst this slough were seen numerous bacterial colonies along with yeast like forms and pseudo hyphae forms of candida admixed with aseptate bulbous mucor hyphae forms (Mucorales). **Special stain** study with PAS &Grocott highlighted the bacterial and fungal elements. An impression of Mixed mycotic etiology was made. **Culture** grew cottony to fluffy, white to yellow colonies on Sabouraud Dextrose Agar. Lactophenol cotton blue (LPCB) mounts show mucor sporangiophore bearing dematiaceous sporangia having sporangiospores. Finally, diagnosis of Post covid Intestinal Mixed mycotic infection with severe liver fibrosis with Type II diabetes mellitus with hypertension was made.

Treatment was done with IV Amphotericin B, Meropenem, Posaconazole, Clexane, Pirfenidone,physiotherapy and supportive treatment. Presently the patient has improved and is in the recovering mode with the antifungal treatment

III. DISCUSSION

In a study published by Song et al[9] in which they have investigated a total of 99 patients of fungalinfections after SARS Covid-19, in China, showed about 5% of these are due to Aspergillus and 7%Mucor species[4,5] They have concluded that impairment of T-cell immunity along with presenceof immunocompromised state is one of the most important pathogenesis.

Invasive fungal infections in post covid patients includes Mucormycosis, presenting clinically assinusitis involving frontal, ethmoid and maxillary sinuses. Cases of rhino -orbital, cerebralMucor mycosis are also not uncommon. Predisposing conditions like diabetes mellitus, high dose systemic corticosteroids, neutropenia, hematological malignancy and immunocompromised status shatters immune system, making post covid Mucormycosis a fatal condition if not treated immediately. Mortality rate due to GI Mucormycosis can be as high as 85%. [3]

In this pandemic, cases of intestinal Mucormycosis and mixed mycotic infections are also emerging as an uncommon new complication, as the common sites until now were rhino- orbital, cerebral and pulmonary attributed to low immunity or immunocompromised status. Clinical suspicion and early diagnosis with expert management are key to prevent morbidity and mortality. CT/MRI, Colonoscopy guided biopsy, Histopathological examination, Special staining, and Culture can be done on the tissue samples as diagnostic modalities, after the clinical picture shows high index of suspicion.

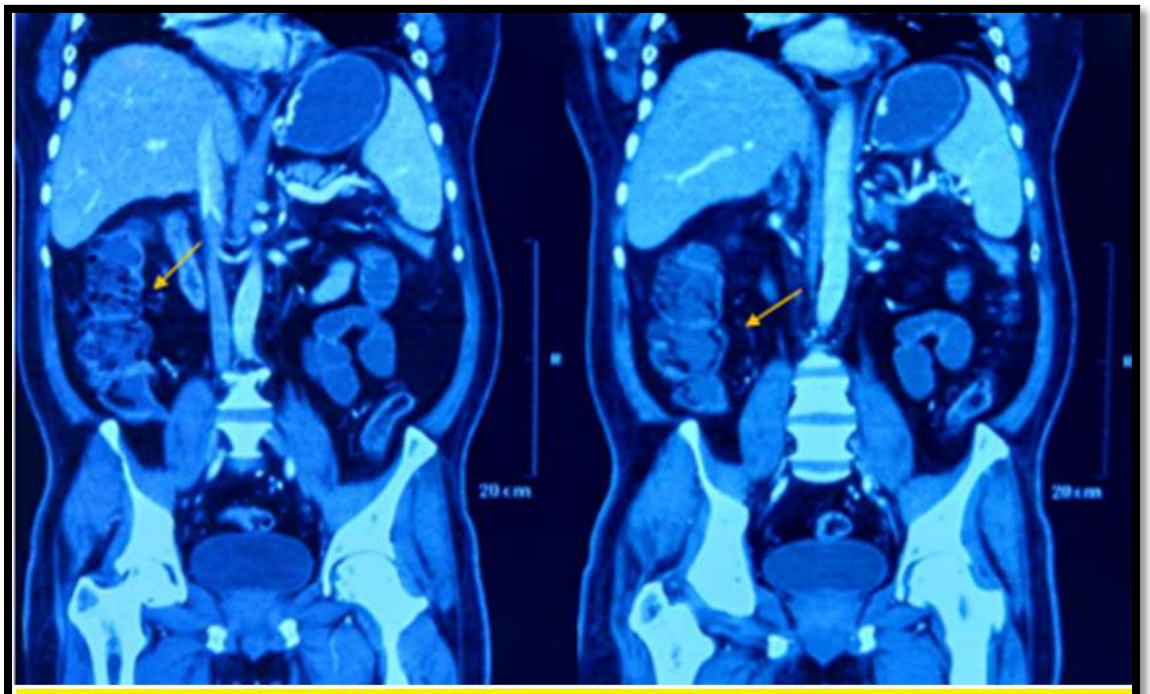

Figure 1: CECT Whole Abdomen: Concentric thickening of proximal ascending colon with mild surrounding fat stranding (arrow).

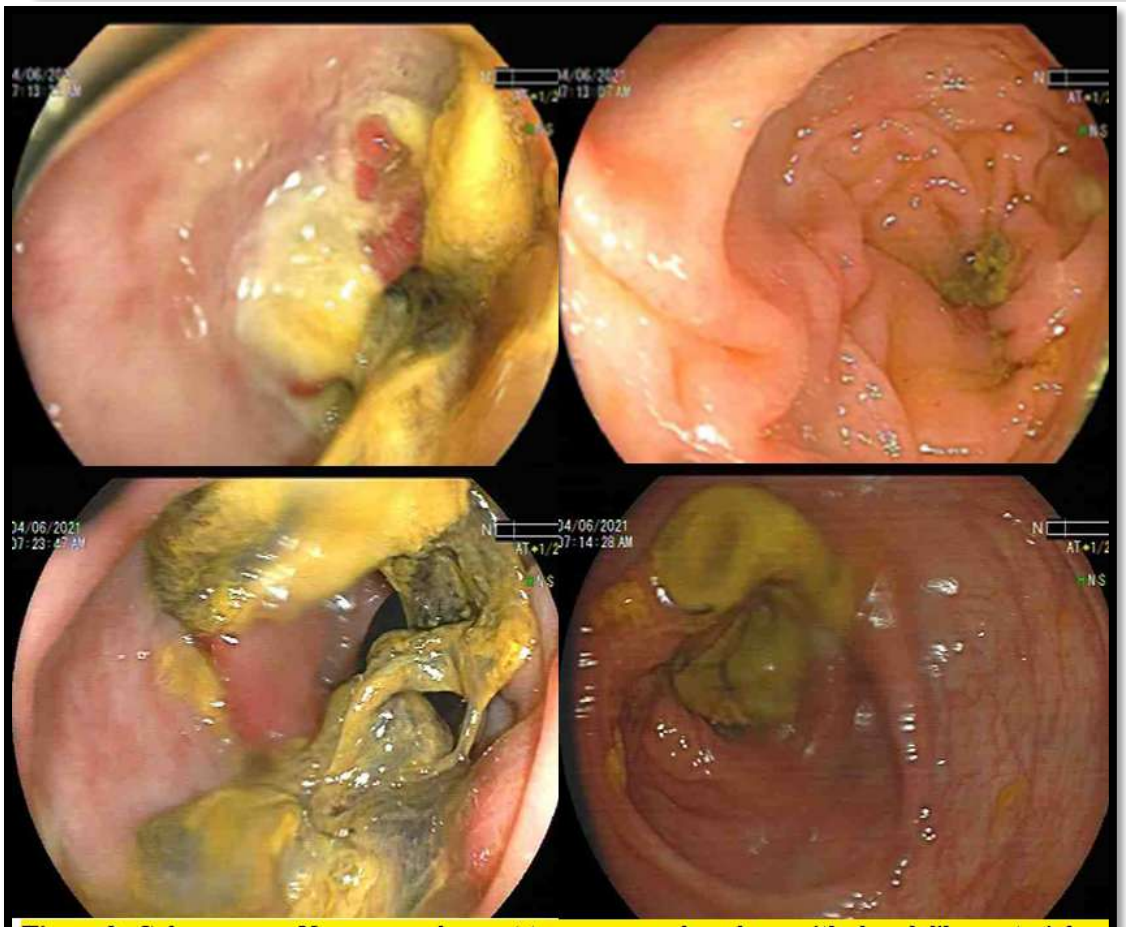

Figure 2: Colonoscopy: Numerous ulcers at transverse colon along with slough like material. Guided biopsy was taken from the same site.

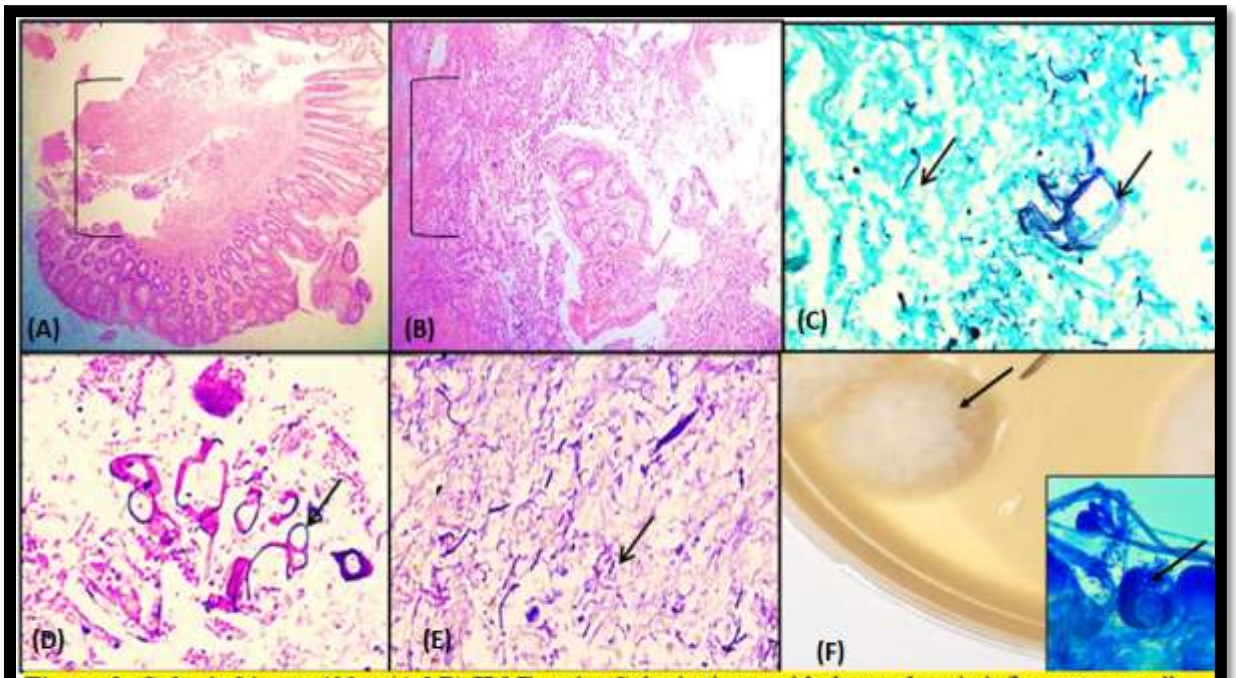

Figure 3: Colonic biopsy 400x: (A&B) H&E stain: Colonic tissue with dense chronic inflammatory cell infiltrate and slough like material in submucosa (bracketed). **(C) Grocott stain**: Broad aseptate hyphae of mucorcmycosis and pseudo hyphae of candida stained black (arrow). **(D&E) PAS Stain**: Mucormycosis hyphae and pseudo hyphae of candida. **(F) SDA Culture plate**: Cottony colonies of Mucor (Inset: Lactophenol cotton blue shows sporangiosis with sporangiospores).

The incidence rate of Mucormycosis varies from 0.005 to 1.7 per million population.[4] Theglobal Mucormycosis case fatality rate is 46%.[6] To our knowledge, very few cases have beenreported with post COVID-19GI Tract involvement by mixed mycotic infections in a patient with severe liver fibrosis. Despite earlydiagnosis and aggressive treatment with medical or surgical modalities, in animmuno-compromised patient, prognosis remains poor. Tissue necrosis is the hallmark of Mucormycosis. Additionally, corticosteroids used for treatment disables the macrophages in preventingthe germination of fungal spores and inadvertently propagating the infection.

Our patient was also diagnosed with severe liver fibrosis, but it was difficult for us to evaluate and corelate at this point if the severe liver fibrosis was an associated complication with Covid – 19 just like the fibrotic changes that happen in the lung or was it coincidently detected due to the ancillary investigations.The pathology of ADRS is due to three overlapping phases: exudative, proliferative, and fibrotic [25]. In fibroproliferative phase, fibrocytes, fibroblasts, and myofibroblasts accumulate in the alveolar compartment, leading matrix deposition components including fibronectin, collagen I, and collagen III [26]. The major player acting as profibrotic cytokine is TGF-ß (27).While it is perhaps too early to predict severe liver fibrosis in the present case as along-term consequence of COVID-19.

Multiple guidelines, recommendations and clinical practices had and has been adopted for the treatment of these patients and prevention. However, the main focus is still on the immediate, day-to-day "anti-COVID fight" ratherthan on a potential future. Not much guidelines can be seen available for postinfectious care or recovery. There is anotable dearth of information on and strategies about howto assess and manage post-COVID patients or persistent post-COVIDsyndrome (PPCS), a newly coined umbrella term, byanalogy to post-sepsis/post-ICU syndrome (24).Factors like pre covid clinical trajectories, pre-existing comorbidities, post covid illness,susceptibility to secondary infections as well as fibrotic remodeling inthe lungs, heart, and brain develop as the end result ofa chronic inflammatory process altogether should be kept in mind which may increase diagnostic and management difficulties.

REFERENCES

[1]. National Institutes of Health. Coronavirus disease 2019 (SARS COVID-19) treatmentguidelines. In: https://www.covid19treatmentguidelines.nih.gov/ [15 July 2020].
[2]. Sargin F, Akbulut M, Karaduman S, Sungurtekin H (2021) Severe RhinocerebralMucormycosis Case Developed After

SARS SARS COVID-19. J Bacteriol Parasitol. 12: 386.
[3]. Monte Junior ESD, Santos MELD, Ribeiro IB, et al. Rare and Fatal GastrointestinalMucormycosis (Zygomycosis) in a COVID-19Patient: A Case Report. Clin Endosc.2020;53(6):746-749. doi:10.5946/ce.2020.180.
[4]. Wang Y, Wang Y, Chen Y, Qin Q. Unique epidemiological and clinical features of theemerging 2019 novel coronavirus pneumonia (SARS SARS COVID-19) implicate special controlmeasures. Journal of Medical Virology. 2020;92(6):568-576. doi: 10.1002/jmv.25748.
[5]. G S, G L, W L. Fungal Co-infections Associated with Global COVID-19Pandemic: AClinical and Diagnostic Perspective from China. PubMed. 2021. [accessed 1 Jun 2021]Available from: https://pubmed.ncbi.nlm.nih.gov/32737747.
[6]. Werthman-Ehrenreich, A., 2021. Mucormycosis with orbital compartment syndrome in apatient with SARS COVID-19. The American Journal of Emergency Medicine, 42, pp.264.e5-264.e8.
[7]. Mishra N, Mutya VS, Thomas A, Rai G, Reddy B, Mohanan AA, Ray S, Thiruvengadem AV, Siddini V, Hegde R. A case series of invasive mucormycosis in patients with COVID-19infection. Int J Otorhinolaryngol Head Neck Surg. 2021 May;7(5):867-70.
[8]. Chowdhary A, Tarai B, Singh A, Sharma A. Multidrug-resistant Candida auris infections in critically Ill coronavirus disease patients, India, April–July 2020. Emerging infectious diseases. 2020 Nov;26(11):2694.
[9]. Song G, Liang G, Liu W. Fungal co-infections associated with global COVID-19pandemic: a clinical and diagnostic perspective from China. Mycopathologia. 2020 Aug;185(4):599-606.
[10]. Yang X, Yu Y, Xu J, Shu H, Liu H, Wu Y, Zhang L, Yu Z, Fang M, Yu T, Wang Y. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. The Lancet Respiratory Medicine. 2020 May 1;8(5):475-81.
[11]. Sharma S, Grover M, Bhargava S, Samdani S, Kataria T. Post coronavirus disease mucormycosis: a deadly addition to the pandemic spectrum. The Journal of Laryngology & Otology. 2021 May;135(5):442-7.
[12]. Ricard JA, Charles R, Tommee CG, Yohe S, Bell WR, Flanagan ME. Epstein virus Barr-positive diffuse large B-cell lymphoma associated with hemophagocytic lymphohistiocytosis. Journal of Neuropathology & Experimental Neurology. 2020 Aug 1;79(8):915-20.
[13]. Chakrabarti A, Denning DW, Ferguson BJ, Ponikau J, Buzina W, Kita H, Marple B, Panda N, Vlaminck S, Kauffmann-Lacroix C, Das A. Fungal rhinosinusitis: a categorization and definitional schema addressing current controversies. The Laryngoscope. 2009 Sep;119(9):1809-18.
[14]. University2015 S. Prevelance of allergic fungal rhino-sinusitis among patients presented with nasal polyps:(prospective study) (Doctoral dissertation, faculty of Medicine, Sohag University).
[15]. Chatterjee P, Nagi N, Agarwal A, Das B, Banerjee S, Sarkar S, Gupta N, Gangakhedkar RR. The 2019 novel coronavirus disease (SARS COVID-19) pandemic: A review of the current evidence. The Indian journal of medical research. 2020 Feb;151(2-3):147.
[16]. Chan KH, Abzug MJ, Coffinet L, Simoes EA, Cool C, Liu AH. Chronic rhinosinusitis in young children differs from adults: a histopathology study. The Journal of pediatrics. 2004 Feb 1;144(2):206-12.
[17]. Gitomer SA, Poore TS, Anand GS, Cañadas KT. Differing rates of fungi in sinonasal cultures from pediatric sinusitis patients. International Journal of Pediatric Otorhinolaryngology. 2022 May 1;156:111125.
[18]. Dokania V, Gaikwad NS, Gite V, Mhashal S, Shetty N, Shinde P, Balakrishnan A. Emergence of invasive fungal rhinosinusitis in recently recovered COVID-19patients. Annals of Otology, Rhinology & Laryngology. 2022 Nov;131(11):1202-9.
[19]. Shaban E, Saleh RA, Ammar MI, Ebeid K. Post-COVID-19acute invasive fungal rhinosinusitis: a systematic radiological approach in the light of clinico-surgical characteristics. Egyptian Journal of Radiology and Nuclear Medicine. 2022 Dec;53(1):1-1.
[20]. Hema VK, Kumar K, Shah VM, Fraser C, Mollan S. Invasive Fungal Sinusitis in Patients with Coronavirus Disease 2019 Seen in South India. Journal of Neuro-Ophthalmology. 2022 Jun 19;42(2):226-9.
[21]. Du Y, Tu L, Zhu P, Mu M, Wang R, Yang P, Wang X, Hu C, Ping R, Hu P, Li T. Clinical features of 85 fatal cases of COVID-19from Wuhan. A retrospective observational study. American journal of respiratory and critical care medicine. 2020 Jun 1;201(11):1372-9.
[22]. Remy KE, Brakenridge SC, Francois B, Daix T, Deutschman CS, Monneret G, Jeannet R, Laterre PF, Hotchkiss RS, Moldawer LL. Immunotherapies for SARS COVID-19: lessons learned from sepsis. Lancet Respir Med. 2020 Oct;8(10):946-949. doi: 10.1016/S2213-2600(20)30217-4. Epub 2020 Apr 28. PMID: 32444269; PMCID: PMC7195015.
[23]. Zheng M, Gao Y, Wang G, Song G, Liu S, Sun D, Xu Y, Tian Z. Functional exhaustion of antiviral lymphocytes in COVID-19patients. Cellular & molecular immunology. 2020 May;17(5):533-5.
[24]. Oronsky B, Larson C, Hammond TC, Oronsky A, Kesari S, Lybeck M, Reid TR. A review of persistent post-COVID syndrome (PPCS). Clinical reviews in allergy & immunology. 2021 Feb 20:1-9.
[25]. Walkey AJ, Summer R, Ho V, Alkana P (2012) Acute respiratory distress syndrome: epidemiology and management approaches.Clin Epidemiol 4:159–169
[26]. Burnham EL, Janssen WJ, Riches DW, Moss M, Downey GP(2014) The fibroproliferative sponse in acute respiratory distresssyndrome: mechanisms and clinical significance. Eur Respir J43(1):276–285
[27]. Wu Q, Zhou L, Sun X (2017) Altered lipid metabolism inrecovered SARS patients twelve years after infection. Sci Rep7:9110

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