CCI JOURNAL CRITICAL CARE INNOVATIONS

CASE REPORT

Crit. Care Innov. 2021; 4(4):45-52

Abdominal wall fungal co-infection mucormycosis associated with COVID-19: a case report.

ISSN 2545-2533

Received: 18.07.2021

Accepted: 30.10.2021

Published: 31.12.2021

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Conceptualization - **A**
Data Curation - **B**
Formal Analysis - **C**
Funding Acquisition - **D**
Investigation - **E**
Methodology - **F**
Project Administration - **G**
Resources - **H**
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Approved the final version - **O**

ABSTRACT

The Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has posed a public health system challenge across the globe. A retrospective analysis of COVID-19 globally surmises that the fungal co-infections associated with COVID-19 might be missed or misdiagnosed. However, data regarding all the signs and symptoms of COVID-19 are insufficient. The available few publications conclude that patients with COVID-19 have a higher susceptibility to fungal coinfections. Mucormycosis is a rare and often life-threatening fungal disease characterized by vascular invasion by hyphae, resulting in thrombosis and necrosis. Based on the available data it seems COVID-19 patients, especially severely ill or immunocompromised, have a higher susceptibility to invasive mycoses. Therefore, it is important to assess the risk factors, the types of invasive mycosis, the strengths and limitations of diagnostic methods, clinical settings, and the need for standard or individualized treatment in COVID-19 patients.

A 33 years old female operated case of laparoscopic ectopic removal with salpingectomy and tubectomy, at post-operative Day 5 had redness and pus discharge from the operative site and was diagnosed with abdominal wall cellulitis. She underwent local exploration and wound wash. At post operative day 5, the patient came to our emergency room with mild disorientation, cellulitis, and pain at the port insertion site. On examination, we highlight BP 90/50 mmg and blood test analysis with HB-8.3, leucocyte count 29.91×109/L, CRP 333mg/L. CT scan revealed necrotizing fasciitis. She then underwent wide local excision and debridement. Post debridement the next day during dressing, the wound showed a cotton fluffy appearance at the edges and part of the base with black necrotic areas. Wound swab was sent for fungal culture, KOH mount, blood culture, pus culture, and tissue for histopathology. In the meantime, she was started on empirical antifungal amphotericin B, meropenem and minocycline antibiotics. Covid antibodies test was done which were reactive: 1.96. Tissue histopathology revealed mucormycosis. A high degree of suspicion and promptness in starting antifungal prevented fatal outcome.

KEY WORDS: Case report, Covid-19, mucormycosis, pregnancy, Fungal Infection.

 doi: 10.32114/CCI.2021.4.4.45.52

INTRODUCTION

Critically ill patients are faced with complex medical and surgical problems: they receive prolonged broad-spectrum antibiotics, total parenteral nutrition due to gut failure, and are usually subjected to multiple invasive procedures, and usually have disrupted natural barriers. All these are associated with an increase in fungal infections in the intensive care unit. Mucormycosis is the third most common infection from the family of Zygomycetes. involving two classes Entomophtorales and Mucorales. The former rarely leads to life-threatening infections however Mucorales are known to cause morbidity and mortality if not treated early [1].

The clinical presentation of mucormycosis varies depending on the location of the disease [2]. It is a devastating disease most commonly seen in immunosuppressed individuals. It has the propensity to disseminate in humans and cause rhinocerebral, pulmonary, gastrointestinal, and cutaneous infections [3]. It is often seen that mucormycosis affects patients with acidosis and granulocytopenia. Mucormycosis is also seen to affect patients with poorly controlled diabetes mellitus type 1 and type 2, steroid users, stem cell transplantation, solid organ transplant recipients, patients with hematologic malignancy, renal failure and burns. Outbreaks of fungal disease have also been associated with natural disasters [4-6]. These patients lack the basic mechanism of cellular defense and hence develop invasive mycosis. However, almost 15 to 20% of patients develop mucormycosis despite the absence of underlying immunosuppression. Thus, we may also encounter cases among immunocompetent hosts [7].

Cutaneous mucormycosis can occur as an opportunistic infection and can also be seen in immunocompetent hosts. This can occur primarily as direct inoculation by contaminated sources or can be secondarily acquired as a result of widespread dissemination. Primary cutaneous mucormycosis can arise due to contaminated dressing, post-surgical wounds, wooden tongue depressors, areas with building construction, contaminated wounds as a result of motor vehicle accidents, direct inoculation in insulin injection site, etc. Rammaert and coworkers in 2012 reported almost 57% of cutaneous mucormycosis among 196 healthcare infections [8]. This infection can present from an indurated erythematous plaque which can progress quite quickly to a fulminant fast-spreading necrotic cellulitis. Among the cutaneous presentation of mucor the fulminant, fast-spreading, necrotic forms are known to be the predominating presentation in the ICU. These patients may present with extreme pain, tachycardia, high WBC count, high lactates, tachypnea, acidosis which then progresses to multisystem organ failure. This infection can prove fatal if intervention (most important being quick wide debridement with antifungals) is not done in the first few days.

We describe a case of an operated surgical site wound mucormycosis in an immunocompetent host post covid not on steroids. To the best of our knowledge, this is one of the few cases of invasive mucormycosis reported in a mild COVID-19 young patient not on steroids.

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CASE REPORT

PATIENT INFORMATION: A 33-years old female submitted to laparoscopic ectopic pregnancy removal in another hospital setting, after a negative RTPCR test done 72 hours before surgery. At post-operative day 5 patient had redness and pus discharge from the operative site and was diagnosed of abdominal wall cellulitis: She underwent local exploration and wound wash (Fig.1).

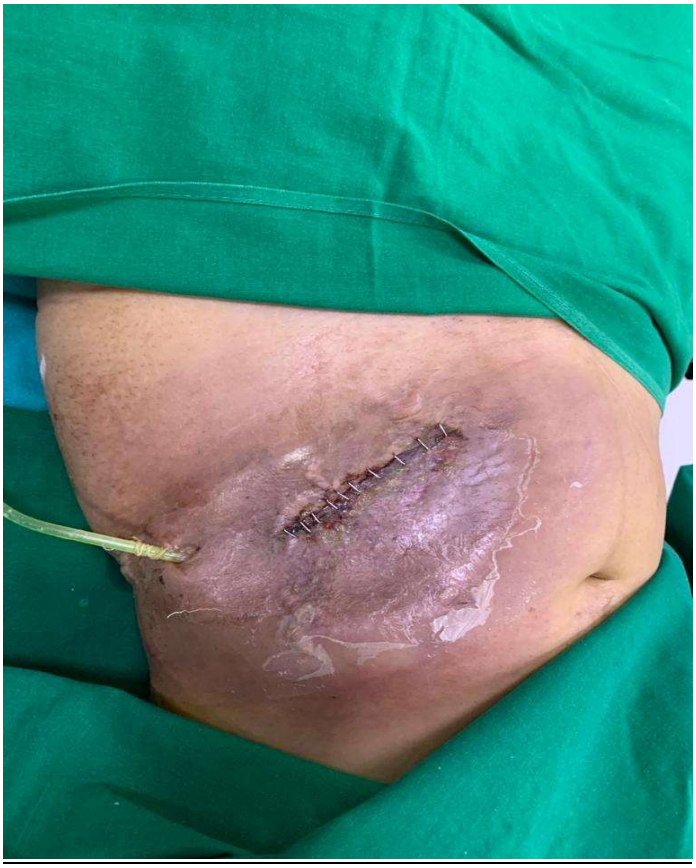

Figure 1. Wound picture at presentation to hospital. Post-laparoscopic ectopic pregnancy removal. Shows stappler at port insertion site with a abdominal drain.

CLINICAL FINDINGS: At post operative day 5, she came to our hospital's emergency room with mild disorientation and pain at the operated site. On examination, the patient was tachycardic, with BP: 90/60 mmHg, febrile, Glasgow Coma Scale: E4M6V4, SpO_2 98% on room air.

INITIAL DIAGNOSTIC TESTING: Blood investigations revealed hemoglobin level of 8.3 mg/dl, leucocyte count 29.91×109/L, CRP 333 mg/L. Computed tomography of abdomen and pelvis revealed necrotizing fasciitis.

INITIAL THERAPEUTIC INTERVENTION: The patient underwent wide local debridement and fasciotomy and blood was transfused perioperatively, regarding Hb of 8.3 (Table 1). Post-wide debridement, the next day during dressing, wound showed fluffy white growth along edges and part of the base. (Fig.2).

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Table 1. Investigation during ICU stay.

LABS	3/2/21	4/2/21	5/2/21	6/2/21	7/2/21	8/2/21	9/2/21	10/2/21
HB (g/dl)	8.3	9.2	13.2	11.3	11.3	10.6	9.8	10.6
WBC (*10^3/ul)	29.91	35.66	43.35	41.4	23.31	17.74	16.41	12.5
PLATELET(*10/ul)	544	422	181	3436	328	313	287	254
UREA (mg/dl)						58.22		
CREATININE(mg/dl)	0.44				0.58			
NA (mEq/L)	139				134	133	135	138
K (mEq/L)	5				3.6	3.6	3.9	2.9
MG (mg/dl)	106				103	103	107	103
PT (sec)	12.8							
PTT(sec)	30							
INR	1.1							
CRP(mg/dl)	333							
LACTATE(mg/dl)	12					10		
PCT (ng/ml)	5.6							

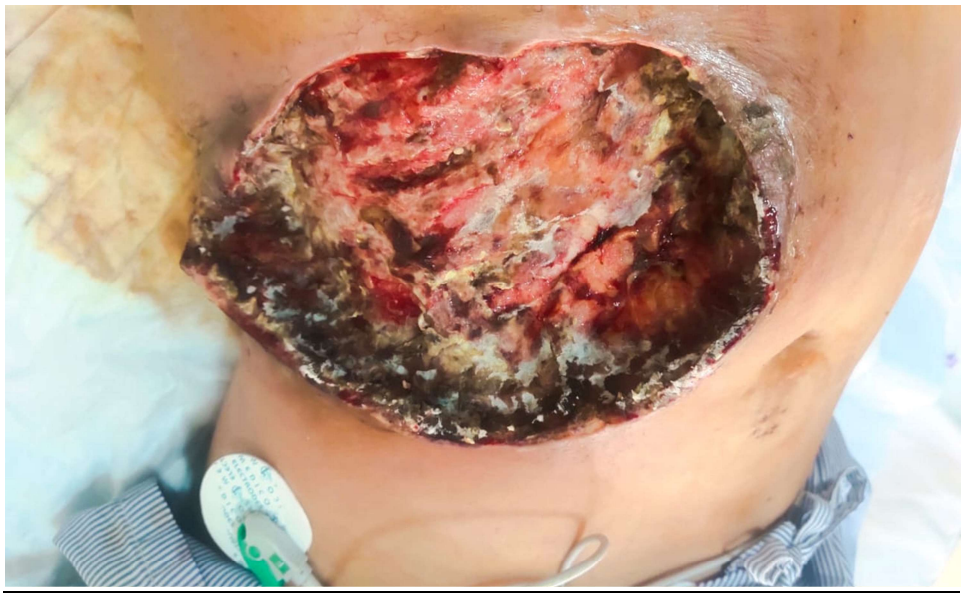

Figure 2. Post-debridement day 2 during dressing.
Appearance of fluufy exudates and wound edges with black necrotic tissue at edges.

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Wound swab was sent for fungal culture, KOH mount, blood culture, pus culture, and tissue for histopathology. With a high degree of suspicion for a fungal infection, she was meanwhile started on amphotericin B along with meropenem and minocycline. An immediate wide local excision was done with wide free margins. Meanwhile, 7 debridements were conducted over the span of 1 month.

FUTHER DIAGNOSTIC TESTING: In the meantime, the Covid antibodies test repeated twice, as routine practice of our institution, were found to be positive. Tissue histopathology revealed non-septate hyphae suggestive of invasive mucormycosis (Fig.3). MRI abdomen findings showed a 15cm large defect involving the entire thickness of subcutaneous fat.

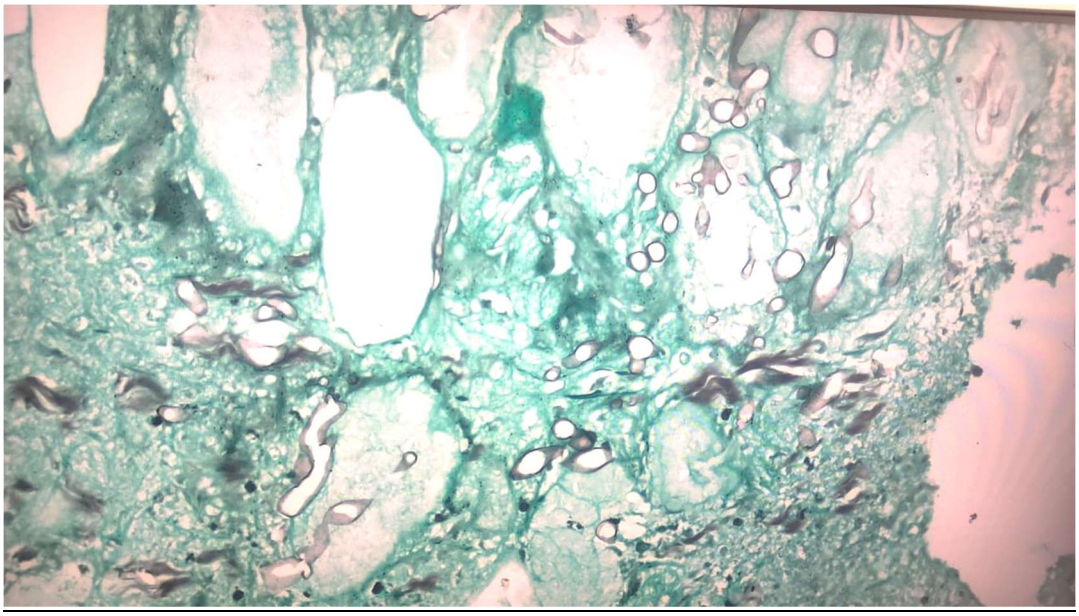

Figure 3. The biopsy reveal a completely necrotic subcutaneous tissue with areas of acute inflammatory exudates. Within the necrotic areas are seen broad, irregular and aseptate fungal hyphae, suggestive of mucromycosis. These fungal hyphae are seen invading the vessel. Impression-invasive mucomycosis.

FOLLOW UP AND OUTCOMES: She underwent wide debridement with VAC (vacuum-assisted closure) dressing of the wound in ICU hospital stay and on the appearance of healthy granulation tissue skin grafting was done. The patient had a high dose opioid requirement 50ug/kg over 24hours due to moderate to severe pain associated with the wound, both at rest and during dressing. A total of seven such repeated debridements at three to four days intervals were conducted over the span of 1 month. On day 30 a VAC (vacuum-assisted closure) dressing of the wound was done .On day 34 , i.e. 4 days after the vacuum dressing there was the appearance of healthy granulation after which a tissue skin grafting was done. The Amphotenericin was stopped on day 36. Meanwhile Antibiotics were continued from hospital admission with a fear of secondary bacterial infection of the large tissue defect and were stopped after 14 day course (i.e. day 14 of hospital admission). Blood cultures were sent at intervals to look for the spread of infection in the blood all of which were negative. The patient had a slow and stable recovery and was discharged home after the completion of days of antifungals.

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DISCUSSION

The ongoing outbreak of COVID-19 originated in Wuhan, China, in December 2019. COVID-19, which is the disease associated with SARS-CoV-2 infection, spread rapidly to produce a global pandemic [9]. The spectrum of symptomatic SARS-CoV-2 infection ranges from mild to critical. The proportion of severe or fatal infections may also vary by location [10]. Patients with COVID-19 might present with markedly higher levels of inflammatory cytokines (such as interleukin [IL]-2R, IL-6, IL-10, and tumor necrosis factor-alpha), associated with impaired cell-mediated immune response, affecting both CD4 + T and CD8 + T cells. In early December 2019, the first cases of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection were identified in Wuhan [10,11]. As this is a relatively novel virus, data regarding all the signs indicative of coronavirus disease (COVID-19) and symptoms that can be caused by the disease are insufficient [12]. The effects of SARS-CoV-2 on the immune system are still not clear with theory revolving around hyper inflammation and dysregulation of the immune system. What is plausible is that there is a weakening of the immune response as a result of T cell exhaustion, chronic viral infection, and the cytokine storm. This may affect the T cell, B cells, and NK cells. The overall general lymphopenia may also be contributing to this immunity reduction [13-16]. We are also not sure the extent to which immune dysregulation would occur, which are the categories of most susceptible patients, and in what period and for how long post covid infection the immune dysregulation would persist. Thus, it is highly likely that these patients would be candidates for opportunistic infections at some point in time [17-19].

One of the fatal opportunistic infections that are encountered among immunocompromised patients is mucor. Mucor is known to occur in patients who have diabetes, renal failure, stem cell transplantation and patients on long-term steroids. Pregnancy has also unique effects on the immunity at different trimesters which may lead to very different immune responses based on the microorganism. Early on in the pregnancy the mother, developing fetus and the placenta is thought to be in a symbiotic relationship thus in an anti-inflammatory phase [20]. Our case involved a young pregnant female, in the first trimester, with no comorbidities and no risk factor for developing mucormycosis. She was admitted to the intensive care unit of our hospital on POD-21 of laparoscopic ectopic pregnancy removal with hypotension, tachycardia, low hemoglobin, raised leukocyte count, and CRP with a very fulminant necrotic skin lesion as shown in Fig.1.This lesion was the site where one of the ports was inserted for laparoscopic surgery done in a different hospital. There was no sign of rhinocerebral involvement and blood cultures were sterile. On history, the patient remarked that she did have fever, sore throat and cough for five days, 4 weeks prior to laparoscopic ectopic pregnancy removal. The history also revealed that two more family members staying in the same house also developed similar symptoms. One of the family members had tested positive for COVID-19 and was isolated separately in another house. Both patient and other family members were treated symptomatically and no tests for COVID-19 were conducted. The culture revealed Rhizopus Arrhizus which was from the mucor family. At this point in time, the reason as to why a young female would develop such a fulminant infection warranting multiple wide local debridements with high opioid requirements throughout the day was not clear.

Similarly, the reason for the underlying poor immune status was not known. Autoimmune workup, HIV, and hepatitis workup were negative.

Hence a Covid antibody test was done, with positive results, confirmed with two successive covid antibody tests. At this stage, we also considered that the covid antibody test could have been a false positive result, due to pre-exposure to another virus of the coronavirus family (not SARS-CoV-2) and thus cross reactivity. However, the presence of one family member affected with the disease makes us believe that our patient could have possibly got exposed to the SARS-CoV-2 virus signaling the presence of the antibodies. Probably, the complex immunity pattern of pregnancy combined with the immunosuppression of Covid could have led to the extremely fulminant course seen in our young patient.

CONCLUSIONS

COVID-19 is itself associated with immune dysregulation and consequently life-threatening infections. Additionally, the prolonged and indiscriminate use of steroids for the treatment of COVID-19 could contribute to this problem of fungal superinfection of mucormycosis. It seems prudent to have a very high suspicion supplemented with a thorough clinical examination and low threshold for imaging in order to diagnose secondary fungal infections, such as mucormycosis. early so that the treatment can be instituted as soon as possible.

SUPPLEMENTARY INFORMATION

Funding: *This research received no external funding.*
Institutional Review Statement: *The study was conducted according to the guidelines of the Declaration of Helsinki.*
Informed Consent Statement: *Informed consent was obtained from all subjects involved in the study.*
Data Availability Statement: *The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.*
Conflicts of Interest: *The authors declare no conflicts of interest.*

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.
doi: https://doi.org/10.12688/wellcomeopenres.15026.2

[2] Kauffman CA, Malani AN. Zygomycosis: an emerging fungal infection with new options for management. Curr Infect Dis Rep 2007; 9(6): 435-440.
doi: https://doi.org/10.1007/s11908-007-0066-4

[3] Herrero EH, Sánchez M, Agrifoglio A, Cachafeiro L, Asensio MJ, Galván B, et al. Cutaneous mucormycosis in the ICU. Crit Care. 2015; 19(Suppl 1): P88.
doi: https://doi.org/10.1186/cc14168

[4] Farmakiotis D, Kontoyiannis DP. Mucormycoses. Infect Dis Clin North Am. 2016; 30(1): 143-163.
doi: https://doi.org/10.1016/j.idc.2015.10.011

[5] Jeong W, Keighley C, Wolfe R, Lee WL, Slavin MA, Kong DCM, et al. The epidemiology and clinical manifestations of mucormycosis: a systematic review and meta-analysis of case reports. Clin Microbiol Infect. 2019; 25(1): 26-34.
doi: https://doi.org/10.1016/j.cmi.2018.07.011

[6] Cornely OA, Alastruey-Izquierdo A, Arenz D, Chen SC, Dannaoui E, Hochhegger B, et al. Global guideline for the diagnosis and management of mucormycosis: an initiative of the European Confederation of Medical Mycology in cooperation with the mycoses study group education and research consortium. Lancet Infect Dis. 2019; 19(12) :e405-e421.
doi: https://doi.org/10.1016/S1473-3099(19)30312-3

[7] Kauffman CA. Zygomycosis: Reemergence of an old pathogen. Clin Infect Dis. 2004; 39(4): 588-590.
doi: https://doi.org/10.1086/422729

[8] Rammaert B, Lanternier F, Zahar JR, Dannaoui E, Bougnoux ME, Lecuit M, et al. Healthcare-associated mucormycosis. Clin Infect Dis. 2012; 54 Suppl 1: S44-54.
doi: https://doi.org/10.1093/cid/cir867

[9] Broughton JP, Deng X, Yu G, Fasching CL, Servellita V, Singh J, et al. CRISPR-Cas12-based detection of SARS-CoV-2. Nat Biotechnol. 2020; 38: 870-874.
doi: https://doi.org/10.1038/s41587-020-0513-4

[10] Guan WJ, Ni ZY, Hu Y, Liang WH, Ou ChQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020; 382: 1708-1720.
doi: https://doi.org/10.1056/NEJMoa2002032

[11] Rothan HA, Byrareddy SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. J Autoimmun 2020; 109: 102433.
doi: https://doi.org/10.1016/j.jaut.2020.102433

[12] de Moura DTH, McCarty TR, Ribeiro IB, Funari MP, de Oliveira PVAG, de Miranda Neto AA et al. Diagnostic characteristics of serological-based COVID-19 testing: a systematic review and meta-analysis. Clinics (Sao Paulo) 2020; 75: e2212.
doi: https://doi.org/10.6061/clinics/2020/e2212

[13] Chiappelli F, Khakshooy A, Greenberg G. COViD-19 immunopathology and immunotherapy. Bioinformation 2020; 16(3): 219–222.
doi: https://doi.org/10.6026/97320630016219

[14] Diao B, Wang C, Tan Y, Chen X, Liu Y, Ning L, et al. Reduction and functional exhaustion of T cells in patients with coronavirus disease 2019 (COVID-19). Front Immunol. 2020; 11: 827.
doi: https://doi.org/10.3389/fimmu.2020.00827

[15] Lin L, Lu L, Cao W, Li T. Hypothesis for potential pathogenesis of SARS-CoV-2 infection – a review of immune changes in patients with viral pneumonia. Emerg Microbes Infect. 2020; 9(1): 727–732.
doi: https://doi.org/10.1080/22221751.2020.1746199

[16] Fathi N, Rezaei N. Lymphopenia in COVID-19: Therapeutic opportunities. Cell Biol Int. 2020; 44: 1792–1797.
doi: https://doi.org/10.1002/cbin.11403

[17] 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(4): 599-606.
doi: https://doi.org/10.1007/s11046-020-00462-9

[18] Chen G, Wu D, Guo W, Cao Y, Hyang D, Wang H, et al. Clinical and immunological features of severe and moderate coronavirus disease 2019. J Clin Invest 2020; 130(5): 2620-2629.
doi: https://doi.org/10.1172/JCI137244

[19] Koehler P, Cornely OA, Böttiger BW, Dusse F, Eichenauer DA, Fuchs F, et al. COVID-19 associated pulmonary aspergillosis. Mycoses 2020; 63(6): 528-534.
doi: https://doi.org/10.1111/myc.13096

[20] Mor G, Cardenas I. The immune system in pregnancy: a unique complexity. Am J Reprod Immunol. 2010; 63(6): 425–433.
doi: https://doi.org/10.1111/j.1600-0897.2010.00836.x