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Letter to Editor

Internal Medicine Section

Opportunistic Oesophageal Candidiasis in a Patient with COVID-19 Infection

ABHIJIT WADEKAR[1], SANYUKTA HEPAT[2], ANAMIKA GIRI[3], SAMARTH SHUKLA[4], SOURYA ACHARYA[5]

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Dear Editor,

Currently, the world is dealing with the catastrophic global pandemic of Coronavrus Disease-2019 (COVID-19). With new mutant strains arising, the complications of COVID-19 are increasing and adding to our anxieties and concerns. The COVID-19 era is also giving rise to new opportunistic infections in the patients. Amongst these opportunistic infections, the most common are fungal infections like mucormycosis, candidiasis, aspergillosis [1,2]. Candidiasis is commonly encountered in the oral cavity in the form of oral thrush. Invasive candidiasis, like oesophageal candidiasis, is a rare occurrence in immunocompetent individuals [2].

The mechanism of such severe infections post COVID-19 can be attributed to the severe immune dysregulation which is caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). These fungal infections can occur in similar way of fever, cough and shortness of breath thus making the diagnosis even more challenging. COVID-19 patients who are admitted in intensive care unit are more vulnerable to such infections [3].

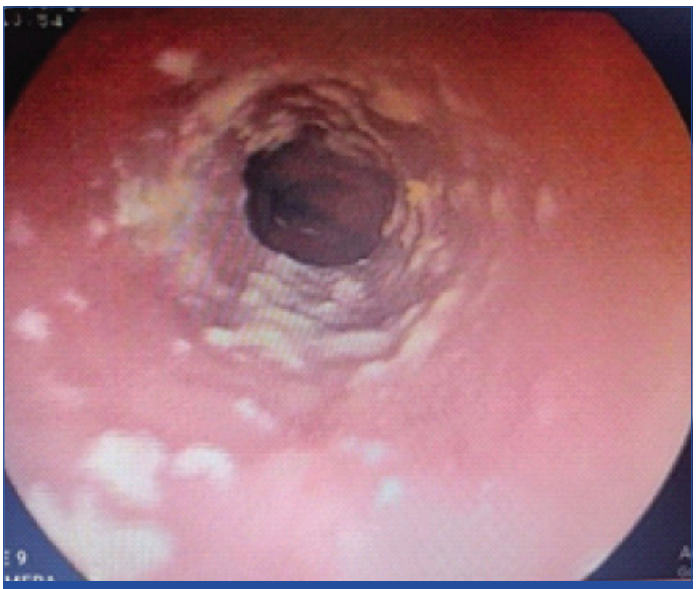
The pathogens causing secondary infections in a SARS-CoV-2 can be either bacterial or fungal, candida being one of them [4]. Early diagnosis and prompt treatment of these life threatening opportunistic infections are mandatory [4].

Inadequate investigations, missing clinical clues, overuse of antibiotics leading to resistance are the underlying reasons for such simple infections to become life threatening [5]. In the current scenario, while the treatment of COVID-19 remains a challenge in itself, thus, it is in the best interest of the patients, that as clinicians we rely on the early diagnosis and prompt treatment to reduce mortality [6].

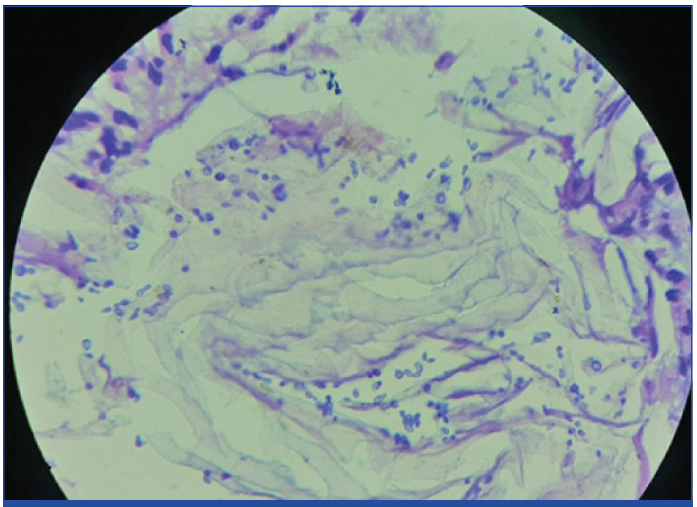
A 59-year-old male was admitted in hospital with diagnosis of moderate COVID-19 infection. He was treated with intravenous (i.v.) antibiotics, injection remdesivir for five days, steroids and anticoagulants and was discharged after seven days in a stable condition.

This patient again presented three weeks later with chief complaints of dysphagia and odynophagia, which was more for solids than liquids. There was no history of hoarseness of voice, swelling of neck, stridor, and diabetes mellitus. On examination, the patient was stable with respiratory rate 16 breaths/min with saturation on room air 95%, blood pressure 120/70 mmHg. Cardiovascular system, respiratory system, central nervous system and per abdomen examination revealed no abnormalities, no cervical lymphadenopathy and goiter. Oral cavity examination revealed no oral thrush, glossitis or ulcers. His COVID-19 panel blood investigations showed raised C-Reactive Protein (CRP) and D-dimer. In view of dysphagia, upper gastrointestinal endoscopy was done, which showed candidiasis growth in oesophagus as shown in [Table/Fig-1]. Sample was sent for histopathology which was suggestive of candidiasis spores shown in [Table/Fig-2].

The patient was treated with injection fluconazole 100 mg twice a day for 15 days post-treatment, he clinically improved and his symptom of dysphagia and odynophagia were resolved. Repeat endoscopy was done which was found to be normal.



[Table/Fig-1]: Gastroscopy showing oesophageal candidiasis.



[Table/Fig-2]: Haematoxylin and Eosin (H&E) stained slide showing pseudohyphae with budding yeast forms along with non specific chronic infiltrate and scattered unremarkable epithelial cells at one or two places, features suggestive of candidiasis.

Candidiasis is a simple fungal infections affecting mankind since hundreds of years. These infections can be in the form of skin infections, oral thrush, vaginosis or affect the gastrointestinal system. These simple conditions become life threatening when they present as secondary infections in post COVID-19 patients [1].

Fungal yeast species belonging to the Candida genus, range from *Candida albicans, Candida glabrata, Candida parapsilosis, Candida tropicalis*, and *Candida krusei*. These are the most prevalent fungal species inhabiting various mucosal surfaces, such as the skin and the respiratory, digestive, and urinary tracts [2]. Although being

commensal within the human host, Candida species are equipped with virulence attributes, enabling them to invade when opportunities arise and causes various infections in humans, especially when the immune system is impaired [7]. Similar cases of opportunistic fungal infections in COVID-19 patients have been reported since the COVID-19 pandemic, few of which have been summarised below in [Table/Fig-3] [8-11].

Authors	Presentation	Treatment	Outcome
Riad A et al., [8]	Dysphagia	Topical antifungal nystatin (Micostatin) four times a day	Complete resolution
Awada B et al., [9]	Acute respiratory distress syndrome	Fluconazole (i.v.), Capsofungin	Death
Kakamad FH et al., [10]	Haemoptysis, dyspnea, cough, fever	Broad spectrum antifungals, antibiotics, lobectomy	Complete resolution
Verma V et al., [11]	Dysphagia	Oral fluconazole	Complete resolution

[Table/Fig-3]: Previous cases of opportunistic fungal infections in COVID-19 patients.

Diagnosis of invasive candidiasis remain challenging. Various investigatory tools like blood culture, non culture entities like β-D-Glucan (BDG) and mannan antigen testing, molecular methods like Polymerase Chain Reaction (PCR) or even Enzyme-Linked Immunosorbent Assay (ELISA) kits can be used for detection [7]. Imaging techniques like MRI, endoscopy can also be used for diagnosis [4].

Invasive candidiasis has a higher mortality rate, if treatment not started at the right time. The management of invasive candidiasis in patients with COVID-19 is similar to that of non COVID-19 patients [5]. Echinocandins are the treatment of choice for invasive Candida infections. Second line alternatives are fluconazole, liposomal amphotericin B, voriconazole, posaconazole and isavuconazole. Other preventive measures include hygiene, source control and even prophylaxis in a prolonged hospitalised patient [6].

As the world fights a battle in the dark, we as clinicians should be well aware of these secondary infections which can be treated rather easily than losing the patient to post COVID-19 complications. Such cases of mortality should be reported, so that the medical fraternity is made well aware of the scenario.

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PARTICULARS OF CONTRIBUTORS:
1. Junior Resident, Department of Medicine, Jawaharlal Nehru Medical College, Sawangi, Wardha, Maharashtra, India.
2. Junior Resident, Department of Medicine, Jawaharlal Nehru Medical College, Sawangi, Wardha, Maharashtra, India.
3. Junior Resident, Department of Medicine, Jawaharlal Nehru Medical College, Sawangi, Wardha, Maharashtra, India.
4. Professor, Department of Pathology, Jawaharlal Nehru Medical College, Sawangi, Wardha, Maharashtra, India.
5. Professor and Head, Department of Medicine, Jawaharlal Nehru Medical College, Sawangi, Wardha, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Sourya Acharya,
Professor and Head, Department of Medicine, Jawaharlal Nehru Medical College, Sawangi, Wardha, Maharashtra, India.
E-mail: souryaacharya74@gmail.com

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