

CASE REPORT

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Rhino-orbito-cerebral invasive fungal sinusitis associated with COVID-19 infection in a malnourished child

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Abstract

Background: Corona virus disease has been associated with a wide variety of fungal and bacterial co-infections. These secondary infections could be due to the irrational use of antibiotics, immunosuppressive therapy, pre-existing co morbidities, and immune modulator effects of the virus. But here, we report a very rare occurring of rhino-orbito-cerebral invasive fungal sinusitis in a malnourished child and no other co morbidities.

Case presentation: This is a case of a 6-year-old boy with severe thinness and no other co-morbidities, with mild COVID-19 infection, during the course of illness developed rhino-orbito-cerebral invasive fungal sinusitis. The child's mother had COVID-19 1 week prior to child's illness. The child then developed fever followed by headache. The child reported to hospital on seventh day of illness and RTPCR for COVID-19, turned positive. The child's vitals were stable and maintaining saturation. Child was being treated with supplements and symptomatic treatment for fever. On his second day of stay at hospital, he started to develop gradually progressive left-sided peri-orbital swelling. Due to the association of COVID-19 with fungal infection, child was started on AMPHOTERICIN-B and given for 4 days and referred to a higher center for further management. Radiological imaging was suggestive of rhino-sinusitis with orbital cellulitis with meningeal enhancement suggestive of fungal etiology. Debridement was done, child was adequately treated with anti-fungal, and the child showed significant improvement along with radiological clearing.

Conclusion: Invasive fungal infection can occur in association with COVID-19 among malnourished pediatric age groups with no other comorbidities.

Keywords: COVID-19, Rhino-cerebral, Invasive fungal infection, Orbital cellulitis

Background

The coronavirus disease 2019 infection is caused by the novel severe acute respiratory syndrome corona virus 2 [1]. In the pediatric age group, the disease may be associated with a wide range of disease patterns, ranging from asymptomatic infection to critical disease progressing to ARDS [2]. The occurrence of a multi-system inflammatory syndrome in children is also known, which was initially named as “Kawasaki like-disease” and then

renamed pediatric multi-system inflammatory syndrome (PIMS) [3]. A wide range of bacterial and fungal co-infections may exist in COVID-19 patients either as a part of hospital acquired infections or those with pre-existing comorbidities [4, 5].

Among children, the most common cause of invasive fungal infection includes *Aspergillus* species, followed by *Candida* and *Mucormycosis* [6]. Acute invasive fungal rhino-sinusitis is an opportunistic infection that occurs mostly in immunocompromised patients [7]. There are increasing reports of invasive fungal infection associated with coronavirus disease especially in India, amongst people with various co-morbidities [8].

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Very few cases have been reported in the pediatric age group with no associated co morbidities. Here, we report a case of child rhino-orbito-cerebral invasive fungal sinusitis associated with coronavirus disease, in a malnourished child. Similar such cases were reported by Turbin et al. among two adolescents with COVID-19 [9].

Case presentation (Fig. 1)

A 6-year-old child hailing from a region of high incidence of COVID 19, from a farming background, came to the hospital with complaints of fever from 1 week. One week prior to the illness mother was tested positive for COVID-19. The child had significant exposure to mother. RTPCR for the child was positive. The child was admitted along with the mother in the hospital. At admission, the child was active and had no difficulty in breathing. On examination, vitals were stable, maintaining saturation, and systemic examination was within normal limits. There was no history of any past hospitalisation for any significant illness in the child and had been healthy since birth. So the child was taken to be Mild COVID-19 illness and was being given symptomatic treatment along with supplements. No steroids were being given .

On the second day of admission, the child started to develop insidious onset, gradually progressing left peri-orbital swelling, tender, appeared red, and proptosis was noted. Vision was intact, but the child could barely open his eyes (Fig. 2). Due to the association of COVID-19 with other co-infections, he was started on

amphotericin-B along with meropenem and vancomycin. CT scan revealed complete lumen filling mucosal thickening with slightly hyper dense internal contents noted at left maxillary sinus, bilateral ethmoid sinus, and sphenoid sinus; Mucosal thickening also noted at fronto-ethmoidal recess; mucosal thickening noted along bilateral inferior turbinate, left middle turbinate, and left osteo-meatal complex; mild axial proptosis of the left eye with bulky medial rectus and surrounding fat stranding along with areas of bony erosion noted. Overall features were suggestive of fungal sinusitis with orbital cellulitis. Contrast-enhanced MRI showed lepto-meningeal enhancement noted along left basifrontal lobe convexity, with areas of patchy mucosal necrosis and other features consistent CT findings, overall suggestive of fungal etiology (Fig. 3). Hence, the child was referred to our center for further management.

At the time of admission to our hospital, vitals were stable, weight is 17 kg, length is 122.5 cm, and BMI is 11.4 kg/m² indicating severe thinness as per WHO growth chart. Local examination revealed lemon-sized left peri-orbital swelling. Diagnostic nasal endoscopy was done, and the soft tissue was sent for KOH mount and fungal/bacterial culture. KOH mount did not show any hyphae and culture did not yield any growth. CBC was then done and showed hemoglobin of 11.4, total count 16,500 (neutrophils 70%/lymphocytes 20%), and platelet count of 5.37L. The blood sugar level was 98 mg/dL, glycated hemoglobin was 4.5, and urine ketone bodies

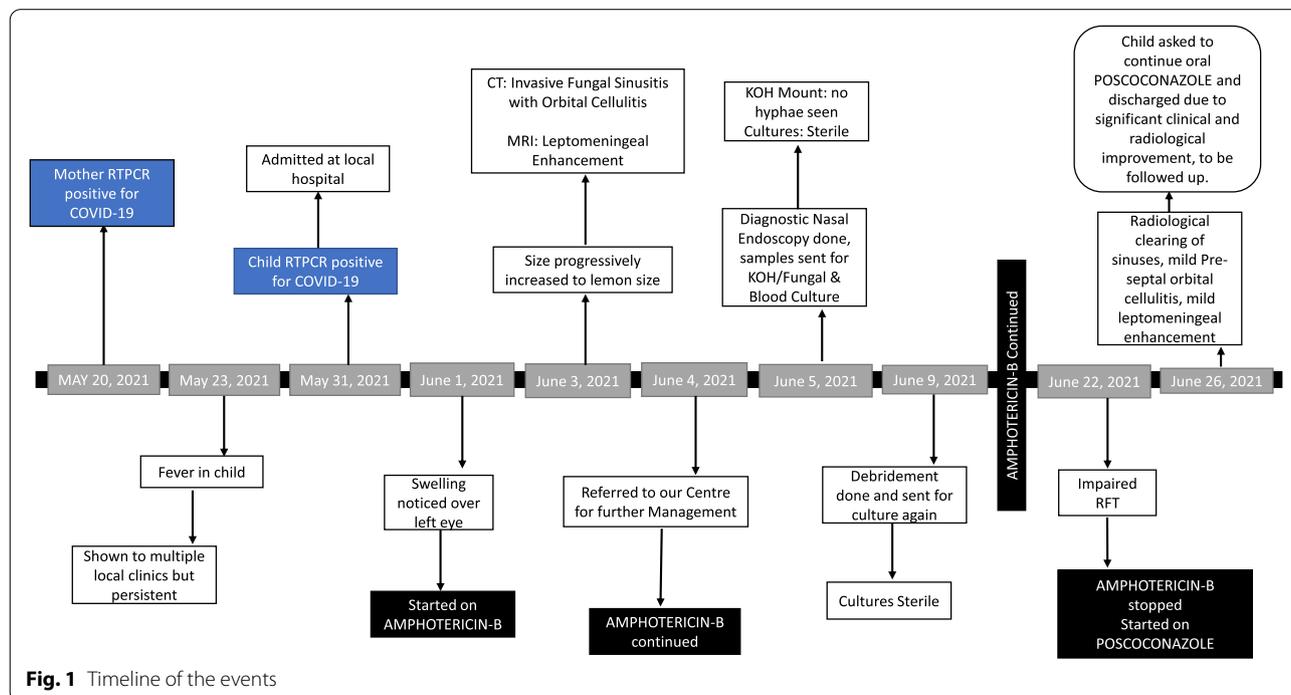


Fig. 1 Timeline of the events

were absent. HIV and HbSag were non-reactive. Inflammatory markers showed C-reactive protein of 72.6 mg/L, serum ferritin of 612.7 nm/mL, lactate dehydrogenase of 358U/L, and D-dimer of 0.04gm/mL. Renal function was within normal limits.

The child was taken up for debridement surgery. Amphotericin B was continued for 22 days. Then, the child developed impaired renal function test. Hence, amphotericin B withheld and started on oral poscoconazole. At the end of 1 month, the child was clinically better with decrease of swelling noticed (Fig. 4). Follow-up MRI was done and showed clear paranasal sinuses, resolution of orbital cellulitis, and regression meningeal

enhancement (Fig. 5). He was asked to continue oral poscoconazole for another 14 days and discharged.

Due to known incidence of acute invasive fungal infection associated with coronavirus disease along with radiological imaging suggestive of fungal infection, he was treated as the same and showed significant improvement with early debridement surgery and early institution of anti-fungal therapy.

Discussion

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel coronavirus previously unknown to mankind. It is classified as a beta-CoV of group 2B and



Fig. 2 Left peri-orbital swelling

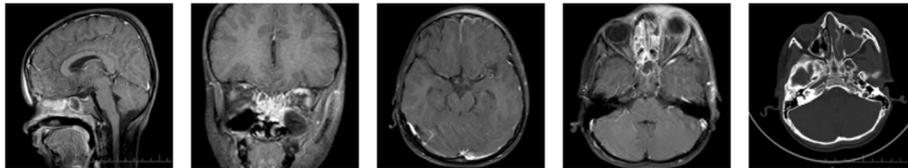


Fig. 3 Contrast-enhanced MRI



Fig. 4 Post-treatment

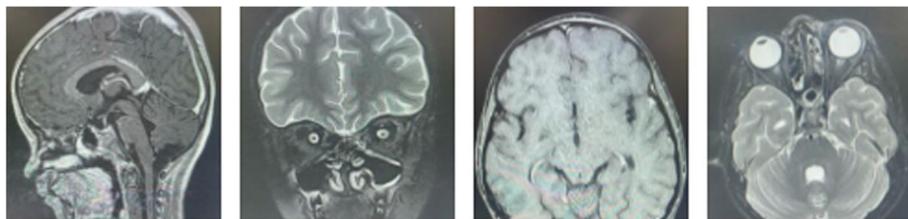


Fig. 5 Follow-up MRI

is the cause of a serious life-threatening disease known as coronavirus disease of 2019 (COVID-19) [10]. SARS-CoV-2 is a virus that is the cause of a serious life-threatening disease known as COVID-19. It was first noted to have occurred in Wuhan, China, in November 2019 and the WHO reported the first case on December 31, 2019. The outbreak was declared a global pandemic on March 11, 2020, and by May 30, 2020 [11].

Beside the acute respiratory distress syndromes (ARDS) caused by it, COVID-19 patients were found to have immune-suppression attributed to a decrease in CD4⁺T and CD8⁺T cells [12]. A complex interplay of factors, including pre-existing diseases, such as diabetes mellitus, previous respiratory pathology, use of immunosuppressive therapy, the risk of hospital-acquired infections, and systemic immune alterations of COVID-19 infection itself may lead to secondary infections, which are increasingly being recognised in view of their impact on morbidity and mortality [13]. Thus, coronavirus disease is known to be associated with several bacterial [10] and fungal co-infections [14]. The main fungal pathogens are *Aspergillus*, *Candida*, *Mucor*, and *Cryptococcus* [15].

This child had mild COVID-19 illness with severe thinness and no other comorbidities, immunosuppressive state, or any other abovementioned risk factors. The fungus could not be cultured due to early institution of therapy. Similar such clinical and radiological findings have been reported in two adolescents with negative culture reports by Turbin et al. [9].

Acute invasive fungal infection has been recently associated with COVID-19 infection, but this has been in patients with several co-morbidities, receiving high-dose steroids, usually in adult patients. But this is one such rare presentation of a malnourished child with invasive fungal infection in association with COVID-19.

Conclusion

Acute invasive fungal infection can also occur as an isolated disease in association with COVID-19. We the treating pediatricians should be aware of the possibility of secondary invasive fungal infections in association with COVID-19, and early diagnosis and treatment

of this deadly infection might reduce the morbidity and mortality.

Abbreviations

WHO: World Health Organization; RTPCR: Reverse transcription–polymerase chain reaction; ARDS: Acute respiratory distress syndrome; CT: Computer tomography; MRI: Magnetic resonance imaging; BMI: Body mass index; KOH: Potassium hydroxide; CBC: Complete blood count; HIV: Human immunodeficiency virus; HbsAg: Hepatitis b S antigen.

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Authors' contributions

Dr. Mallesh Kariyappa, Dr. Dhanalakshmi K, Dr. Dhakshayani B, and Dr. Ashray S. Patel were all involved in the evaluation and management of the case. Dr. Ashray S. Patel and Dr. Dhanalakshmi K were involved in the writing the manuscript. Dr. Mallesh Kariyappa and Dr. Dhakshayani B have reviewed the manuscript. The authors read and approved the final manuscript.

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Availability of data and materials

All data and materials available with the authors can be reached on reasonable request.

Declarations

Ethics approval and consent to participate

Approval was taken from the ethical committee, and consent to participate was obtained. Institute name: Bangalore Medical College and Research Institute.

Consent for publication

We obtained written consent for publication from the parent of the participant along with consent for photography because it contains photographs and radiological images.

Competing interests

The authors declare that they have no competing interests.

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