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Pediatrics

A RARE CASE OF COVID-19 ASSOCIATED MUCORMYCOSIS IN A NEWLY DIAGNOSED TYPE-1 DIABETIC CHILD

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ABSTRACT Mucormycosis is an invasive fungal infection, occurring in patients with an underlying immunocompromised condition. Secondary infections after Covid 19 infection can be of bacterial and fungal origin. While COVID 19 associated pulmonary aspergillosis (CAPA) has predominated internationally, mucormycosis has been on the rise in India observed even in patients with mild to moderate SARS-coV2 infections. The strongest predisposing factor being hyperglycaemia. We report a case of a 6years 6 months female child with newly diagnosed juvenile onset diabetes mellitus with rhino-orbital mucormycosis post COVID-19 infection, who was successfully treated. To the best of our knowledge this is the first paediatric mucormycosis associated with Covid 19. With this case we highlight the importance of considering mycotic co infections with COVID 19 even in paediatric population with underlying co morbidities like diabetes and the need for prompt, multidisciplinary aggressive treatment for successful outcome.

KEYWORDS : COVID 19, Mucormycosis, Juvenile onset Diabetes Mellitus, Liposomal Amphotericin B, Posaconazole

INTRODUCTION

Mucormycosis is a fungal infection that belongs to the order Mucorales. It is an acute opportunistic infection, being the second most frequent invasive fungal disease in children.Infection occurs by implantation of the fungal spores in the mucous membranes, inhalation or ingestion of contaminated food. COVID 19 associated mucormycosis is being increasingly reported since the start of the pandemic, especially in diabetic adult patients. Here we present a case of rhino-orbital mucormycosis after Covid 19 infection in a 6year6months old female child, who was recently diagnosed with juvenile onset diabetes mellitus.

CASE REPORT

A 6years 6months old female child born 1st by birth order, of non-consanguineous marriage was referred to our tertiary health centre with the complaints of a pain over the medial aspect of her left eye associated with serosanguineous discharge for 1month and swelling over the left mid face region for the past 15 days. There was no history of any fever, cough, cold, nasal stuffiness, restriction of eye movements, blackish discharge. She was developmentally normal and immunised for age. 2 months prior she had a history of admission for altered sensorium, fever and swelling over the left eye. For which she was diagnosed as a case of severe diabetic ketoacidosis associated with left eye orbital cellulits, in a newly diagnosed type 1 diabetic (HbA1C-13.5). She was managed conservatively with broad spectrum antibiotics given for a total duration of 14 days, topical steroids, and started on basal bolus insulin regimen and discharged.

On examination she was well-nourished with a weight 19kg (-1SD to median) and height 116cm (-1SD to median).Conscious, afebrile, vitally and hemodynamically stable. On local examination facial oedema was present over the left malar region, left eye showed mild proptosis, lower eyelid oedema, conjunctival congestion near limbus and a sinus present near medial canthus of the left eye. Rhinoscopy revealed oedema of the left nasal mucosa but no necrotic tissue or discharge. Remaining systemic examination was unremarkable. For these above complaints a Contrast enhanced CT of the Orbit and Paranasal sinus was done which was s/o focal erosions at left lamina papyracea and medial wall of left orbit with soft tissue thickening suggesting inflammatory sinusitis involving left ethmoid, maxillary and frontal sinus.

She underwent a necrotic bone debridement under local anaesthesia with removal of the eroded bones and a tissue sample was sent for culture and histopathology. The Biopsy revealed the presence of aseptate hyphae with right angled branching typical of mucormycosis.

All baseline Investigations were sent which were within normal ranges for her age/sex except for an elevated HBA1c of 7.6, and a RBS-302. Fungal cultures and KOH mounds were negative. Covid 19 -RTPCR was negative, but the child was reactive for Covid antibody (total) with a titre of 27.195 (non-reactive =<1.0).

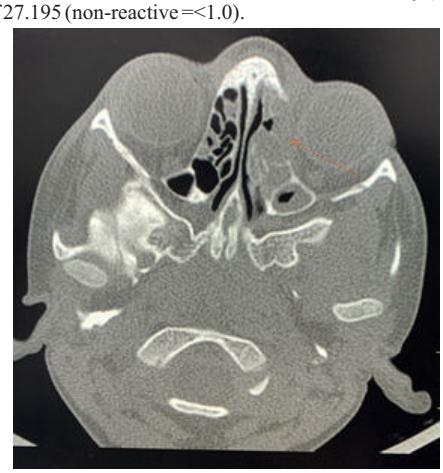

Figure 1-Bony erosions of lamina papyracea (arrow)

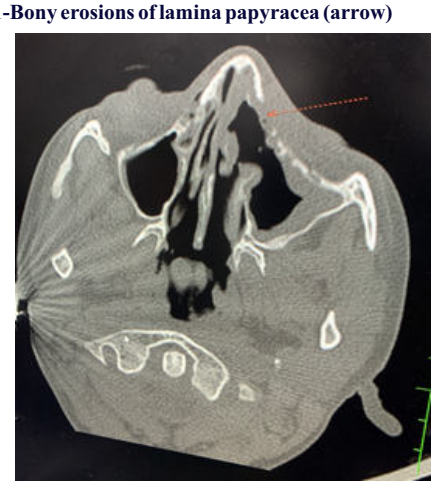

Figure 2-Bony erosions and soft tissue enhancement of the ethmoid sinus (arrow)

Repeat contrast enhanced CT scan (brain/orbit/PNS) was done on day 40 of symptoms to determine the extent of the disease which showed involvement of left ethmoid, maxillary and frontal sinus with bony erosion and extension to preseptal compartment of left globe. There was no cerebral, retro-orbital involvement or angioinvasion. She was treated with Injectable Liposomal Amphotericin B (5mkd) for 21 days with serum creatinine and electrolytes monitoring and then switched over to oral Posaconazole (12mkd) for a total duration of 9 weeks after clinical improvement and radiological resolution. Strict euglycemia was ensured. The total daily dose of insulin being given as 40% basal regimen of Glargine and 60% bolus of Glulisine. The Child underwent FESS (functional endoscopic sinus surgery) procedure with Debridement and nasal crust which was sent for Culture which was negative. The child is following up on outpatient basis with no adverse effects to antifungals or recurrence.

DISCUSSION

Mucormycosis is primarily an opportunistic fungal infection, with an estimated prevalence 70 times higher India than that globally, but with only few cases being reported in the pediatric age group.[1,3] It's an invasive fungal infection occurring in rhinocerebral, cutaneous, disseminated, gastrointestinal, and pulmonary forms. Immuno compromised individuals are at increased risk of development of the disease risks including diabetes mellitus, haematological malignancies, stem cell/organ transplantation, HIV, trauma, injectable drug use, dessferoaxime therapy.[2]

Uncontrolled diabetes Mellitus appears to be the leading risk factor specially in the Indian setup accounting for 54-76% of cases presenting as Rhino-orbital cerebral mucormycosis.[3,4] Hyperglycemia induces Glucose-regulated protein 78 (GRP78) expression identified as a putative endothelial cell receptor for Mucorales enhancing endothelial cell invasion and fungal damage.[5] Rhizopus oryzae species inherently possess enzyme keto-reductase which utilise hosts ketones for their own growth leaving patients vulnerable.[6]

Since the start of the Coronavirus pandemic cases of mucormycosis associated with the recovered or recovering COVID 19 patients has increased exponentially leading to increased concern.[7]Cytokine storm, ciliary dysfunction, dysregulated innate immune response triggered by the virus ,vulnerable host population with co morbidities ,immunosuppressive therapy(corticosteroids), prolonged ICU stay, invasive procedures, high fungal spore count, and humid environment all have created an ideal setting for mould infections.[8]

Diagnosis involves a combination of examination findings, radiographic evidence (CT/MRI) to see the extent of the disease, fungal cultures for confirmation although often yielding no growth due to fragile nature of tissue, and histopathological identification of typical fungal structure. Serum studies and newer 18S rRNA targeted PCR based tests have showed promise in culture negative situations.[9]

Approach to treatment is multidisciplinary involving strict control of underlying risk factors especially glycemic control, surgical management such as debridement/debunking surgeries, and anti-fungal agents. The anti-fungal agent of choice is intravenous liposomal Amphotericin B given at a dose of 5-10mkd for minimum of 3 weeks with strict monitoring of electrolytes and renal function. Alternatively, Posaconazole/ Isavuconazole or Capsofungin in combination therapy can be tried.[2,9]Posaconazole given as a delayed release tablet in doses of 12-15mkd is most commonly used for step down therapy post initial treatment with Amphotercin B and monitoring its trough levels on follow up is advised. Isavuconazole has a better safety profile but limited use in paediatrics due to minimal data.[10]

Most cases that have been reported till date involve adult population, to the best of our knowledge this is a first case report of COVID 19 associated mucormycosis in a newly diagnosed Type 1 diabetic in the pediatric population. There is an increased need for keeping a high index of suspicion in such cases and recognising ominous signs to prevent erroneous diagnosis and delay in management.

CONCLUSION

With children now making up for a growing share of new COVID 19 cases worldwide and in India, and pediatric cases daily being on the rise we are seeing a wide spectrum of the disease in them. This is ranging from mild to severe disease, Multi-system inflammatory in Children(MIS-C) and presentations similar to that of the adult spectrum of the disease.[12]We must therefore be vigilant to such opportunistic co-infections being seen commonly in adult COVID19 in our vulnerable paediatric population and act promptly to ensure successful outcome and decrease the overall burden of the disease.

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