



Mucormycosis with COVID-19 in Tertiary Care Hospital of Southern Rajasthan: A Case Series

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Abstract

Background and Aims

There are increasing case reports of rhino-orbital mucormycosis in people with coronavirus disease 2019 (COVID-19), especially from India. Diabetes mellitus (DM) is an independent risk factor for both severe COVID-19 and mucormycosis. The present study was carried out to understand the relation to COVID-19, relation to inflammatory markers, relation to steroid use during COVID-19 treatment, clinical course, and outcome of the disease.

Materials and methods

The present case series was conducted at RNT Medical College Udaipur. This study was done over a period of one month after getting approval from institutional ethics committee. Written and informed consent from patients were taken. In this case series 25 patients admitted in COVID wards, medical wards, mucormycosis ward and ICU were taken if they found fungal hyphae positive on KOH mount and history of COVID19 illness and negative KOH mount patients were excluded.

Results

In present case series on admission out of 25 patients 13(52%) patients admitted with mean NLR >5.5, mean CRP 148, mean D-Dimer 2710, 7(28%) patients admitted with mean NLR 3.5-5.5, mean CRP 74, mean D-Dimer 758 and 5(20%) patients admitted with mean NLR <3.5, mean CRP 23, mean D-Dimer 414. Out of total 13 patients who admitted with NLR >5.5, 5(38.5%) patients admitted with orbital cellulitis and 8(61.5%) patients admitted with invasive sinusitis, out of 7 patients who admitted with NLR 3.5-5.5, 3(42.9%) patients admitted with orbital cellulitis and 4(57.1%) patients admitted with invasive sinusitis, out of 5 patients who admitted with NLR <3.5, 2(40%) patient admitted with orbital cellulitis and 3(60%) patients admitted with invasive sinusitis. Out of total 10 patients who admitted with orbital cellulitis, in 70% Patients steroid was used during COVID19 treatment and out of 15 patients who admitted with invasive sinusitis, in 73.3% Patients steroid was used during COVID19 treatment, intracranial extension was seen in 3(12%) patients . In present case series 72% patients were male and 28% patients were females. 68% patients were from rural area and 32% patients were from urban area. In present case series 74% cases treated with Amphotericin B, out of these 36% cases were orbital cellulitis patients and 38% cases were invasive sinusitis patients. 26% cases treated with posaconazole, out of these 9% were orbital cellulitis cases and 17% were invasive sinusitis cases. 85.72% cases of orbital cellulitis were improved and 75% cases of invasive sinusitis were improved. 39.28% cases who admitted with NLR >5.5 were not improved with effective treatment.

Discussion

Mucormycosis were developed most commonly in patients who were admitted with severe form of COVID19 illness with cytokine storm and treated with steroid during their COVID illness.

Conclusion

As per present case series inflammatory markers of COVID-19, NLR and history of steroid during treatment can be taken as predictor of mucormycosis occurrence and their outcome.

Keywords

COVID, NLR, CRP, LDH, IL6

Introduction

Phycomycosis or zygomycosis was first described in 1885 by Paltauf¹ and later coined as Mucormycosis in 1957 by Baker² an American pathologist for an aggressive infection caused by *Rhizopus*. Mucormycosis is an uncommon but a fatal fungal infection that usually affects patients with altered immunity. Mucormycosis is an angioinvasive disease caused by mold fungi of the genus *Rhizopus*, *Mucor*, *Rhizomucor*,

Cunninghamella and *Absidia* of Order-Mucorales, Class - Zygomycetes³. The *Rhizopus Oryzae* is most common type and responsible for nearly 60% of mucormycosis cases in humans and also accounts for 90% of the Rhino-orbital-cerebral (ROCM) form⁴. Mode of contamination occurs through the inhalation of fungal spores.

Globally, the prevalence of mucormycosis varied from 0.005 to 1.7 per million population, while its prevalence is nearly 80 times higher (0.14 per 1000) in India compared to developed countries, in a recent estimate of year 2019–2020⁵⁻⁷. In other words, India has highest cases of the mucormycosis in the world. Notwithstanding, India is already having second largest

population with diabetes mellitus (DM) and was the diabetes capital of the world, until recently⁸. Importantly, DM has been the most common risk factor linked with mucormycosis in India, although hematological malignancies and organ transplant takes the lead in Europe and the USA⁷. Nevertheless, DM remains the leading risk factor associated with mucormycosis globally, with an overall mortality of 46%⁹. While long term use of corticosteroids have often been associated with several opportunistic fungal infection including aspergillosis and mucormycosis, even a short course of corticosteroids has recently been reported to link with mucormycosis especially in people with DM. A cumulative prednisone dose of greater than 600 mg or a total methyl prednisone dose of 2–7 g given during the month before, predisposes immunocompromised people to mucormycosis¹⁰. There are few case reports of mucormycosis resulting from even a short course (5–14 days) of steroid therapy,

especially in people with DM¹¹. Surprisingly, 46% of the patients had received corticosteroids within the month before the diagnosis of mucormycosis in the European Confederation of Medical Mycology study¹². These findings need a relook in the context of COVID-19 pandemic where corticosteroids are often being used. There has been a steep rise in case reports/series of mucormycosis in people with COVID-19 especially from India. These finding are unprecedented and carry an immense public health importance, primarily because fatality rate with mucormycosis is pretty high. Especially the intracranial involvement of mucormycosis increases the fatality rate to as high as 90%¹³. Moreover, rapidity of dissemination of mucormycosis is an extraordinary phenomenon and even a delay of 12 h in the diagnosis could be fatal, the reason 50% of cases of mucormycosis have been historically diagnosed only in the post-mortem autopsy series¹⁴.

Observations

Table 1

Mean NLR	N	Mean CRP
<3.5	5	23
3.5-5.5	7	74
>5.5	13	148

In present case series on admission out of 25 patients 13(52%) patients admitted with mean NLR >5.5 and mean CRP 148, 7(28%) patients admitted with mean NLR 3.5-5.5 and mean CRP 74, 5(20%) patients admitted with mean NLR <3.5 and mean CRP 23.

Table 2

Mean NLR	N	Mean D- dimer
<3.5	5	414
3.5-5.5	7	758
>5.5	13	2710

In present case series on admission out of 25 patients 13(52%) patients admitted with mean NLR >5.5 and mean D-Dimer 2710, 7(28%) patients admitted with mean NLR 3.5-5.5 and mean D-Dimer 758, 5(20%) patients admitted with mean NLR <3.5 and mean D-Dimer 414.

Table 3

NLR	Orbital Cellulitis (N) (%)	Invasive Sinusitis (N) (%)	Total (N)(%)
<3.5	2(40)	3(60)	5(100)
3.5-5.5	3(42.9)	4(57.14)	7(100)
>5.5	5(38.5)	8(61.5)	13(100)

In present case series out of total 13 patients who admitted with NLR >5.5, 5(38.5%) patients admitted with orbital cellulitis and 8(61.5%) patients admitted with invasive sinusitis, out of 7 patients who admitted with NLR 3.5-5.5, 3(42.9%) patients admitted with orbital cellulitis and 4(57.14%) patients admitted with invasive sinusitis, out of 5 patients who admitted with NLR <3.5, 2(40%) patient admitted with orbital cellulitis and 3(60%) patients admitted with invasive sinusitis.

Table 4

Steroid	Orbital Cellulitis	Invasive Sinusitis	Total
Used	7(70%)	11(73.3%)	18(72%)
Not used	3(30%)	4(26.7%)	7(28%)

In present case series out of total 10 patients who admitted with orbital cellulitis, in 70% Patients steroid was used during COVID19 treatment and out of 15 patients who admitted with invasive sinusitis, in 73.3% Patients steroid was used during COVID19 treatment.

Table 5

Intracranial extention

Yes	No
3(12%)	22(88%)

In present case series intracranial extention was seen in 3(12%) patients.

Table 6

Males	Females
72%	28%

In present case series 72% patients were male and 28% patients were females.

Table 7

Rural	Urban
68%	32%

In present case series 68% patients were from rural area and 32% patients were from urban area.

Table 8

Amphotericin B Used	Posaconazole Used	Orbital Cellulitis	Invasive Sinusitis
74%	-	36%	38%
	26%	9%	17%

In present case series 74% cases treated with Amphotericin B, out of these 36% cases were diagnosed with orbital cellulitis and 38% cases were diagnosed with invasive sinusitis. 26% cases treated with posaconazole, out of these 9% were orbital cellulitis cases and 17% were invasive sinusitis cases.

Table 9

Improved	Orbital Cellulitis	Invasive Sinusitis	Total
Yes	85.72%	75%	80%
No	14.28%	25%	20%

In present case series 85.72% cases of orbital cellulitis were improved and 75% cases of invasive sinusitis were improved.

Table 10

NLR	Orbital Cellulitis (N) (%)	Invasive Sinusitis (N) (%)	Improved With Treatment	Not Improved With Treatment
<3.5	2(40)	3(60)	100%	-
3.5-5.5	3(42.9)	4(57.1)	100%	-
>5.5	5(38.5)	8(61.5)	60.72%	39.28%

In present case series 39.28% cases who admitted with NLR >5.5 were not improved with effective treatment.

Discussion

In present case series more patients were males and from rural background, more number of patients were admitted with severe COVID19 disease with NLR >5.5, mean CRP >50, mean D-Dimer >1000, more number of cases were diagnosed with invasive sinusitis than orbital cellulitis and in these cases more number of

patients were admitted with severe COVID19 disease. Mucormycosis were developed most commonly in patients who were treated with steroid during their COVID illness and they were admitted with severe form of COVID19 illness with cytokine storm. Amphotericin B was used more commonly than

posaconazole in their mucormycosis treatment. 60.72% patients were improved with treatment and they were mild and moderate severity disease category patients of COVID19 and 39.28% patients were not improved who were admitted with severe form of COVID19 illness with cytokine storm.

Conclusion

As per present case series inflammatory markers of COVID19, NLR and history of steroid during treatment can be taken as predictor of mucormycosis occurrence and their outcome.

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