Rhino-orbital mucormycosis and off label use: 13 case reports

In a case series, 13 patients (10 men and 3 women) aged 33–65 years were described, who developed rhino-orbital mucormycosis following treatment with dexamethasone, favipiravir, hydrocortisone, ivermectin, methylprednisolone, prednisolone or Withania somnifera. Out of these 13 patients, three patients received off-label treatment with prednisolone or dexamethasone for COVID-19 (routes and durations of treatments to reactions onsets not stated; not all dosages and outcomes stated).

Patient 1: The 46-year-old man, who had diabetes and hypothyroidism, was found to have COVID-19. He had been receiving metformin, glimepiride, levethoxyroxine-sodium [thyroxine], amoxicillin/clavulanic-acid [co-amoxiclav], antiviral therapy with ivermectin, zinc, ascorbic-acid [vitamin C] and steroid therapy with methylprednisolone 16mg twice a day for 5 days. Subsequently, he presented to the hospital due to nasal blockage, yellowish discharge, right-side cheek swelling, right peri-orbital pain and headache. A CT scan showed right maxillary and right ethmoid, sphenoid and frontal sinusitis. Blood tests showed Hb 9.5, total leucocyte count 13 300 and platelet count 3 50 000. Thus, rhino-orbital mucormycosis was suspected and debridement was performed. Thereafter, a postoperative tissue smear showed broad aseptate hyphae. Based on these findings, rhino-orbital mucormycosis was confirmed secondary to the steroid therapy and antiviral therapy with ivermectin. Thus, treatment with unspecified antifungal medication was given and he was discharged alive.

Patient 2: The 33-year-old man, who had diabetes mellitus and dyslipidaemia, was found to have COVID-19. He had been receiving metformin, teneligliptin, glimepiride, azithromycin, antiviral therapy with favipiravir, remdesivir and ivermectin, zinc, pirilenidone, ascorbic-acid [vitamin C], oxygen therapy and steroid therapy with dexamethasone 6mg twice every day for 14 days, hydrocortisone 100 mg/day for 2 days and methylprednisolone 8 mg/day for 7 days. Subsequently, he presented to the hospital due to headache and right-side facial swelling. A CT scan showed at right maxillary and sphenoid sinusitis. Blood tests showed Hb 13.5, total leucocyte count 10 200 and platelet count 2 28 000. Thus, rhino-orbital mucormycosis was suspected and debridement was performed. Thereafter, a postoperative tissue smear showed broad aseptate hyphae. Based on these findings, rhino-orbital mucormycosis was confirmed secondary to the steroid therapy and antiviral therapy with remdesivir, favipiravir and ivermectin. Thus, treatment with unspecified antifungal medication was given and he was discharged alive.

Patient 3: The 40-year-old woman, who had diabetes mellitus, was found to have COVID-19. She had been receiving metformin, teneligliptin, glimepiride, azithromycin, antiviral therapy with ivermectin and zinc. Subsequently, she presented to the hospital due to pain in and swelling of right eye. A CT scan showed bilateral frontal ethmoid, sphenoid (right left) sinusitis and right-side optic neuritis. Blood tests showed Hb 10.5, total leucocyte count 11 230 and platelet count 3 30 000. Thus, rhino-orbital mucormycosis was suspected and debridement was performed. Thereafter, a postoperative tissue smear showed broad aseptate hyphae. She lost vision in the right eye. Based on these findings, rhino-orbital mucormycosis with an intracranial involvement and it was considered that the mucormycosis was secondary to antiviral therapy with ivermectin. Thus, treatment with unspecified antifungal medication was given and she was discharged alive.

Patient 4: The 47-year-old man, who had diabetes mellitus and hypertension, was found to have COVID-19. He had been receiving insulin-suspension-isophane/insulin [insulin; 30/70 pre-mix], amlodipine, steroid therapy with methylprednisolone 8mg twice a day for cough and dyspnoea, cefixime, ofloxacin, azithromycin, clarithromycin, antiviral therapy with ivermectin, zinc and ascorbic-acid [vitamin C]. The Methylprednisolone was tapered over a period of 8 days. Subsequently, he presented to the hospital due to pain and swelling in the right side of face. A CT scan showed right maxillary and right ethmoid, frontal and sphenoid sinusitis. Blood tests showed Hb 11.9, total leucocyte count 6 390 and platelet count 2 10 000. Thus, rhino-orbital mucormycosis was suspected and debridement was performed. A preoperative culture revealed Mucor sp., histopathological evaluation showed granulomatous inflammation and postoperative tissue smear showed broad aseptate hyphae. Based on these findings, mucormycosis was confirmed secondary to steroid therapy and antiviral therapy with ivermectin. He also had renal function abnormalities. Thus, treatment with unspecified antifungal medication was given and he was discharged alive.

Patient 5: The 65-year-old man, who had hypothyroidism, was found to have COVID-19. He had been receiving azithromycin, moxifloxacin, levofloxacin, doxycycline, meropenem, ascorbic-acid [vitamin C], zinc, fluconazole, oxygen therapy, antiviral therapy with favipiravir and steroid therapy with methylprednisolone 40mg thrice every day for 5 days. The methylprednisolone was tapered over a period of 20 days. Subsequently, he presented to the hospital due to swelling of both eyes and headache. A CT scan showed bilateral frontal, ethmoid, sphenoid and maxillary sinusitis. Blood tests showed Hb 9.6, total leucocyte count 68 000 and platelet count 4 80 000. Thus, rhino-orbital mucormycosis was suspected and debridement was performed. Thereafter, a postoperative tissue smear showed broad aseptate hyphae. Based on these findings, rhino-orbital mucormycosis was confirmed secondary to the steroid therapy and antiviral therapy with favipiravir. Thus, treatment with unspecified antifungal medication was given and he was discharged alive.

Patient 6: The 53-year-old woman, who had diabetes mellitus and hypertension, was found to have COVID-19. She had been receiving metformin, warfarin, telmisartan, cepodoxime, ceftriaxone, antiviral therapy with favipiravir, ascorbic-acid [vitamin C], steroid therapy with dexamethasone 6mg twice a day for 12 days as an off-label use for COVID-19 and oxygen therapy. Subsequently, she presented to the hospital due to facial pain and swelling. A CT scan showed right-sided maxillary, sphenoid and ethmoid sinusitis. Blood tests showed Hb 8, total leucocyte count 3 200 and platelets count 2 07 000. Thus, rhino-orbital mucormycosis was suspected and debridement was performed. Thereafter, a postoperative tissue smear showed broad aseptate hyphae. Based on these findings, mucormycosis was confirmed secondary to the steroid therapy and antiviral therapy with ivermectin. Thus, treatment with unspecified antifungal medication was given and he was discharged alive.

Patient 7: The 62-year-old man, who had diabetes mellitus and hypertension, was found to have COVID-19. He had been receiving amlostidine, telmisartan, antiviral therapy with ivermectin and steroid therapy with dexamethasone 6 mg/day for 12 days and methylprednisolone 125 mg/day for 2 days, meropenem, zinc, itraconazole, ascorbic-acid [vitamin C] and oxygen therapy. Subsequently, he presented to the hospital due to left-side facial swelling and purulent discharge from left eye. A CT scan showed left maxillary, frontal, ethmoid sinusitis and mild erosion of left lamina papryacea. Blood tests showed Hb 13, total leucocyte count 14 600 and platelet count 1 74 000. Thus, rhino-orbital mucormycosis was suspected and debridement was performed. A preoperative and postoperative examination showed broad, aseptate hyphae and histopathology was suggestive of mucormycosis. Based on these findings, mucormycosis was confirmed and secondary to the steroid therapy and antiviral therapy with ivermectin. Thus, treatment with unspecified antifungal medication was given and he was discharged alive.

Patient 8: The 58-year-old man, who had diabetes mellitus, was found to have COVID-19. He had been receiving azithromycin,
doxycycline, Withania somnifera [ashwagandha; indication not stated], antiviral therapy with ivermectin and steroid therapy with dexamethasone 4 mg/day for 5 days. Subsequently, he presented to the hospital due to vomiting, headache, right eye pain and delirium. A CT scan showed right maxillary, sphenoid and bilateral ethmoid sinusitis and acute infarction in the right frontoparietal lobe. Blood tests showed Hb 14, total leucocyte count 8 670 and platelet count 2 43 000. Thus, rhino-orbital mucormycosis was suspected and debridement was performed. A post-operative examination showed broad, aseptate hyphae. Based on these findings, mucormycosis was confirmed secondary to the steroid therapy and antiviral therapy with ivermectin. Thus, treatment with unspecified antifungal medication was given and he was discharged alive.

Patient 9: The 40-year-old man, who had diabetes mellitus, was found to have COVID-19. He had been receiving gentamicin, linezolid, meropenem and steroid therapy with dexamethasone 8 mg/day for 10 days. Subsequently, he presented to the hospital due to headache and facial swelling and pain. A CT scan showed bilateral ethmoid, maxillary and sphenoid sinusitis with extensive orbital and intracranial involvement. Blood tests showed Hb 13, total leucocyte count 14 700 and platelet count 3 000 000. Thus, rhino-orbital mucormycosis was suspected and debridement was performed. A post-operative examination showed broad, aseptate hyphae. Based on these findings, mucormycosis was confirmed secondary to the steroid therapy. Thus, treatment with unspecified antifungal medication was given and he was discharged alive.

Patient 10: The 60-year-old man, who had diabetes mellitus and hypertension, was found to have COVID-19. He had been receiving metformin, telmisartan, glimepiride, doxycycline, azithromycin, cefuroxime, vitamin D, zinc, ascorbic-acid [vitamin C], oxygen therapy, steroid therapy with prednisolone 30 mg/day as an off label use for COVID-19 and antiviral therapy with ivermectin. Subsequently, he presented to the hospital due to right facial pain and swelling. A CT scan showed right-sided frontal and ethmoidal sinusitis and soft tissue oedema in right-side periorbital region. Blood tests showed Hb 10.2, total leucocyte count 10 600 and platelet count 2 26 000. Thus, rhino-orbital mucormycosis was suspected and debridement was performed. A post-operative examination showed broad, aseptate hyphae. Based on these findings, mucormycosis was confirmed secondary to the antiviral therapy with ivermectin and steroid therapy. Thus, treatment with unspecified antifungal medication was given. However, he died after 76 days.

Patient 11: The 65-year-old man, who had diabetes mellitus, hypertension and coronary artery disease, was found to have COVID-19. He had been receiving cilnidipine, clopidogrel, rosuvastatin, isosorbide dinitrate, tamsulosin, dutasteride, ascorbic-acid [vitamin C], antiviral therapy with ivermectin, amoxicillin/clavulanic-acid [co-amoxiclav], cefuroxime and steroid therapy with dexamethasone 2mg three times a day for 5 days. He had received one dose of BBV-152 [COVAXIN]. Subsequently, he presented to the hospital due to headache, facial pain and eye discharge. A CT scan showed bilateral maxillary, sphenoid and ethmoid sinusitis with right orbital cellulitis. Blood tests showed Hb 10.8, total leucocyte count 51 400 and platelet count 1 85 000. Thus, rhino-orbital mucormycosis was suspected and debridement was performed. A post-operative examination showed fragmented hyphae. Based on these findings, mucormycosis was confirmed secondary to the antiviral therapy with ivermectin and steroid therapy. Thus, treatment with unspecified antifungal medication was given and he was discharged alive.

Patient 12: The 42-year-old man, who had diabetes mellitus, was found to have COVID-19. He had been receiving insulin, piperacillin/tazobactam, zinc, cefuroxime, ascorbic-acid [vitamin C] and steroid therapy with prednisolone 40 mg/day for 5 days and methylprednisolone 8mg three times a day for 5 days followed by methylprednisolone 16 mg/day for 5 days. Subsequently, he presented to the hospital due to facial swelling and pain and swelling of right eye. A CT scan showed right maxillary, ethmoid and sphenoid sinusitis with right eye involvement. Blood tests showed Hb 9.2, total leucocyte count 7 060 and platelet count 1 90 000. Thus, rhino-orbital mucormycosis was suspected and debridement was performed. A post-operative examination showed broad, aseptate hyphae. Based on these findings, mucormycosis was confirmed secondary to the antiviral therapy with ivermectin and steroid therapy. Thus, treatment with unspecified antifungal medication was given and he was discharged alive.

Patient 13: The 58-year-old woman, who had diabetes mellitus, was found to have COVID-19. She had been receiving azithromycin, doxycycline, antiviral therapy with ivermectin, ascorbic-acid [vitamin C], zinc, steroid therapy with dexamethasone 8 mg/day for 5 days as an off-label use for COVID-19 and oxygen therapy. She had received AZD-1222 [Covishield]. Subsequently, she presented to the hospital due to swelling of left eye and left-side of the face. A CT scan showed left maxillary, ethmoid sinusitis and left-sided orbital cellulitis with possible cavernous sinus thrombosis. Blood tests showed Hb 7.7, total leucocyte count 16 030 and platelet count 2 78 000. Thus, rhino-orbital mucormycosis was suspected and debridement was performed. Her preoperative smear showed broad, aseptate hyphae. Based on these findings, mucormycosis was confirmed secondary to the steroid therapy and antiviral therapy with ivermectin. Thus, treatment with unspecified antifungal medication was given. However, she died after 64 days [cause of death not stated].

Aggarwal SK, et al. Case Report. Rhino-orbital Mucormycosis Related to COVID-19: A Case Series Exploring Risk Factors. American Journal of Tropical Medicine and Hygiene 106: 566-570, No. 2, 2022. Available from: URL: http://doi.org/10.4269/ajtmh.21-0777