Aggressive Coccidioidomycosis following Glucocorticoid Therapy: 2 patients

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Introduction

Glucocorticoids have been historically utilized for immune system modulation. Nonetheless, cell-mediated immunity is required for the control of CM infection. Patients undergoing immunosuppressive therapy have a high risk of severe primary pulmonary infection, disseminated, or reactivated infection. In regions endemic to CM, there are no established guidelines for CM screening prior to initiating immunosuppressive therapy.

Case summaries

A 49-year-old male patient with no significant past medical history received dexamethasone as part of his treatment for SARS-CoV-2 infection. Less than 3 weeks later, the patient developed acute respiratory distress syndrome. Radiological and serological testing led to a diagnosis of acute hypoxic miliary CM.

A 52-year-old male with a past medical history of chronic kidney disease (CKD) was treated with prednisone for focal segmental glomerulosclerosis (FSGS). Within 2 weeks, this patient developed bilateral lower extremity weakness. Radiology, serology, and lumbar puncture proved a diagnosis of reactivated CM with miliary pattern and CM meningoencephalitis with arachnoiditis. Whether treatment with glucocorticoids caused reactivation of CM is discussed in this case series.

Case 1 Presentation

The first patient is a 49-year-old Latinx male field worker with tobacco and alcohol abuse. He was in his usual state of health until he developed a nonproductive cough. He tested positive for SARS-CoV-2 by ABBOT COVID-19 testing at an urgent care facility. He presented to the Kern Medical ED one day later. CXR revealed bibasilar infiltrates. The patient was deemed stable, with SpO2 96% and was discharged on supportive management.

The patient re-presented six days later with increased cough and shortness of breath with subjective fevers. Vital signs revealed HR 112, RR 36, and SpO2 90%, and the patient was admitted. CXR demonstrated increased infiltrates. He was treated with nasal oxygen, convalescent plasma, and dexamethasone 6mg daily for 10 days. His oxygenation improved, and he was discharged on hospital day five to finish dexamethasone 6mg daily and on 2L of nasal oxygen.

Subsequent to discharge, the patient completed dexamethasone and improved. Eighteen days after discharge he re-presented with two days of increasing cough, shortness of breath, subjective fevers, and night sweats. His vital signs included HR 135 bpm, RR 24 breaths per minute, and SpO2 89% on 2L of oxygen via nasal cannula. Physical examination revealed labored breathing, decreased bronchovesicular breath sounds in the right lower lobe, and wheezes and crackles in the left lung base. Integumentary examination revealed six new 4mm lesions, including two erythematous macules, two verrucous papules, and two nodules with eschars.

CXR revealed bilateral miliary nodules. CT of the chest with contrast confirmed this and demonstrated right middle lobe consolidation with central cavitation. Serum coccidioidomycosis (CM) serology revealed immunodiffusion IgM reactive, immunodiffusion IgG reactive, and complement fixation (CF) 1:16. Sputum culture grew *Coccidioides immitis*. The patient was diagnosed with acute hypoxic miliary CM. Treatment was initiated with AmBisome 5 mg/kg IV daily and IV methylprednisolone tapered over 21 days.

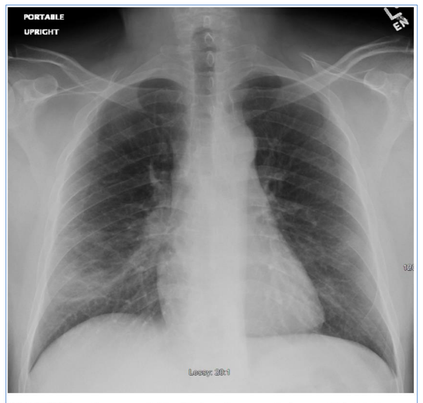
Despite a turbulent hospital course, vigorous treatment resulted in a hospital discharge with continued outpatient care for disseminated CM.

Case 2 Presentation

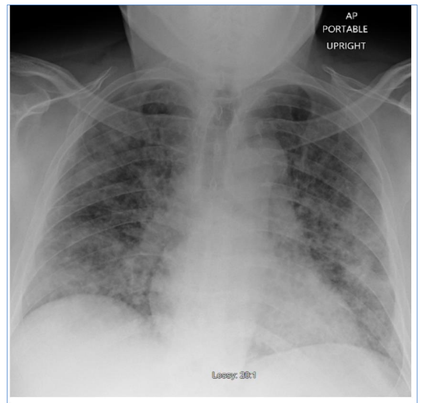
The second patient is a 52-year-old Latinx man with diabetes mellitus type II. He was found to have chronic kidney disease and kidney biopsy demonstrated FSGS. Subsequently, nephrology initiated prednisone 60mg daily.

Ten days after initiation of treatment, the patient presented to the Kern Medical ED for progressive bilateral lower extremity weakness. Physical exam revealed paraplegia and the patient was admitted. MRI of the axial skeleton without contrast revealed leptomeningeal enhancement of the thoracic, lumbar, and sacral spine.

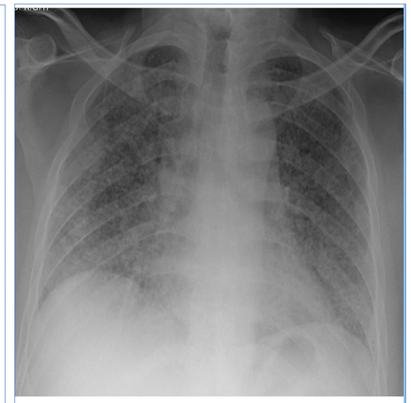
Case 1 Imaging & Integumentary Physical Exam Findings



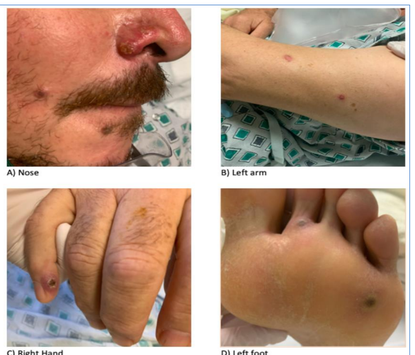
CXR 12/19/2020 revealing segmental right mid to lower lung zone and subsegmental left mid to lower lung zone airspace disease.



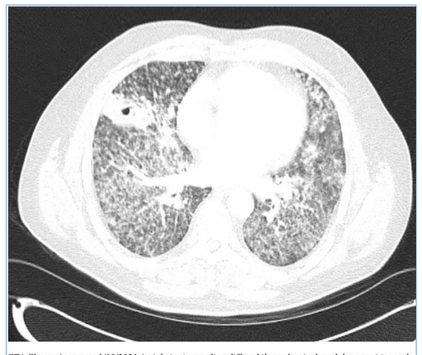
CXR 12/20/2020 revealing diffuse ground glass infiltrates, may represent Covid, with usual differential consideration.



CXR 12/25/2020 revealing atypical/viral pneumonia.

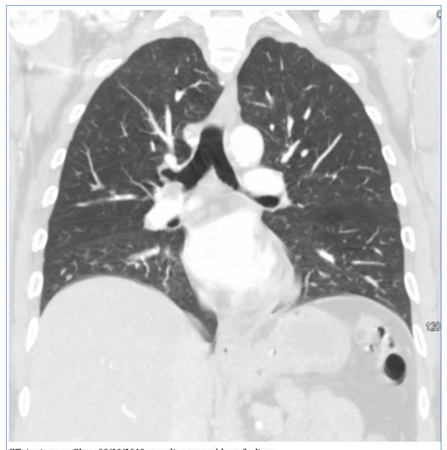


(A) Papule with eschar. B) Two erythematous macules. C) Papule with eschar. D) Two verrucous papules.

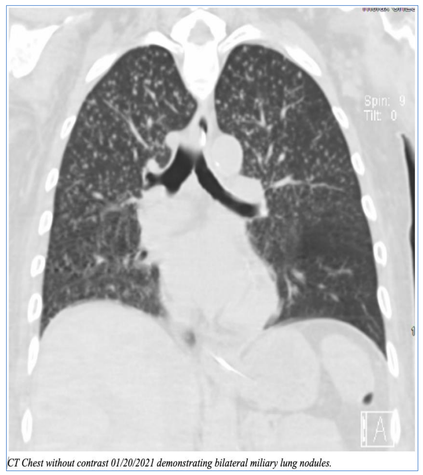


CTA Chest w/ contrast 1/18/2021 (axial view) revealing diffuse bilateral reticulonodular opacities and right middle lobe consolidation with central cavitation.

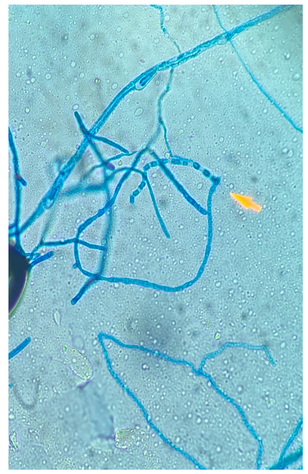
Case 2 Imaging & Microbiology



CT Angiogram Chest 08/30/2019 revealing normal lung findings.



CT Chest without contrast 01/20/2021 demonstrating bilateral miliary lung nodules.



Case 2 Presentation Cont.

The patient developed fevers to 39°C, nuchal rigidity, and disorientation (not alert, nor oriented to person, place, or time). MRI of the brain without contrast demonstrated punctate foci in the bilateral mesial temporal lobes, peripheral right cerebellar hemisphere, and left midbrain cerebral peduncle. Interventional-radiology-guided lumbar puncture revealed an opening pressure of 17 mmH20 (normal 8-15), xanthochromia, WBC 665 cells (normal 0-5), Neutrophils 96%, Lymphocytes 1%, glucose 2 mg/dL (normal 50-80), and protein 242 mg/dL (normal 15-45). CSF CM titers were immunodiffusion IgM non-reactive, immunodiffusion IgG reactive, and CF 1:8. CSF fungal culture grew *C. immitis*.

Pulmonary imaging was compared to prior CXR and CT with angiogram of the chest. CXR demonstrated new diffuse nodular densities throughout both lungs. CT chest without contrast demonstrated bilateral miliary nodules. Serum CM serology revealed immunodiffusion IgM reactive, immunodiffusion IgG reactive, and CF antibodies (1:64).

The patient was diagnosed with reactivated CM with miliary pattern and CM meningoencephalitis with arachnoiditis, resulting in his chief complaint of bilateral lower extremity weakness. Empiric treatment was initiated with fluconazole 1,000 mg intravenous daily, AmBisome 5mg/kg IV daily, along with dexamethasone for 15 days.

After a 42-day tempestuous hospital course, the patient was unable to be weaned off of mechanical ventilation and he suffered a neurological death.

Discussion & Conclusion

CM causes asymptomatic disease in the majority of patients, yet it often leaves behind an immunological footprint. Serological testing has allowed for CM detection in nearly all affected individuals. CM serology is a staple laboratory order for symptomatic disease in endemic areas; yet asymptomatic patients are rarely screened. A challenge arises: when should asymptomatic screening be a requisite?

Glucocorticoids are a double-edged sword. In high doses, they demonstrate a broad spectrum of immune suppression. This may advantage patients with an excessive immune response. Moreover, they may contribute to the treatment of acute, severe CM. However, immune suppression unopposed by antifungal therapy may lead to severe reactivation of CM.

In our patients, glucocorticoids were part of the treatment for SARS-CoV-2 and FSGS. However, lack of initial CM screening followed by glucocorticoid use - led to acute hypoxic miliary CM in one patient and miliary CM with meningoencephalitis and arachnoiditis in the other. We believe these cases of miliary CM are due to immunosuppression short of antifungal treatment. Therefore, we share this presentation with the scientific community, to urge screening of all patients in endemic regions for CM prior to immunosuppressive treatment initiation.

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