CLINICAL VIGNETTE

Cough and Confusion, A Case of Coccidioidal Meningitis

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A 69-year-old male with hypertension, hyperlipidemia, and pre-diabetes presented for a Medicare Annual Wellness visit. He also complained of upper respiratory symptoms that started about 10 days prior to his visit. Symptoms included arthralgias, loss of appetite, loose stools, and lingering cough. He had a telemedicine visit with another provider the prior week, with negative COVID PCR testing. Vitals: BP 140/79 | Pulse 99 | Temp (!) 38.4 °C (101.1 °F) (Tympanic) | Ht 5' 4.76" (1.645 m) | Wt 176 lb (79.8 kg) | SpO2 95% | BMI 29.50 kg/m² General: NAD, A+OX3, pleasant; HEENT: PERRL, EOMI, TM clear; Neck: no thyromegaly, no lymphadenopathy, supple; Lungs: scattered wheezing on expiration, coughing, normal respiratory effort; Cardio: borderline tachycardic, no murmurs/gallops/rubs; Neuro: no sensory/motor/cerebellar deficits. Normal gait. Remainder of the exam was unremarkable.

He was started on azithromycin 500mg daily for 5 days. He continued to have fever and cough despite antibiotics, and on the fourth day was seen again via telemedicine for further evaluation of ongoing symptoms. Blood work was ordered including CBC, CMP, CRP, and chest x ray (CXR). Notable results were white blood cell count of 13.27 and CXR showing *focal opacification in the left mid and inferior lung, likely corresponding to the left upper lobe with diffuse interstitial prominence, concerning for pneumonia.* He continued to have fevers to 102°F and night sweats, along with dry persistent cough for three more days and presented to the emergency room and was admitted. Pulmonary coccidioidomycosis was diagnosed after serologies returned positive. Chest CT and CXR showed *LUL consolidation with central cavitation as well and centrilobular scattered nodular densities.* He was initially started on ceftriaxone/ azithromycin antibiotics and switched to fluconazole 600mg daily which continued upon home discharged. His cough improved, fever resolved and energy and appetite returned. He remained in close follow up with infectious disease and pulmonary specialty for six months, while taking daily fluconazole and steroid inhaler.

After about seven months of treatment, he stopped taking fluconazole and relapsed after nine days with cough, fever, and new headache. He restarted on fluconazole, but continued to develop worsening headache over the following two months. Lumbar puncture, with serologies indicated coccidioidal meningitis. Fluconazole was increased to 1000mg daily, and Infectious Disease monitored his cocci serum CF and symptoms. His symptoms remained stable with mild cough, but no further headache. However, the CF level remained elevated and medication was changed to voriconazole and titrated up to therapeutic trough. He remained stable for ten months with monthly follow up with infectious diseases and pulmonary. Unfortunately, his daughter reported that he missed five or more days of medication and presented to the office with altered mental status – sleeping all the time, displaying unusual behaviors in the last few days with vomiting and headache the prior night. He was admitted to hospital and found to have hydrocephalus likely secondary to coccidioidomycosis meningitis. A right parieto-occipital V-P shunt was placed, antifungal medication continued and was transferred to inpatient rehab and subsequently home. His symptoms improved somewhat over a month, however then he developed worsening gait instability and nausea. He was admitted for further management but unfortunately developed progressive worsened altered mental status, atrial fibrillation and hypotension. He developed progressive hypoxic respiratory failure and shock, requiring intubation and attempted management on four vasopressors in the ICU. Ultimately a decision was made by the family to transition to comfort care.

Discussion

Coccidioidomycosis is acquired by inhaling spores of the fungi *Coccidioides immitis* and *C. posadasii* that are present in soil and can become airborne in dust, which can travel downwind. Epidemics have occurred after heavy rains, promoting growth of mycelia, are followed by drought and winds. Once inhaled the spores convert to large tissue-invasive spherules, which can enlarge and subsequently rupture, releasing thousands of small endospores, which then form more spherules. Most patients with primary coccidioidomycosis are asymptomatic, but non-specific respiratory symptoms resembling influenza, acute bronchitis, or acute pneumonia or pleural effusion sometimes occur. Pulmonary disease can be acute, subacute, or chronic granulomatous reactions with varying extent of fibrosis. Lesions may cavitate or form coin-like lesions.[1] Progressive symptoms are uncommon in otherwise healthy people, but can extend to widespread lung involvement and systemic dissemination. Focal lesions may form in any tissue, most commonly in skin, subcutaneous tissues, bones, joints, and meninges. Endemic areas in North America are Southwest US and Northern Mexico. Affected areas of the southwestern US include: Arizona, central valley California, part of New Mexico, and Texas west of El Paso. Because of travel and delayed onset of clinical symptoms for weeks, months, or occasionally years

after primary infection, disease can become evident outside endemic areas.

The most impactful extrapulmonary dissemination is the spread of Coccidioides spp. to the central nervous system causing meningitis. When left untreated CM is uniformly fatal. Fatality rates have improved with the use of antifungals and amphotericin B, but morbidity is still substantial due to complications from the disease, devices used for treatment management, and side effects of medications, as much higher recommended doses are necessary for prolonged period of time.[2] Common life-threatening complications of meningitis include hydrocephalus, CNS vasculitis, cerebral ischemia, infarction, vasospasm and hemorrhage. Patients with hydrocephalus, need a ventricular shunt for decompression. Subsequently, shunt complications can occur, including secondary infection, obstruction due to persistent coccidioidomycosis, and/or abdominal pseudocysts.

The disease is only suppressed in patients with coccidioidal meningitis who achieve remission while receiving azole therapy. Most clinicians prefer oral therapy with fluconazole. With fluconazole treatment symptoms resolve within 4-8 months. Based on clinical experience and due to extremely high relapse rates up to 78% reported in small series when therapy is discontinued, lifelong treatment with azoles is warranted.[3] Adherence counseling, assessment of drug-drug interactions, therapeutic drug monitoring, and consideration of alternative antifungal therapy is of utmost importance.

REFERENCES

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