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CLINICAL VIGNETTE

Rare Case of Disseminated Coccidiomycosis with Septic Arthritis and Empyema

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A 62-year-old male with poorly controlled DMII presented with two months of progressively worsening subacute left knee pain. He initially presented to local emergency departments in the San Joaquin Valley of California. He reported several unsuccessful arthrocentesis attempts at different ED's. His symptoms fluctuated and he relocated to Los Angeles to live with his daughters. When his knee pain worsened he presented to the Emergency Department at Olive View and was admitted.

On admission he complained of both progressively worsening subacute left knee pain and a painful left wrist nodule that had been present for more than a year. A purulent discharge was noted from the wrist. Review of systems was notable for a dry cough and worsening respiratory complaints for three weeks prior to admission. Successful arthrocentesis of the left knee revealed a purulent, orange fluid with 31,050 RBCs/mm^3, 216,000 cells with 98% neutrophils. He was taken to the OR for joint washout. Joint fluid cultures were positive for both Coccidioides immitis and Coccidioides posadasii. Serologies were positive for IgG Cocci, negative for IgM Cocci, other serologies were negative (QFG, legionella, histoplasma, and aspergillus). Because of dissemination to the knee, lumbar puncture was performed with CNS studies negative for white cells or infection (CSF EIA negative). CXR and Chest CT revealed a bronchopleural fistula and consolidations concerning for empyema. The patient underwent video assisted thoracoscopic surgery (VATS) decortication with placement of three chest tubes. Green purulent fluid was drained with 6.69, 915,000 PMNs, 66% neutrophils, glucose 139, LDH >8100, protein >36, triglycerides 46, +pus and positive gram stain (Strep viridans) and positive cocci cultures. During his hospitalization he was initially started on broad spectrum parenteral Vancomycin and piperacillian/tazobactam. These were changed to parenteral ampicillin/sulbactam and oral fluconazole for the remainder of the hospitalization. He was hospitalized for 25 days before discharge on oral amoxicillin /clavulanate and fluconazole 800 mg/day, with ID, Ortho and General Surgery follow up.

Several weeks post-discharge the patient returned to the ED with two weeks of increasing redness and drainage from the left wrist. The wrist lesion was incised and drained (I&D), and a wrist splint was placed. Review of final biopsy results from the prior admission revealed cutaneous cocci. He was maintained on daily fluconazole 800mg. At his one week ID follow up there was increase in redness, drainage and tenderness of the site. Wrist XR demonstrated osteomyelitis (OM) of the distal left radius, which was confirmed with MRI. He was readmitted for bone debridement and I&D of the radial abscess. Wound cultures were positive for MSSA, with negative fungal cultures. He was eventually discharged on a six week course of cefazolin via PICC line, with a left wrist splint and wound packing.

Discussion

Coccidiomycosis is most commonly a local pulmonary disease without extrapulmonary disseminated features. To date, few reports have described extrapulmonary disseminated cocci cases, especially to the joints.

Coccidiomycosis, otherwise known as Valley Fever or San Joaquin Valley Fever, is a dimorphic fungus found predominantly in the southwestern region of the United States. There are two species that are most common: *Coccidiomycosis posadasii*, found in Arizona, Texas and Central and South America, and *Coccidiomycosis immitis*, found in California.[1] More than 70% of cases occur in Arizona, and over 25% occur in California.[2,3] In 2011, more than 20,000 cases of cocci were reported, twice as many as tuberculosis.[2,3] More than 40% of Valley Fever cocci cases require hospitalization and cost an average of $50,000.[2,3] Of these cases, 4.7% generally have extrapulmonary symptoms. According to a medical chart review by the Arizona Department of Health Services (DHS), there were 8% with evidence of clinical and/or laboratory infection beyond the lungs.[4] The mechanism of spread is via the inhalation of spores, leading to hilar adenopathy. It is thought that the hilar adenopathy is secondary to coccidioidal pneumonia spreading into the paratracheal and supraclavicular lymph nodes, which then drain through the lymphatic system into the IVC, and subsequent hematogenous spread throughout the body.

The typical clinical presentation is of a patient presenting with a "flu-like" illness, particularly nonspecific respiratory symptoms. However, disseminated cocci may present with skin/ subcutaneous soft tissue, meningeal, spinal cord, and even

skeletal manifestations. It less commonly disseminates to the eye, liver, peritoneal cavity, monoarticular joints and various other locations.[5-8] Diagnosis can be made with visualization of spherules in histopathology specimens or by culture of a suspicious lesion. In situations where a biopsy is too difficult or unsafe checking antibody titers and correlating to the destructive lesion.[9-12] The diagnostic workup for disseminated extrapulmonary cocci includes Magnetic Resonance Image (MRI) and Lumbar Puncture (LP) for meningeal and spinal cord involvement; CT scan for suspected pulmonary empyemas, CSF and blood cocci antibodies, fungal blood cultures, and tissue culture of a suspected lesion. Disseminated cocci can be treated with fluconazole (400 mg PO daily) or itraconazole (200 mg PO BID). Treatment duration should be for the patient's lifetime for systemic dissemination, especially to the meninges or spinal cord, as relapses are common and potentially fatal. If a patient does not respond to oral therapy, intrathecal amphotericin B should be considered.[9]

In 1998 Acree et al published a case of disseminated cocci. This was diagnosed with serologies, fungal cultures and histology.[13] In 2016, a case of tenosynovitis was reported with an atypical presentation of C. immitis peroneal tenosynovitis, initially treated with high dose of fluconazole followed by usual 400mg oral dose of fluconazole for four weeks.[14] A 26 year single institution review identified nine cases of coccidioidal tenosynovitis. There was a high overall relapse rate of 50% with 71% relapse in patients who discontinued antifungal treatment.[15]

In our case, the patient had already been evaluated for his knee pain at an outside hospital, and as no records were available to us, we considered common and uncommon pathogens that potentially were not treated with standard antibiotics. A thorough medical history was obtained, including personal, travel and occupational history. This patient was a farm worker in the San Joaquin Valley. The gold standard diagnostic workup was initiated which included an arthrocentesis.

A comprehensive physical exam raised suspicion for a septic knee (confirmed by arthrocentesis), and also identified a left wrist nodule. During the initial hospitalization, imaging or biopsy of the left wrist nodule was not pursued as our priority was treating the empyema and septic joint. The readmission may have been prevented if a wrist XR or needle aspiration of the left wrist nodule was performed. This could have resulted in earlier identification of an underlying osteomyelitis and earlier debridement of the site.

Conclusion

There are multiple learning points in this case of disseminated coccidiomycosis. First, in any admission, consider previous hospitalizations and obtain any relevent records. Also, consider past successful or unsuccessful treatments of the current disease, as well as potential barriers to treatment, such as medication non-adherence. Lastly, critical in this case, always consider the patient's personal, environmental and occupational factors. Consider atypical infections, particularly in immunocompromised patients living in locations where atypical infections are more common.

Where localized cocci is suspected, be sure to focus the history and physical exam to rule out disseminated cocci. Omitting imaging of our patient's wrist nodule may have contributed to his readmission. To our knowledge, this is one of the few cases in which a patient presented with disseminated cocci manifested by a septic joint, empyema and osteomyelitis of the wrist.

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