CLINICAL VIGNETTE

A Curious Case of Cutaneous Coccidioidomycosis

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Case

A 50-year-old Mandarin speaking female gardener with no significant past medical history presented for an office visit with a lump on her collar bone for 3-4 days along with facial rash. She reported having a URI 2 months prior with fever, cough, myalgias, which resolved after a few days. Denied B symptoms, including pain, fevers/chills, SOB, cough.

On physical exam, her vitals were normal and appeared well. A one cm soft, mobile nodule in the right supraclavicular region. Skin was remarkable for a less than 1 cm right cheek papule with acneiform. The remainder of her exam was unremarkable.

She was started on Tretinoin cream for possible acne and an ultrasound was ordered to evaluate the supraclavicular nodule. Ultrasound showed a morphologically normal lymph node measuring subcentimeter in short axis, likely benign/reactive. Given the high-risk location of the supracervical lymph node a CT chest/abdomen/pelvis was ordered. Screening mammogram was updated, which showed calcifications in the right breast. She ultimately had a core needle biopsy, which was negative for malignancy.

Her facial rash worsened over the next 1-2 weeks and began to secrete purulent discharge. She was seen by another PCP who started treatment with Doxycycline for possible folliculitis. Rash continued to progress and she was evaluated by an outside teledoc who prescribed TMP/SMX and Valacyclovir 500 mg TID for presumed shingles. The rash worsened and the patient was evaluated by dermatology two weeks after initial presentation. They noted papules and pustules some with scabbing coalescing on the right cheek on exam. Swabs for HSV, VZV and a bacterial culture were performed, which were all negative but did note mold on the culture. At dermatology follow up she was started on Minocycline and a punch biopsy was performed which showed ulcerated skin with underlying acute/chronic and granulomatous inflammation with a spherule identified within a granuloma that was PAS+. This was ultimately diagnosed as cutaneous coccidioides immitis, and started on Fluconazole 400 mg daily was added QD, and referred to Infectious Disease. ID checked Cocci Complement Fixation titers, which was elevated to 1:64 and increased Fluconazole to 800 mg QD and stopped minocycline. Clinically, her facial lesion ultimately scabbed over and resolved and cocci CF titers declined to 1:4.

CT chest/abdomen/pelvis to evaluate supraclavicular lymphadenopathy to show prominent nodule in the superior segment of right lower lobe with surrounding peribronchial thickening and satellite nodules with associated regional lymphadenopathy with consideration for infectious granuloma with reactive adenopathy. CT abdomen was unremarkable. Repeat CT chest performed 6 months later showed no change in the right lower lobe nodular consolidations with peripheral satellite nodules reflecting sequela of reported cocci infection. The supraclavicular lymphadenopathy was attributed to disseminated coccidioides immitis infection, and resolved with treatment.

Discussion

Coccidioidomycosis is a fungal infection caused by coccidioides posadasii and immitis. The latter is endemic to Southern California.[1] Transmission usually occurs via inhalation of the spores, also known as arthroconidia, from disturbed soil. Once inside the lung tissue, the spores transform into spherules and release endospores causing an inflammatory response that produces the systemic features of the disease. Clinical disease manifests 1-3 weeks after exposure and usually causes a self-limited, acute to subacute pneumonia, which is thought to represent approximately 17-29% of all cases of community acquired pneumonia.[2]

Disseminated disease develops in less than 5% of clinically affected individuals with a risk estimated from 0.2-4.7% , during an endemic.[3] Dissemination is defined by coccidioidal infection that is clinically apparent outside the thoracic cavity. Sites of infection include: soft tissue with cutaneous granulomatous lesions, abscesses, supraclavicular adenopathy; bone/joint with monoarticular infectious arthritis, vertebral body osteomyelitis without involvement of the end plate or adjacent disk space, meningitis, and other less frequent sites including endocrine glands, eye, liver, kidney, genitals, prostate, and peritoneal cavity. Immune-mediated, transient cutaneous rashes described as toxic erythema, erythema nodosum, and erythema multiforme can occur in up to 10-50% of patients with primary pulmonary coccidioidomycosis. The development of erythema nodosum and erythema multiforme are positive predictors of a favorable response.[4]

Diagnosis of disseminated disease is confirmed by the presence of Coccidiodes in one or more extrathoracic sites. Diagnosis can be further supported by complement fixing antibody titers of 1:16 or greater, coccidioidal antigen urine/blood/CSF assay, and PCR.[5] Other associated laboratory findings can include

mild leukocytosis, eosinophilia, and/or elevated ESR. Chest imaging findings can include unilateral pulmonary infiltrates, commonly affecting upper lobes with ipsilateral hilar lymphadenopathy, mediastinal lymphadenopathy, pleural effusion, pulmonary nodules, or thin-walled pulmonary cavities.[6]

In contrast to primary pulmonary coccidioidomycosis, disseminated disease should always be treated with antifungal therapy due to risk of developing more severe infection. Treatment with oral azoles, particularly fluconazole or itraconazole, is recommended as a first line therapy for extrapulmonary soft tissue, bone/joint, and meningeal Coccidioidomycosis consistent with 2016 IDSA guidelines.[7] Fluconazole is dosed at 400-800 mg once daily for soft tissue infection and 800 mg once daily for bone/joint infection. Itraconazole is 200 mg twice daily for both soft tissue and bone/joint infections. IV Amphotericin B is reserved for pregnant women during their first trimester with non-meningeal Coccidioidomycosis with intrathecal Amphotericin B for meningeal Coccidioidomycosis and patients with severe osseous infection with surgical consultation recommended for vertebral involvement. The recommended duration of treatment with antifungal therapy is at least 6-12 months due to high relapse rates ranging from 60% after 45 days of treatment to 11% after 12 months.[8] Patients should be monitored with Coccidioides Complement Fixation Titers every 12 weeks while on therapy and for at least 1 year after discontinuation of antifungal therapy. Hepatic function should be monitored periodically due to risk of hepatotoxicity with azoles.

REFERENCES

1. **Galgiani JN, Ampel NM, Blair JE, Catanzaro A, Johnson RH, Stevens DA, Williams PL; Infectious Diseases Society of America**. Coccidioidomycosis. *Clin Infect Dis*. 2005 Nov 1;41(9):1217-23. doi: 10.1086/496991. Epub 2005 Sep 20. PMID: 16206093.
2. **Herrick KR, Trondle ME, Febles TT**. Coccidioidomycosis (Valley Fever) in Primary Care. *Am Fam Physician*. 2020 Feb 15;101(4):221-228. PMID: 32053327.
3. **Welsh O, Vera-Cabrera L, Rendon A, Gonzalez G, Bonifaz A.** Coccidioidomycosis. *Clin Dermatol*. 2012 Nov-Dec;30(6):573-91. doi: 10.1016/j.clindermatol.2012.01.003. PMID: 23068145.
4. **Crum NF, Lederman ER, Stafford CM, Parrish JS, Wallace MR**. Coccidioidomycosis: a descriptive survey of a reemerging disease. Clinical characteristics and current controversies. *Medicine (Baltimore)*. 2004 May;83(3):149-175. doi: 10.1097/01.md.0000126762.91040.fd. PMID: 15118543.
5. **Binnicker MJ, Buckwalter SP, Eisberner JJ, Stewart RA, McCullough AE, Wohlfiel SL, Wengenack NL**. Detection of Coccidioides species in clinical specimens by real-time PCR. *J Clin Microbiol*. 2007 Jan;45(1):173-8. doi: 10.1128/JCM.01776-06. Epub 2006 Nov 15. PMID: 17108077; PMCID: PMC1828991.
6. **Merchant M, Romero AO, Libke RD, Joseph J**. Pleural effusion in hospitalized patients with Coccidioidomycosis. *Respir Med*. 2008 Apr;102(4):537-40. doi: 10.1016/j.rmed.2007.11.014. Epub 2007 Dec 31. PMID: 18164951.
7. **Galgiani JN, Ampel NM, Blair JE, Catanzaro A, Geertsma F, Hoover SE, Johnson RH, Kusne S, Lisse J, MacDonald JD, Meyerson SL, Raksin PB, Siever J, Stevens DA, Sunenshine R, Theodore N**. 2016 Infectious Diseases Society of America (IDSA) Clinical Practice Guideline for the Treatment of Coccidioidomycosis. *Clin Infect Dis*. 2016 Sep 15;63(6):e112-46. doi: 10.1093/cid/ciw360. Epub 2016 Jul 27. PMID: 27470238.
8. **Blair JE**. State-of-the-art treatment of coccidioidomycosis: skin and soft-tissue infections. *Ann N Y Acad Sci*. 2007 Sep;1111:411-21. doi: 10.1196/annals.1406.010. Epub 2007 Mar 1. PMID: 17332079.