386. A Reexamination of Disseminated Coccidioidomycosis: The Natural History in the Pre-Antifungal Era

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Background. While it has been previously well described that central nervous system (CNS) coccidioidomycosis (CM) is nearly always fatal without treatment, the natural history of non-CNS disseminated coccidioidomycosis (DCM) infections is not well characterized. The historical VA-Armed forces CM patient group provides a unique cohort of patients not treated with standard antifungals to characterize the natural history of non-CNS DCM.

Methods. We conducted a retrospective study of 595 VA-Armed forces CM patients diagnosed between 1955 and 1958 and followed to 1966. Cohorts were identified as non-disseminated disease (487 patients), non-CNS DCM (72 patients), and CNS DCM (36). A combination of statistical analyses were used to compare demographic information, laboratory data including serologies and complete blood count data, symptom severity, late of primary infection, and mortality.

Results. There were significant differences in the ethnicity between the cohorts with trends toward a higher percentage of Black and Filipino patients in the disseminated cohorts (P < 0.001). There was a trend showing increased frequency of leukocytosis regardless of eosinophilia in the disseminated cohorts (P = 0.009). Patients with disseminated disease presented with more severe symptoms (P = 0.008). Primary fate of infection dissemination was determined by the identification of residual pathogens were observed in DCM, 13.89% in non-CNS DCM, and 19.44% in CNS DCM (P < 0.001). In addition, there were decreased rates of residual cavities in DCM: 33.26% in non-CNS DCM, 8.33% in non-CNS DCM, and 8.33% in CNS DCM (P < 0.001). Forty-five percent and 53% of patients in the non-CNS DCM and CNS DCM cohorts, respectively, developed disseminated meningitis at initial infection. Mortality at last known follow-up due to CM was significantly different across the cohorts: 1.03% in non-DNM, 15.28% in non-CNS DCM, and 77.78% in CNS DCM (P < 0.001).

Conclusion. This large retrospective cohort study helps further characterize the natural history of non-CNS DCM in comparison to CNS DCM in a population that was not treated with conventional antifungal therapy. While not as fatal as CNS DCM, non-CNS DCM shares many characteristics and has a high associated morbidity.

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387. Coccidioidomycosis in Children Younger Than 2 Years of Age: A Retrospective Review

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Background. Coccidioidomycosis, a disease endemic to the southwestern United States, is associated with significant morbidity, especially in patients in the extremes of age and patients with immunodeficiency or other comorbidities. This review aims to study the disease burden in infants and young children.

Methods. A review of coccidioidomycosis cases in patients younger than 2 years of age seen at Valley Children’s Hospital over a 10-year period, between June 1, 2007 and December 31, 2017.

Results. Forty cases were identified. Median age was 10.9 months (IQR, 5.3–15.8), majority were males (60%), Hispanic (80%), and without comorbid conditions (93%). Fever and cough were the most common symptoms occurring in 83% and 75% of the cases, respectively; Erythema nodosum was seen in only 10% of the patients. Forty percent of the patients had disseminated disease, while 58% had pulmonary disease alone. The most commonly involved extra-pulmonary sites were: bone (12%), central nervous system (10%), larynx (7%), and skin (7%). Majority of patients required hospitalization (75%) and received antifungal therapy (95%), with 55% of them requiring two or more drugs. Patients with disseminated disease presented at a younger age than with pulmonary disease alone (median 6.7 vs. 12.5 months, P = 0.007); had higher coccidioidal complement fixation titers at the time of diagnosis (median 132 vs. 11.6; P = 0.05); required longer duration of hospitilization (median 79 vs. 2 days, P = 0.002); and were more frequently treated with combination antifungal therapy (87% vs. 36%; P = 0.001). In regards to outcome, disease resolution was achieved in 75% of the cases while 25% had active but stable disease on maintenance therapy. A relapse occurred in 5% of the cases. No deaths occurred in this cohort.

Conclusion. Coccidioidomycosis in children younger than 2 years of age is associated with significant morbidity and healthcare burden. Disseminated disease is frequently encountered in this age group and should be considered when formulating the plan for treatment and diagnostic investigations.

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388. New Observations in Coccidioidomycosis Serology

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Background. Coccidioidomycosis is associated with a broad spectrum of illness severity, ranging from asymptomatic or self-limited pulmonary infection to life-threatening disseminated disease. Current understanding of serologic kinetics and serologic features are largely based on serologic studies from the 1950s before antifungals were widely available. The effects of antifungal therapy on serologic characteristics has not previously been evaluated.

Methods. We retrospectively analyzed chart history and complement fixation titer trends of 434 patients classified by infectious disease physicians as having either uncomplicated pulmonary coccidioidomycosis (UPC) (n = 248), chronic pulmonary coccidioidomycosis (CPC) (n = 64), disseminated coccidioidomycosis not including meningitis (DC) (n = 86), or coccidoidal meningitis (CM) (n = 36). All patients received azole antifungal therapy. Serologic kinetics and features were analyzed and compared between groups.

Results. Roughly 94% of UPC, 61% of CPC, 29% of DC, and 56% of CM patients developed maximum complement fixation titers ≥1:128. Surprisingly, 25.4% of UPC, 63% of CPC, 23% of DC, and 8.3% of CM patients did not develop a detectable complement fixation titers during the study period (at least 3 years after diagnosis for each patient). The median maximum titer was 1:4 (range <1:2 – 1:512) for UPC, 1:24 (range <1:2 – 12:048) for CPC, 1:128 (range <1:2 – 14:096) for DC, and 1:32 (range <1:2 – 14:096) for CM. There were significant differences in the ethnicity between the cohorts (P < 0.009). Patients with disseminated disease presented with more severe symptoms (<90 days from initial positive serology). Meanwhile, 15% of UPC, 25% of CPC, 31% of DC, and 25% of CM patients exhibited a serofast phenotype despite antifungal therapy.

Conclusion. Our findings provide an update to serologic studies performed prior to the long-term triazole therapy. An understanding of the serologic features and kinetics for patients with varying forms of coccidioidomycosis receiving antifungal therapy is key to clinical evaluation and therapeutic decision making.

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389. Pediatric Musculoskeletal Coccidioidomycosis in Central California: Single-Center Experience

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Background. Coccidioidomycosis is an infection caused by the fungus Coccidioides (coccii), endemic to the southwest region of the United States. The burden of coccidioidomycosis in Central California continues to be significant among children.

Methods. We reviewed literature on disseminated coccidioidomycosis, including musculoskeletal coccidioidomycosis (MSKC) currently exists.

Methods. Describe the clinical course and outcomes of MSKC in a tertiary children’s hospital.

Results. Thirty cases were identified. Median age was 13.1 years (IQR, 5.1–14.5). Majority was male (63%), Hispanic (63%), and without comorbid conditions (70%). Common presenting features included limb swelling (60%), bony pain (50%), joint pain (43%), and fever (40%), and the majority of patients were hospitalized (90%). Pulmonary disease occurred in 57%, and 7% had meningitis. Cocci ElA antibody was positive in 63% (90%) and positive by Immunodiffusion/median serum coccidioidal complement fixation (CF) titers were 1:128 (IQR, 64–512). Tissue/Fluid culture was positive in 92%. The most commonly involved bony sites were: Craniofacial (33%), vertebrae (17%), and rib (13%). Most required surgery (77%) and underwent median duration of 2 years (IQR, 1.7–2.6). Overall, 83% had resolved and/or stable disease, whereas 17% experienced relapse and/or progressive disease. Additionally, older patients (≥21 years) were more likely to have two or more procedures as compared with younger patients (P < 0.05).

Conclusion. To our knowledge, this is the largest case series of MSKC. Older patients seem to be at higher risk for MSKC with more aggressive disease requiring multiple surgeries. This may prompt early consideration and evaluation, including skeletal scintigraphy and MRI of involved area, especially in an endemic region.

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