386. A Reexamination of Disseminated Coccidioidomycosis: The Natural History in the Pre-Antifungal Era
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Session: 56. Fungal Disease: Management and Outcomes
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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 more 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 = 0.006). Primary fate of infection dissemination determined by the sites of residual pulmonary pathology 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, 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 dissemination with initial infection. Mortality at last known follow-up due to CM was signiﬁcantly different across the cohorts: 1.03% in non-DCM, 15.28% in non-CNS DCM, and 77.78% in CNS DCM (P < 0.001).

Conclusion. The details of 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. 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 those with pulmonary disease alone (median 6.7 vs. 12.5 months, P = 0.07); had higher coccidioidal complement ﬁxation titer at the time of diagnosis (median 1:32 vs. 1:16, P = 0.05); required longer duration of hospitalization (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 utilization. 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-threaten- ing 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 titre 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 = 46), or coccidioidal 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 ≥1:32. Surprisingly, 25.4% of UPC, 6.3% of CPC, 2.3% of DC, and 8.3% of CM patients did not develop a detectable complement ﬁxation titer 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 – 1:128) for CPC, 1:128 (range <1:2 – 1:14,096) for DC, and 1:32 (range <1:2 – 1:14,096) for CM. Few signiﬁcant differences were observed in the mean titers for UPC, CPC, 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 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 Coccidiodes (coccidioides) endemic to the southwest region of the United States. The burden of coccidioidomycosis in Central California continues to be significant among children.

Methods. We performed a literature review on dissemination of 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 EIA antibody was positive in 63% (10% were positive by Immunodiﬁlusion; 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%), vertebral (17%), and rib (13%). Most required surgery (77%) and 39% underwent 2 procedures. Twenty-six patients (86%) required 2 antifungal therapies with 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 (78% vs. 22%, P = 0.03). Therapy failures was also seen in older patients as compared with younger ones (1.25 vs. 1.64).

Conclusion. To our knowledge, this is the largest case series of MSKC. Older patients seem to be at high risk for MSKC with more aggressive disease requiring multiple surgeries. Any musculoskeletal symptoms or high coccidioidal CF titers should prompt early consideration and evaluation, including skeletal scintigraphy and MRI of involved area, especially in an endemic region.

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