H81 Cryptococcal Central Nervous System (CNS) Disease in a Large Urban Forensic Population

Jonee Taylor, MD, Office of the Chief Medical Examiner, New York, NY; Rebecca Folkerth, MD, PhD, Office of the Chief Medical Examiner, New York, NY 10016*

Learning Overview: The goals of this presentation are to: (1) alert attendees to the continued presence of CNS Cryptococcal disease in a forensic population in New York City, a relatively resource-abundant setting during the era of Highly Active Retroviral Therapy (HAART); and (2) provide an overview of organism burden, degree of inflammation, and neuroanatomic localization in CNS Cryptococcal disease, and correlation with the type of immune compromise and other demographic factors.

Impact on the Forensic Science Community: This presentation will impact the forensic science community by reminding practitioners that CNS Cryptococcal infection is still noted in a relatively resource-abundant urban forensic setting, even during the era of HAART.

Background: Despite the introduction and now widespread availability of HAART, fatal opportunistic infections are still a major problem, especially in the developing world. For example, in 2016, >1 million deaths occurred worldwide from AIDS-related illness, and as many as 15%–20% were attributed to meningitis due to Cryptococcus species. In contrast to hospital-based autopsy practice, which focuses on patients already in the health care system (and has limited autopsy volume), forensic practice involves high numbers of unattended deaths, very often among vulnerable or underserved populations. Thus, forensic autopsies, particularly in a large, diverse urban setting, can contribute to a public health surveillance function by highlighting underappreciated trends. The goal of this study was to characterize all cases with autopsy evidence of Cryptococcal CNS infection from the office of the Chief Medical Examiner in the City of New York, during the HAART era.

Methods: This study screened its database of cases referred for neuropathology consultation from 2004 to 2014 for decedents diagnosed with Cryptococcal disease and identified 14 cases. (For reference, during this period, 10,916 cases were referred for neuropathology evaluation, of which 313 were decedents with HIV/AIDS.) Microscopic sections included frontal lobe, thalamus, basal ganglia, hippocampus, midbrain, pons, medulla, and cerebellum, stained with hematoxylin and eosin. A variable combination of standard ancillary stains, including methenamine silver, periodic acid-Schiff, and mucicarmine, was used in 11 cases. Neuropathology reports on all, and microscopic slides on 9, were reviewed to semi-quantitatively evaluate: (1) organism burden (scale of 1 [rare or sparse], 2 [moderate numbers], and 3 [numerous]); (2) degree of inflammation (0 [none], 1 [sparse], and 2 [robust, including granuloma formation]; and (3) anatomic location (leptomeninges; perivascular space; and parenchyma). Additionally, demographic features were recorded.

Results: Among the 14 cases, 8 were female and 6 male, ranging in age from 20 to 74 years. A majority (n=11) were born in the United States, and 2 were born in Haiti; the country of origin for one was unknown. There were 9 Black decedents, 4 Hispanic, and 1 White. Of the 14 cases, 11 carried the diagnosis of HIV/AIDS, and 3 were immune-compromised due to other medical illness. Macroscopically, leptomeningeal opacification was noted in 12, particularly over the cerebellum. Histologically, 12 cases had leptomeningeal involvement, 9 had perivascular, and 9 had parenchymal (most cases had more than one pattern). The organism burden was high in 3, moderate in 7, and sparse in 2. In 2 cases, Cryptococcal meningitis was noted as a premortem diagnosis; however, no inflammation or organisms were seen on microscopy. The degree of inflammation was sparse in 7, and robust in 5, including granuloma formation in 3. The neuroanatomic site most frequently affected was the cerebellum (n=8), followed by brainstem (n=6), and diencephalon (n=5). Of note, one case, with a clinical history of blindness, showed histologic involvement of the optic nerve. Only the non-HIV cases demonstrated granulomatous inflammation, including multinucleated giant cell formation engulfing Cryptococcal organisms.

Limitations: The numbers of cases are small and likely reflect selection bias, as not all brains were referred for neuropathology consultation. Sampling bias likely prevented postmortem confirmation of a premortem diagnosis of CNS Cryptococcal disease in a minority of cases.

Conclusion: Cryptococcus, as an opportunistic fungal infection of the immune-compromised, showed a spectrum of CNS involvement regarding distribution of organisms and host response. Of note, only the HIV-negative immune-compromised individuals were able to mount a granulomatous response. It is further pointed out that, even during the HAART era in our relatively resource-abundant forensic setting, CNS Cryptococcal disease is still a significant finding. If anything, this experience likely underrepresents the true incidence of Cryptococcal disease among the large diverse urban population. This study emphasizes the role of neuropathologic evaluation of immune-compromised decedents for public health surveillance of this fatal complication.

HIV, Meningoencephalitis, Opportunistic