G129 Fatal Progressive Disseminated Histoplasmosis Presenting as FUO in an Immunocompetent Italian Host

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The goal of this presentation is to focus on a fatal case of undiagnosed disseminated histoplasmosis occurring in an immunocompetent Italian host. A forensic approach by means of autopsy, microscopic examination, and microbiological studies led to the conclusion that the cause of death was septic shock caused by *Hstoplasma capsulatum* with pulmonary origin and overlapping of other fungal species infection.

This presentation will impact the forensic science community by demonstrating how important a thorough forensic investigation is to reach the correct postmortem diagnosis as well as showing that histoplasmosis could be an emerging sporadic infection in Western countries which needs to be addressed in clinical differential diagnosis in order to avoid unexpected death.

Histoplasmosis is a relatively rare infectious disease endemic in certain moist areas, such as East Africa, eastern and central United States, western Mexico, central and South America, and is mainly related to contact with soil containing feces of birds and bats. Most cases (95%) are acute, self-limited, and completely asymptomatic. Disseminated histoplasmosis has been described almost exclusively in immunocompromised hosts and in AIDS patients. Indeed, histoplasmosis is generally caused by a primary pulmonary lesion with a possible subsequent sporadic hematogenous dissemination.

Presented is a case of a 43-year-old Italian woman, previously splenectomized (due to the complications of a road accident) but clinically immunocompetent, who was admitted to a regional hospital with a Fever of Unknown Origin (FUO) for several days. Two weeks later, in August, under suspicion of a lymphoproliferative disease, she underwent mediastinoscopy with incisional biopsy which revealed the absence of neoplastic lesions and specific granulomatous structures. Approximately one month later, following the appearance of hepatomegaly with altered indices of cholestasis (without jaundice) and the persistency of fever, the patient underwent liver biopsy with the sole evidence of a necrotizing granulomatous inflammation. Finally, ten days later, a bone marrow biopsy was suggestive for necrotizing inflammatory lesions of infectious etiology. Due to the rapid onset of sepsis, a sudden deterioration of general conditions occurred and the patient died.

A forensic autopsy was performed within 48 hours after death in order not only to find the real cause of death but also to investigate the hypothesis of medical liability (delay in diagnosis, lack of adequate therapy, and so on) of the clinician who had taken care of her.

On the basis of internal examination (sectioning the lung, an apparently capsulated blackish round lesion—1.5cm in diameter—appeared; also a reddish-brown focus with a yellowish central area was found. Other multiple dense spots in the pulmonary parenchyma were observed) and evaluation of histological specimens obtained from autoptic samples (jeweled oval cells of 1 – 5 microns in diameter), it was possible to formulate a diagnosis of histoplasmosis with polivisceral localization (lung, liver, brain, bone marrow), with overlapping—in the lungs—of other fungal species infection (Candida sp.) and arterial embolization of hyphae and pseudo-hyphae.

The diagnostic difficulties due to the inability to document a histoplasmosis in the early stages of the disease, more so in any clinical-radiological pictures which were not sufficiently specific and consequently clinically subtle, led to the accused clinicians being found not guilty of manslaughter. However, this case underlines the need to keep attention levels high in the clinical and forensic analysis of all the granulomatous lesions of unclear etiology which require histological and microbiological studies of blood and infected organs as well as detection of antigens in blood or urine samples by ELISA or PCR.

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