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Case Report Open Access

A Case of Mistaken Identity - Ocular Histoplasmosis in Florida

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Abstract

Ocular Histoplasmosis Syndrome (OHS) is thought to develop when *Histoplasmosis capsulatum* spores settle in the choroid, obstruct choroidal vessels and stimulate neovascular growth. OHS is characterized by retinal scarring and Choroidal Neovascularization (CNV). Diagnosis of OHS is usually confirmed through the presence of 'histo' spots and retinal swelling. The former is considered presumptive of exposure to histoplasmosis spores and the latter results from the growth of abnormal blood vessels. Multifocal Choroiditis (MFC) mimics the presentation of OHS and diagnostic errors may occur. A thorough patient history, in conjunction with confirmatory laboratory testing for *H. capsulatum* exposure, can avoid misdiagnosis. We report a case of MFC misdiagnosed as OHS in a patient evaluated foroccupational exposure.

Keywords: Ocular histoplasmosis syndrome; *Histoplasmosiscapsulatum;* Choroiditis; Retinal neovascularization; Multifocal choroiditis

Introduction

Histoplasmosis is an infection caused by exposure to *Histoplasma capsulatum* spores, a fungus common to damp soil and nourished by accumulated bird droppings and bat guano. *H. capsulatum* has also been found in older buildings and may present a danger during demolition. Inhalation of *H. capsulatum* spores is the primary exposure route. Respiratory histoplasmosis infections may be asymptomatic; when symptoms do manifest they are often dismissed as a mild cold. A small fraction of people who contract histoplasmosis will go on to developOHS, where spores lodge in the choroid and cause the inflammation and scarring commonly called 'histo' spots [1]. Attempts to biopsy 'histo' spots for spores have proven unsuccessful. The impact of these spots on vision is determined by their location in the eye; central scarring in the macula may result in a large blind spot. Peripheral vision is generally unaffected. Ocular histoplasmosis is a leading cause of vision loss for Americans aged 20 to 40 residing in the 'Histo Belt'[2,3]. The 'Histo Belt' refers to the southeastern, midatlantic and central United States, particularly the Ohio and Mississippi River valleys, where a majority of the adult population has been infected [4,5]. Multifocal Choroiditis (MFC) should be considered as a differential diagnosis in cases of OHS that present without confirmatory laboratory test results or inconsistent exposure history. In this article we highlight the importance of comprehensive patient histories in a case of MFC misdiagnosed as OHS in an individual with suspected occupational fungal exposure and a review of the relevant scientific literature necessary to evaluate risk factors for the disease.

Case Presentation

An immunocompetent 25-year old white female, native of Florida, was referred for a medical examination to assess vision complaints possibly related to occupational fungal exposure. The patient complained of decreased vision and the presence of a 'grey spot' in the center of the visual field of the left eye. Additional minor complaints included nonanaphylactic allergic symptoms, frequent rashes on the lower extremities and nasal congestion.

All physical examination outcomes were normal with the exception of decreased vision in the left eye and pruritic rash on the lower extremities. The patient's medical history revealed elevated cholesterol and nonanaphylactic sensitization to animal dander(s), pollen and dusts. Prior ocular history was unremarkable and included Laser-Assisted, In-Situ Keratomileusis (LASIK) for both eyes in 2005. In 2009, the patient underwent surgical removal of an arachnoid cyst in her left temporal lobe. A shunt was placed several months later to reduce post-surgical hydrocephalus, and recent Magnetic Resonance Imaging (MRI) was clear.

Diagnostic criteria for OHS include the presence of 'histo' spots, retinal swelling secondary to neovascular growth and positive serology. Ophthalmoscopy of the right eye indicated evidence of peripapillary Subretinal Neovascular Membranes (SRNVM) on the temporal edge, while the left eye revealed macular Retinal Pigment Epithelial (RPE) changes, subretinal fluid consistent with wet Age-Related Macular Degeneration (ARMD) and evidence of SRNVM. Multiple atrophic peripheral chorioretinal scars were observed in both eyes. Ocular coherence tomography results for the right eye were normal; however, the left eye exhibited a loss of foveal contour with subretinal fluid within the macular region and a well-defined SRNVM with moderate retinal edema and intraretinal cysts. Fluorescein angiography of the left macula confirmed moderate RPE pigmentary changes and subfoveal SRNVM. Assay results were negative for histoplasmosis antibody Immunediffusion (ID) reaction, histoplasmosis antibody Complement Fixation (CF) and urinary histoplasmosis antigen.

The clinical and angiographic evidence was consistent with OHS. Secondary and tertiary diagnoses included retinal neovascularization, SRNVM and peripheral choroiditis. The patient was treated with intravitreal injection of 0.05 cc Avastin (bevacizumab) solution in the left eye. Laser Photocoagulation (LPC) was used to treat the lesion in the right eye. LPC reduces the odds of additional CNV and concomitant vision loss by clearing the existing CNV; however, it cannot restore lost vision.

For the previous 4 years, the patient had been employed as clerical

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staff by a large supermarket chain. The patient indicated that there was an 'old odor' in the building where she worked and that HVAC (heating, ventilation, and air conditioning) problems were common. She also reported an increase in symptoms consistent with mucosal irritant exposure (nasal congestion, bronchitis and respiratory irritation) while employed in this capacity. Her prior occupational history included 5 years of counter work in various restaurants. The patient denied hobbies or activities outside the workplace that would have involved significant exposure to fungal spores such as *H. capsulatum*. Lifetime travel within the 'Histo Belt' had been limited to several short trips to North Carolina, Alabama and Georgia. These regions are considered the outskirts of the 'Histo Belt' as the overwhelming majority of OHS cases occur in the Mississippi, Arkansas and the Ohio River Valley. During these time-constrained trips her activities were primarily indoors and related to family gatherings. Contact with *H. capsulatum*spore laden soil appears unlikely as does occupational contact. The remainder of the patient's life had been spent in one central Florida County. The patient also denied use of tobacco, alcohol or illicit substances.

Discussion

Histoplasma is a common mycosis carried by bats and birds. Spores are found worldwide, although they are especially abundant in the moist soil of the Ohio and Mississippi river valleys [6]. *H. capsulatum* spores may be released in the air by any activity (construction, agriculture, etc.) that disturb the soil. Local outbreaks have also been linked to building renovations that disseminated large numbers of spores [7]. These spores of *H. capsulatum* may be inhaled into the lungs and researchers believe the spores can later spread from the lungs to the eyes [8].

There are 4 primary clinical manifestations of OHS: maculopathy, 'histo' spots, peripapillary pigment changes, and clear vitreous fluid [9,10]. OHS may also be referred to as Presumed Ocular Histoplasmosis Syndrome (POHS) because diagnosis often relies on the appearance of 'histo' spots and evidence of CNV rather than a single definitive laboratory test [11]. Attempts to isolate *Histoplasma* from ocular tissue have not been successful.As CNV is associated with multiple ocular pathologies the differential diagnosis should include multifocal choroiditis (MFC), Age-Related Macular Degeneration (AMD), Behcet syndrome and toxoplasmosis.It has also been weakly associated with LASIK, though evidence is anecdotal, with an incidence of 0.003% to 0.33% [12,13].

Multifocal Choroiditis (MFC), also called MCP for multifocal choroiditis and panuveitis, was initially referred to as 'inflammatory pseudohistoplasmosis'. MFC patients develop the peripapillary scarring, macular and peripapillaryCNV membranes considered characteristic of OHS. MFC patients also exhibit 4 primary fundal manifestations; 'punched out' scarring similar to 'histo' spots, peripapillary scars, CNV and aggregates of punched out scars. MFC primarily affects younger women. Similar clinical presentations make MFC a likely differential diagnosis in cases of suspected OHS.

The 'histo' spots seen in the early stages of OHS are largely asymptomatic, while the decline in visual acuity is associated with CNV that occurs after the initial infection. It is thought that CNV results from a complex interaction between the *H. capsulatum* and the immune system. The pathogenesis of OHS has not been elucidated. The characteristic 'histo' spots that appear in the early phase of OHS are linked to subretinal lymphocytic aggregation that leads to chorioretinal scarring. When the scarring is in the peripapillary or macular region, progression to CNV is more likely. There is also an inflammatory component in the CNV that appears later in the disease course [14]. Recent improvements in histoplasmosis antibody Immunodiffusion (ID) reaction, histoplasmosis antibody Complement Fixation (CF) and urinary histoplasmosis antigen assays have significantly improved sensitivity and specificity [15,16]. Histoplasmin skin tests are not performed in OHS patients because testing may activate inactive ocular lesions [17,18]. Laboratory testing should be performed to rule out MFC and other conditions that mimic OHS.

Differentiation between OHS and MFC can be quite challenging. Comprehensive patient history can help determine if the patient has spent time in areas where *H. capsulatum* is endemic. Serological testing should be employed to further refine the diagnosis. Given the absence of confirmatory laboratory testing and incompatible patient history in this case, it is unlikely the patient suffers from OHS. A diagnosis of MFC is more appropriate.

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