Expression of Platelet-Associated Marker CD42b on Histoplasma

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Abstract

Background

in histopathologic specimens, Histoplasma capsulatum, can be readily identified by morphology and specific stains such as GMS and PAS. It is known that patients are rarely symptomatic, if not asymptomatic, despite heavy exposure. Histoplasma may infect the body in three distinct ways: while accidentally swallowing contaminated dust, while inhaling dust containing fungal spores, and when inhaling dust containing the fungal spores while sleeping. When a person inhales the spores, the fungi will multiply in the lung to form a warm, moist environment. It is during this period that symptoms start to appear. Histoplasma can spread to other parts of the body, and the infection can become more severe. However, most people infected with Histoplasma remain asymptomatic and do not require specific treatment.

Cases were identified by known or suspected diagnoses of fungal infections from the files of Neogenomics (Aliso Viejo, CA; DPO), City of Hope National Medical Center (Duarte, CA, YSK), and Indiana University Medical Center (Indianapolis, IN, LCG). All samples were obtained with respect to local standards for ethical research.

In each case, H&E and GMS stains were reviewed (DPO) to confirm the presence of fungal organisms. CD42b staining was performed on Verdana Benchmark (Tucson, AZ) using anti-CD42b antibody (Dako; Carpinteria, CA) using standard techniques.

Results

We identified an index case of histoplasmosis in a bone marrow biopsy of a 23 year male. The index patient had a history of living in the southwest United States, with recent U.S. military service in the area. The bone marrow core biopsy was hypercellular for age (near 100%), but the overall hematopoietic marrow was reduced to approximately 25%. In the bone marrow aspirate smear, we found an abundance of atypical lymphoid cells, many resembling Reed-Sternberg cells. In the bone marrow, we found numerous histocytes, numerous T cells with scattered J cells associated with the increased macrophages. Scattered T cells were seen within the bone marrow, which was also infiltrated by numerous histiocytes. Staining for CD34 and CD117 did not show any increase of immature myeloid elements or mast cells.

Immunohistochemical stains were also performed to evaluate the underlying marrow elements, as part of evaluation for other causes for the pancytopenia. CD34 and CD117 did not show any increase of immature myeloid elements or mast cells. CD3 stains increased scattered T cells associated with the increased macrophages. In the index case, immunohistochemical staining for CD42b highlighted decreased numbers of megakaryocytes. It also highlighted numerous small organisms within the cytoplasm of most macrophages, with far more positivity than either GMS or PAS stain.

Discussion

in most circumstances, infection with Histoplasma is asymptomatic. The majority of primary infections go unrecognized and only significant immunosuppression or severe infection lead to symptoms (Guimaraes 2008). Diagnosis typically requires a combination of clinical findings, serologic studies as well as histopathologic confirmation of organisms.

Our study supports that Histoplasma can be identified by CD42b immunohistochemical staining.

CD42b, also referred to as Gp1ba, is a platelet surface membrane glycoprotein. It binds with other platelet glycoproteins to bond to von Willebrand factor and cause platelet adhesion to surfaces.

We suggest the possibility that a fungal 14-3-3 protein, which are known to bind to Gp1ba (Zhang 2012), may share enough homology with CD42b (e.g. Gp1ba), to cause the staining effect that we have observed.

While this could present a potential pitfall in diagnosis, e.g. platelets misidentified as organisms and vice versa, we would suggest that it presents an interesting opportunity for both sensitive and relatively specific identification of pathogenic fungi in a variety of histopathologic samples. The presence of positivity for CD42b within macrophages with an appropriate morphology could lead to better identification of fungal organisms.

The histopathologic appearance of Histoplasma can be similar to other pathogens including Candida, Penicillium, Pneumocystis, Toxoplasma, Leishmania and Cryptococcus. Testing of CD42b on a variety of other pathogenic fungal or other infectious organisms (e.g. Candida, Aspergillus, Cryptococcus, Coccioides, Blastomyces, etc.), will provide insight into the range of reactive species. Cross-reactivity may be present. However, even if a broad range of pathogenic fungi are identified, staining for CD42b would still allow for a sensitive immunohistochemical approach to identify fungi in histopathologic specimen.

References