Chronic Histoplasmosis and Lymphoma: A Possible Association?

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Background:
• Histoplasma capsulatum is a dimorphic fungus that can cause pulmonary, mediastinal, pericardial, mucocutaneous, and disseminated infections.
• There have been sporadic reports of chronic histoplasmosis infections subsequently developing into reticulo-endothelial tumors, including lymphoma, in the same anatomic location [1].
• Murray and Brandt in 1951 postulated that either the fungal infection of the reticulo-endothelial system or a cellular reaction of the reticulo-endothelial system caused the formation of lymphoma [1].
• As shown by our case and also with the increasing incidence of histoplasmosis infection and lymphoma in patients treated with anti-tumor necrosis factor therapy, one has to be aware of a possible common etiological association [2].

Case:
• A 48 year old female, presented with painful erythematous nodular skin lesions.
• Skin biopsy showed fungal organisms compatible with histoplasmosis.
• Patient also had positive urine histoplasmosis antigen titer.
• Skin biopsy was negative for malignancy.
• Patient was successfully treated with Itraconazole 100mg BID.
• The following year, the patient returned with non-tender nodules in the skin.
• This time, the skin biopsy showed an atypical cutaneous lymphoid infiltrate highly suspicious for a large B cell lymphoma.
• Immunoperoxidase studies were positive for CD20, CD 68, and CD 30.
• PET scan showed that these nodules were compatible with metabolically active tumors.
• The patient was started on rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone.
• The patient has been in remission since treatment and no new nodules have been seen.

Methods:
• Review of the literature included a database search at Pubmed and Ovid.
• Search terms used: lymphoma, Histoplasma capsulatum, Histoplasma associated with malignancy
• Limited to English literature

Conclusion:
• This is the first documented case since 1960 to illustrate a possible association between a cutaneous histoplasmosis infection and B cell lymphoma.
• We hypothesized that this may relate to altered immunity affecting immune surveillance secondary to chronic inflammation in predisposed individuals.
• We recommend further studies to investigate this association.
• Clinicians should have increasing vigilance and long-term monitoring of patients with chronic histoplasmosis infection.
• It is important to be aware of a possible association between histoplasmosis and lymphoma, as early investigation will establish a diagnosis at an earlier stage with improved prognosis.

References:
3. US Food and Drug Administration Black Box Warning. Tumor Necrosis Factor (TNF) Blockers. August 2009