DISSEMINATED HISTOPLASMOSIS LEADING TO HAEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS IN AN IMMUNOCOMPETENT PATIENT
(case report)

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Background: Emerging fungal infections can pose a serious threat in contemporary healthcare due to host variations, clinical presentation and emerging resistance. Histoplasma capsulatum is a thermally dimorphic fungus, which acts as a Trojan horse by residing inside macrophages. Histoplasmosis is an emerging infection and its association with hemophagocytic lymphohistiocytosis (HLH) in immunocompetent patients has been scantily reported in the literature.

Objective: The aim of the study was to explore disseminated histoplasmosis with the help of case report.

Methods: A case report of histoid leprosy is presented.

Results: A male patient of 47 years of age, under treatment for chronic obstructive pulmonary disease for five years and diabetes mellitus Type-II for two years, presented with fever of unknown origin (FUO) with evidence of HLH in the bone marrow. Core biopsy of the liver and spleen showed a dense tissue infiltrate with vacuolated histiocytes containing Histoplasma capsulatum, eosinophils, some lymphocytes and plasma cells.

Conclusion: Histoid leprosy is a discrete infrequent form of multibacillary leprosy with distinctive clinical, bacteriological and histomorphological features. Histopathologic examination with modified fite stain remains the mainstay of diagnosis.

KEY WORDS: histoplasmosis; hemophagocytic lymphohistiocytosis.

Introduction

Histoplasma capsulatum is a thermally dimorphic fungus, which acts as a Trojan Horse by residing inside macrophages [1]. Most individuals with intact cellular immunity are asymptomatic. A patient presented with fever of unknown origin (FUO) with evidence of hemophagocytic lymphohistiocytosis (HLH) in the bone marrow. Emerging fungal infections can pose a serious threat in contemporary healthcare due to host variations, clinical presentation and emerging resistance [2-8]. There are diagnostic stringencies in resource limited facilities [9, 10]. Histoplasmosis is an emerging infection and its association with HLH in immunocompetent patients has been scantily reported in the literature [11-16].

Case Report

A male patient of 47 years old, under treatment for chronic obstructive pulmonary disease for five years and diabetes mellitus Type-II for two years, presented with rashes around knee for 6 months, fever for 2 weeks and black stools for 3 days. Pallor, pedal edema, hepatomegaly 7 cm below right subcostal margin and splenomegaly 9 cm below left subcostal margin were evidenced. Investigated for FUO, hemoglobin was 5.5-8.3 gm/dl, total leucocytes 3600-4200/cumm with normal differential, serum ferritin was 306 ng/dl, while other tests were non-contributory towards diagnosis. CT thorax and abdomen revealed hepatosplenomegaly, retroperitoneal lymphadenopathy with mild ascites and solitary lesion in spleen. Colonoscopy was non-contributory. Bone marrow aspirate and biopsy showed evidence of HLH (Fig. 1).

While on treatment, the patient succumbed to his illness. Consented post-mortem needle biopsy from liver, spleen, lungs and kidneys was done. Core biopsy of the liver and spleen showed a dense tissue infiltrate with vacuolated histiocytes containing histoplasma capsulatum, eosinophils, some lymphocytes and plasma cells.

Discussion

Histoplasmosis is an endemic infection in most of the USA, Asia and Africa caused by
infectious bat and bird excretions. Disseminated histoplasmosis, classically described in the immunocompromised, can occur in immunocompetent patients. Clinical presentations vary depending on the size of the inoculum, host’s immune status and presence of underlying lung disease. Overt symptoms occur in 5% healthy individuals after low-level exposure; however 75% may get affected with heavy exposure. Mostly asymptomatic, mild flu-like illness, fever, chills, sweating, cough, chest and joint pain may occur. Acute histoplasmosis may last 1-5 days whereas chronic histoplasmosis, mostly associated with lung infections, can last 10-21 days and is associated with weight loss, persistent fatigue and night sweats. Associated acute or subacute pulmonary disease, progressive disseminated disease, pericarditis, arthritis, mediastinitis, hepatomegaly, splenomegaly and bone marrow suppression may occur [17-19]. The patient presented with fever, fatigue, polyarthralgia, skin rashes and black stools with underlying chronic obstructive pulmonary disease. Along with anemia and hepatosplenomegaly, the clinical picture fits histoplasmosis [11-16].

HLH is an overwhelming inflammatory response, resulting in cytokine storm and activation of monocyte-macrophage system resulting in multiorgan dysfunction. It is a secondary phenomenon to infections, malignancies, autoimmune disorders and drug reaction. HLH is associated with high mortality although successful treatment has been registered [11,14,15].

Diagnosis of histoplasmosis involves staining, isolation, serology and antigen detection. Bone marrow gives the highest diagnostic yield. Antigen detection in urine and serum by radioimmunoassay is useful in an immunocompromised patient when antibody production may be impaired. Other laboratory abnormalities include anemia, leukopenia, pancytopenia, elevated liver enzymes, increased ferritin and lactate dehydrogenase. Our diagnosis was based on clinical presentation and histopathology of liver and spleen [6], when culture was negative.

A high index of suspicion is required as 100% mortality seen in untreated histoplasmosis, can fall to 70% when adequately treated with Amphotericin-B [4, 20-25]. Risk factors for acquiring acute or chronic histoplasmosis in immunocompetent patients are for farmers and travelers having prolonged contact with rural or endemic environment, speleologists/spelunkers coming in contact with bat guano, and farmers coming in contact with soil enriched with bird guano. Heavy infective inoculum leads to acute presentation whereas low inoculum may lead to asymptomatic or chronic infection. Prolonged exposure to endemic area in Brazil led to histoplasmosis in 43.9-82.9% of immunocompetent patients [26-29].

Conclusion
Disseminated histoplasmosis needs to be differentiated from common diseases like tuberculosis, lymphoma or metastatic malignancy. Emerging opportunistic resistant infections warrant a high degree of clinical intuition and mental mobility for optimal management.

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Conflict of Interests
The authors declare no conflict of interest.

Author’s Contributions
I.D. Khan – study concept/design, conduct of study, drafting and manuscript revision, final approval of manuscript; M. Brijwal – study concept/design, final approval of manuscript; I. Joshi – study concept/design, final approval of manuscript; B. Singh – conduct of study; B. Poonia, G. Gonimadatala, S. Mangalesh, A. Yadav – statistical analysis, drafting and manuscript revision; H. Rajput – drafting and manuscript revision, N. Bhuttay – drafting and manuscript revision.
ДИСЕМІНОВАНИЙ ГІСТОПЛАЗМОЗ ЯК ЕТІОЛОГІЧНИЙ ЧИННИК ГЕМОФАГОЦИТАРНОГО ЛІМФОГІСТІОЦИТОЗУ У ІМУНОКОМПЕТЕНТНОГО ПАЦІЄНТА (клінічний випадок)

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Вступ. Зростання кількості та частоти грибкових інфекцій може становити серйозну загрозу сучасній системі охорони здоров'я через варіативність клінічного перебігу, симптомів та ознак захворювання, резистентність до лікування. Histoplasma capsulatum – це диморфний гриб, який поодинокує в середовищі макрофагів. Гістоплазмоз – захворювання, що останнім часом все частіше діагностується, однак про його взаємозв'язок з гемофагоцитарним лімфогістіоцитозом у імунокомпетентних осіб надзвичайно мало інформації.

Мета роботи – дослідити перебіг дисемінованого гістоплазмозу.

Методи. Описано клінічний випадок гістоїдної лепри у пацієнта.

Результати. Чоловік, 47 років, котрий останніх п'ять років лікувався від ХОЗЛ та цукрового діабету другого типу, звернувся до лікаря зі скаргами на лихоманку невідомого генезу. Було діагностовано гемофагоцитарний лімфогістіоцитоз кісткового мозку. На препаратах печінки та селезінки посмертної біопсії органів знайдено щільний тканинний інфільтрат з вакуолізованими гістіоцитами, які містили Histoplasma capsulatum, еозинофіли, невелику кількість лімфоцитів та плазмоцитів.

Висновки. Гістоїдна лепра – рідкісна форма мультибацилярної лепри з характерними клінічними, бактеріологічними та гістоморфологічними ознаками. Проведення гістологічного дослідження дозволяє діагностувати захворювання.

КЛЮЧОВІ СЛОВА: гістоплазмоз; гемофагоцитарний лімфогістіоцитоз.
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