

Case Report

## DISSEMINATED HISTOPLASMOSIS IN HIV-PATIENT IN NEPAL: A CASE REPORT

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### ABSTRACT

The risk of disseminated Histoplasmosis increases among immunocompromised HIV infected patients. It can clinically present with skin manifestation. We report a forty years HIV infected male with severe immunodeficiency clinically presenting as a disseminated Histoplasmosis with dermatological manifestation and diagnosis.

**Keywords:** COVID-19, Pandemic, Tuberculosis, Nepal

### INTRODUCTION

Histoplasmosis is a systemic fungal infection caused by *Histoplasma capsulatum*, a dimorphic fungus. It is found in soil contaminated by bat and bird droppings. During farming, construction and chicken coups handling fungal microconidia are aerosolized which on inhalation reach the lung. In lungs conidia form a yeast causing localized or patchy infection. Furthermore, they are taken up by alveolar macrophages and reach the blood stream through the lymphatics. It is a self-limiting condition in immunocompetent person due to cell mediated immunity but in immunodeficient individuals it can disseminate to reticulo-endothelial organs such as liver spleen bone marrow and sometimes gastrointestinal system, bones, skin, eyes and

brain. It manifests as acute, sub-acute, chronic and progressive disseminated disease.<sup>1-4</sup>

*Histoplasma capsulatum* is endemic in United states, certain parts of Mexico, Central and South America, Africa.<sup>5-7</sup> However, recently cases have been increasing in other non-endemic regions due to HIV, primary immunodeficiency, immunosuppressive drugs and solid organ transplantation. The cases are also in increasing trend in South East Asian region such as Bangladesh, India and China.<sup>7-9</sup> To the best of our knowledge only few cases were reported from Nepal. Hence, we report a case of 40 years old male with HIV and TB not improving inspite of appropriate treatment. He presented clinically with cutaneous nodules diagnosed as Histoplasmosis on microscopy.

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### CASE REPORT

A 40 years male from Kusma, Parbat presented in local hospital in Pokhara with history of fever for 3 months and multiple episodes of loose stool for 2 months. Cervical lymph node biopsy showed

infectious reactive hyperplasia and treated with antibiotics. In spite of appropriate antibiotics course his symptoms did not improve. He was referred to a tertiary care center in Kathmandu. Repeat cervical lymph node biopsy showed granulomatous lymphadenopathy suggestive of TB lymphadenitis. He was put on category I ATT at National TB Control Center. He showed improvement for few days, however his symptoms persisted. Three months later he presented to Sukraraj Tropical and Infectious Disease Hospital (STIDH) with complaints of dysphagia, odynophagia, generalized weakness, anorexia, weight loss and multiple itchy skin lesions over the face and neck.

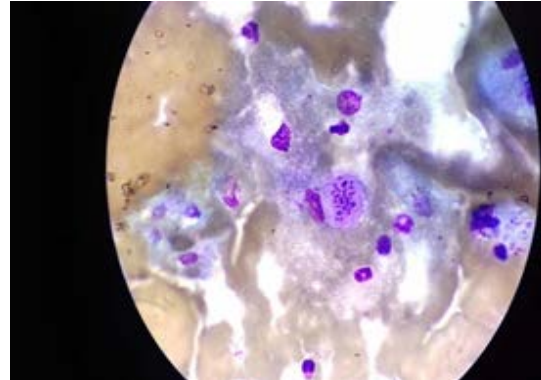
On examination patients was pale and cachectic (Weight=37kg). He had multiple papulo-nodular erythematous, painful, molluscum like lesions with central crusting over chin, cheeks, forehead and neck. Bilateral pitting pedal edema and anterior cervical lymphadenopathy was present. There were whitish patches on the buccal and pharyngeal mucosa with peripheral redness. Systemic examination showed no neurological deficit or any respiratory system findings. Abdominal examination showed hepatomegaly 4 finger below the right costal margins.

Blood parameters were Hb-6.1gm/dl, TLC 2700/mm<sup>3</sup>, Total bilirubin 3.6 mg/dL, Bilirubin direct 2.2 mg/dL, Serum ALT 27 U/L, AST 80 U/L, Sodium 125mEq/L. Potassium 4.3 mEq/L and random blood sugar 140mg/dL. Urine routine and microscopy were normal. Blood culture showed no growth. Serology for syphilis, serum cryptococcal antigen, toxoplasmosis, rubella, cytomegalovirus and herpes simplex virus was negative. HIV serology was positive with CD4 count of 39/mm<sup>3</sup>. Chest X-ray was within normal limit. Fine needle aspiration of the right cervical lymph node showed granulomatous lesion suggestive of tubercular lymphadenitis. Peripheral blood smear showed normocytic, normochromic and normal morphology of red blood cells and platelets. Sputum for AFB stain was negative. Fungal stain could not be done because of lack of facility at the hospital.

CT chest showed moderate bilateral pleural effusion with sub-segmental consolidation collapse of adjacent parenchyma and multiple small nodules scattered in bilateral lungs. CT abdomen and pelvis showed multiple discrete as well as coalesced necrotic lymph nodes in right paraaortic, periportal,

peripancreatic, celiac, mesentery, retroperitoneal, paraaortic aortocaval and bilateral inguinal region.

Microscopy of scrapping from the skin lesions on the face showed fungal elements morphologically consistent with Histoplasma. (Figure 2)



**Figure 1:** Smear from skin scrapping shows structure with basophilic center and surrounding halo arranged in clusters and singly within and outside macrophages consistent with Histoplasmosis



**Figure 2:** Multiple papulo-nodular erythematous lesion with central crusting over chin, cheeks, forehead

He was prescribed with Itraconazole 200mg/day orally. However, patient deteriorated during treatment in the hospital and taken to High Dependency Care Unit (HDU) due to respiratory failure. Patients was later absconded from HDU management. The reason for abscondment was not known and he could not be traced for further management and the outcome was unknown.

## DISCUSSION

The increasing trend of reported histoplasmosis cases have been observed in many Asian countries. First case in Nepal was reported from B.P.Koirala Institute of Health Sciences, Dharan, Nepal in a

male patient from Bihar, India.<sup>10</sup> Since then few cases have been reported<sup>11,12</sup> and hence the prevalence of the disease is yet to be studied. Histoplasmosis is an opportunistic infection in HIV that occurs when CD4 cell count is <200 cells/ $\mu$ L.<sup>13</sup> Histoplasmosis may be asymptomatic; an acute or chronic pulmonary infection; or disseminated histoplasmosis (DH). The acute form of DH is seen mostly in the immunocompromised people and is characterized by fever, malaise, weight loss, cough, dyspnea abdominal pain and diarrhea. Other clinical and laboratory findings include anemia, hepatosplenomegaly, lymphadenopathy, leucopenia and thrombocytopenia. The chronic form has an indolent course with focal lesions due to effective cell mediated immunity.<sup>14</sup> It presents as disseminated disease in 95% of cases.<sup>15</sup> Disseminated disease can involve gastrointestinal tract (GI) and skin. GI involvement can cause bowel obstruction, perforation and bleeding.<sup>16</sup> Skin lesions presents as polymorphic papules or plaque, pustules, nodules and ulcer like molluscum contagiosum or acne.<sup>17</sup> Due to clinical resemblance to TB and occurrence with TB in HIV patients, it is a diagnostic challenge in regions with high prevalence of TB. Lack of diagnostic facilities and low level of clinical suspicion leads to misdiagnosis of TB.<sup>18</sup> This patient also had diagnosis of Histoplasmosis delayed because of clinical and cytological features resembling Tuberculosis. Delayed diagnosis and treatment have poor outcome.

Diagnosis of Histoplasmosis requires understanding of test, their accuracy and limitations. The gold standard is growth of the *H. capsulatum* on specific culture media or direct visualization of the yeast in clinical specimens with the Gomori methenamine silver (GMS) and Periodic acid-Schiff (PAS). However, low sensitivity for mild cases and diagnosing invasive growth which requires 4 to 6 weeks are some of the limitations in routine laboratory set-up and requires Biosafety level 3 set-up. Antigen detection in serum and urine has higher sensitivity in disseminated histoplasmosis in HIV/AIDS. Among people living with HIV, it is recommended to diagnose disseminated histoplasmosis by detecting circulating *Histoplasma* antigens.<sup>19</sup> But the test is not widely available. Since antigen tests were not available in our setup, diagnosis in our patient was established using direct microscopy.

Cytopathologic evaluation of bronchoalveolar lavage (BAL) alone has lower sensitivity however, combined with *Histoplasma* antigen testing the sensitivity rises to 97%.<sup>20</sup> Fine-needle aspiration cytology is safe and useful test for diagnosis from lymph nodes and adrenal glands. Antigen detection in serum when combined with urine is a very useful test in patients with severe acute or disseminated Histoplasmosis. Serological test takes 4 to 8 weeks to become positive so it is useful for subacute and chronic forms of Histoplasmosis.<sup>21</sup>

## CONCLUSION

Although Nepal is non-endemic region for histoplasmosis it should be suspected in HIV patients who present with fever, weight loss and lymphadenopathy. High clinical suspicion and diagnostic facilities is key to early diagnosis. With high burden of HIV and increasing number of Histoplasmosis cases, there should be efforts to increase the availability of the test for urinary antigen detection in DH diagnosis and diagnostic center with well-trained medical personnel needs to be increased. Diagnostic facilities with microscopy examination of cutaneous lesion can aid in diagnosis of disseminated Histoplasmosis.

## CONFLICT OF INTEREST

None

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