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A CLINICOPATHOLOGICAL STUDY ON DISSEMINATED HISTOPLASMOSIS WITH SPECIAL REFERENCE TO ATYPICAL CASES IN A TERTIARY CARE CENTRE -IN EASTERN INDIA.

Pathology

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ABSTRACT

INTRODUCTION: Untreated Histoplasmosis is fatal for all, immunocompetent or immunocompromised. Histoplasmosis has seen a steady increase in incidence from a single recorded case in Kolkata, India in 1954 to 388 cases from 2004-17 and 161 from 2017-till date all over India. Yet, it has been consistently relegated to a niche of opportunistic infections without a proper diagnostic protocol. **OBJECTIVES:** To study the clinical features and natural history of disseminated histoplasmosis(DH) and analysis of cases with atypical clinical presentation of Histoplasmosis simulating malignancy in search of a consolidated and efficient diagnostic algorithm in a tertiary care centre. **MATERIALS AND METHODS:** The retrospective institution-based study was conducted in the Department of Pathology, CSTM from February 2011 to July 2019 in collaboration of Dept. of Tropical Medicine on specimens collected from 33 cases of Skin biopsy, Lymph node biopsy and FNAC aspirate from enlarged lymphnodes, slit skin smear followed by BM Aspirate analysis done in cases of disseminated histoplasmosis, Bone Marrow Biopsy was done in selected cases. Histoplasma capsulatum like yeast cells were detected with Leishman Giemsa stained slit skin smears in 9 cases and in FNA smears in 13cases and they were PAS positive. Diagnosis were confirmed in Histopathological examination along with special stain for fungus in all cases. Radiological investigations (CXR, USG, CT), Routine investigations (Haemogram, LFT, RFT, Electrolytes) along with CD4 count in ART clinic and microbiological tests like Gram stain of SSS, India Ink, KOH preparation, Cryptococcal Ag testing, urine C/S) were corroborated with. **RESULTS:** All 33 cases FNAC (13),slit skin smear(9) and HPE on rest of the specimen show small, oval yeast cells on LG stain. Biopsy showed histiocytic phagocytosis of yeast cells with foamy macrophages and PMN infiltration with NO granulomas in seroposive cases. Gomori Methenamine Silver stain of BM biopsy showed black intracellular yeast consistent with *Histoplasma capsulatum*. PAS stained FNAC smears showed yeast cells with chromatin dot and surrounding halos with no kinetoplasts. Mycological cultures were in agreement. Here, in most cases, CD4 count and Disseminated Histoplasmosis findings were not in accordance. **CONCLUSION:** DH is not uncommon in India and is being increasing day by day and it should be considered in the diagnosis of patients with prolonged fever, weight loss, oropharyngeal ulcers, hepatosplenomegaly, lymphadenopathy and adrenal enlargement. Correct diagnosis by well designed analytical studies utilising appropriate diagnostic modalities in an immunocompromised patient even with minimum suspicion of opportunistic infection, a consolidation of selective investigations like FNAC, HPE and relevant microbiological tests into a diagnostic design for maximum utilization of finances, resources and time, all of which can help to understand the epidemiology of this neglected disease for accurate treatment leading to a favourable outcome.

KEYWORDS

Histoplasmosis, atypical cases, diagnosis, outcome

INTRODUCTION:

Disseminated Histoplasmosis is a chronic granulomatous disease caused by the dimorphic fungus, Histoplasma capsulatum. It can occur in immune compromised as well as immunocompetent hosts. Its clinical presentation varies from acute/chronic pulmonary Histoplasmosis to chronic disseminated form involving skin ,bone marrow, adrenal gland ,lymph nodes. In India the disease can be present with similar clinical features of tuberculosis or pyrexia of unknown origin, malignancy or other diseases. It is often misdiagnosed due to rarity of the disease to and to lack of awareness and inadequate mycological diagnostic facilities.[1]Histoplasmosis is the most prevalent endemic mycosis in the United States with the highest incidence in the Mississippi and Ohio River Valleys.[2]

Histoplasmosis has seen a steady increase in incidence from a single recorded case in Kolkata in 1954.[3] .The number rises to 388 cases from 2004-17 and showed a rising trend of reporting 200 cases being recorded during the period 2004–2013 and 161 from 2017-till date all over India.[4] Most cases were recorded from northern and north east states of India along the rivers Ganges, Yamuna and Brahmaputra usually in people associated with agricultural activities. West Bengal has the highest recorded number at 56cases topping the charts.[5] The prevalence of 12.3% histoplasmin sensitivity found in the riverine -A survey on skin testing with histoplasmin on small segments of population residing in rural, urban and riverine area was performed by Viswanathan et al was the highest reported from any part of India.[6]

DH is not uncommon in India and should be considered in the diagnosis of patients with prolonged fever, weight loss, oropharyngeal ulcers, hepatosplenomegaly, lymphadenopathy and adrenal enlargement. Correct diagnosis and treatment leads to a favourable outcome.[7] Yet, it has been consistently relegated to a niche of opportunistic infections without a proper diagnostic protocol. This is such a disease which in its severest form often in immunocompromised person, mimics sepsis and accelerates death. Although it can be rapidly diagnosed with selective investigations and responds to early treatment in most typical cases but unfortunately it is not done in most of the cases.[3]

Histoplasma capsulatum, the opportunistic pathogen in immunocompromised especially HIV seropositive cases is a thermally (25°C and 37°C) dimorphic fungal form with saprophytic mycelia in soil rich in phosphates and nitrogenous compounds from avian droppings and bat guano.[8] It is endemic in warm, humid areas like American Ohio and Mississippi River valleys, Central America and southeast Asia. It is associated with cave dwellings/ excavations/ trekking/ spelunkingand agricultural occupational hazards as entry into system occurs by inhalation of microconidia. Engulfmentof the organism by lung macrophages and subsequent dissemination by haematogenous route in immunocompromised patients leads to multi-organ failure.[7]

Samuel Taylor Darling discovered that intracellular yeasts inside "Histio"-cytes appearing like "plasmo"-dium and apparently having a "capsule"; so named it *Histoplasma capsulatum*. In his honour, classical/ American Histoplasmosis is called Darling's disease.

Clinical differential Diagnoses:

1. Tuberculosis
2. *Leishmania donovani*
3. *Cryptococcosis*
4. *Candida glabrata*
5. Carcinoma especially vascular tumours eg. Kaposi Sarcoma
6. Lymphoma
7. *Mycoplasma pneumoniae*
8. *Toxoplasma gondi*

HPE/FNAC/SSS

Histoplasmosis in all

OBJECTIVES:
To study the clinical features and natural history of disseminated histoplasmosis(DH) and analysis of cases with atypical clinical presentation of Histoplasmosis simulating malignancy in search of a consolidated and efficient diagnostic algorithm in a tertiary care centre.

MATERIALS AND METHODS:
The retrospective institution-based study was conducted in the Department of Pathology, Calcutta School of Tropical Medicine (CSTM) from February 2011 to January 2020 in collaboration with the Dept, of Tropical Medicine on specimens collected from 33 cases. Skin biopsy, Lymph node biopsy and FNAC aspirate from enlarged lymphnodes, slit skin smear followed by BM Aspirate analysis done in cases of disseminated histoplasmosis, Bone Marrow Biopsy was done in selected cases. Histoplasma capsulatum like yeast cells were detected with Leishman Giemsa stained slit skin smears in 9 cases and in FNA smears in 13cases and they were PAS positive. Diagnosis were confirmed in Histopathological examination along with special stain for fungus in all cases.

Routine HE and PAS stains were done for HP sections and examined under 40X and Oil Immersion Lens (100X). Special stains like Gomori Methenamine Silver stain was used on Bone marrow biopsy and histopathological sections.

Radiological investigations (CXR, USG, CT), Routine investigations (Complete Haemogram, LFT, RFT, serum Electrolytes) along with CD4 count in ART clinic. Microbiological tests like Gram stain of slit skin smear (SSS), India Ink, KOH preparation, Cryptococcal Ag testing, urine for C/S were done and corroborated with. STD panel mandatorily done in serological tests in CSTM. Fungal culture inoculation done on SDA with actidione (inhibitory to *H. capsulatum*) and yeast extract phosphate agar for mycelial to yeast conversion monitoring at 37°C

In acute cases admitted to CCU, ABG was also performed in accordance with critical care protocols. MRCP was performed in 01 case to ascertain presence of gall stones though unrelated to histoplasmosis.

RESULTS:
In our study 27 were males (81.81%) and 6 were females (18.18%) out of total 33 cases with M:F ratio 4.5:1. Average age varies from 8-53 yrs, male 37.92 yrs and female 31.33yrs. Out of 33 cases 29 was seropositive and 4 were seronegative for HIV. Majority of the male patients were farmer or driver, others are businessmen, vegetable seller, unemployed. All the female patients were house wife. Two school children infected from their parents. Duration of onset of acute illness 1-6 months. Majority of the patients presented with fever,skin rash and oral lesions.Fig.I &II. Some of the patients are on ART therapy, most of them were diagnosed as HIV positive in 2017, one patient diagnosed in 2011. Among the other associated illness Tuberculosis was the commonest one ,others are Diabetes mellitus, chronic liver disease, toxoplasmosis (CNS),chronic lung disease etc.

Out of 4 immunocompetent patients 2 presented with adrenal mass of which one had adrenal insufficiency.

One patient presented with bilateral inguinal lymph adenopathy clinically diagnosed as lymphoma.

One 8yrs boy presented with cervical lymphnodes with low grade fever and weight loss clinically diagnosed as tuberculosis.

Table- 1. Distribution of cases according to clinical presentation:

Sign & symptoms	No. of cases	%age
Fever	30	90.9%
Weight loss	28	84.8%
Seropositivity	29	87.8%
Skin rash	27	81.8%
Oral lesion	20	60.6%
Lymph adenopathy	30	90.9%
Hepatosplenomegaly	21	63.6%
CD4 count <150/µL	9	27.7%
Pancytopenia	26	78.7%
Associated Tuberculosis	12	36.3%

- Out of all 33 cases FNAC (13), SSS (09) and HPE in rest of the cases show small, oval yeast cells on LG stain. Routine haemogram showed Pancytopenia and related features in all with almost normal DC in 06 cases and elevated lymphocyte in 01 chronic-PDH case.
- Biopsy showed histiocytic phagocytosis of yeast cells with foamy macrophages and PMN infiltration with no granulomas in immunocompromised cases.Fig.III a,b,c
- Gomori Methenamine Silver stain of lymph node and BM biopsy showed black intracellular yeast consistent with *Histoplasma capsulatum. FigIV*
- PAS stained FNAC smears showed yeast cells with chromatin dot and surrounding halos with no kinetoplasts.
- Mycological cultures were in agreement.
- Here, in most cases, CD4 count and Disseminated Histoplasmosis findings were not in accordance.
- The critically ill patients were terminal, admitted to CCU of STM, and while one patient made a recovery &was shifted to IPD, 01 patient with CD4 count-10cells/µL succumbed to his compromised immunity and expired.

Default correlations useful for administration of ART:
CD4 count > 350 cells/µL: pneumonia and limited to respiratory tract.

CD4 count < 150 cells/µ : BM infiltration, PDH, IRIS(immune reconstitution inflammatory syndrome)

Only 9 of our 33 cases have CD4 count <150 cells/µ (27.27%) with PDH, rest have PDH with CD4 count > 250cells/µL

OBSERVATION:
Case details of some patients →
1. 35yr old male shopkeeper from North 24 parganas c/o HGF 2months with loss of appetite. o/e pallor ++, cervical LAP, mild HSM. MP, SPUTUM, Blood culture- negative. Lab: Pancytopenia with DC[N40,L50,E3,M1], LFT altered [increased],

MCV: 32.4fl | CD4 count- 14cells/µL, admitted to CCU. CXR-WNL,USG- HSM, RPLN+, CT thorax- hilar LAP in paraoesophageal region. On CAT1 , Cotrimoxazole, steroid but recurrence of maculopapular rash and petechial oral lesions. Post diagnosis of atypical PDH by HPE, empirical therapy was converted to Liposomal Amphotericin B I/V and steroid which led to remarkable good response and eventual discharge.

2. 53 yr male farmer from Baruipur c/o LGF 2months, increased wt loss > 6kg in 2months. Diagnosed HIV1 + in 2008 with PTB, Jaundice 1.5months; O/E: splenomegaly, multiple LN swellings [Left cervical > rt axillary] 2LE . Lab: Pancytopenia but with normal blood indices and DC normal, LFT elevated, no history of blood transfusion. CD4 fluctuates over 7 years from 575 cells/µL in 2012 to 666cells/µL in 2014 to 321cells/µL in 2015. [**FNAC**]

3. 30 yr old female resident of Kolkata complained of high grade fever 6-7months with PTB 1.5yrs on ATD for 6months. Lab: pancytopenia with normal indices. Urine C/S: E. coli. Admitted to CCU, CD4 count-14cells/µL. H/o 4 PRBC transfusion.

4. 44yr old male driver from Kolkata complained of Low grade fever for 4months, Loss of appetite for 4months, with past history of abdominal TB 7yrs back (on ATD cat2) and HIV1 seropositive with ART start in Dec 2015.[TLE]. USG showed Hepatosplenomegaly, CT thorax and abdomen showed 2 subpleural cysts with LAP (largest abdominal periaortic LN 20mm). CD4 in nov15- 14cells/µl, ART, then CD4 count-325cells/µL but did not continue response to treatment and reverted back to CD4-16cells/µL in Jan2016. Lab reports: Pancytopenia with abnormal RFT, H/O 3 whole blood transfusions and 2 PRBC.

5.48 yrs unemployed male from Kolkata admitted with HIV1 + with disseminated TB and PDH on ART(01 July 2019) and ATD. No orientation and altered sensorium. Maculopapular rashes all over , raised and hyperpigmented non-pruritic rash, HGF with esophageal Candidiasis, skin necrosis. O/E- splenomegaly. USG shows no ascites, no RPLN. Admitted in CCU with 1U whole blood / day for 4 days f/b 4 U PRBC. On Ceftriaxone, CTX, condom catheterised pt. post diagnosis of PDH started on I/V liposomal Amphotericin B in 100ml DW. Lab: SEVERE PANCYTOPENIA.

6. 32 yr male resident of Malda, farmer by profession came with LGF

for 6months. HIV1+ in 2011. CD4 count on adm in 2011-325cells/μL,lab: pancytopenia with normal indices. CD4 count-635cells/μL in jan 2017. On oral Itraconazole lifelong treatment.

7. 40 yr old male businessman from Kolkata came with dry cough, shortness of breath and low grade fever for 1month in 2018 May. HIV1+ in 2018, CD4 count- 576cells/μL in May 2018. Lab: pancytopenia with increased neutrophils in DC presumably acute pulmonary. CXR- patchy pulmonary infiltrates. No HSM.

8. 40yr male farmer of North 24 parganas diagnosed with HIV1+ in 2016 with CD4 count of 700cells/μL appeared with maculopapular non-pruritic hyperpigmented rash all over lower extremities and back, trunk, abdomen. Lab: pancytopenia with normal LFT, RFT. USG showed mild HSM. Diagnosed with cutaneous histoplasmosis.

9. 32yr old female resident of Malda, diagnosed with HIV1+ in 2017 with CD4 count of 678cells/μL appeared with multiple LN swellings in right axillary and inguinal region bilaterally. USG showed hepatosplenomegaly, CXR showed patchy hilar infiltrates in lung with features of pericarditis/mediastinitis. On Ceftriaxone, post diagnosis of PDH recovered well. No Transfusion history.

10. 30yr old female from Kolkata diagnosed HIV+ in 2016 with CD4-650cells/μL c/o maculopapular rash all over with petechial lesions in oral mucosa. pancytopenia in lab and CXR-WNL, with no ascites or HSM in USG. Diagnosed with mucocutaneous Histoplasmosis. [**FNAC**]

11. 42 yr male vegetable seller from south 24 parganas, complained of low grade fever and loss of appetite for 5months with dry cough. CXR showed hilar LAP with pulmonary infiltrates and Usg showed mild splenomegaly. Pancytopenia with normal blood indices but increased neutrophil. Diagnosed with HIV1+ in 2017 and ART started 2017. CD4 count- 485cells/μL in 2017. Diagnosed with acute pulmonary histoplasmosis.

12. 46 yr male from Kolkata ,working in a poultry farm presented with skin lesions for 2 months ,known case of HIV and on ART for 4yrs,. His CXR show military mottling ,CD 4count <100/μL clinically diagnosed as kaposi's sarcoma.

13. 33yrs female patent ,known case of HIV with history of CNS toxoplasmosis (treated) presented with low grade fever, generalised weakness, jaundice , recurrent diarrhoea, pancytopenia with CD4 count <50.

DISCUSSION :

Histoplasmosis poses a difficult diagnostic challenge because of its similarity and clinical manifestationswith other diseases specially with tuberculosis. The primary pathogen, the etiologic agent, *H. capsulatum* var c*apsulatum* infects the immunocompetent as well as immunocompromised patients.

In our study 27 were males (81.81%) and 6 were females (18.18%) out of total 33 cases with M:F ratio 4.5:1. Average age varies from 8-53 yrs, male 37.92 yrs and female 31.33yrs. Out of 33 cases 29 was seropositive and 4 were seronegative for HIV. Majority of the male patients were farmer or driver, others are businessmen, vegetable seller, unemployed. All the female patients were house wife. Two school children infected from their parents. Majority of the patient presented with skin rash (81.8% and oral lesion (61.6%). Clinical differential diagnoses were as follows:

1. Tuberculosis(commonest)
2. *Leishmania donovani*
3. *Cryptococcosis*
4. *Candida glabrata*
5. Carcinoma especially vascular tumours eg. Kaposi Sarcoma
6. Lymphoma
7. *Mycoplasma pneumoniae*
8. *Toxoplasma gondi*

HPE/FNAC/SSS shows Histoplasmosis in all cases.

Out of 4 immunocompetent patients 2 presented with adrenal mass of which one had adrenal insufficiency.

One patient presented with bilateral inguinal lymph adenopathy clinically diagnosed as lymphoma.

One 8yrs boy presented with cervical lymphnodes with low grade fever and weight loss clinically diagnosed as tuberculosis.

In this study it has been observed that efault correlations useful for administration of ART:

CD4 count > 350 cells/μL: pneumonia and limited to respiratory tract.

CD4 count < 150 cells/μ: BM infiltration, PDH, IRIS(immune reconstitution inflammatory syndrome)

Only 9 of our 33 cases have CD4 count <150 cells/μ (27.27%) with PDH, rest have PDH with CD4 count > 250cells/μL

Biopsy showed histiocytic phagocytosis of yeast cells with foamy macrophages and PMN infiltration with no granulomas in immunocompromised cases. Ill defined granulomas were found in 2 cases of imunocompetent patients.Gomori Methenamine Silver stain of BM biopsy showed black intracellular yeast consistent with *Histoplasma capsulatum.*

Although culture has been considered as the gold standard among the laboratory diagnostic tests, its value is limited by the fact Sabouraud agar routinely used as a mycological medium is unsuitable for this fastidious fungal pathogen. On the other hand direct microscopy of wet mounts or stained tissue sections/smears of clinical specimens requires expertise of a cytopathologist/histopathologist for interpretation. Though with the development of PCR it can be overcome but this molecular technology is not accessible to a vast majority of centres in Indian subcontinent.[7]

In patients with prolonged fever, hepatosplenomegaly, and lymphadenopathy, histoplasmosis must be considered in the differential diagnosis, particularly, if there is no response to empirical anti-tubercular therapy (ATT). Also, many cases of histoplasmosis in the subcontinent may present as non-healing oral ulcers mimicking mucocutaneous leishmaniasis. It needs to be emphasized that histoplasmosis should be considered in the differential diagnosis of patients with mucocutaneous lesions.[4] Histoplasmosis is an under-recognized disease in India and should be considered in the differential diagnosis patients with prolonged fever, granulomatous disease on histopathology without response to ATT. Tissue biopsy specimens show granulomas, fungal stains should be routinely performed. Treatment with itraconazole leads to an excellent outcome in most patients.[13]

Intracellular mycosis of Reticuloendothelial system involving spleen, adrenals, liver , kidney, skin and CNS(rare) and others, so CMI plays a crucial defensive role. Hence AIDS patients are at an exceptionally high risk .In mild cases, self resolution in 2-3 weeks in immunocompetent person. Clinical types can be broadly classified into

a. Acute Pulmonary : yeast within histiocytes; C/F: low grade fever with dry cough, dyspnoea X-ray chest shows pulmonary infiltrates and hilar lymphadenopathy typically.
b. Chronic pulmonary: ulcerative lesions on mucosa of lip, nose with typical pulmonary lesions with central necrosis. Histoplasmoma is a uniformly calcified zone with peripheral fibrosis around healed focus. This stage atypically mimics malignancy with mucocutaneous lesions like vascular tumours or radiologically appearing as neoplastic lymphadenopathy with profuse calcified foci.
c. Mucocutaneous Histoplasmosis: oral cavity lesions
d. Progressive Disseminated Histoplamosis (PDH): pancytopenia with hepato splenomegaly and lymphadenopathy[7]

The diagnosis of histoplasmosis is based on a multi-faceted approach that includes clinical, radiographic and laboratory evidence of disease.[9]

In this study the following factors /atypical findings deviated clinical diagnosis towards malignancy:

- CD4 count in 24 out of 33 cases remained above 480-500cells/μL at the time of diagnosis with Histoplasmosis any form while conventionally, CD4 count < 150 cells/μL is said to be the standard cut-off for Histoplasmosis attack.
- Almost 27 out of 33 cases appeared with skin lesions associated with organ dysfunction seen by radiology and later bone marrow aspiration/biopsy. Another variant of H.capsulatum var duboisii (African Histoplasmosis) mainly is associated with skin lesions to this extent but our study cases were conclusively classical H.

capsulatum by fungal culture. Also 4cases of PDH did not show any pulmonary involvement in CXR which is a known clinical sign of classical (acute/ chronic) Histoplasmosis. skin lesions made diagnosis reconsidered against vascular tumours like Kaposi sarcoma as all are HIV1+.

- One of the study cases showed adrenal insufficiency.
- 11 out of 33 cases were initially non-responsive to empirical treatment with antibiotics like ceftriaxone, CTX or steroid and showed recurrence (which is a feature of chronic Histoplasmosis).

The spectrum of disseminated infection includes acute, severe, life-threatening sepsis and chronic, slowly progressive infection. Diagnostic accuracy has improved with the use of an assay for Histoplasma antigen in the urine; serology remains useful for certain forms of histoplasmosis, and culture is the ultimate confirming diagnostic test. Classically, histoplasmosis has been treated with long courses of amphotericin B.

In an immunocompromised patient, even with minimum suspicion of opportunistic infection, there is a need for consolidation of selective investigations like FNAC, HPE and relevant microbiological tests into a diagnostic design for maximum utilization of finances, resources and time, all of which are scarce for the average Indian patient. Choosing the relevant test requires an understanding of the performance of various diagnostic methods attributed to each clinical setting. While HP examination remains gold standard and quite time-efficient, presumptive rapid diagnosis can be made by careful evaluation of cytolysis of centrifuged BAL fluid>Bone marrow aspirate> blood {buffy coat}. Fungal culture, although time consuming remains the currently approved confirmatory test as well for species identification. But often, tuberculate macroconidia *of Histoplasma* can be doubted with confusers like *Renispora flavissima, Sepedonium sp.* Also, SDA is not quite so effective and that is the most commonly available in laboratory[10]. CSTM is equipped with a Mycology dept. with biosafety level 3 infrastructure required for *Histoplasma sp* culture but not many such laboratories are accessible or affordable for the ailing patient.

Soon, with the advent of FISH AccuProbe™, even Nested PCR would become mainstay for prompt diagnosis[11]. While that remains in distant future, resource-poor institutions can apply a back to basics approach with the amalgamation of radiological and clinical signs with histopathology/FNAC. Through Immunological tests like Ag detection from BAL fluid, Urine, serum or CSF in HIV+ patients (if allowed by finances), even the active or past staging of disease can be done promptly. Hence, a simplified diagnostic algorithm with the clinical picture, prompt HPE/FNAC and if necessary Ag detection test would benefit not only the clinicians and pathologists, but effectively accelerates life-saving treatment for patients.

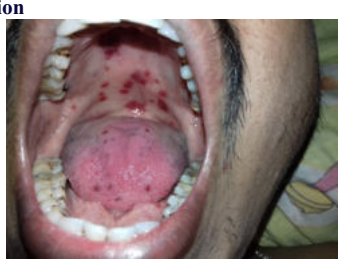
Disseminated histoplasmosis is a rare in immunocompetent host. In India, histoplasmosis is rare as it is thought to be endemic only in small regions in West Bengal in Western India.[14]

Liposomal amphotericin B appears to be a better choice compared to deoxycholate amphotericin B for treating PDH in people with HIV; and fluconazole performed poorly compared to other azoles.[15]

CONCLUSION:

DH is not uncommon in India and is being increasing day by day and it should be considered in the diagnosis of patients with prolonged fever, weight loss, oropharyngeal ulcers, hepatosplenomegaly, lymphadenopathy and adrenal enlargement. Correct diagnosis by well designed analytical studies utilising appropriate diagnostic modalities to understand the epidemiology of this neglected disease is necessary for accurate treatment leading to a favourable outcome.

Fig. I oral lesion



Oral lesions in a HIV positive case with DH

Fig .II. Skin rash –clinical diagnosis –Kaposi sarcoma

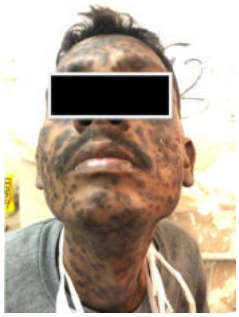
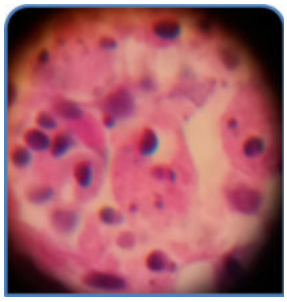
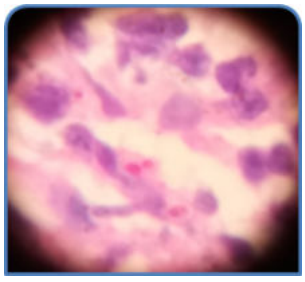


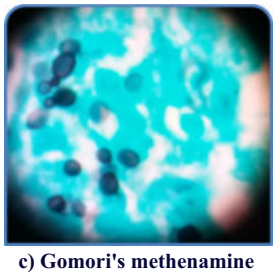
Fig.III. Photo micrograph of Lymph node biopsy



a)H&E in(100x oil immersion)



b) PAS stain (100x)



c) Gomori's methenamine silver(100x)

Fig. IV .Bone marrow aspirate Leishman stain (100x)

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