Disseminated Cutaneous Histoplasmosis In Aids

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Introduction

There have been very few reports of histoplasmosis from India. It could be because of its varied clinical presentation and lack of awareness. Panja and Sen first reported histoplasmosis from India in 1959 [1]. Histoplasma capsulatum is considered to be endemic in certain North Indian states like West Bengal, where a study showed a prevalence of skin positivity of 9.4% to histoplasmin antigen [2]. There are a few sporadic case reports from South India as well[3]. With the advent of HIV infection more and more cases of Histoplasmosis are observed.In this patient who presented with disseminated cutaneous histoplasmosis we were faced with 2 major therapeutic problems.First was diagnosis and management of Histoplasmosis and second was treatment of AIDS.As she was already on standard ART regimen she had probably developed failure to first line drugs due to drug resistance.So she was started on second line of antiretroviral therapy.However she failed to respond and Histoplasmosis turned out be the fatal opportunistic infection for her.

Case Report

A 30 year old female a diagnosed case of Acquired immunodeficiency syndrome on treatment with Stavudine,Lamivudine,Nevirapine was admitted with chief complaints of Fever off and on, dry cough and nodular skin lesions over face since 5 months.Patient was clinically stable on ART (antiretroviral therapy) till recent symptoms and had not done any investigations to monitor the disease or treatment.

On general examination she was febrile with pulse rate of 80/min,regular,BP of 110/70 mmof Hg ,tachypnoeic with respiratory rate of 28/min,but was maintaining spO2 of 96%.She had oral thrush, but no oral ulcers or lymphadenopathy. On Local examination she had multiple subcutaneous nodules on left lower eye lid, right arm and right thigh.She had crusted as well as keratotic nodules over right cheek (Figure 1), bridge of nose and left lower eyelid which were non tender(Figure 2). Biopsy was taken from the lesion on right cheek.Her systemic examination was normal except for few scattered rales on chest auscultation.

On investigations her Hb% was 9.9 gms/dl,Total leucocyte count of 3000/cu mm.Polymorphs were 84% and lymphocytes 16%.Her CD4 count was only 16.Viral load estimation was not done.Sputum examination by microscopy revealed - few gram positive cocci in pairs & small groups, numerous fungal spores & hyphae.Sputum was negative for acid fast bacilli.X-ray chest showed diffuse infiltrates with cavitatary and consolidatory changes on both sides (Figure 3).CT scan head was normal.

Sputum culture in Sabbouraud's medium grew histoplasma capsulatum.Histological examination of biopsy specimen from the nodule showed nodular aggregates of histiocytes with multiple intracellular yeast form of histoplasma (Figure 4).

She was given Inj.Fluconazole 150 mg IV for 2 weeks followed for Tab Itraconazole 100 mg BD for 1 month.She was also given Tab Sulfamethoxazole-Trimethoprim twice daily.Her ART regimen was changed to HAART PLUS i.e. Emtricitabine, Tenofovir,Atazanavir. Initially she showed response, but after 1 month the nodules and respiratory symptoms recurred.Then she was given Inj.Amphotericin B 15 mg daily for 15 days.She failed to respond.She continued to detiorate and developed severe wasting syndrome and loss of appetite.She went home against medical advice and died after one and a half month at home.

She represents a typical terminal AIDS patient with fatal Disseminated Cutaneous Histoplasmosis.

Discussion

Histoplasmosis, also called as Darling's disease, is

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caused by a dimorphic fungus Histoplasma capsulatum. The fungus has two variants viz. Histoplasma capsulatum var. capsulatum, which is found in America and the tropics, and Histoplasma capsulatum var. duboisii, which is found in Africa. The pulmonary and disseminated forms of histoplasmosis are very common in AIDS patients and cause great morbidity and mortality. Primary cutaneous histoplasmosis is rare [4].

There should be a very high index of suspicion of histoplasmosis in an immunocompromised patient who has a CD4 count of less than 200.Our patient had a CD4 cont of 16 only.The clinical manifestations of histoplasmosis are different in immunocompetent and immunocompromised host.

In an immunocompetent host it is asymptomatic or mild self limited infection.It presents with Flu like illness with fever, chills, headache, myalgia, cough, dyspnoea.Chest radiographs usually show signs of pneumonitis with hilar or mediastinal adenopathy.5-10%may show rheumatologic symptoms of arthralgia or arthritis often associated with erythma nodosum. Dhar S. et al. reported seven cases of histoplasmosis; 6 males and one female. Their ages ranged from 40 to 78 years. Of 7 patients, 5 had skin lesions, 4 with palatal ulcer, one with papules and nodules. None of the patients were HIV positive. In all patients either cytology, or skin biopsy or both revealed Histoplasma. Culture was positive in two patients[5].

In immunocompromised host risk factors for Progressive Disseminated Histoplasmosis (PDH) include AIDS [cd4 <200] , extremes of age, use of immunosuppressive medications.Like our patient the common symptoms are Fever , weight loss,cough, breathlessness.Cutaneous involvement is seen usually in the form of multiple subcutaneous nodules and mucocutaneous involvement also occurs in the form of palatal and oral ulcers.The infection disseminates through the reticuloendotehlial system.There may be hepatosplenomegaly.CNS histoplasmosis also occurs in late stage.Surprisingly our patient did not have CNS histoplasmosis.PDH in AIDS patient has an acute rapidly fatal course with diffuse interstitial or reticulonodular lung infiltrates or causing respiratory failure , shock, coagulopathy & multiorgan failure.Recently Bonifaz et al. have reported a series of 23 cases (21 men, two women; median age 29 years) with disseminated cutaneous histoplasmosis in AIDS patients . Most of the patients were classified as stage C3. The most common dermatological findings were papules, crusting plaques, nodules and ulcers, mainly located on the face and chest. 65% had pulmonary involvement.They have not reported a single case of Progressive Disseminated Histoplasmosis [6].

Diagnosis of Histoplasmosis is usually achieved by high index of suspicion and demonstration of Histoplasma capsulatum organisms as intracellular inclusion bodies on biopsy specimen.Cultures may sometimes be negative.Serological tests against histoplasma antigen are still not widely available.

Treatment is indicated for all pts with PDH or chronic pulmonary histoplasmosis or symptomatic patients with acute pulmonary histoplasmosis. In immunocompetent patients, in majority of cases acute pulmonary histoplasmosis resolves without therapy & treatment is not recommended.In immunocompromised host ART improves outcome of PDH & is recommended.Our patient was already on ART,and as her CD4 count was only 16 regimen was changed to HAART PLUS.Whether our patient had primary drug resistance to initial drugs or developed resistance later is difficult to comment because resistance testing was not done prior to starting treatment.Drug resistance during the course of ART usually develops when HIV replication is not fully suppressed.WHO now recommends that drug resistance should be carefully monitored.Fibrosing mediastinitis which represent a chronic fibrotic reaction does not respond to antifungal therapy.The management guidelines[7] are as follows :

1. Ac. Pulmonary Histoplasmosis: moderate to severe- Inj.Amphotericin.B+ glucocorticoids for 1-2 weeks. Then Itraconazole 200mg B.D. for 12 weeks.
2. Chronic pulmonary Histoplasmosis:Oral Itraconazole 200mg.OD/BD for 12months
3. Progressive disseminated Histoplasmosis –Inj. AmphotericinB for 1-2 weeks. Then Itraconazole 200mg BD for 12 months.
4. CNS Histoplasmosis: Inj.Amphotericin.B for 4-6 weeks then Itraconazole 200mg BD/TDS. for 1 year.

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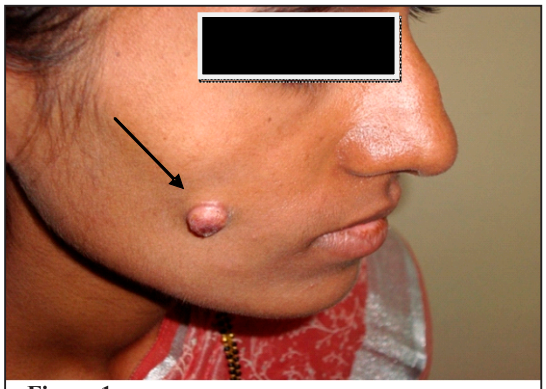

Figure 1
Showing Hyperkeratotic Nodule Over Right Cheek

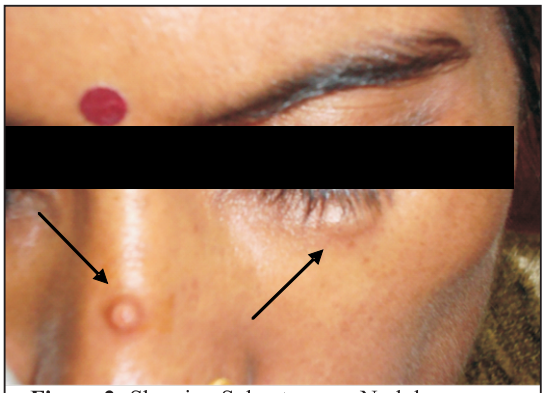

Figure 2: Showing Subcutaneous Nodules over Bridge of Nose and Lower Eyelid

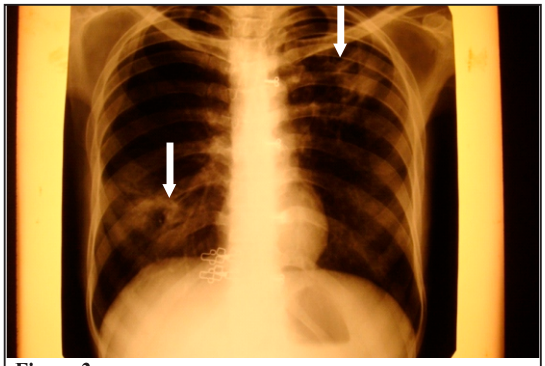

Figure 3
X-ray Chest Showing Infiltration, Diffuse Reticulonodular Shadows And Cavitation Lt.upper Zone And Rt.lower Zone

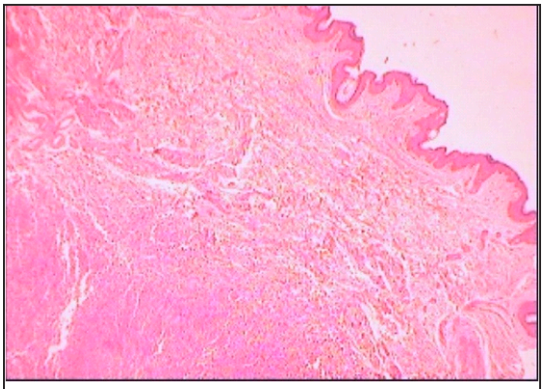

FIGURE 4
Biopsy from subcutaneous Nodule showing histiocytic infiltrate in the dermis

FIGURE 5 Multiple tiny regular intracytoplasmic bodies, surrounded by a clear halo s/o histoplasma capsulatum

colour