Case Report

Granulomatous skin lesions; a rare manifestation of histoplasmosis A Case Report

Welagedara PGRUM[1], Sigera LSM[1], Liyanage SPM[2], Dissanayake DMUI[1], Udugama SG[2], Jayasekera PI[1]

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Abstract

Histoplasma capsulatum is a dimorphic fungus which can cause severe disease in humans. This case describes a patient with disseminated histoplasma infection with granulomatous skin lesions which is rarely encountered in Sri Lanka. A farmer who presented with multiple granulomatous nodules on face and upper trunk was found to be infected with *Histoplasma capsulatum* following isolation in fungal culture. He was diagnosed with histoplasmosis four years ago but had defaulted on treatment. He was treated with IV amphotericin B for 10 days and oral itraconazole for one year and achieved complete cure without any complications. Close contact with bat guano was considered as the source of his infection and measures were taken to prevent further exposure.

Histoplasma infection needs to be ruled out in patients presenting with granulomatous cutaneous lesions as good clinical responses can be achieved by rapid diagnosis and appropriate therapy with antifungal drugs.

Keywords: *Histoplasmosis, histoplasma, disseminated, granulomatous*

Introduction

Histoplasma capsulatum is a soil saprophyte which is highly endemic in the Americas. Southeast Asis is also known as an endemic region for *Histoplasma* infections. *Histoplasma* can cause a spectrum of diseases from asymptomatic to severe progressive disseminated infection, specially seen in patients with decreased cell mediated immunity.[1] Evidence for this infection in Sri Lanka is limited to a few case reports.[2–5] The patient described here had disseminated disease with *Histoplasma* which is a rare occurrence in Sri Lanka.

[1] *Department of Mycology, Medical Research Institute, Colombo 8, Sri Lanka*
[2] *Department of Microbiology, Army Hospital, Colombo-05, Sri Lanka*

Address for correspondence: Dr. PGRUM Welagedara, Department of Mycology, Medical Research Institute, Colombo 8 Tel: +94714398741 Email: pgrumw@gmail.com https://orcid.org/0000-0002-2824-0140

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Case history

A fifty-seven-year-old farmer, father of a military officer, presented to the Military Hospital, Colombo, complaining of multiple nodular cutaneous lesions. These lesions were mainly seen on his upper trunk, including face and arms (Figure 1). He had been experiencing tender, pus discharging nodules for one month. His oral cavity was also badly affected with these lesions, including prominent swelling of his lips. He had difficulty in swallowing, and a poor appetite due

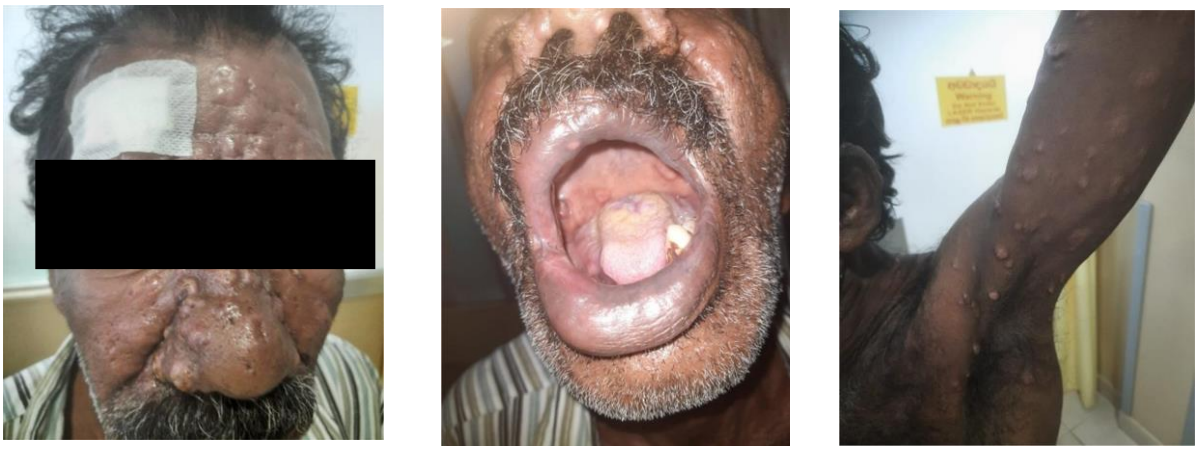

Figure 1: Granulomatous lesions in the face, oral cavity, upper limbs and trunk

to oral mucosal involvement resulting in weight loss. He was a diabetic but had defaulted on follow-up treatment.

He was investigated for a similar episode 4 years ago in a different hospital. During that admission, apart from skin nodules, he had mild hepatomegaly, chronic calcified pancreatitis and multiple para-aortic lymphadenopathy. Histology of an axillary lymph node biopsy revealed granulomatous lymphadenitis favoring sarcoidosis and he was treated with prednisolone. Additionally , a re-biopsy was done for fungal culture to exclude histoplasmosis. *Histoplasma capsulatum* was isolated in a culture at the Mycology Reference Laboratory and he started on oral itraconazole. However, he defaulted on treatment and follow-up.

Investigations done on the current admission to hospital showed elevated liver function (SGPT 87U/L; SGOT 97U/L; ALP 790IU/L; bilirubin 0.6mg/dl), with normal full blood count and renal function. Pus swab and axillary nodular tissue direct smear showed yeast cells with no bacterial growth on culture. Histopathology of the forehead nodular lesion was compatible with histoplasmosis. The right axillary nodular lesion had multiple small yeasts on direct microscopy with potassium hydroxide (10%). After 2 weeks of incubation at 26 ℃ on Sabouraud Dextrose Agar (SDA), *Histoplasma capsulatum* was isolated at the Mycology Reference Laboratory (Figure 2).

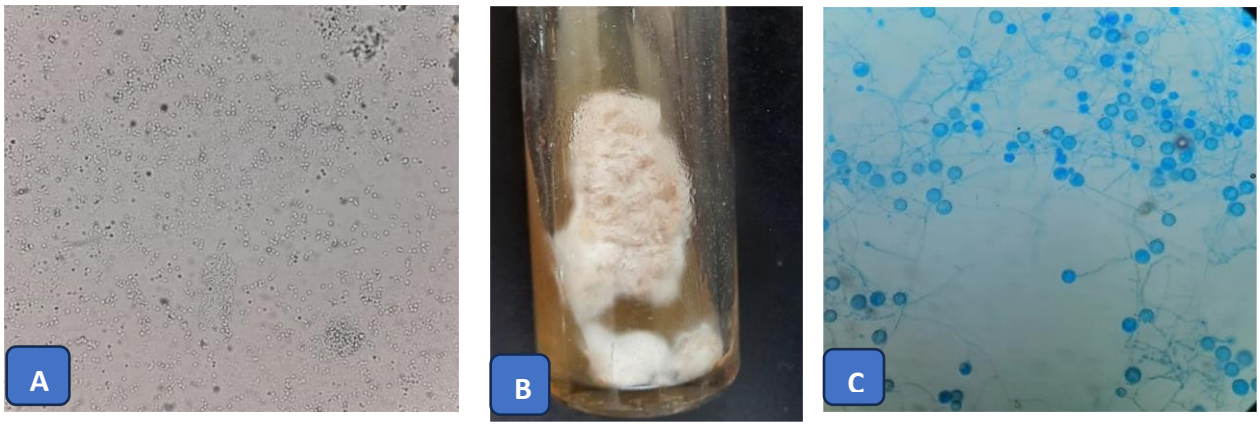

Figure 2: Laboratory findings on tissue : direct microscopy and culture

A. Direct 10% KOH mount of nodules - small budding yeast cells
B. Culture on SDA agar after 14 days of incubation at 26 ℃ - expanding, granular to cottony, white color colony with cream colored reverse
C. Microscopic appearance – thick-walled macroconidia with tuberculate projections, arising from short conidiophores and hyaline microconidia arising on short stalks from undifferentiated hyphae

Chest X-ray revealed a paravertebral density in the upper abdomen and a density in the left lower zone of lung overlapping a rib. Multiple pancreatic calcifications were noted in contrast-enhanced computed tomography. No other organs were involved.

The patient was treated for disseminated *Histoplasma* infection with intravenous (IV) liposomal amphotericin B 3mg/kg daily followed by oral itraconazole 200mg twice daily for which he achieved adequate clinical response. Oral swelling and the size of skin nodules gradually subsided. He received only 10 days of IV amphotericin B due to unavailability of the drug.

After 40 days of itraconazole treatment he was discharged on oral itraconazole 200mg twice daily. He was followed up at the clinic regularly and showed good clinical response to treatment. At the end of one year of oral itraconazole, all the skin lesions were resolved, and he was completely asymptomatic (Figure 3).

Frequent exposure to bat guano was considered the major source of his infection and he was advised to prevent further exposure to bat guano. In addition, he was advised to maintain good glycaemic control and to comply with the prescribed oral hypoglycemic drug regime.

Timeline of his clinical course is given in Figure 3.

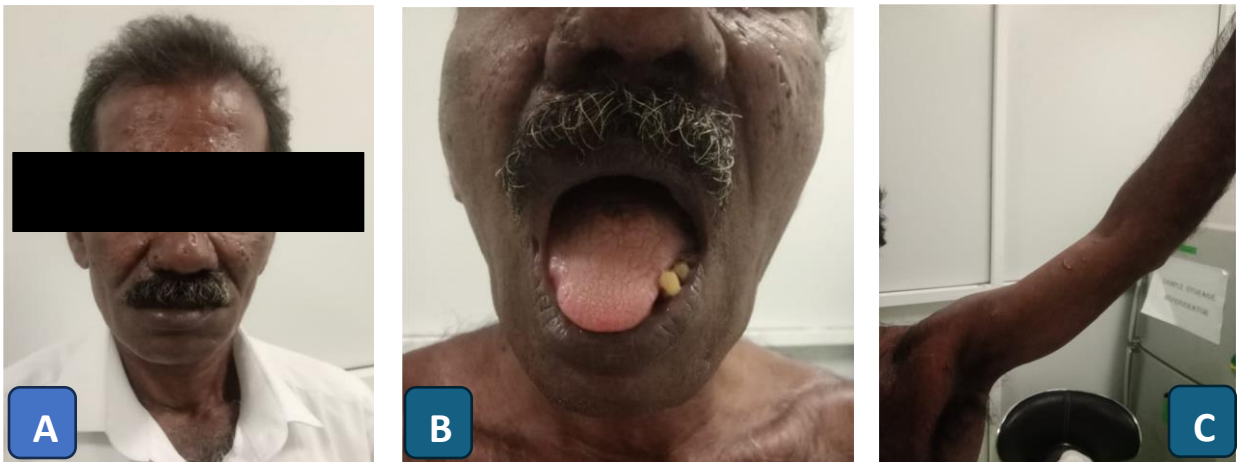

Figure 3: Response to antifungal treatment after 3 months

A. Resolving skin lesions on face.
B. Reduced oral swelling and subsiding of oral lesions.
C. Resolving lesions on upper limb

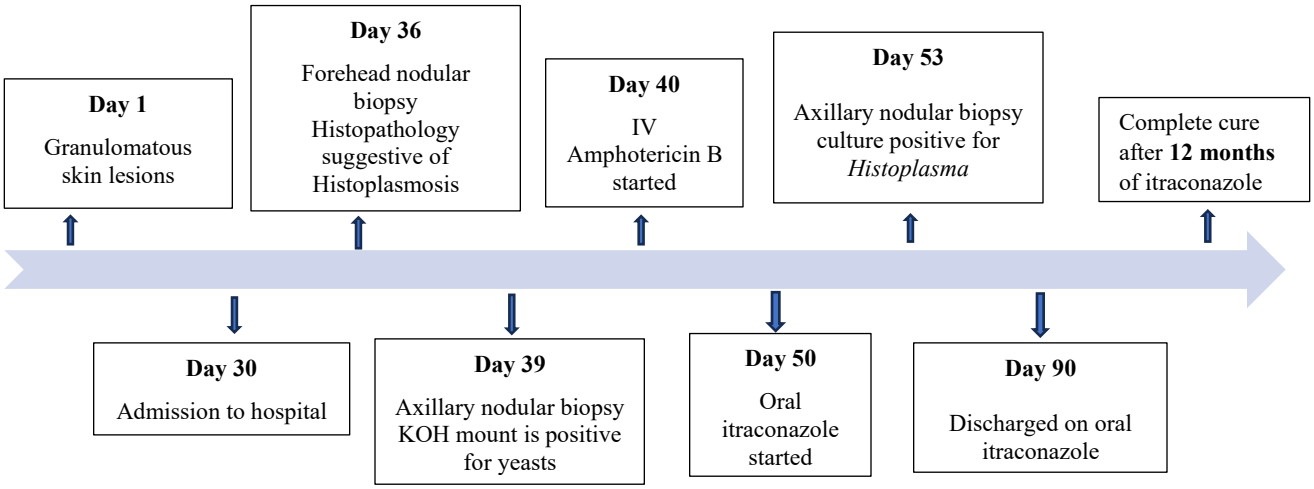

Figure 4: Timeline of the clinical course

Discussion

Histoplasmosis, which is highly endemic in the Americas, is being increasingly recognised beyond that region. Southeast Asia and Southern Europe are also now considered to be endemic for *Histoplasma capsulatum var capsulatum* while *Histoplasma capsulatum var duboisii* is prevalent in the central and western regions of Africa causing African histoplasmosis.[6,7]

It is a thermally dimorphic fungi which is mainly seen in soil rich with birds, especially bat, excreta. Inhalation of aerosolised microconidia is the main mode of transmission when the environment is disturbed due to various activities such as demolition, construction and renovation activities.[1]

An epidemiological survey found that 77% reported cases of histoplasmosis were due to exposure to bats, birds or their droppings.[8] Similarly, the patient described in this case was a farmer from a rural village in the Hambantota district who had been exposed to bat caves in his garden.

The gastrointestinal tract, especially the oral mucosa, is one of the commonest sites of dissemination of histoplasma infection and was seen in this patient as well. In contrast to other endemic mycoses, the skin is not a common extra pulmonary site for this infection other than in HIV patients.[7] However, this patient presented with multiple granulomatous skin nodules and his retroviral studies were negative. Tuberculosis is another infectious cause for disseminated cutaneous granulomas while sarcoidosis and interstitial granulomatous dermatitis are other non-infectious causes.[9]

Disseminated histoplasmosis should always be treated with antifungals to prevent fatalities.[10] Most patients initially need IV amphotericin B followed by step down therapy with itraconazole after 1–2 weeks. This patient responded well to amphotericin B and itraconazole and was able to be discharged from hospital with itraconazole maintenance therapy. A minimum of 12 months of treatment is recommended with the assessment of clinical, laboratory and radiological parameters to prevent relapses.[7]

Conclusion

Histoplasma infection should be considered as a differential diagnosis when patients present with granulomatous cutaneous lesions, especially if there is high exposure to fungal spores. Disseminated histoplasmosis can be fatal if not treated adequately. Accurate and rapid diagnosis and appropriate antifungal treatment for adequate duration will favor good responses in patients with histoplasmosis.

Declaration

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