



## Original Research Article

### Primary cutaneous histoplasmosis in 56 years old male – A rare case report

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#### A B S T R A C T

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Histoplasmosis was considered a rare and always fatal disease for many years after it was first described by Darling in 1906. It is a granulomatous fungal disease caused by *histoplasma capsulatum*, a dimorphic fungus. 56 years old, post transplant male presented with raised erythematous skin lesion on face. Histology showed a granulomatous skin infiltrate with numerous intracellular PAS positive rounded yeast cells within macrophages. Treatment with itraconazole showed an excellent response. The purpose of this paper is to report a case of primary cutaneous histoplasmosis which is very rare and resulted from direct inoculation of the fungus through the skin.

## Introduction

Histoplasmosis refers to an infection caused by *histoplasma capsulatum*, a dimorphic fungus and it was first described by Darling in 1906. [1] Histoplasmosis is widely distributed throughout the world, occurring in more than 60 temperate and tropical countries in USA, Africa and Australia. [2] Primary cutaneous histoplasmosis infection is quite rare and presents as variety of the cutaneous lesions such as pustule, papule, plaque, ulcer, warty nodule or rarely as Erythema Nodosum. Because of a variety of clinical presentations and lack of awareness amongst dermatologists, histoplasmosis is reported rarely in India. First case of histoplasmosis was reported in India in 1959[3].

Here, we are presenting a case of 56 years old, post transplant male patient with raised erythematous skin lesions on face with no evidence of any internal organ involvement. Although fungal culture is a useful to diagnose histoplasmosis, the culture often yields negative results and because of this reason histopathological examination of the skin biopsy remains gold standard tool for final diagnosis.

## Case report

56 years old male presented with raised erythematous skin lesion on face. The lesion first appeared a month before consultation. On examination, multiple erythematous

papules and nodules were present all over the face. Patient experienced mild burning and pain in the lesions. Some of them also showed spontaneous ulceration and crusting. The patient was a known case of Diabetes Mellitus type-II with renal failure for which he underwent renal transplantation before 15 months. There was no history of exposure to birds, trauma preceding the onset of skin lesions. On clinical examination, neither hepatosplenomegaly nor lymphadenopathy was found. Examination of other systems revealed no significant abnormality. The clinical diagnosis was uncertain. Laboratory investigations including routine hemogram, urine and stool examination, and renal and liver function tests were within normal limits. Roentgenogram of the chest and bones were normal. Mantoux test, VDRL test and ELISA for HIV were negative. Biopsy was taken from the skin lesion and sent for histopathological examination.

Histopathology showed a thinned out epidermis with loss of normal dermal architecture. There was presence of granulomatous infiltrate involving the dermis and subcutaneous tissue mainly consisting of macrophages and scattered giant cells. (Photo – 1) Small (2-4 microns), PAS positive, round to oval organisms with a clear halo were seen. (Photo - 2, Photo - 3) The causative organisms were stained by the usual fungal stains such the PAS reaction and methenamine silver. We found aggregates of histiocytes containing intensely PAS positive smaller yeast forms. (Photo – 4) GMS stain showed spores of *histoplasma capsulatum* within the cytoplasm of macrophages. (Photo - 5, Photo – 6) The histopathology was compatible with the diagnosis of histoplasmosis. Patient showed an excellent response to itraconazole 100 mg twice a day. The patient was followed up regularly for the tolerance of the treatment. The skin

lesions were resolved and there was no recurrence.

## Discussion

Histoplasmosis is caused by two species, *histoplasma capsulatum* found in America and the Tropics and *histoplasma duboisii* found in Africa. *H. capsulatum* exists as a saprophyte in nature and the spores of these organisms, which are infectious to man, are found in soil, thorns and bird droppings. The route of infection to humans is via inhalation of the spores. [1] There are two variants of *histoplasma capsulatum*, one is *capsulatum* and the other is *duboisii*. The variant *capsulatum* is found in America and tropical countries, whereas the variant *Duboisii* is seen in Africa. In the *capsulatum* type, pulmonary changes dominate, whereas in the *Duboisii* type, lesion of skin and bones are seen. [4]

Histoplasmosis may occur in three forms: primary cutaneous inoculation histoplasmosis, primary pulmonary histoplasmosis caused by inhalation, and disseminated histoplasmosis. Primary cutaneous inoculation histoplasmosis, a very rare event, is benign and self limited in duration. It generally occurs as a laboratory infection and presents as a chancriform syndrome, with a nodule or ulcer at the site of inoculation and associated lymphangitis and lymphadenitis. [5, 6]

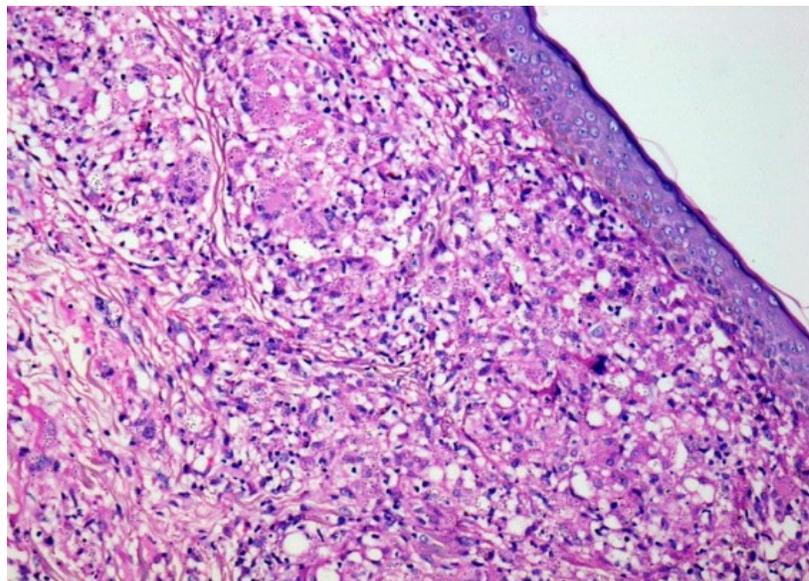
Histoplasmosis has emerged as an important opportunistic fungal infection in immunocompromised patients, including those with AIDS. [7] Infections have been reported after a median of 11 months (range, 1.2–90 months) after organ transplant [8] however our patient presented first within 14 months of renal transplant.

Cutaneous lesions occur in a wide variety of forms, none of which can be said to be characteristic. Most commonly they consist of primary ulcers, often with annular, heaped-up borders. [9, 10] They may also consist of papules, nodules, or large plaque-like lesions. [11, 12] Papules may umbilicate, causing a resemblance to lesions of molluscum contagiosum. [13] In addition, there may be a number of nonspecific cutaneous manifestations associated with histoplasmosis, including erythema nodosum and erythema multiforme. [14]

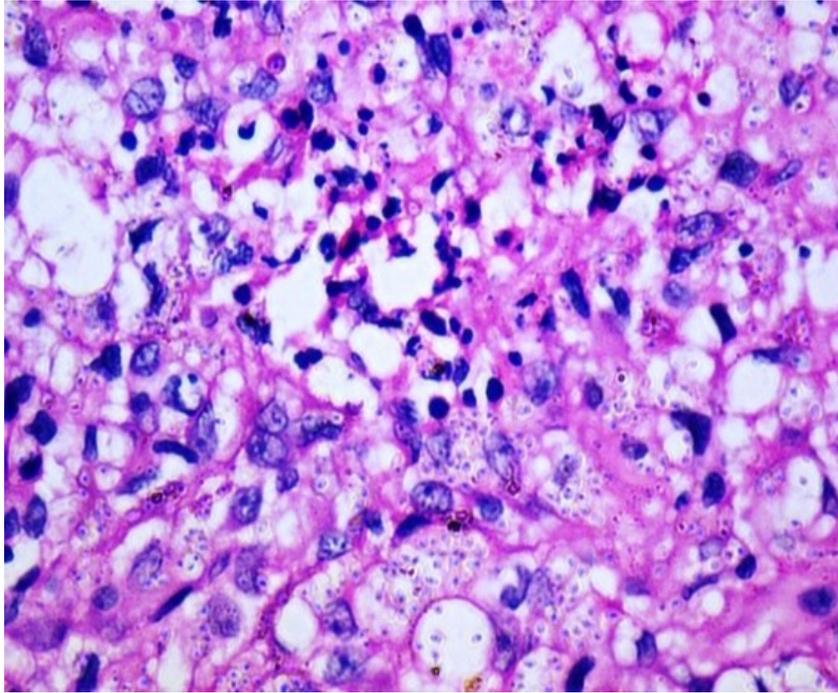
Fungal cultures for this fastidious organism are often negative. Culture yield is highest for bronchi alveolar lavage, bone marrow aspirate, blood and sputum. Cultures are negative however in other forms of Histoplasmosis. [15] As culture may require up to a 4-week incubation period also [16], biopsy of a cutaneous lesion is the most rapid method of arriving at a specific diagnosis.

The diagnostic feature in all types of cutaneous histoplasmosis is the presence of tiny 2 to 4  $\mu\text{m}$  spores within the cytoplasm of macrophages and variably within giant cells. [12, 17] We are able to see the spores of *H. capsulatum* in sections stained with hematoxylin and eosin, Gram stain, or Giemsa stain. They appear as round or oval bodies surrounded by a clear space that was originally interpreted as a capsule, giving rise to the name *H. capsulatum*. Silver impregnation stains like GMS (Gomori's methanamine silver) shows spores of *Histoplasma capsulatum* within the cytoplasm of macrophages and absence of capsule. On electron microscopy, *H. capsulatum* does not possess a capsule and that the inner portion of the clear space represents the cell wall of the fungus and the clear space itself is filled with granular material that separates the cell wall of the fungus from the cytoplasm of the macrophage. [17]

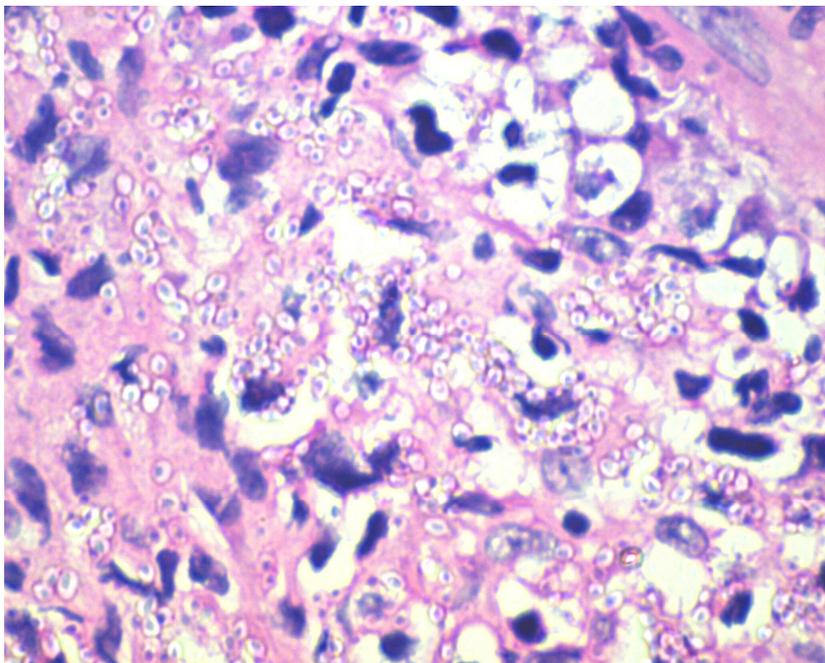
**Photo.1** Showed thinned out epidermis with loss of normal dermal architecture with presence of plenty of macrophages. [H & E stain, 10X]



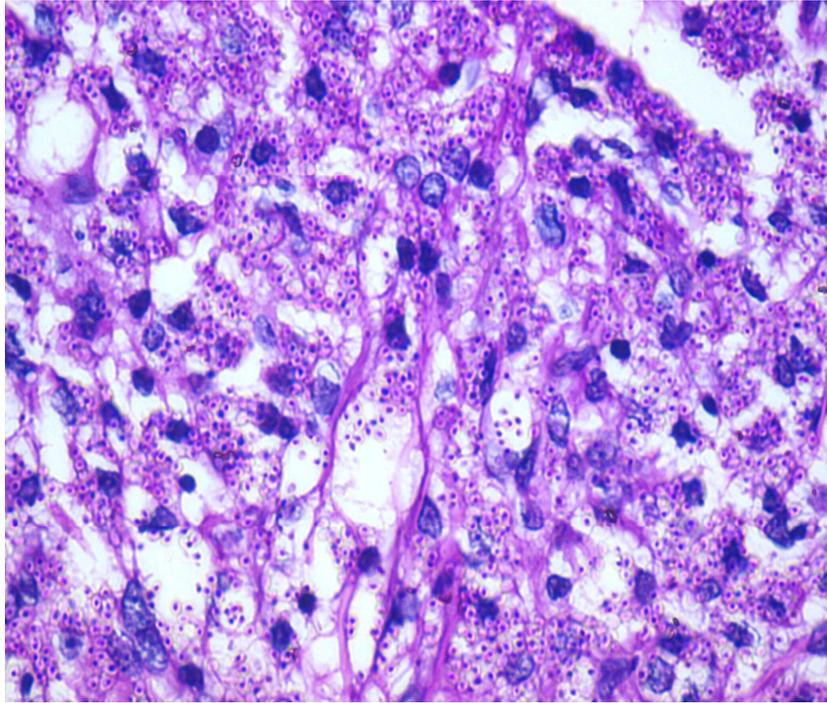
**Photo.2** Histiocytes containing numerous intracellular small, ovoid cysts surrounded by a clear space. [H&E stain, 40X]



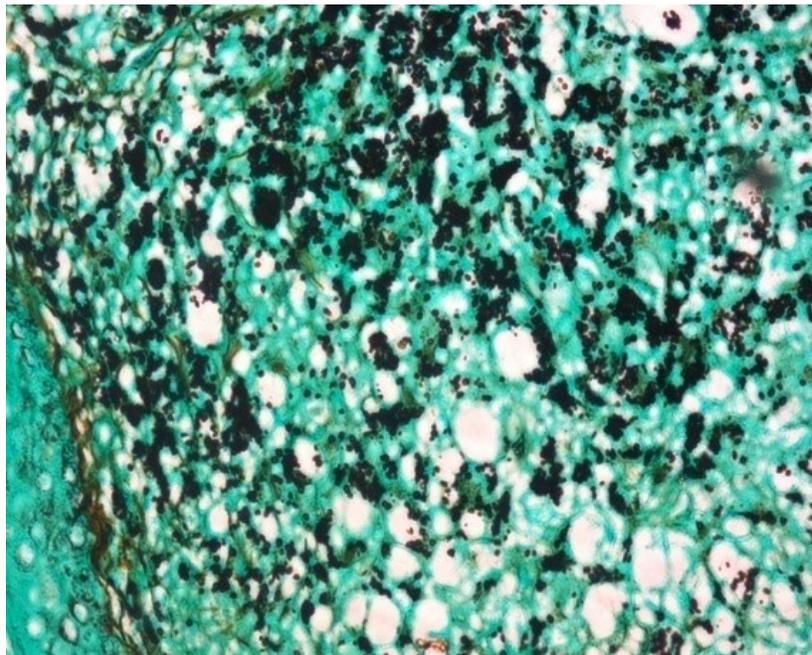
**Photo.3** Ovoid cysts surrounded by a clear space. [H& E stain, 60X]



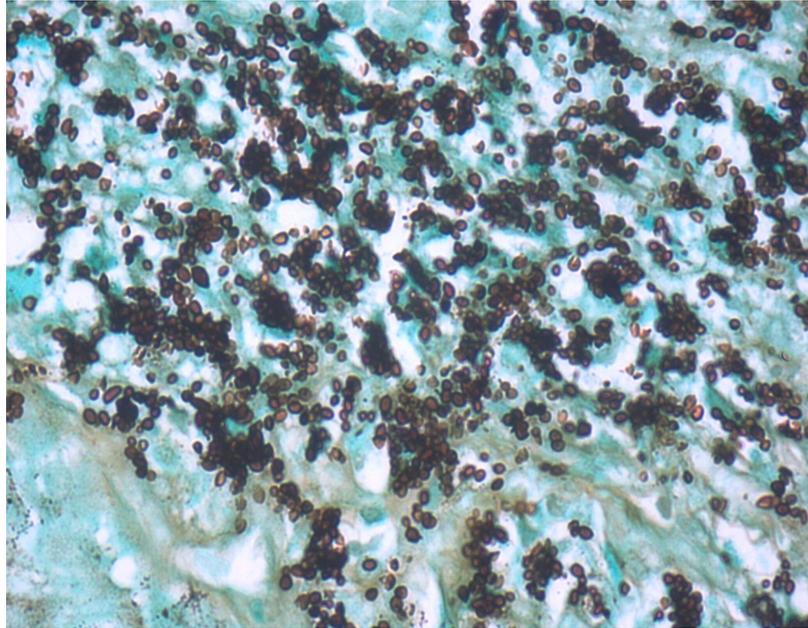
**Photo.4** The histoplasma showed intense staining on Periodic-Acid Schiff method.  
[PAS, 40 X]



**Photo.5** Spores of *Histoplasma capsulatum* within the cytoplasm of macrophages.  
[GMS stain, 40X]



**Photo.6** Spores of *Histoplasma capsulatum* within the cytoplasm of macrophages and absence of capsule. [GMS stain, 60X]



In present case, patient was immunosuppressed for renal transplant with cutaneous lesions no evidence of systemic involvement. Only a high degree of suspicion can pick up cases of histoplasmosis. We are afraid that many cases are probably being missed out and the mystery is never unravelled. A properly done biopsy and histopathological examination with routine and special stains for fungus can reliably diagnose a case of histoplasmosis.

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