A rare case of disseminated cutaneous histoplasmosis

Sir,

Histoplasmosis, a systemic mycotic infection is caused by the dimorphic fungus, *Histoplasma capsulatum*. It is acquired through the inhalation of fungal spores present in soil contaminated with bat or bird faeces.[1] It is endemic in some regions of America, Africa, and West Bengal (Eastern India), with few sporadic cases reported from southern India.[1,2] Disseminated cutaneous histoplasmosis is commonly seen in immunocompromised patients. Conditions that increase the risk of dissemination include acquired immunodeficiency syndrome, organ transplant, hematologic malignancies, and immunosuppressive agents.[1] We herein report a case of disseminated cutaneous histoplasmosis in an HIV seronegative patient on long term methotrexate therapy from a non-endemic region.

A 65-year-old female presented with multiple, painful, red elevated lesions over the face and trunk with oral cavity erosions of five months duration. Few lesions were associated with purulent discharge and crusting. She had fever associated with chills and rigour, weight loss, dry cough, and shortness of breath one month prior to the onset of skin lesions and was treated as an acute exacerbation of asthma, following which systemic symptoms improved. She gave a history of working in an area that was heavily inhabited by birds, with plenty of bird excreta in soil. There was no significant travel history in the recent past. She was on treatment with low dose methotrexate (20 mg weekly once) and intermittent oral steroids, since the last four years for rheumatoid arthritis. On physical examination, she was undernourished and cachectic with pallor. On clinical systemic examination, there was no organomegaly. Cutaneous examination showed small hyperpigmented, crusted plaques over the face [Figure 1a] and multiple erythematous, annular to polycyclic plaques with erosions and crusting over the anterior and posterior aspects of the trunk [Figure 1b and c]. Multiple erosions were seen over the tongue and hard plate [Figure 1d]. Differential diagnoses considered were nutritional dermatosis, pemphigus foliaceous, necrolytic migratory erythema and acquired zinc deficiency. Skin biopsy revealed plenty of macrophages containing yeast forms with basophilic nucleus with perinuclear halo throughout the dermis [Figure 2a]. On periodic acid Schiff staining, dermis showed periodic acid Schiff-positive organisms with a perinuclear halo [Figure 2b]. Gomori's methenamine silver staining showed multiple, small, black yeast cells [Figure 2c]. Direct immunofluorescence from perilesional skin was negative. Bone marrow aspirate showed plenty of macrophages with numerous organisms showing yeast-like appearance with encapsulation [Figure 2d]. Routine lab investigations revealed anaemia, hypoalbuminemia, and thrombocytosis. Tissue culture was not done due to the unavailability of Biosafety level 3 laboratory. Computed tomography of the abdomen revealed multiple, tiny, calcified granulomas in both lobes of the liver. Computed tomography of the chest revealed patchy fibrotic changes and subpleural fibrotic strands. A diagnosis of disseminated cutaneous histoplasmosis was made and the patient was started on oral itraconazole 200 mg per day, following which there was an improvement in lesions. The patient was later lost to follow up.

Histoplasmosis has a worldwide distribution, with the first case from India reported by Panja and Sen.[3] Thereafter many cases were reported from Bengal, with sporadic reports from Maharashtra and other parts of the country.[3] Our patient was a resident of a non-endemic region from South India but worked in an area where the soil was contaminated with bird excreta. We assume that our patient acquired the disease via inhalation of airborne conidia of Histoplasma capsulatum from the soil.

There are three clinical presentations of histoplasmosis, namely, primary cutaneous, pulmonary, and progressive disseminated (PDH) forms. Histoplasmosis is asymptomatic in 95% of the patients.[4] However, the pulmonary infection may disseminate hematogenously to liver, spleen, kidney, lymph nodes, bone marrow and mucocutaneous tissues, resulting in progressive disseminated histoplasmosis which usually occurs in immunocompromised hosts. Cutaneous lesions are non-specific with varied presentations such as mucocutaneous erosions/ulcers, or multiple erythematous papules/nodules with scaling or crusting.[5] However, annular to polycyclic erythematous plaques as seen in our case, have rarely been reported.

How to cite this article: Panuganti S, Varala S, Damarla SV, Prasad JVDS. A rare case of disseminated cutaneous histoplasmosis. Indian J Dermatol Venereol Leprol 2022;88:533-6.

Received: December, 2021 **Accepted:** February, 2022 **EPub Ahead of Print:** April, 2022 **Published:** June, 2022

DOI: 10.25259/IJDVL_1184_2021 **PMID:** 35593285

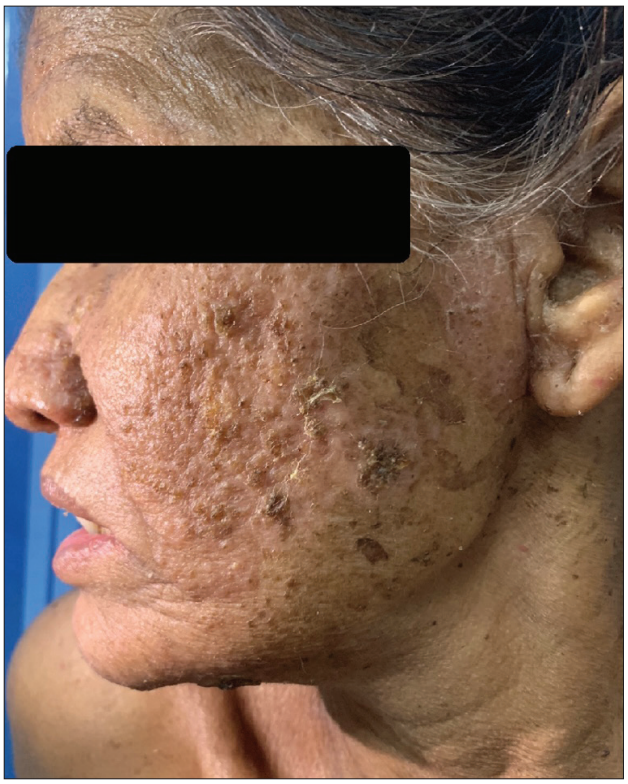

Figure 1a: Small crusted plaques over the face

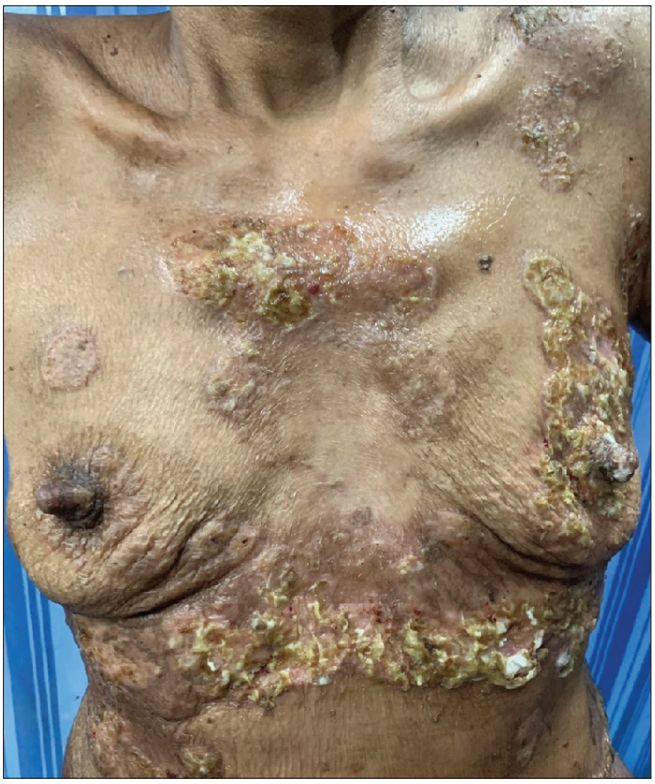

Figure 1b: Multiple, well defined, annular to polycyclic plaques with erosions and crusting over anterior aspect of trunk

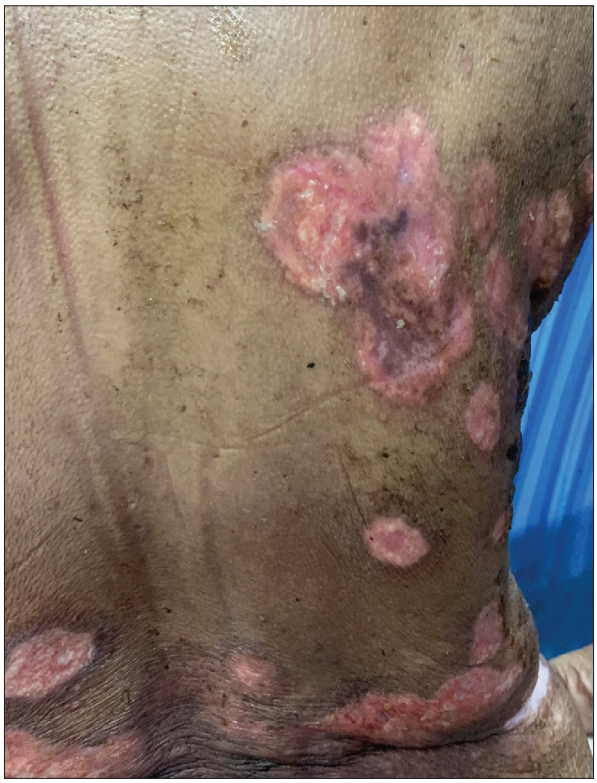

Figure 1c: Multiple, well defined, annular plaques with erosions over posterior aspect of trunk

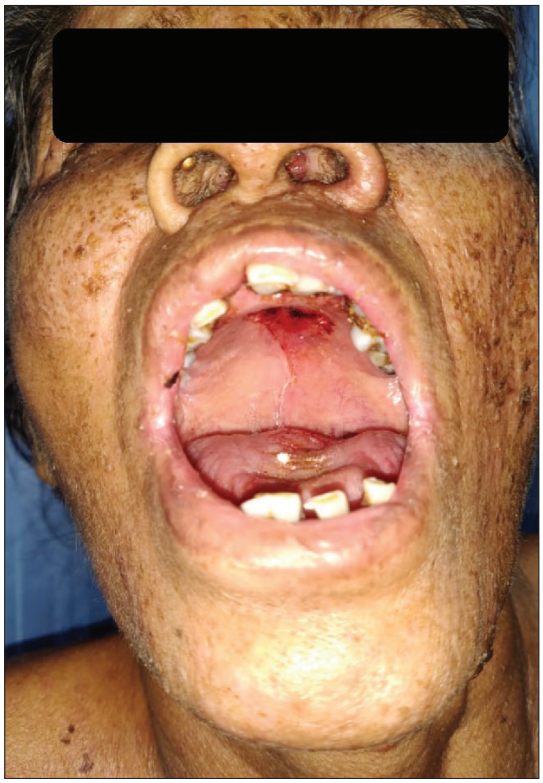

Figure 1d: Erosions over hard palate

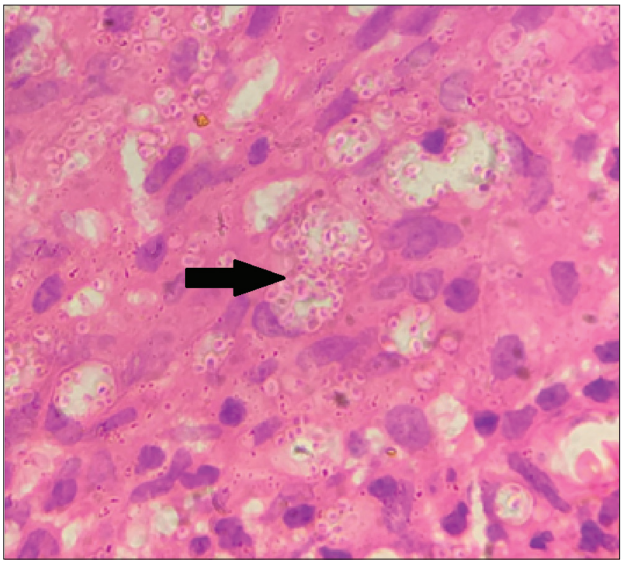

Figure 2a: Plenty of parasitized macrophages in dermis (arrow) (H & E, ×100)

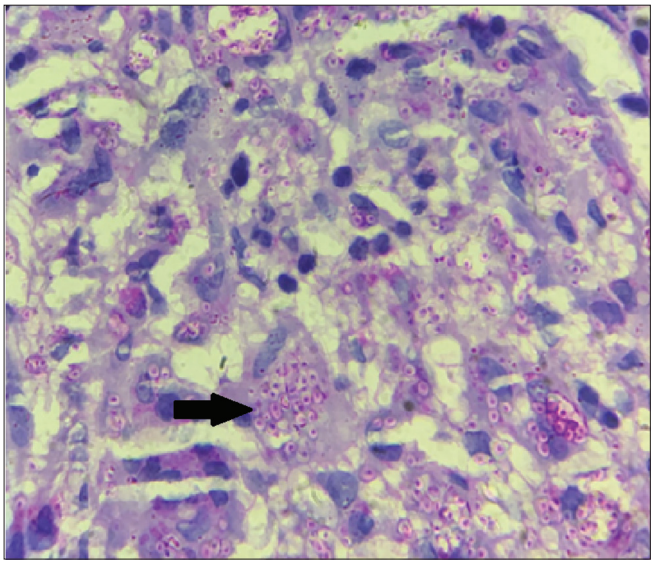

Figure 2b: Periodic acid Schiff positive organisms within the macrophages with perinuclear halo (arrow) (PAS stain, ×100)

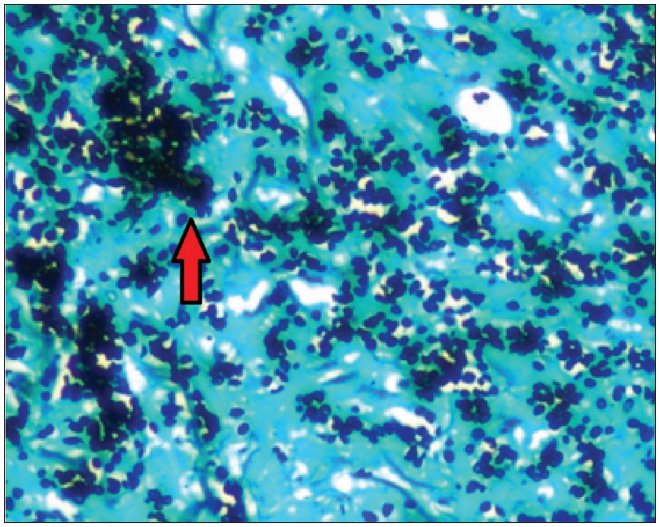

Figure 2c: Gomori's methenamine silver stain showing yeast forms (arrow) (GMS stain, ×100)

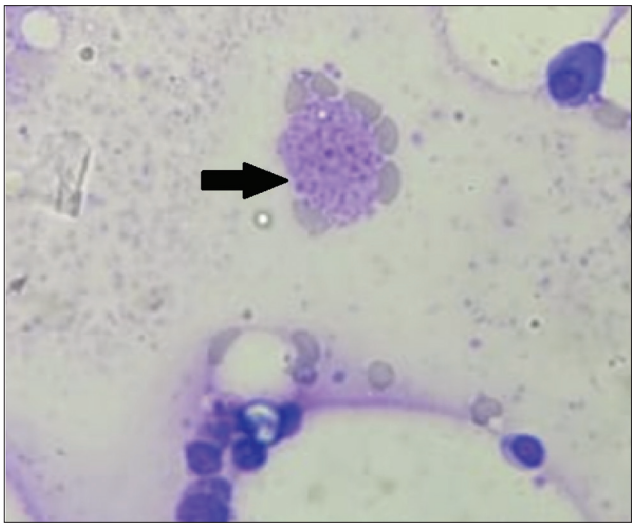

Figure 2d: Bone marrow aspirate smear showing macrophages with yeast like organisms (arrow) (Giemsa stain, ×100)

Our patient developed progressive disseminated histoplasmosis presumably due to immunosuppression secondary to chronic methotrexate therapy and oral steroids. Similar to our case, Roy *et al.*[6] reported disseminated histoplasmosis following prolonged low dose methotrexate therapy, in whom the diagnosis was confirmed by bone marrow biopsy. Dussouil *et al.*[7] reported a patient treated with methotrexate and corticosteroid therapy for rheumatoid arthritis who presented with disseminated histoplasmosis that partially mimicked dermatomyositis.

In our case, the diagnosis was made based on histopathology and bone marrow aspirate examination with special staining. Histopathology, a primary tool in the diagnosis of the disease, typically shows tiny 2–4 μm spores within the cytoplasm of macrophages which appear as round or oval bodies surrounded by a clear space and stains with special stains like periodic acid Schiff or Giemsa stain.[8]

Focal calcifications were seen in the liver in our case, which indicate prior infection with histoplasma. Focal calcifications are also seen in tuberculosis, which is a major public health problem in India leading to diagnostic difficulties.[9] Amphotericin B is the drug of choice for disseminated histoplasmosis. However, in patients who cannot tolerate amphotericin B, itraconazole is a highly effective and alternative therapy and histoplasma is one of the rare opportunistic deep fungal infections causing organ damage**.** It is usually missed clinically, especially in non-endemic areas, in which case, a proper clinical history along with

histopathology and special stains help in making an accurate diagnosis. Our case is unique in its morphological presentation with large erythematous polycyclic plaques as opposed to the classical presentation with papules and nodules.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Sowmya Panuganti, Sirisha Varala, Sudha Vani Damarla, JVDS Prasad

Department of Dermatology, Osmania Medical College, Hyderabad, Telangana, India

Corresponding author:
Dr. Sirisha Varala,
Department of Dermatology, Osmania Medical College, Afzalgunj, Hyderabad, 500012, Telangana, India.
itsme.siri@yahoo.com

References

1. Mignogna MD, Fedele S, Lo Russo L, Ruoppo E, Lo Muzio L. A case of oral localized histoplasmosis in an immunocompetent patient. Eur J Clin Microbiol Infect Dis 2001;20:753–55.
2. Harnalikar M, Kharkar V, Khopkar U. Disseminated cutaneous histoplasmosis in an immunocompetent adult. Indian J Dermatol 2012;57:206–9.
3. Sane SY, Patel MG, Patel BM, Kokal K. Disseminated histoplasmosis (a case report). J Postgrad Med 1983;29:270–3.PMID: 6672189
4. Mukherjee A, Tangri R, Verma N, Gautam D. Chronic disseminated histoplasmosis bone marrow involvement in an immunocompetent patient. Indian J Hematol Blood Transfus 2010;26:65–7.
5. Mahajan VK, Raina RK, Singh S, Rashpa RS, Sood A, Chauhan PS, *et al.* Case report: Histoplasmosis in Himachal Pradesh (India): An emerging endemic focus. Am J Trop Med Hyg 2017;97:1749–56.
6. Roy V, Hammerschmidt DE. Disseminated histoplasmosis following prolonged low-dose methotrexate therapy. Am J Hematol 2000;63:59–60.
7. Dussouil AS, Allardet-Servent J, Dunogeant L, Grauer JL, Ranque S, Nasser V. Disseminated histoplasmosis partially mimicking a dermatomyositis in a patient with rheumatoid arthritis. Br J Dermatol 2015;173:797–800.
8. Vidyanath S, Shameena P, Sudha S, Nair RG. Disseminated histoplasmosis with oral and cutaneous manifestations. J Oral Maxillofac Pathol 2013;17:139–42.
9. Patnana M, Menias CO, Pickhardt PJ, Elshikh M, Javadi S, Gaballah A, *et al.* Liver calcifications and calcified liver masses: Pattern recognition approach on CT. Am J Roentgenol 2018;211:76–86.
10. Calza L, Manfredi R, Donzelli C, Marinacci G, Colangeli V, Chiodo F. Disseminated histoplasmosis with atypical cutaneous lesions in an Italian HIV-infected patient: Another autochtonous case. HIV Med 2003;4:145–8.

Unilateral areolar leiomyoma with sebaceous hyperplasia

Sir,

Leiomyoma frequently develops in the uterus, but its occurrence in the areola is rare. Similarly, sebaceous hyperplasia, usually located on the nose and forehead, also rarely occurs in the areola. However, cases where both leiomyoma and sebaceous hyperplasia developed in the same areolar lesion have not been reported. Here, we report such a case in the unilateral areola.

A 41-year-old man noticed a nodule on his left areola one year before his initial visit to our hospital. On physical examination, a 1-cm, yellowish nodule was found on the upper part of the left areola [Figures 1a and b]. Polarized light dermatoscopy (Heine Delta 20 plus; Heine Optotechnik, Herrsching, Germany) revealed white reticular lines with yellowish globular structures [Figure 1c] and a biopsy was performed. Histopathology of the lesion showed numerous, mature sebaceous glands whose ducts directly led to the epidermis [Figures 1d and e]. In addition, moderate epidermal hyperplasia with elongated rete ridges was also observed [Figures 1d and e] and, in the dermis, tumour nests composed of α-smooth muscle actin-positive spindle-shaped cells with intermingled collagen were seen [Figures 1d, f and Figure 2a]. These results led to a diagnosis of areolar leiomyoma with sebaceous hyperplasia. Additional immunohistochemical studies revealed that the leiomyoma was positive for estrogen and progesterone receptors but the proliferated sebocytes were negative [Figures 2b and c]. In contrast, the sebocytes were positive for androgen receptors but the leiomyoma was negative [Figure 2d]. Epidermal growth factor, insulin-like growth factor-1 and fibroblast growth factor-2 were highly expressed in the leiomyoma [Figures 3a-c and 4a-d]. Epidermal growth factor receptor, insulin-like growth factor-1 receptor β and fibroblast growth factor receptor 2, a receptor for fibroblast growth factor-2, were expressed in

How to cite this article: Oya K, Nakamura Y, Fujisawa Y. Unilateral areolar leiomyoma with sebaceous hyperplasia. Indian J Dermatol Venereol Leprol 2022;88:536-40.

Received: December, 2020 **Accepted:** February, 2022 **EPub Ahead of Print:** May, 2022 **Published:** June, 2022

DOI: 10.25259/IJDVL_7_2020 **PMID:** 35593282