Primary cutaneous histoplasmosis in an immunocompetent patient presenting with severe pruritus

Sir,
A 60-year-old man presented with severe generalized pruritus of 1-year duration. In the initial 6 months, the pruritus was not associated with any skin lesions. The pruritus was severe enough to disturb his sleep and daily activities. It was not relieved by over-the-counter oral antihistamines and topical steroids. Over the next 6 months, he developed multiple erythematous papules on the trunk, followed by face and extremities. There was no history of fever, malaise, weight loss or other systemic symptoms. He did not report any comorbidities other than a single episode of angina 3 years back. At presentation, he had multiple monomorphic, shiny, erythematous-to-skin colored, 0.2 cm × 0.3 cm papules and small nodules on the face, upper trunk and upper limbs [Figure 1a-c]. The papules coalesced to form plaques on the eyelids and nape of the neck. There was also diffuse infiltration of the face and ears. The scalp, flexures and mucosae were spared. Systemic examination revealed mild splenomegaly. Clinical diagnoses of lepromatous leprosy, post kala-azar dermal leishmaniasis and sarcoidosis were considered.
Skin biopsy revealed a dense dermal inflammatory infiltrate of histiocytes, epithelioid cells and multinucleated giant cells with numerous ovoid-shaped yeasts with a peripheral halo which stained positively with Periodic Acid-Schiff stain, suggestive of *Histoplasma capsulatum* [Figure 2a]. Potassium hydroxide preparation of a tissue sample also revealed yeasts. However, the fungus could not be isolated on culture. On further questioning, the patient reported living near a poultry farm, though he did not have any direct exposure to birds. Based on the presence of yeasts resembling *Histoplasma* in the biopsy, a clinical diagnosis of cutaneous histoplasmosis was considered and the patient was evaluated for systemic involvement.

Routine hematological and biochemical investigations were unremarkable. Serological evaluation for human immunodeficiency virus-1 and -2 were negative and CD4 counts were within normal limits. Contrast-enhanced computed tomography of the chest and abdomen revealed splenomegaly with multifocal splenic infiltrates [Figure 2b]. Fine needle aspiration cytology from the spleen showed reactive hyperplasia. Bone marrow biopsy, serum cortisol, adrenocorticotropic hormone and thyroid stimulating hormone were within normal limits. The patient was treated with intravenous liposomal amphotericin 3 mg/kg/day. Within 3 days of initiation of treatment, there was significant flattening of papules, reduction of infiltration and erythema with a moderate improvement in pruritus. Amphotericin was stopped after 8 injections due to elevation in urea (90 mg/dl) and creatinine (2.3 mg/dl) and the patient was shifted to itraconazole, 200 mg twice daily. Two months later, there was near-complete resolution of lesions with significant improvement in pruritus [Figure 1d].

Histoplasmosis is a common granulomatous infection worldwide caused by *Histoplasma capsulatum*, a dimorphic fungus. Pulmonary involvement is the most common clinical presentation. Cutaneous manifestations are reported to occur in 10% to 25% of

**Table 1: Various reported morphological patterns of cutaneous histoplasmosis in immunocompetent patients**

| Authors          | Clinical presentation                                      | Risk factors | Mode of diagnosis             | Treatment and follow-up                                      |
|------------------|-----------------------------------------------------------|--------------|-------------------------------|-------------------------------------------------------------|
| Lacaz *et al.*   | Erythematous infiltrated cutaneous nodules, surrounded by hypocromic halo | Nil          | Culture                       | Itraconazole 100 mg per day, complete cure in 3 months       |
| Gupta and Bhardwaj | Molluscum contagiosum-like skin lesions, lymphadenopathy and splenomegaly | Nil          | Fine needle aspiration cytology of cervical lymph node | Amphotericin B, died on day 5 due to disseminated intravenous coagulation |
| Harnalikar *et al.* | Asymptomatic swelling of the hard palate and crusted papules and nodules over the extremities, face and trunk | Nil          | Histology                     | Amphotericin B, died on day 2                               |
| Nair *et al.*    | Diffuse swelling of thumb and ulceration                   | History of thorn pricks | Histology                     | Itraconazole 200 mg twice daily, good response              |

Figure 1a: Multiple, monomorphic, erythematous, infiltrated papules and plaques over the face

Figure 1b: Multiple, monomorphic, erythematous, infiltrated papules and plaques over the arm
immunosuppressed patients with disseminated histoplasmosis. The occurrence of cutaneous involvement in immunocompetent patients is rare and limited to a few case reports. Varied morphological patterns have been described in these reports causing a diagnostic dilemma [Table 1]. Inhalation of fungal conidia from soil contaminated by excreta of bats or birds is the primary mode of infection for histoplasmosis.

Cutaneous lesions of histoplasmosis are usually asymptomatic, and we were unable to find previous reports of severe pruritus as a presenting sign preceding the development of skin lesions. The improvement in intractable pruritus after antifungal therapy indicates that it is probably related to histoplasmosis and not an independent or coincidental phenomenon. Interestingly, pruritus is diminished but persists even after skin lesions have cleared, providing us an additional clinical marker by which to monitor the length of the therapy. We plan to continue itraconazole for 6 months after pruritus subsides.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Nil.

Figure 1c: Multiple, monomorphic, erythematous, infiltrated papules and plaques over trunk

Figure 1d: Significant improvement in skin lesions noted after 2 months of antifungal therapy

Figure 2a: Histological evaluation on hematoxylin and eosin stain showed dense infiltrate of histiocytes, epithelioid cells and multinucleated giant cells, numerous ovoid shaped yeasts with a peripheral halo (arrow) suggestive of Histoplasma capsulatum (×400)

Figure 2b: Contrast-enhanced computed tomography of the abdomen showing multiple hypodense lesions (arrow) in the spleen
Conflicts of interest
There are no conflicts of interest.

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Generalized multinucleate cell angiohistiocytoma with involvement of palms and soles: An unusual manifestation

Sir,
We describe a case of a Thai male diagnosed with generalized multinucleate cell angiohistiocytoma, along with lesions presenting on palms and soles. Such a case has not been documented in the literature yet.

A healthy 42-year-old male presented with an 8-year history of multiple disseminated asymptomatic lesions on his trunk and extremities. The lesions began on his trunk which subsequently spread to the upper and lower extremities. Physical examination showed multiple dark-red-to-violaceous, dome-shaped papules of varying size, with a smooth surface, scattered on the trunk, arms and legs, including palms and soles [Figures 1 and 2]. The lesions developed slowly over the years with partial regression of some lesions. Rest of the physical examination was unremarkable. The initial clinical impressions were multiple angioma, multiple eruptive dermatofibroma, eruptive microvenular hemangioma and Kaposi’s sarcoma. Biopsy from the lesion on his back demonstrated proliferation of thick-walled small blood vessels in association with scattered stellate fibroblasts, bizarre shaped and angulated cytoplasm of multinucleate giant cells, infiltrate of lymphocytes and plasma cells in the entire dermis [Figure 3]. Overlying epidermis also showed hyperplasia and hyperpigmentation. Immunohistochemically, vascular endothelial cells expressed vimentin and CD34. Mononucleated spindle cells expressed vimentin and factor XIIIA but not CD68 and estrogen receptor. Multinucleate cells were positive for vimentin [Figure 3], but negative for factor XIIIA, CD68 and estrogen receptor. HHV-8 stain was also negative. The final diagnosis of generalized multinucleate cell angiohistiocytoma was made. There was no evidence of other systemic disease. The patient was lost to follow-up.

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