DOI: 10.7860/JCDR/2021/48863.14747

Case Report

Microbiology Section

Primary Cutaneous Cryptococcosis: A Rare Masquerading Presentation of *Cryptococcus* Infection

TANISHA BHARARA[1], SHALINI UPADHYAY[2], MOHINDER PAL SINGH SAWHNEY[3], MANISHA KHANDAIT[4]

ABSTRACT

The yeast, *Cryptococcus* is widely present in the environment. Its main portal of entry is the respiratory tract. Clinical and experimental evidences indicate that cryptococcosis is usually a reactivation of a dormant infection. They have been recovered from soil contaminated with avian excreta, especially pigeon droppings and from decaying wood, fruits, vegetables and dust. *Cryptococcus* may be found on skin of healthy subjects without causing any manifestation but it is known to cause life threatening infection in immunocompromised hosts. Primary Cutaneous Cryptococcosis (PCC) is an uncommon condition which is characterised by localised cryptococcal skin eruptions without dissemination to internal organs. Clinicians are aware of the typical presentation of cryptococcal infections occurring mostly in immunocompromised patients. Rare manifestations like PCC may go unnoticed leading to prolonged morbidity and health care cost. The present article is a case report of PCC in a 39-year-old immunocompetent male who presented with two months history of scattered erythematous indurated papules and plaques on his right foot, arm and abdominal region developed after having suffered minor injury at the cement factory. The patient was started on fluconazole to which he responded well.

Keywords: Fungal infection, Immunocompetent, Skin eruptions, Yeast

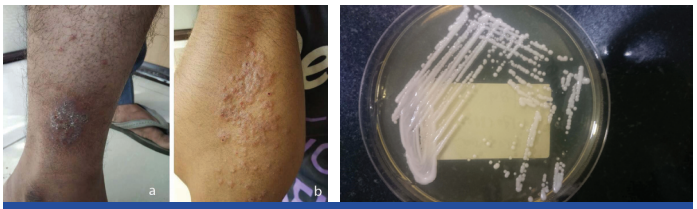
CASE REPORT

A 39-year-old male patient, labourer in cement factory, presented to Dermatology, Outpatient Department with rapidly enlarging plaques on his right foot, forearm, thigh region and lower abdomen. Two months back patient was asymptomatic, when he got a superficial bruise on his right foot at his work place. Subsequently, he developed pruritus and erythema at the site of injury. Initially the erythematous itchy area changed to red rash which eventually changed to black flaky lesion. He consulted a quack nearby, who prescribed him steroids. He took the medication for two months, but his symptoms were not relieved. The lesion had subsequently spread to his left forearm, groin region, thighs and lower abdomen [Table/Fig-1]. An appropriate consent was obtained from the patient.

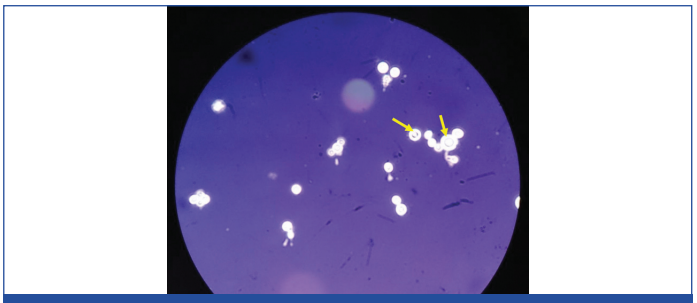
He denied fever, night sweats, malaise or other systemic symptoms. On physical examination, he was found to be afebrile and lymphadenopathy was absent. Laboratory testing showed normal total leucocyte count and haemoglobin. Skin scraping was taken from the site of the lesion and was sent to the Microbiology laboratory for potassium hydroxide (KOH) mount and fungal culture. One part of the sample was inoculated in two tubes of Sabouraud Dextrose Agar (SDA) and incubated at 37°C and 25°C, respectively. Other part of the specimen was incubated in a tube containing 10% KOH at 37°C for two hours.

The KOH findings revealed round yeast cells. The culture on SDA, incubated at 37°C grew moist, creamy colonies after 24 hours [Table/Fig-2]. Lactophenol cotton blue staining revealed round, budding yeast cells and nigrosine staining showed capsulated, round, budding yeast cells [Table/Fig-3]. Urease test was subsequently performed and was found to be positive. On the basis of above findings, the organism was identified as *Cryptococcus* species. The patient was HIV negative and did not give any history of prolonged past illness.

Upon confirmation of fungal infection, he was started on fluconazole (400 mg daily) based on the culture report. The patient's lesion improved remarkably over the course of his treatment with near resolution of the surrounding erythema. His steroid was gradually weaned down. Patient responded well to the medication. He was asked to continue the medication for three months and follow-up after one week. At first-week follow-up, his wound showed great improvement. He tolerated fluconazole well and was continued on the same treatment for an additional three months for a total duration of six months. From the start of lesion till his last visit, he never showed sign of relapse or any disseminated disease.



[Table/Fig-1]: Primary cutaneous cryptococcosis lesions: a) Ulcerative lesion on patient's right lower leg; and b) Erythematous papules on patient's right forearm.
[Table/Fig-2]: The moist, creamy white colonies of *Cryptococcus* on Sabouraud's dextrose agar. (Images left ot right)



[Table/Fig-3]: The negative staining of capsule marked with yellow arrows seen around round budding yeast cells at 40x magnification with nigrosine stain.

DISCUSSION

Primary Cutaneous Cryptococcosis (PCC) is defined as isolation of *Cryptococcus* species from a skin lesion without evidence of simultaneous disseminated disease [1]. The cases of PCC reported from all over the world and even occasionally from India, over the last 10 years have been depicted in [Table/Fig-4] [2-26]. A survey conducted by the French Cryptococcosis Study Group (1985-2000) identified 28 cases of PCC from 1,974 Cryptococcosis cases reported to

the National Reference Centre for Mycoses. Of these 28 patients, 14 were immunocompetent suggesting that PCC can develop regardless of immune status. PCC usually presents as solitary lesions mostly located on unclothed areas while disseminated disease present as scattered umbilicated papules resembling Molluscum contagiosum [1].

The most common sites of PCC infection are the extremities, probably because they are mostly exposed and prone to minor injuries. In most of the patients, certain areas having underlying skin disease or site of injury provide a portal of entry for PCC [14]. There was history of bruise at the cement factory preceding the lesion in the presented case. The patient had affirmed the presence of pigeons at his work place. So, it can be hypothesised that the patient may have got the infection through exposure to either infested soil or bird droppings. The cutaneous manifestations of cryptococcosis may mimic other dermatological conditions, such as, fungal infections (*Sporothrix schenckii, Coccidioides immitis, Blastomyces dermatitidis* and *Histoplasma capsulatum*), varicella lesions, lepromatous leprosy and insect bite. Based on the cases reviewed as well as the findings in the present case a checklist has been prepared to aid in diagnosis of PCC [Table/Fig-5] [1,5,11,14].

Year of Publication	Authors/ Reference	Region	Age (years)/ Gender	Immune status	Occupation/ Exposure	Site of lesion	Type of lesion	Outcome
2011	Leão CA et al., [2]	Brazil	75/M	Immunocompetent	Eucalyptus logs handler	Forearm	Nodule	Recovery
2011	Lingegowda BP et al., [3]	Singapore	37/M	Immunocompetent	Forklift driver	Scalp	Nodule	Recovery
2012	Kulkarni A et al., [4]	India	55/M	Immunocompromised	Repeated insulin and heparin subcutaneous injections	Thigh	Umbilicated	Unrelated death
2012	Marques SA et al., [5]	Brazil	11 patients, mean age 71.2/9M2F	5 immunocompetent, 6 on corticosteroid therapy	5 out of the 11 cases reported trauma or exposure to contaminated sources	Upper limbs	Circumscribed lesions ranged from an infiltrative plaque to a solid tumour mass	9 cured, 1 unrelated death, 1 marked improvement
2012	Spiliopoulou A et al., [6]	Greece	58/M	Immunocompetent	Poultry farmer	Hand	Ulceration	Recovery
2012	Pasa CR et al., [7]	Brazil	59/M	Immunocompetent	Firewood collection	Forearm	Ulceration	Recovery
2012	Narváez-Moreno et al., [8]	Rural Central America	66/M	Immunocompetent	Not reported	Penis	Nodule	Recovery
2013	Lu YY et al., [9]	Rural area of Taiwan	87/M	Immunocompetent	Not reported	Arm	Indurated papules and plaques	Recovery
2013	Molina-Leyva A et al., [10]	Spain	8/F	Immunocompetent	None	Forearm	Macule	Recovery
2014	Nascimento E et al., [11]	Southeast Brazil	68/M	Immunocompetent	Bus driver	Forearm	Nodule	Recovery
2014	Leechawengwongs M et al., [12]	Thailand	48/F	Immunocompetent	Reported trauma	Lower leg	Inflamed wound	Recovery
2014	Drogari-Apiranthitou M et al., [13]	Greece	61/M	Immunocompromised	Injury with a plant thorn	Finger	Ulceration	Recovery
2015	Wang J et al., [14]	USA	56/M	Immunocompromised	Carpenter	Right forearm	Plaque	Recovery
2015	Srivastava GN et al., [15]	India	56/M	Immunocompetent	Reported trauma	Forehead and ala of nose	Ulcerated nodule	Recovery
2016	Forrestel AK et al., [16]	Philadelphia	62/F	Immunocompromised	Reported trauma	Forehead	Nodule	Recovery
2016	Ajam T et al., [17]	USA	76/F	Immunocompromised	Gardener	Forearm	Papule	Recovery
2016	Hyde K et al., [18]	Rural Central Texas	10/F	Immunocompetent	None	Foot	Ulcerated nodule	Recovery
2017	Landucci G et al., [19]	Italy	75/M	Immunocompromised	Not reported	Forearm	Papule	Recovery
2017	Arjona-Aguilera C et al., [20]	Spain	42/F	Immunocompromised	Probable contact with pigeon	Thigh	Edematous painful plaques	Recovery
2018	Henderson GP and Dreyer S [21]	California	69/M	Immunocompromised	Reported trauma	Forearm	Ulceration and bullae	Recovery
2018	Hobbs M et al., [22]	Rural Mississippi	6/F	Immunocompetent	Not reported	Right Eyelid	Abscess	Recovery
2019	Beatson M et al., [23]	USA	80/M	Immunocompetent	Pigeon breeder	Cheek, ear	Papules	Recovery
2020	Shalom G and Horev A [24]	Israel	30/F	Immunocompromised	Owned birds and pigeons	Erythropoietin derivative injection sites	Ulcer	Recovery
2021	Gaviria Morales E et al., [25]	Switzerland	60/F	Immunocompetent	Injury caused by a rose thorn	Right thumb	Erythematous ulcerated nodule	Recovery
2020	Patil SM et al., [26]	USA	63/M	Immunocompromised	None	Occipital scalp	Plaque lesion	Recovery
2021	Present case	India	39/M	Immunocompetent	Trauma	Lower leg and forearm	Papule and ulcer	Recovery

[Table/Fig-4]: Reports of primary cutaneous cryptococcosis around the world in the last decade [2-26].

Criteria	Evidence of PCC
Skin lesion	Confined to limited body area
Site of origin	Unclothed area (limbs)
Injury	• History of prior injury or former skin lesion • Identical body site for prior injury or former skin lesion • Hobby or occupation predisposing to skin injury
Exposure	Possible contaminated source
Living area	Rural
Underlying disease predisposing to cryptococcosis	None
Extracutaneous sites positive for *Cryptococcus*	None
Outcome of infection	Favourable

[Table/Fig-5]: Checklist for identification of primary cutaneous cryptococcosis [1,5,11,14].

The majority of patients diagnosed with PCC underwent laboratory investigations to evaluate host immune status and to rule out disease dissemination. Many patients had serum and Cerebrospinal Fluid (CSF) cryptococcal antigen studies and/or cultures (sputum, blood, urine or CSF) performed and all cultures and CSF antigen were reported as negative [9,11,18,24,25]. In a few immunocompetent patients no culture or latex agglutination data were obtained, and had no radiographic evaluation for pulmonary cryptococcosis [7,11]. Although, the present case was HIV negative and he did not any history of prolonged illness in the past; one of the limitations of this study was that extensive work up to rule out disseminated disease could not be performed on the patient neither serotyping of the isolated strain was done due to resource constraints.

The treatment for cryptococcosis is determined by the type of infection and the immune status of the host. The Infectious Disease Society of America (IDSA) recommends oral azole therapy for 6-12 months for patients with non-central nervous system, non-disseminated *Cryptococcus* [26]. The present case had a favourable response to fluconazole monotherapy and topical wound care after only a few weeks of treatment. A single documented treatment failure reported in literature, in an immunocompromised patient, was discovered at autopsy after three months of antifungal therapy [27].

CONCLUSION(S)

This case was an aide memoire about the risk factors, clinical presentation and prompt response to therapy in a case of PCC. It illustrated the importance of prompt microbiological investigations and thorough evaluation for atypical infections such as PCC.

REFERENCES

[1] Neuville S, Dromer F, Morin O, Dupont B, Ronin O, Lortholary O, et al. Primary cutaneous cryptococcosis: A distinct clinical entity. Clin Infect Dis. 2003;36(3):337-47.
[2] Leão CA, Ferreira-Paim K, Andrade-Silva L. Primary cutaneous cryptococcosis caused by *Cryptococcus gattii* in an immunocompetent host. Med Mycol. 2011;49(4):352-55.
[3] Lingegowda BP, Koh TH, Ong HS, Tan TT. Primary cutaneous cryptococcosis due to *Cryptococcus gattii* in Singapore. Singapore Med J. 2011;52(7):e160-62.
[4] Kulkarni A, Sinha M, Anandh U. Primary cutaneous cryptococcosis due to *Cryptococcous laurentii* in a renal transplant recipient. Saudi J Kidney Dis Transpl. 2012;23:102-05.
[5] Marques SA, Bastazini Jr I, Martins ALGP. Primary cutaneous cryptococcosis in Brazil: Report of 11 cases in immunocompetent and immunosuppressed patients. Int J Dermatol. 2012;51(7):780-84.
[6] Spiliopoulou A, Anastassiou ED, Christofidou M. Primary cutaneous cryptococcosis in immunocompetent hosts. Mycoses. 2012;55(2):e45-47.
[7] Pasa CR, Chang MR, Hans-Filho G. Post-trauma primary cutaneous cryptococcosis in an immunocompetent host by *Cryptococcus gattii* VGII. Mycoses. 2012;55(2):01-03.
[8] Narváez-Moreno B, Bernabeu-Wittel J, Zulueta-Dorado T, Conejo-Mir J, Lissen E. Primary cutaneous cryptococcosis of the penis. Sexually Transmitted Diseases. 2012;39(10):792-93.
[9] Lu YY, Wu CS, Hong CH. Primary cutaneous cryptococcosis in an immunocompetent man: A case report. Dermatologica Sinica. 2013;31(2):90-93.
[10] Molina-Leyva A, Ruiz-Carrascosa JC, Leyva-Garcia A, Husein-Elahmed H. Cutaneous *Cryptococcus laurentii* infection in an immunocompetent child. Int J Infectious Dis. 2013;17(12):e1232-33.
[11] Nascimento E, da Silva MEMB, Martinez R, Kress MRVZ. Primary cutaneous cryptococcosis in an immunocompetent patient due to *Cryptococcus gattii* molecular type VGI in Brazil: A case report and review of literature. Mycoses. 2014;57(7):442-47.
[12] Leechawengwongs M, Milindankura S, Sathirapongsasuti K, Tangkoskul T, Punyagupta S. Primary cutaneous cryptococcosis caused by *Cryptococcus gattii* VGII in a tsunami survivor from Thailand. Med Mycol Case Rep. 2014;11(6):31-33.
[13] Drogari-Apiranthitou M, Panayiotides IG, Mastoris I, Theodoropoulos K, Gouloumi A-R, Hagen F, et al. Primary cutaneous cryptococcosis and a surprise finding in a chronically immunosuppressed patient. JMM Case Reports. 2014;1(3). DOI 10.1099/jmmcr.0.003426.
[14] Wang J, Bartelt L, Yu D, Joshi A, Weinbaum B, Pierson T, et al. Primary cutaneous cryptococcosis treated with debridement and fluconazole monotherapy in an immunosuppressed patient: A case report and review of the literature. Case Rep Infect Dis. 2015;2015:131356.
[15] Srivastava GN, Tilak R, Yadav J, Bansal M. Cutaneous *Cryptococcus*: Marker for disseminated infection. BMJ Case Rep. 2015;2015:bcr2015210898.
[16] Forrestel AK, Modi BG, Longworth S, Wilck MB, Micheletti RG. Primary cutaneous Cryptococcus in a patient with multiple sclerosis treated with fingolimod. JAMA Neurol. 2016;73(3):355-56.
[17] Ajam T, Hyun G, Blue BJ, Rajeh N. Primary cutaneous cryptococcosis in a patient with chronic lymphocytic leukemia: A case report. Ann Hematol Oncol. 2016;3(3):1082.
[18] Hyde K, Warren D, Gavino AC. Primary cutaneous cryptococcal infection with subsequent erythema nodosum in a 10-year-old immunocompetent girl. JAAD Case Rep. 2016;2(6):494-96.
[19] Landucci G, Farinelli P, Zavattaro E, Giorgione R, Gironi LC, Veronese F, et al. Complete remission of primary cutaneous cryptococcosis in an immunosuppressed patient after fluconazole treatment. J Infect Dis Ther. 2017;5(4):326.
[20] Arjona-Aguilera C, Jiménez-Gallo D, Collantes-Rodríguez C, Linares-Barrios M. Primary cutaneous cryptococcosis: A new case of this rare entity. Open Forum Infect Dis. 2017;4(1):ofw276.
[21] Henderson GP, Dreyer S. Ulcerative cellulitis of the arm: A case of primary cutaneous cryptococcosis. Dermatol Online J. 2018;24(2):13030.
[22] Hobbs M, King J, Feghaly RE, Brodell R. Primary cutaneous cryptococcosis in an immunocompetent 6-year-old female. Skin. 2018;2(4):240-42.
[23] Beatson M, Harwood M, Reese V, Robinson-Bostom L. Primary cutaneous cryptococcosis in an elderly pigeon breeder. JAAD Case Rep. 2019;5(5):433-35.
[24] Shalom G, Horev A. Primary cutaneous cryptococcosis: An unusual injection site infection. Case Rep Dermatol. 2020;12:138-43.
[25] Gaviria Morales E, Guidi M, Peterka T, Rabufetti A, Blum R, Mainetti C. Primary cutaneous cryptococcosis due to *Cryptococcus neoformans* in an immunocompetent host treated with itraconazole and drainage: Case report and review of the literature. Case Rep Dermatol. 2021;13(1):89-97.
[26] Patil SM, Beck PP, Arora N, Acevedo BA, Dandachi D. Primary cutaneous cryptococcal infection due to fingolimod- Induced lymphopenia with literature review. ID Cases. 2020;21:e00810.
[27] Perfect JR, Dismukes WE, Dromer F, Goldman DL, Graybill JR, Hamill RJ, et al. Clinical practice guidelines for the management of cryptococcal disease: 2010 update by the infectious diseases society of America. Clin Infect Dis. 2010;50(3):291-322.

PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of Microbiology, SGT University, Gurgaon, Haryana, India.
2. Assistant Professor, Department of Microbiology, SGT University, Gurgaon, Haryana, India.
3. Professor and Head, Department of Dermatology, SGT University, Gurgaon, Haryana, India.
4. Professor and Head, Department of Microbiology, SGT University, Gurgaon, Haryana, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Shalini Upadhyay,
SGT University, Gurgaon-Badli Road, Chandu, Budhera, Gurgaon, Haryana, India.
E-mail: shalini.upd@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Feb 06, 2021
- Manual Googling: Mar 03, 2021
- iThenticate Software: Mar 31, 2021 (19%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Feb 04, 2021**
Date of Peer Review: **Mar 04, 2021**
Date of Acceptance: **Mar 11, 2021**
Date of Publishing: **Apr 01, 2021**