Scientific Research Publishing

Case Reports in Clinical Medicine, 2023, 12, 418-424
https://www.scirp.org/journal/crcm
ISSN Online: 2325-7083
ISSN Print: 2325-7075

Cutaneous Cryptococcosis Arising in a Patient with Idiopathic Lung Disease: Related Illnesses or "Ticks and Fleas"

Zoe Parker[1], Cary Chisholm[2]

[1]Lubbock Christian University, Lubbock, USA
[2]Dermatopathology Laboratory, Epiphany Dermatology, Waco, USA
Email: cary.chisholm@gmail.com

How to cite this paper: Parker, Z. and Chisholm, C. (2023) Cutaneous Cryptococcosis Arising in a Patient with Idiopathic Lung Disease: Related Illnesses or "Ticks and Fleas". *Case Reports in Clinical Medicine*, **12**, 418-424.
https://doi.org/10.4236/crcm.2023.1210056

Received: September 6, 2023
Accepted: October 15, 2023
Published: October 18, 2023

Abstract

Cryptococcus is a yeast typically found in bird feces such as pigeon droppings. Infection may occur through inhalation of spores or via direct inoculation into the skin. Typically there is a history of immunosuppression, but cases are also reported in immunocompetent hosts. *Cryptococcus* may manifest as pulmonary disease or primary cutaneous infection, but dissemination to a systemic illness is the most life-threatening concern. We present the case of a 71-year-old man with a four-year history of idiopathic lung disease, treated with oral prednisone and mycophenolate, presents with a new onset skin rash on the right wrist. He has a history of cleaning and clearing barns and sheds after a recent storm devastated the area. Birds and bats were present in these structures while he was working. Initial therapy failed, and subsequent biopsy showed the presence of *Cryptococcus* yeast. Further investigation yielded a positive, low titer *Cryptococcus* antigen screen but negative blood cultures. This case illustrates three valuable facets of patient care. Ideally, one diagnosis will explain all of the clinical presentation, but when that is not the case then multiple etiologies must be explored. Sometimes first-line therapy is ineffective, and the clinician should not be afraid to recognize that and change course. Importantly with skin lesions, failure to respond to treatment or worsening of the lesion in the face of topical and/or oral steroids should lead one to consider the possibility of infection, particularly in an immunosuppressed patient, and prompt biopsy is prudent.

Keywords

Cryptococcosis, Cryptococcus, Dermatitis, Chronic Lung Disease, Skin Infection

1. Introduction

Cryptococcus is a species of fungus is a dimorphic fungus that may infect humans, typically as an opportunistic pathogen especially in cutaneous cases [1]. As a dimorphic fungus, it may exist as yeast or as hyphae, but most human infections occur from inhalation of yeast form [2]. This organism is classically associated with meningitis and sepsis as part of human immunodeficiency virus (HIV) infection and subsequent acquired immunodeficiency syndrome (AIDS) and as such is regarded as an AIDS-defining illness [3]. Improved antiviral medications and improved adherence to antiviral regimens has led to a drastic reduction in AIDS cases, although HIV infections have increased, with HIV-infected individuals now capable of living a much more normal life [4].

Cryptococcus is a cause of pulmonary infections. Rarely they can disseminate to other organs such as the skin. There are no pathognomonic signs of cutaneous Cryptococcosis, and this diagnosis may often come as a surprise when the skin is biopsied for an uncertain dermatitis. Furthermore, the presence of cutaneous Cryptococcosis may be a primary infection from direct inoculation which further complicates clinical decision making as a secondary infection must be excluded. Cutaneous lesions may manifest as nonhealing ulcers, papules, plaques, nodules, or abscesses, and they typically resolve completely with fluconazole treatment [5] [6] [7] [8]. We report a case of cutaneous Cryptococcosis arising in a patient with pre-existing idiopathic pulmonary disease including the considerations for determining a primary infection versus secondary dissemination.

2. Case Presentation

A 71-year-old male presents to the dermatologist with a red papule on his right wrist. Initial treatment with topical steroids failed to alleviate the dermatitis. The lesion continued to spread such that there was now circumferential erythema of the right wrist and distal forearm (**Figure 1**). No associated signs or symptoms, such as headaches, fever, chills, night sweats or neurological impairments, are reported. Physical examination reveals no other notable findings. Social history reveals that the patient works for an asphalt company in the lab. Due to many severe storms where he lives in the Ohio River Valley, there has been significant storm damage to buildings. To help with recovery of the community he has recently been working to help clean up barns, sheds, and other damaged buildings where he often encountered birds and bats. He does not remember direct trauma to this site but states that, due to the nature of the work, it is possible.

His past medical history includes four years of pulmonologist follow-up for idiopathic interstitial lung disease. His prescribed medication regimen during that time consists of prednisone and mycophenolate, but the lung disease has persisted during the course of treatment. A skin biopsy was performed, and it showed the presence of *Cryptococcus* yeast. Subsequent testing revealed a *Cryptococcus* serum antigen titer of 1:20 and negative blood cultures. Further com-

puted tomography (CT) and magnetic resonance imaging (MRI) scans showed no evidence of other sites of infection or central nervous system (CNS) involvement. He was prescribed oral fluconazole 400 mg daily for six months until resolution of the wrist lesion. He was next seen for follow-up 12 months later and that visit showed complete resolution of the wrist lesion. He is not expected to have any sequelae from this infection now that it has fully resolved.

Histologic sections from the skin biopsy show a mixed dermal inflammatory cell infiltrate punctuated by collections of neutrophils. Within several of these microabscesses are small yeast of varying size (Figure 2). The capsule surrounding each yeast spore stains prominently with a mucicarmine stain (Figure 3).

Figure 1. Circumferential erythema is noted on the right wrist.

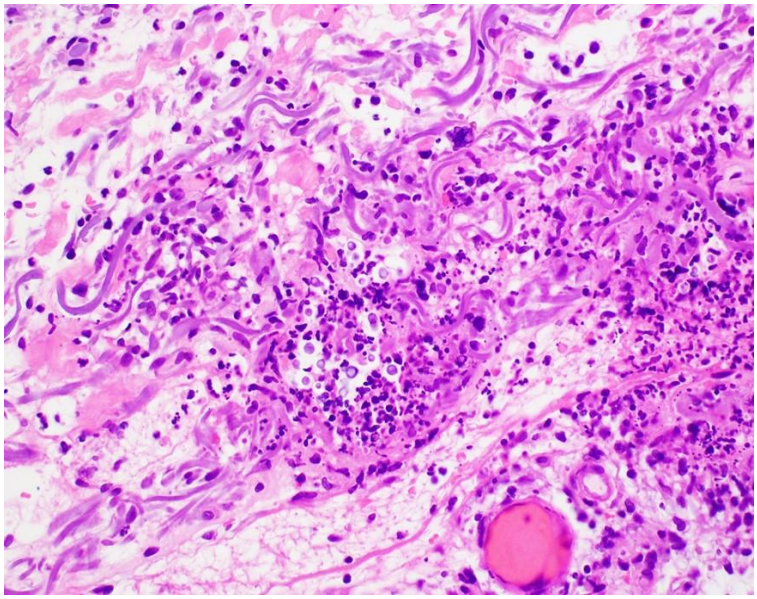

Figure 2. Cryptcoccus yeast are present within a cluster of neutrophils.

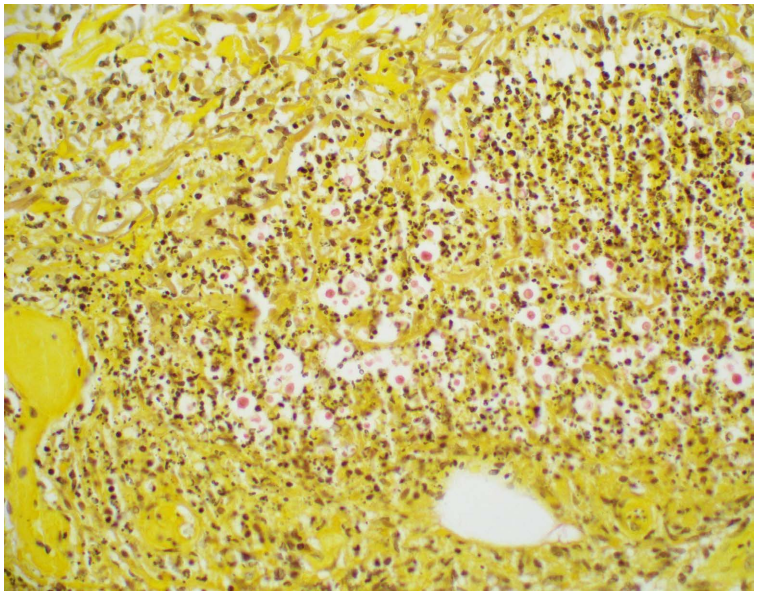

Figure 3. Mucicarmine highlights the yeast (pink) which are embedded in a background of inflammation.

3. Discussion

Cutaneous cryptococcosis typically occurs secondary to direct inoculation by an infectious source in patients with some history of pre-existing immunosuppression [9]. Immunocompetent patients are less commonly afflicted with this infection. Sources of immunosuppression include depletion and/or dysfunction of T cell lymphocytes (*i.e.* HIV infection) and solid organ transplantation followed by immunosuppressive medications [10] [11] [12] [13]. Cases have also been reported to arise in patients who have a malignant tumor that may or may not have been treated with chemotherapeutic agents at the time of infection [14] [15].

Physical presentation may vary, and there are no pathognomonic features of primary cutaneous cryptococcosis [16]. Lesions may be papules, ulcers, or erythematous plaques [17] [18] [19] [20] [21].

Our patient had been followed for the previous two years for an idiopathic lung disease. His treatment regimen included two immunosuppressive medications—prednisone and mycophenolate. Upon receiving the diagnostic results from the skin biopsy, the concern by the infectious disease physician was to evaluate for the possibility of pulmonary cryptococcosis with secondary dissemination due to these medications.

Further investigation discovered that the patient had a positive *Cryptococcus* antigen screen, albeit with a low titer at 1:20. Fungal blood culture yielded negative results. Morphological patterns concerning for dissemination were not identified with imaging studies. When combining the patient's laboratory and radiologic findings with his exposure history, it was determined that this is most likely a primary skin inoculation without dissemination and therefore unrelated to the etiology of his pre-existing lung disease. In fact, eventual completion of

the fluconazole failed to improve the underlying lung disease while successfully eliminating the wrist lesion.

Cryptococcus may cause pulmonary disease in patients with immunosuppression and adequate exposure history, much like in primary cutaneous infection [22], and it would have been convenient if both lung and skin lesions could be explained by this one organism. The clinician correctly investigated this possibility first before ruling it a primary cutaneous process. This eventual determination altered the treatment regimen so that the patient was able to take oral fluconazole 400 mg for six months with follow-up exclusively via telemedicine.

Medical training usually includes the strategy that one should, when possible, find one diagnosis that will encompass and explain all the patient's presenting signs and symptoms. It is prudent to remember that patients often carry multiple diagnoses indicating several concurrent disease conditions.

The patient did not respond to initial therapy, and his physical findings actually worsened with topical steroids and the systemic steroids already in place to treat idiopathic lung disease. Instead of trying multiple treatment strategies the clinician understood that the patient's history of immunosuppression increased his likelihood for either an uncommon disease (such as infection) or an uncommon presentation of a common illness. Worsening of cutaneous signs in the presence of topical and/or systemic steroids raises the possibility of an infectious process, and, recognizing this, the provider was quick to perform a punch biopsy for diagnosis by a dermatopathologist. Prompt biopsy and diagnosis allowed for rapid intervention and prevention of subsequent dissemination.

This case illustrates three important facets of patient care that are part and parcel of optimum patient care and patient outcomes, particularly when concerning skin lesions. Firstly, evaluate if one diagnosis may explain all the presenting signs and symptoms, and if a single diagnosis does not fit then pivot to find the fewest best etiologies (so-called "ticks and fleas"). Secondly, do not be afraid to conclude that the first-line therapy is not effective and change tactics. Third, if the diagnosis is in doubt then utilization of skin biopsy with subsequent evaluation by a board-certified dermatopathologist may yield specific results which dramatically alter the course of treatment.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Akram, S.M. and Koirala, J. (2023)Cutaneous Cryptococcus. StatPearls, Treasure Island.

[2] Heung, L.J., Wiesner, D.L., Wang, K., Rivera, A. and Hohl, T.M. (2023) Immunity to Fungi in the Lung. *Seminars in Immunology*, **66**, Article ID: 101728. https://doi.org/10.1016/j.smim.2023.101728

[3] Ibe, C., Okoye, C.A., Nweze, E. and Out, A. (2023) Cryptococcus in Africa: What

the Data Tell Us. *Medical Mycology*, **61**, myad049.
https://doi.org/10.1093/mmy/myad049

[4] Dailey, A., Johnson, A.S., Hu, X., *et al.* (2021) Trends in HIV Care Outcomes among Adults and Adolescents-33 Jurisdictions, United States, 2014-2018. *Journal of Acquired Immune Deficiency Syndromes*, **88**, 333-339.
https://doi.org/10.1097/QAI.0000000000002778

[5] Belda Jr, W., Casolato, A.T.S., Luppi, J.B., Passero, L.F.D. and Criado, P.R. (2022) Primary Cutaneous Cryptococcosis Caused by *Cryptococcus gatti* in an Elderly Patient. *Tropical Medicine and Infectious Disease*, **7**, Article 206.
https://doi.org/10.3390/tropicalmed7090206

[6] Nishiyama-Fujita, Y., Kondapi, D.S., Parkerson III, G.R. and Xu, Y. (2022) Primary Cutaneous Cryptococcosis of Nose with Extensive Tissue Destruction: A Rare Case Report. *Ear, Nose & Throat Journal*. https://pubmed.ncbi.nlm.nih.gov/36065638/
https://doi.org/10.1177/01455613221126324

[7] Premjith, T.J., Prathap, P., Asokan, N. and Balakrishnan, S. (2022) Non-Healing Cutaneous Ulcer as the Initial Presentation of Disseminated Cryptococcosis. *Indian Journal of Dermatology, Venereology and Leprology*, 88, 873.
https://doi.org/10.25259/IJDVL_854_2021

[8] John, M., Norsworthy, S. and Richards, L. (2021) Cutaneous Lesions in the Setting of Disseminated *Cryptococcus neoformans* Infection. *Southern African Journal of HIV Medicine*, **22**, a1315. https://doi.org/10.4102/sajhivmed.v22i1.1315

[9] Noguchi, H., Matsumoto, T., Kimura, U., Hiruma, M., Kusuhara, M. and Ihn, H. (2019) Cutaneous Cryptococcosis. *Medical Mycology Journal*, **60**, 101-107.
https://doi.org/10.3314/mmj.19.008

[10] Becker, J., Wolde-Semait, H. and Wollstein, R. (2023) Cutaneous Cryptococcus Infection and Suspected Kaposi Sarcoma of the Hand in an Immunocompromised Patient. *The Journal of Hand Surgery* (*Asian-Pacific Volume*), **28**, 273-277.
https://doi.org/10.1142/S2424835523720104

[11] McCann, T., Patel, A.S., Patel, D.N., Sharath, D.B., Mansouri, B. and Contreras, C. (2022) Cutaneous Cryptococcal Infection: Initial Manifestation of Acquired T-Cell Immunodeficiency Due to Malignant Thymoma. *Current Medical Mycology*, **8**, 55-58.
https://doi.org/10.18502/cmm.8.2.10334

[12] Ozawa, S., Hanada, S., Uruga, H., Ito, H., Nakahama, H., Ishikawa, N., Moriguchi, S., Murase, K., Miyamoto, A., Hayashi, N. and Takai, D. (2022) Disseminated Cryptococcosis in a Renal Transplant Recipient. *Respirology Case Reports*, **10**, e01011.
https://doi.org/10.1002/rcr2.1011

[13] Tan, W.H., Koniman, R., Tan, A.L., Wijaya, L., Lim, K.H. and Oh, C.C. (2022) Solitary Leg Ulcer in a Renal Transplant Recipient. *JAAD Case Reports*, **23**, 93-95.
https://doi.org/10.1016/j.jdcr.2021.12.046

[14] Hu, M., Chai, S., Lei, W., Liao, K. and Zhang, R. (2021) Mediastinal Small Cell Carcinoma with Primary Cutaneous Cryptococcosis: A Rare Case Report. *Infection and Drug Resistance*, **14**, 3693-3697. https://doi.org/10.2147/IDR.S325826

[15] Passerini, M., Terzi, R., Piscaglia, M., Passerini, S. and Piconi, S. (2020) Disseminated Cryptococcosis in a Patient with Metastatic Prostate Cancer Who Died in the Coronavirus Disease 2019 (COVID-19) Outbreak. *Cureus*, **12**, e8254.
https://doi.org/10.7759/cureus.8254

[16] Silva Souza, C.D., Takada, M.H., Ambiel, M.V. and Nakai, V.T. (2021) Primary Cutaneous Cryptococcosis: The Importance of Early Diagnosis. *Anais Brasileiros de Dermatologia*, **96**, 482-484. https://doi.org/10.1016/j.abd.2020.12.004

[17] Cartron, A.M., Challa, N., Chung, C. and Trinidad, J.C. (2020) Umbilicated Papules on the Bilateral Upper and Lower Extremities. *Dermatology Online Journal*, **26**, Article ID: 13. https://doi.org/10.5070/D3266049325

[18] Choi, H., Kim, Y.I., Na, C.H., Kim, M.S. and Shin, B.S. (2020) Primary Cutaneous Cryptococcosis in an Older Immunocompetent Patient: A Case Report. *Annals of Geriatric Medicine and Research*, **24**, 148-151. https://doi.org/10.4235/agmr.20.0012

[19] Nowak, M.A., Putynkowska, A., Barańska-Rybak, W., Czarnacka, K. and Dębska-Ślizień, M.A. (2020) *Cutaneous cryptococcosis*: An Underlying Immunosuppression? Clinical Manifestations, Pathogenesis, Diagnostic Examinations and Treatment. *Postępy Dermatologii i Alergologii*, **37**, 154-158. https://doi.org/10.5114/ada.2020.94833

[20] Oppenheimer, A.R., Valente, N.Y.S. and Silva, D.H.M. (2020) Cutaneous Cryptococcosis Simulating Pyoderma Gangrenosum. *Revista da Sociedade Brasileira de Medicina Tropical*, **53**, e20200120. https://doi.org/10.1590/0037-8682-0120-2020

[21] Carrasco-Zuber, J.E., Navarrete-Dechent, C., Bonifaz, A., Fich, F., Vial-Letelier, V. and Berroeta-Mauriziano, D. (2016) Cutaneous Involvement in the Deep Mycoses: A Review. Part II—Systemic Mycoses. *Actas Dermo-Sifiliográficas*, **107**, 816-822. https://doi.org/10.1016/j.ad.2016.06.001

[22] Wang, Y., Gu, Y., Shen, K., Cui, X., Min, R., Sun, S., Feng, C., Chen, Y., Wang, L., Ma, G., Chen, B., Ni, Y., Zhong, H., Shi, Y. and Su, X. (2023) The Management and Outcome of Cryptococcosis in Patients with Different Immune Statuses and Treatment Protocols: A Multicenter Real-World Study in Jiangsu Province—China. *Journal of Medical Mycology*, **33**, Article ID: 101389. https://doi.org/10.1016/j.mycmed.2023.101389