Cutaneous nodules secondary to *Mycobacterium avium* complex in a patient with human immunodeficiency virus

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Abstract

We present a patient with human immunodeficiency virus who developed multiple painful lesions that previously in the past had speciated as *Cryptococcus neoformans* cutaneously, and in the lung. Despite induction therapy for presumed re-infection, the patient did not improve so a biopsy was performed and this was speciated as *Mycobacterium avium* complex, with final diagnosis being disseminated *Mycobacterium avium* complex. This case highlights the importance of considering a broad differential diagnosis for any new lesions regardless of prior culture data.

Keywords: Cryptococcus neoformans, HIV, Mycobacterium avium

Introduction

We present a case of a 49-year-old-man experiencing homelessness with human immunodeficiency virus (HIV) and a CD4 count of 56 cells/mm^3, and an undetectable viral load who had developed new acutely painful nodules on the arms. Similar lesions present one year ago had previously revealed *Cryptococcus neoformans* on culture. Owing to this, the new nodules were attributed to the same fungal organism. However, there was no clinical improvement despite therapy with amphotericin B and flucytosine treatment being directed for presumed cryptococcal infection. For example, there was no lesional resolution and lesional pain continued to increase. Thus, a dermatology consultant was enlisted and elected to perform two biopsies of different appearing lesions, which yielded positive culture for *Mycobacterium avium* complex (MAC). This case highlights the critical importance of keeping a broad differential diagnosis in mind, despite any prior proven illnesses. This is especially true when dealing with the immunocompromised.

Case Synopsis

A 49-year-old man experiencing homelessness with a history of HIV inconsistently taking prescribed anti-retroviral therapy presented to the emergency department owing to a one-month history of fatigue with generalized weakness, a 5-day history of several painful erythematous papules and nodules on his hands, forearms, and abdominal wall, and profuse diarrhea. The individual had a notable history of multiple opportunistic infections during the prior two years, including recurrent cryptococcal meningitis requiring multiple inductions, *Pneumocystis jirovecii* pneumonia, chronic diarrhea due to *Cryptosporidium* species, cavitary lung lesions secondary to *C. neoformans*, and numerous cutaneous nodules, also secondary to *C. neoformans*. The patient had stable vital signs. A complete blood count was notable for moderate anemia and a comprehensive metabolic panel was normal. HIV parameters disclosed a CD4 count of 56 cells/mm^3 with an undetectable viral load. A dermatologist was consulted to evaluate the painful cutaneous nodules. The latter were understandably initially attributed to cutaneous *C. neoformans*. However, the

skin lesions were not improving despite induction therapy with amphotericin B and flucytosine; the patient continued to feel pain from these nodules (**Figure 1**).

Two punch biopsies were performed of these lesions and submitted for both routine stain and cultures. Hematoxylin and eosin stain showed granulomatous inflammation with sparse necrosis located in the deep dermis (**Figure 2**). This suggested fungal or mycobacterial infection, with cultures ultimately growing MAC. Culture results in conjunction with compatible histology established the diagnosis of disseminated MAC. Infectious disease consultants concurred with this conclusion. An ophthalmology consult was obtained for ocular evaluation but no evidence of ocular MAC was found. The patient had computed tomography scans of the chest, abdomen, and pelvis which disclosed no evidence of internal organ MAC involvement. The patient's current antiretroviral therapy was changed from bictegravir/emtricitabine/tenofovir alafenamide to emtricitabine/tenofovir disoproxil fumarate/dolutegravir. In addition, the patient was started on a combination of rifabutin 300mg daily, ethambutol 800mg daily and azithromycin 500mg daily to be taken for one year related to the disseminated MAC. The patient initially did well following discharge but was subsequently lost to follow-up one month after.

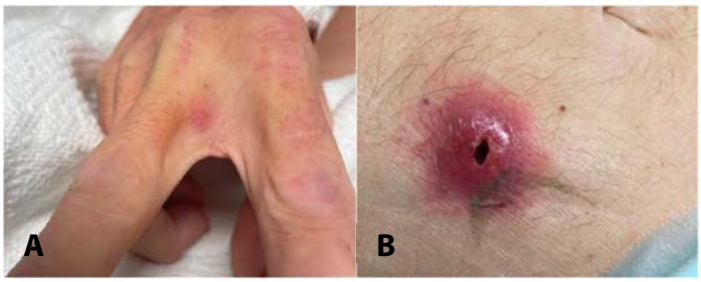

Figure 1. ***A)*** *Right hand second webspace with tender erythematous papule.* ***B)*** *Right abdominal tender, erythematous nodule.*

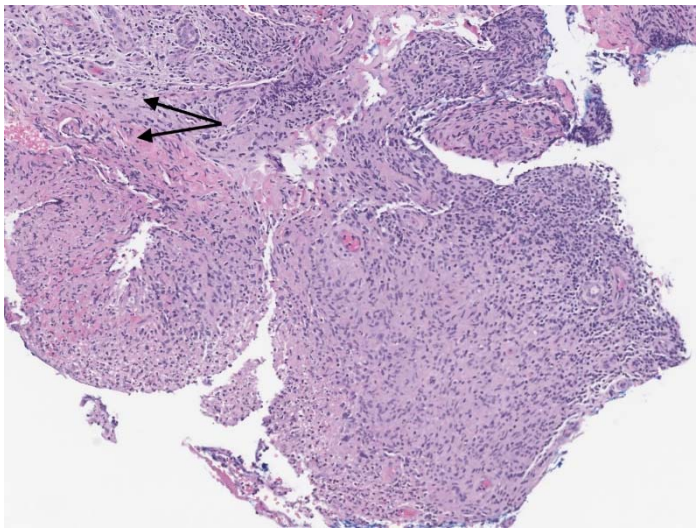

Figure 2. *H&E histopathology. Deep dermis section demonstrating granulomatous inflammation and sparse necrosis as shown by the black arrows, 100×.*

Case Discussion

Overall, MAC is a fairly ubiquitous organism commonly encountered via environmental exposure (animals, water sources, and soil) rather than via contact with other humans [1]. Cutaneous MAC is a fairly rare entity with protean manifestations such as painful nodules, painless granulomas, and verrucous ulcers. Cutaneous MAC primarily manifests on areas of skin above the clavicle [2,3]. Uniquely, MAC can present with either localized or disseminated involvement, run a varying clinical course, and can be difficult to culture, making this a challenging diagnosis to establish [3]. Although cutaneous disease can manifest in immunocompetent hosts, it is much more common among those who are immunocompromised, such as solid organ transplant recipients, those suffering from autoimmune disease, and acquired immunodeficiency syndrome patients with CD4 counts <50 cells/mm^3 [3]. Our patient is unique in the sense that, whereas he did have a low CD4 count, his viral load was undetectable. In addition, the patient did not have evidence of lung MAC and he actually demonstrated two different morphologies of cutaneous MAC lesions that both demonstrated such when biopsied, which is extremely rare to have without concomitant pulmonary involvement [4]. Uniquely in immunocompromised patients, multiple pathogens can manifest in the same lesion appearance, resulting in polymicrobial infections [5].

Numerous treatment options have been reported for MAC, including macrolides, different rifamycins, ethambutol, quinolones, and aminoglycosides, with macrolides often playing a central role in therapy [6]. The standard therapy is to use a triple drug regimen

with a macrolide, rifampin, and ethambutol, with aminoglycosides only added for severe fibrocavitary disease; however, benefit is mixed [7]. In our case, rifampin was substituted for rifabutin given medication interaction with his prior antiretroviral therapy.

Conclusion

Overall, our case highlights the importance of keeping a broad differential diagnosis in mind when working with an immunocompromised patient population presenting with a variety of nonspecific cutaneous findings. Although endemic deep fungal and saprophytic fungal infection might be more common, disseminated MAC (and other mycobacterial infections) remain possible. Despite a well-defined prior infection caused by *C. neoformans*, new lesions in this patient actually represented a new infection. It is paramount to entertain a broad differential diagnosis as this can help decrease treatment delays and ensure patients get appropriate treatment.

Potential conflicts of interest

The authors declare no conflicts of interest

References

1. Rahmani M, Alroy J, Zoukhri D, Wein RO, Tischler AS. Mycobacterial pseudotumor of the skin. *Virchows Arch*. 2013;463:843-6. [PMID: 24114192].
2. Hirt PA, Gonzalez AM, Acosta AS, et al. Cutaneous Mycobacterium avium-intracellulare infection masquerading as sarcoidosis. *Pediatr Dermatol*. 2024;41:497-500. [PMID: 38173086]. [
3. Kollipara R, Richards K, Tschen J, et al. Disseminated Mycobacterium avium Complex With Cutaneous Lesions. *J Cutan Med Surg*. 2016;20:272-4. [PMID: 26740021].
4. Sivanesan SP, Khera P, Buckthal-McCuin J, English JC, 3rd. Cutaneous Mycobacterium avium-intracellulare complex associated with immune reconstitution inflammatory syndrome. *J Am Acad Dermatol*. 2010;62:e25-6. [PMID: 20466168].
5. Cohen PR. Evaluation of clinically normal appearing skin for systemic infectious diseases in human immunodeficiency virus seropositive patients. *Med Hypotheses*. 1991;34:193-7. [PMID: 2062253].
6. Griffith DE. Treatment of Mycobacterium avium Complex (MAC). *Semin Respir Crit Care Med*. 2018;39:351-61. [PMID: 30071550].
7. Hendrix C, McCrary M, Hou R, Abate G. Diagnosis and Management of Pulmonary NTM with a Focus on Mycobacterium avium Complex and Mycobacterium abscessus: Challenges and Prospects. *Microorganisms*. 2022;11:47. [PMID: 36677340].