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Co-infection of Aspergillosis and Nasal Demodicosis in an Aplastic Anemia Patient with COVID-19: A Case Report

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Abstract

Demodex mites normally live in the pilosebaceous unit and gland, the presence of them can be harmless on the human skin. They are usually diagnosed in young adults or immunodeficiency states. We report a possible case of demodicosis in aplastic anemia patient with co-infection of aspergillosis and COVID-19. Direct microscopic examination of Sinus debridement was positive for both fungal elements as well as *Demodex* mites and they were diagnosed as *Aspergillus flavus* by sequencing and *Demodex folliculorum* respectively.

Keywords Co-infection; Aspergillosis; Demodicosis; *Aspergillus flavus*; *Demodex folliculorum*

Introduction

Demodex is a genus of mites that normally live in the pilosebaceous unit and gland [1]. Two species live in humans: *D. folliculorum* and *D. brevis* [2]. Their presence can be harmless on the human skin and transmitted by skin-to-skin contact. *Demodex* mites are usually diagnosed in young adults or immunodeficiency states [3]. There are two types of demodicosis: primary and secondary demodicosis. Primary demodicosis could be the causative agent of pityriasis folliculorum, papulopustular, ocular and auricular demodicosis. Secondary demodicosis is usually related to systemic or local immuno-suppression and studies show increased severity of demodicosis [2]. For demodectic diagnosis, skin scraping from different regions like the nose, cheeks, chin, or forehead by direct examination or a skin biopsy under the microscopic examination. Demodicosis is diagnosed when there is a high density of *Demodex* mite (>5/cm^2) in a 1cm^2 area using a light microscope [3]. In this study, we demonstrate aplastic anemia, in a COVID-19 patient who simultaneously had *D. folliculorum* and *Aspergillus flavus* in his paranasal sinuses.

Case presentation

A 31-year-old male was a known case of aplastic anemia on a treatment of cyclosporine, was admitted with symptoms of high fever, dyspnea, and severe thrombocytopenia at the Imam Khomeini Hospital Complex, in June 2022. Due to the COVID-19 pandemic, a chest CT scan was done and ground glass opacities were seen (Figure 1). Real-time polymerase chain reaction (PCR) from nasopharyngeal swab was reported positive for SARS-CoV-2 and the patient took remdesivir (200mg/stat and 100mg/daily) and dexamethasone 8mg/daily for 5 days. The patient's fever and dyspnea got better. After 5 days, she was discharged with a relatively good general condition. Three days later, he was referred with a fever of T: 38.6°C. The patient had hematuria in the early urination and had pain in the perianal area. A routine laboratory examination revealed pancytopenia and infection. Leukocytes (1.2×103/µl), Hemoglobin (7.6 g/dl), platelet (14×103/µl), erythrocyte sedimentation rate (106mm/hr.), and C- reactive protein (25mg/lit), other blood tests were within normal ranges.

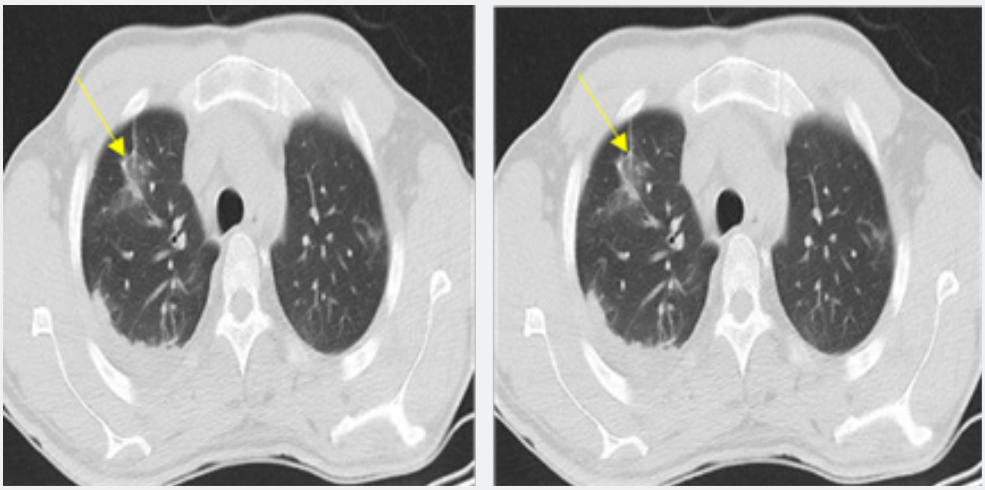

Figure 1: A contrast - enhanced computed tomography chest showing ground - glass opacities.

Klebsiella pneumonia (sensitive: Meropenem and Amikacin, resistance: ceftriaxone, ciprofloxacin, co-trimoxazole) was isolated from blood culture, he also had hemoptysis. The patient was treated with meropenem (2 g/TDS/IV/Infusion). After one week, while the patient's fever had stopped and her general condition had improved, he complained of facial pain and headache. Para-nasal CT scan revealed pan sinusitis with bone destruction (Figure 2). Liposomal amphotericin B (350mg/daily/IV) was started. He also presented a lot of red papules and pustules surrounded by inflammatory redness and flushing in his trunk and limbs (Figure 3). The patient was referred for microscopic examination for Scabies, and the result was positive (Figure 4a). A potassium hydroxide 10 % of sinus debridement examination showed the presence of mite Figure 4(b) and fungal septate elements hyaline hyphae (Figure 4c).

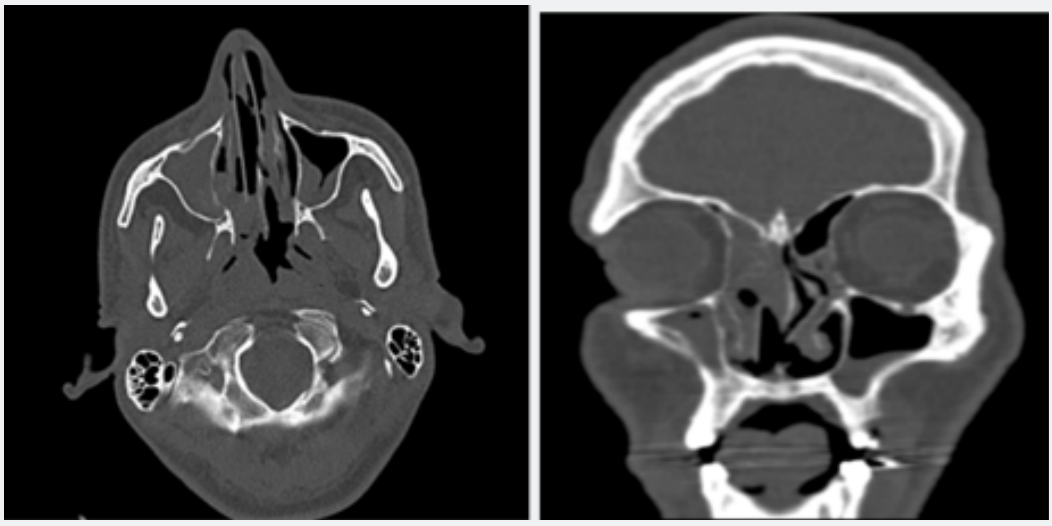

Figure 2: Para- nasal CT scan showing pan sinusitis with bone destruction.

Examination of the mite morphology (long striated posterior segment with four legs) and size (0.3-0.4mm long) detected it as *D. folliculorum* [4]. The sinus debridement was cultured on SDA for conventional and molecular methods at 37c and 25c for 4 weeks. Microscopic examination showed *Aspergillus spp*. For molecular identification DNA of *Aspergillus spp*. was extracted from SDA and purified. The entire internal transcribed spacer (ITS) region (ITS1-5.8S rDNA-ITS2) was amplified by PCR with the universal

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primers ITS1 (5'-TCC GTA GGT GAA CCT GCG G-3') and ITS4 (5'-TCC TCC GCT TAT TGA TAT GC-3'). The PCR amplicon was sent for Sanger sequencing. *Aspergillus flavus* was identified using a basic local alignment search tool (BLAST) (http://www.ncbi.nlm.nih.gov/BLAST/) and the sequence was deposited into GenBank Data.

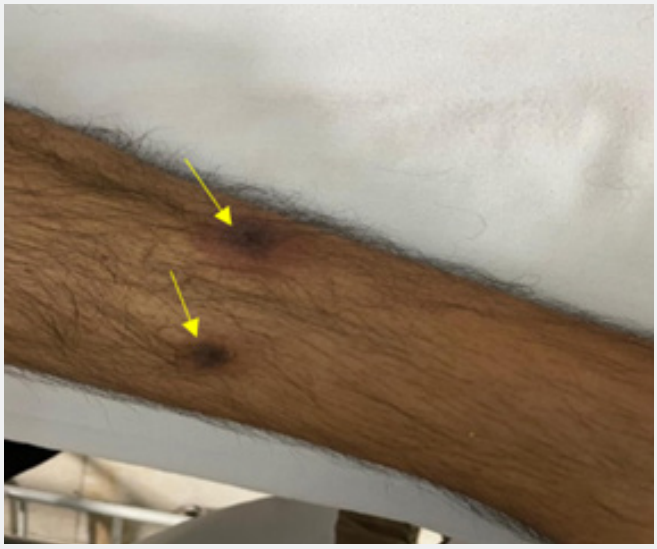

Figure 3: Red papules and pustules surrounded by inflammatory redness and flushing.

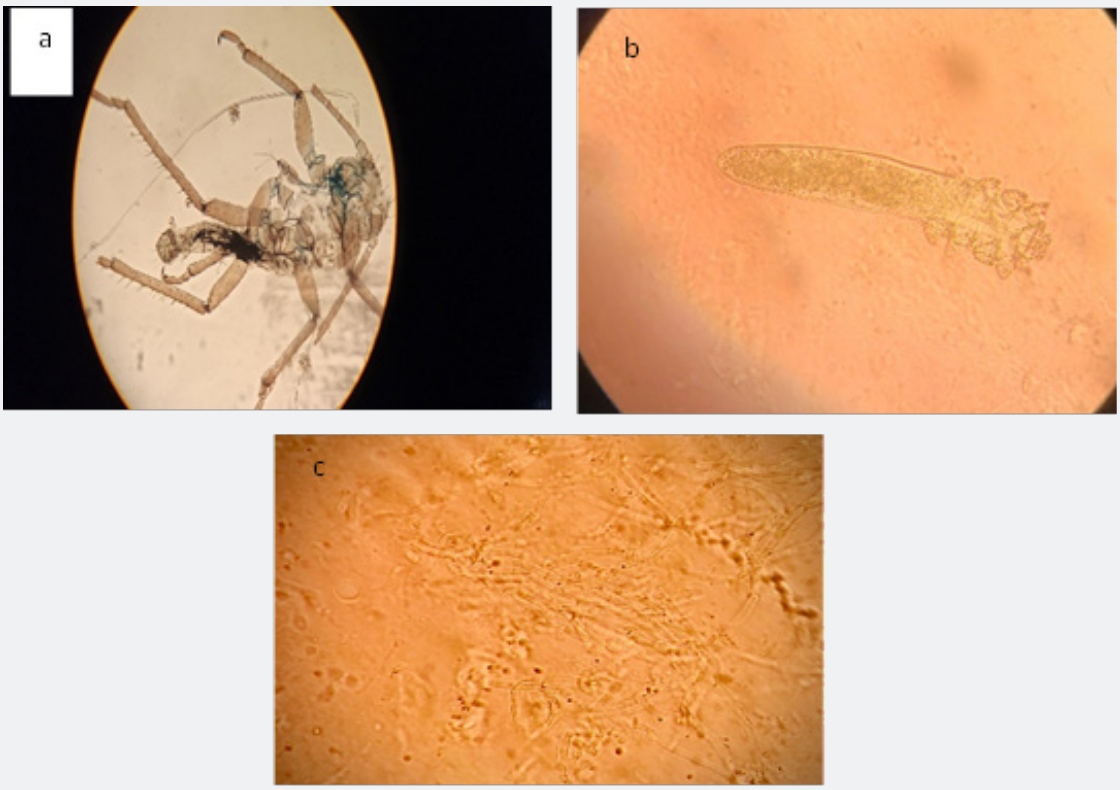

Figure 4: Mite of Sarcoptes scabiei from lesion scraping (a), KOH mount of paranasal sinuses debridement characteristic features of Demodex folliculorum (b) (magnification× 40) and septate hyphae (c) (magnification ×40).

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Discussion

Invasive aspergillosis was diagnosed in this immunocompromised person as he had aplastic anemia on a treatment of cyclosporine. Patients with aplastic anemia are the leading candidates for invasive fungal infections and invasive aspergillosis is among the most common infection in patients with hematological malignancy [5]. The diagnosis was confirmed by conventional and molecular methods from the sinus debridement sample and *A. flavus* was identified. The predisposing factors of invasive aspergillosis are commonly by species of *A. fumigatus* (about 80%), *A. flavus* (about 15-20%), and less common are *A. terreus* and *A. niger*. Although the majority (approximately 80%) of invasive aspergillosis is caused by *A. fumigatus* overall in the United States, *A. flavus* is the predominant pathogen in our study and tropical as well as sub-tropical areas like; most of the Middle East, southeast Asia and Africa. This pathogen can survive in dry conditions and higher temperatures, experimental in vivo studies in both normal and immunocompromised mice have shown more virulence of *A. flavus* compared to *A. fumigatus* [6-9]. The inability of host defenses in our pancytopenia patient predisposed the development of *A. flavus* and Demodex mites simultaneously in paranasal sinuses. For proliferation in the human body, *Demodex* mites need immunosuppression.

Studies showed severe demodicosis in immunocompromised patients with allogenic bone marrow transplant, stem cell transplantation, hematological malignancies, corticosteroid therapy [10,11] and scalp demodicosis in COVID-19 patient [12]. Even though the presence of *D. follicullorum* in debridement of the paranasal sinus increases suspicious rhino sinusitis due to the loss of patient, more investigation couldn't be done to find out its pathogenic implementation. Apart from this probable role, a study has suspended mites in transferring the fungal spores into sinuses [13]. To the best of our knowledge, this is the first case of possible demodicosis associated with an aplastic anemia COVID-19 patient with a coinfection of invasive aspergillosis. In conclusion, this case shows more attention from clinicians and laboratory physicians about *Demodex*, especially in immunosuppressed patients. More studies are needed to investigate the role of aplastic anemia in the susceptibility of demodicosis.

Acknowledgments

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