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Magnusiomyces capitatus in Immune-Competent Patients with Pulmonary Haemorrhage and Systemic Lupus Erythematosus

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Abstract

Invasive fungal infections have grown significantly over the last two decades, owing to an increase in immunocompromised hosts and geriatric patients. When the host's defenses are compromised, such infections are associated with severe morbidity and mortality. Here, a rare case of fungal infection in a 61-year-old immunocompetent male patient from Saudi Arabia was reported, who suffered from pulmonary hemorrhage and Systemic Lupus Erythematous. Bronchoalveolar Lavage was used as a diagnostic tool to identify the fungus reported in the case. The pathogenic fungal specie identified as *Magnusiomyces capitatus*, in macroscopic and microscopic morphological characteristics of the colonies. Based on clinical evidence, liposomal amphotericin formulation was recommended for initial therapy against fungal infection. Also, liposomal amphotericin B induced mycological eradication up to 70 percent in patients with proven *Magnusiomyces capitatus* infection. In addition to addressing suspected Systemic lupus erythematosus, the patient's health has improved with no evidence of pulmonary bleeding and hemoptysis.

Keywords

Magnusiomyces capitatus, Fungal Infection, Bronchoalveolar Lavage, Pulmonary Haemorrhage, SLE (Systemic Lupus Erythematosus), Amphotericin, A Case Report

1. Introduction

Magnusiomyces capitatus is a rare Ascomycetes yeast-like organism and has the order Sacchromycetales in the family Dipodsscaceae [1]. *M capitatus* is a ubiquitous global fungus in the typical microbial ecology colonizing humans. It can cause intrusive disease among immunosuppressed patients, particularly those with hematologic issues [2] [3]. Furthermore, it has the ability to infect individuals with a healthy immune system and is extremely rare in those who possess a fully functioning immune system. Patients with systemic lupus erythematosus (SLE) exhibit a predisposition to fungal infections as a result of specific immune system dysregulation. Nevertheless, there is a lack of case reports documenting the coexistence of SLE and *Magnusiomyces capitatus* in the same individual. This was the first case reported from Saudi Arabia, which displays a rare association between *Magnusiomyces capitatus* with Systemic lupus erythematosus (SLE).

2. Case History

In December 2021, a 61-year-old male resident in Saudi Arabia who retired from the military was admitted to a hospital, namely Security Forces Hospital Program, located in Makkah, Saudi Arabia. He had a history of heavy smoking, diabetes mellitus, hypertension, resolved HBV infection, and chronic kidney disease stage G4/A3. The patient's initial physical screening showed no change in his degree of consciousness or signs of gastrointestinal or urinary problems. Notable findings also included a temperature of 37˚C, Blood pressure of 147/59 mm Hg, Pulse rate of 69 beats per minute, and oxygen saturation of 96% on room air. Pulmonary and neurological examination was normal. The patient appeared to be in good health, mindful, alert, and not in pain, pale or jaundiced. All the body parts were sound and stable. On day +0, the patient was admitted to the intensive care unit for acute coronary syndrome.

Initial Laboratory investigations revealed:

Renal profile: Creatinine 286 umol/L (normal range 60 - 115) base line 169

Urea 37 mmol/L (normal 3 - 9) base line 15.7

Na^+ 134 mmol/L (136 - 154) K^+ 4.6 mmol/L (3.3 - 5.1) Chloride 101 mmol/L (98 - 107)

Urine protein/Urine Creatinine 192 (Normal <15)

Calcium 2.08 mmol/L (2.2 - 2.5) PTH 21 pmol/L (Normal 1.6 - 6.9)

Urine analysis: Negative Glucose, Negative Ketones, Negative Nitrates, Urine/Protein 2+ leucocytes/Urine 10 - 15, RBCs/Urine 3 - 5

CBC: Hemoglobin 9.9 g/dl (13 - 16) MCV 81 f L (Normal Range) MCH 29 pg (normal range) Platelets 133 (150 - 450) WBCs 4 (4 - 11) Lymphocytes 0.9 (1 - 3) Neutrophils 2.0 (2 - 7) Monocytes 0.8 (0 - 0.9) Eosinophil's 0.35 (0 - 0.7)

Coagulation profile revealed normal PT, PTT

Troponin 0.07 (Normal <0.03)

Liver function test: Albumin 28 g/L (34 - 48), Bilirubin Direct 15 umol/L (0.00

- 9) Total Bilirubin 26 umol/L (3.4 - 20), ALT 26 U/L (5 - 55), AST 10 U/L (5 - 34), Alkaline phosphatase 143 U/L (40 - 150), Protein 53 g/L (60 - 83)

Lactate Dehydrogenase 307 U/L (Normal 125 - 220)

ESR 65 mm/Hr (Normal 0 - 14)

C-Reactive Protein 21.4 mg/L (Normal 0.0 - 5.0)

Hepatitis B Surface Antigen Negative

Hepatitis C Antibody Non-reactive

HIV 1 and HIV 2 Antibody/Antigen Non-reactive

HbA1C 6.00% (Normal 4.8 - 5.9)

His initial ECG showed a left bundle branch block with mild elevation in troponin 0.078 ng/Ml. For two days (day +1 and day +2), he was introduced to Heparin infusion and dual antiplatelet agents (Aspirin and Plavix). On day +3 in ICU, the patient again experienced Dyspnea with high blood pressure, managed by intravenous Nitroglycerin. His CXR revealed bilateral consolidation in the right middle lobe and left upper lobe with bilateral effusion with pulmonary congestion; his oxygen saturation started to drop to 85% - 88% on room air. The patient was supplied with oxygen via nasal cannula, placed on BIPAP, and treated with Intravenous diuretics for pulmonary edema. His renal function started to raise Creatinine to 380 umol/L, and he developed oliguria. On ICU day, +4 patients developed Hemoptysis (2 attacks) in moderate amounts. His repeated Hemoglobin showed a drop of 2 g, and he received a blood transfusion in 2 units, and both Heparin and dual antiplatelet (Aspirin and Plavix) were discontinued.

CT chest was ordered and revealed bilateral dense consolidation and bilateral effusion (**Figure 1**).

The patient was suspected of having Rapid progressive glomerulonephritis on top of his chronic kidney disease and developed pulmonary hemorrhage. Workups for possible underlying autoimmune processes causing his rapidly progressive renal deterioration and lung hemorrhage were requested.

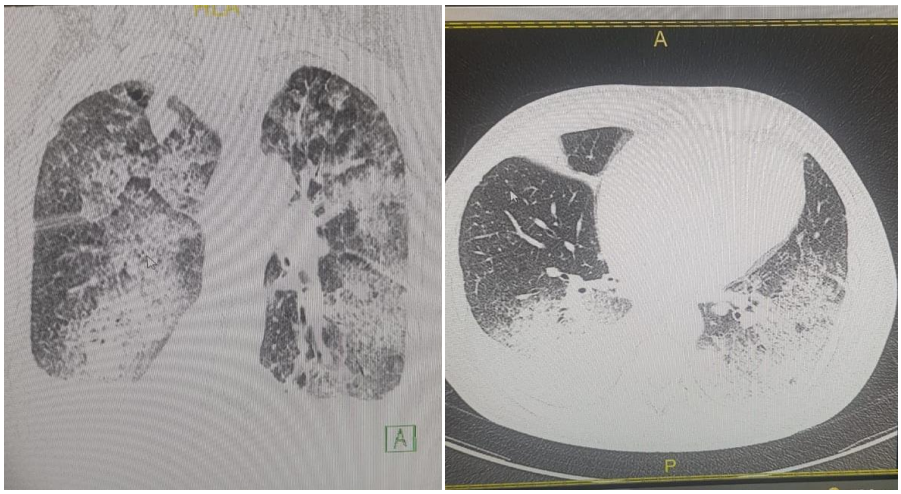


Figure 1. CT chest (bilateral consolidation and bilateral pleural effusion).

Autoimmune workup:
Anti-Nuclear Antibody Positive
Complement C4 < 0.03 g/L (0.15 - 0.5) C3 0.56 g/L (0.82 - 1.8)
Ant ds-DNA Antibody 202 IU/ml (0.0 - 200)
Anti-cyclic citrullinated peptide Antibody 0.5 U/ml (0.0 - 5.0)
Rheumatoid Factor <20 IU/ml (0.00 - 30)
Anti-Ribonuclear Protein (RNP) Negative
Anti-scleroderma Antigen (SCL-70) Positive
Anti-Sjogren s Syndrome—Antigen A Negative
Anti-Sjogren s Syndrome—Antigen B Negative
Anti-Smith Antigen (Sm) Negative
Anti-Centromere Antibody Negative
C-ANCA 1.73 Units (Normal <20)
P-ANCA 1.87 Units (Normal <20)
Glomerular Basement Membrane Ab (IgG) Not detected
Lupus Anticoagulant Not detected
Beta 2 Glycoprotein I AB (IgA) < 2.0 (Normal 0 - 20)
Anti-Cardiolypin Antibody (IgM) 3.2 MPL (Normal <20)
Anti-Cardiolypin Antibody (IgG) 4.3 GPL (Normal <20)

The rheumatology team made the diagnosis of Systemic Lupus Erythematosus (SLE). The plan was to treat him with pulse steroid therapy, Cyclophosphamide, and plasma exchange for SLE with possible SLE nephritis and Pulmonary hemorrhage secondary to SLE. On day +5 of ICU admission, the patient was electively intubated and ventilated because of further deterioration in his oxygen saturation despite a high flow oxygen supply of 40 L 100%. Also, he became more oliguric and started on Hemodialysis. In addition, plasma exchange was initiated (planned for ten sessions), and he received the first dose of pulse steroid therapy and the first dose of Cyclophosphamide. On day +6 of ICU admission, a bronchoscopy was performed, during which bloody secretions were noticed in the trachea, carina, and bronchial trees. Left and right lower lobes, LUL, and RML Bronchoalveolar lavage were done.

The cytological analysis from Bronchoalveolar lavage (BAL) showed abundant septated Hyphae with negative malignant cells (**Figure 2**, black arrow).

Later on, the microbiology analysis for the fungal culture reported unidentified rapidly growing fungi (unlikely to be aspergillus, and it looked like trichosporon in direct wet mount).

The fungus-infected sample was cultured for 48 hours producing creamy-colored, moist colonies that rapidly grew at 25˚C (**Figure 3(a)**).

Direct microscopic examination showed hyaline hyphae segmentation into arthroconidia of varying lengths (**Figure 3(b)**, black arrow).

The patient was switched on empirical Liposomal Amphotericin (5 mg/kg IV daily). After he received 7 days of Amphotericin, his respiratory condition started to improve with low setting ventilator support.

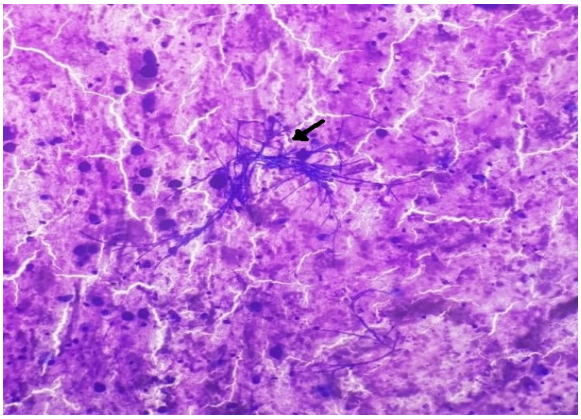
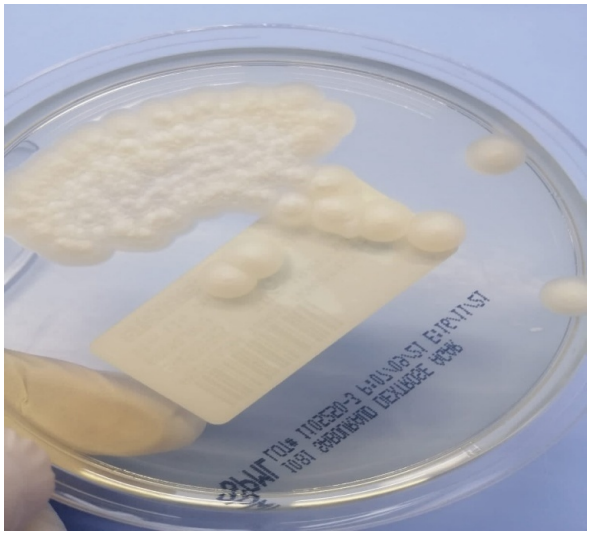
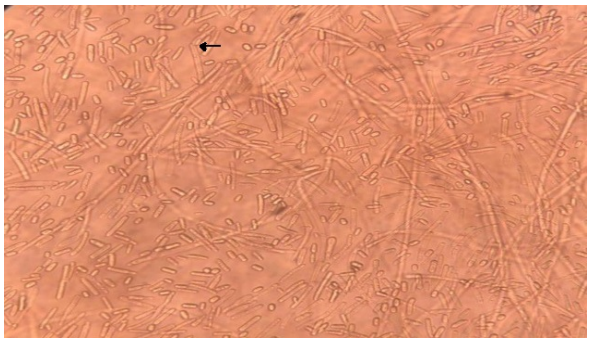


Figure 2. Abundant septated Hyphae, black arrow.



(a)



(b)

Figure 3. (a) *Magnusiomyces capitatus*, BAL, 48 hours culture on Sabouraud Dextrose Agar: Creamy-colored and moist colony; (b) direct wet mount, 40 X magnifications, hyaline hyphae segmentation into arthroconidia of varying lengths, black arrow.

Gene sequencing (PCR) from the BAL fungal culture sample was sent and reported as *Magnusiomyces capitatus*, and the infectious disease team decided to

continue Amphotericin for 14 days. Few days later, the patient was started on a weaning trial from the ventilator and finally disconnected successfully from the ventilator, and his CXR was improving in congestion and consolidation.

After a few days, the patient was transferred to a general ward where he received ongoing general support alongside his prescribed treatment from the infectious diseases, nephrology, and rheumatology teams. He made significant progress and was ultimately released in favorable overall health, with arrangements for further monitoring and care at the outpatient clinics.

3. Discussion

Magnusiomyces capitatus (formerly known as *Geotrichum capitatum*) is an emerging opportunistic fungal pathogen that has gained attention due to its ability to cause invasive infections, especially in immunocompromised individuals. However, there have been limited studies focusing on the impact of *Magnusiomyces capitatus* on immunocompetent individuals.

One study conducted by Cohen-Naftaly *et al.* [4] reported a series of cases in which *Magnusiomyces capitatus* caused invasive infections in immunocompetent patients. The study described four cases of disseminated infections, including fungemia and endocarditis, in patients without apparent immunodeficiency. These findings suggest that *Magnusiomyces capitatus* has the potential to cause invasive disease even in individuals with intact immune systems, challenging the assumption that it primarily affects immunocompromised patients.

Another study by Ortoneda *et al.* [5] provided further evidence of the pathogenicity of *Magnusiomyces capitatus* in immunocompetent individuals. The researchers investigated a cluster of cutaneous infections caused by this fungus among healthy newborns in a maternity ward. The study highlighted the ability of *Magnusiomyces capitatus* to cause localized infections in immunocompetent hosts, indicating that the fungus may be more prevalent and clinically significant than previously anticipated.

In this case report, our patient presented without any apparent immunodeficiency or underlying diseases that could weaken his immune system and make him more susceptible to opportunistic fungal infections like *Magnusiomyces capitatus*. However, a diagnosis of Systemic Lupus Erythematosus (SLE), a disease characterized by chronic inflammation and immune system dysregulation, was made. This condition renders the patient more vulnerable to fungal infections compared to individuals without the disease [6] [7] [8].

SLE is primarily characterized by the production of autoantibodies and dysregulation of the immune system. Activation of immune cells triggers an inflammatory response. However, in the absence of immunosuppressive medications, the immune system may remain hyperactive, leading to chronic inflammation. This persistent immune activation weakens the immune response against fungal pathogens and enhances the likelihood of acquiring opportunistic fungal infections.

A study by Li *et al.* (2018) investigated the immunological dysfunction in SLE patients without immunosuppressive medications. They observed impaired immune responses against *Candida albicans*, a common fungal pathogen, indicating a compromised antifungal defense mechanism in these patients.

SLE patients often exhibit imbalances in T cell subsets, with reduced regulatory T cells (Tregs) and increased effector T cells. Tregs are crucial for maintaining immune self-tolerance and homeostasis, whereas effector T cells contribute to inflammation. The disturbed T cell balance in SLE patients without immunosuppressive drugs further weakens the defense against fungal infections.

A study conducted by Cheng *et al.* (2020) investigated Treg cell populations in SLE patients and immunosuppressive drug-free SLE patients. They found that SLE patients without immunosuppressive medications had significantly lower Treg cell levels, implying an impaired ability to suppress inappropriate immune responses and control fungal infections.

Phagocytic cells such as neutrophils and macrophages play a crucial role in eliminating fungal pathogens. In SLE, these cells may exhibit functional abnormalities, impacting their ability to efficiently clear fungi. The deficiency in phagocytosis increases the susceptibility to fungal infections.

An experimental study by Denton *et al.* (2019) explored the phagocytic function of neutrophils in SLE patients lacking immunosuppressive medications. Results indicated impaired phagocytic activity against *Candida albicans*, suggesting decreased clearance capacity and increased susceptibility to fungal infections.

Although the exact mechanisms of pathogenesis of *Magnusiomyces capitatus* in immunocompetent individuals remain uncertain, some factors could contribute to the development of invasive infections. *Magnusiomyces capitatus* possesses a variety of virulence factors, including adhesins, protease enzymes, and biofilm formation ability (Castro *et al.*, 2016) [9]. These factors may facilitate tissue invasion, colonization, and evasion of the immune response, thereby leading to infection.

The diagnosis of *Magnusiomyces capitatus* infections in immunocompetent individuals can be challenging since the fungus is often misidentified or disregarded as a contaminant due to its resemblance to other yeasts [10]. The use of molecular identification techniques, such as DNA sequencing, can improve accuracy in identifying this pathogen. Additionally, susceptibility testing is crucial to guide appropriate antifungal therapy, considering the emerging resistance to commonly used antifungal agents [10].

The definitive diagnosis of *Magnusiomyces capitatus* in our case report was determined through the use of gene sequencing and polymerase chain reaction (PCR) on a bronchoalveolar lavage fungal culture sample.

Magnusiomyces capitatus demonstrates intrinsic resistance to many antifungal agents, making treatment challenging. Amphotericin B, a widely used antifungal medication, has shown promising efficacy against *M. capitatus*.

Several studies have elucidated the efficacy of amphotericin B in treating *M. capitatus* infections [11] [12]. In a study by Antachopoulos *et al.* (2012), amphotericin B was found to have a favorable response rate of approximately 75% in patients with *M. capitatus* bloodstream infections. These findings were further supported by a study conducted by Girmenia *et al.* (2014), which demonstrated successful outcomes in approximately 85% of patients treated with amphotericin B for *M. capitatus* infections.

The patient described in our case report underwent treatment using amphotericin B and exhibited a highly favorable response, without any negative side effects.

The primary difficulty encountered in the management of this patient was distinguishing whether his pulmonary symptoms were attributable to the fungal infection or a complication of systemic lupus erythematosus (SLE) manifested as pulmonary renal syndrome with pulmonary hemorrhage. Nevertheless, the patient's remarkable response to fungal treatment suggests that his pulmonary manifestations were primarily linked to the fungal infection caused by *Magnusiomyces capitatus*.

4. Conclusions

Most fungal infections are caused by immune system malfunctions. Environmental and genetic variables contribute to disease pathogenesis. *M. capitatus* was identified as a significant opportunist, causing pulmonary and disseminated infections in patients with hematological malignancies, and other immune disorder.

Opportunistic fungal infections often arise in patients with Systemic Lupus Erythematosus (SLE) as a complication of prolonged immunosuppression treatment. However, we present here a rare association between SLE and *Magnusiomyces capitatus* in a patient who was newly diagnosed with SLE.

Healthcare providers should maintain vigilance regarding the potential occurrence of these potentially lethal infections in patients with SLE, considering their compromised immune system.

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 understands that his name and initials will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

Research Quality and Ethics Statement

The authors followed applicable EQUATOR Network http://www.equator-network.org/ guidelines, notably the CARE guideline, during the conduct of this report.

Declaration for All Articles

We also certify that none of the authors is a member of the Editorial board of the JGID.

Key Message

• This was the first case reported, which displays a rare association between *Magnusiomyces capitatus* with Systemic lupus erythematosus (SLE).

Conflicts of Interest

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

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