

# A Case of Pulmonary Infection Due to *Magnusiomyces capitatus* in a Non-Immunocompromised Patient with Cerebral Palsy

Yanyan Jiang<sup>1</sup>, Zhengzheng Chen<sup>1</sup>, Huoyang Lv<sup>2</sup>, Lihua Jiang<sup>1</sup>, Zhiyuan Fan<sup>3</sup>

<sup>1</sup>Medical Laboratory Center, Tongxiang First People's Hospital, Jiaxing, Zhejiang, People's Republic of China; <sup>2</sup>Medical Laboratory Center, Zhejiang Provincial People's Hospital, Hangzhou, Zhejiang, People's Republic of China; <sup>3</sup>Department of Emergency Medicine, Tongxiang First People's Hospital, Jiaxing, Zhejiang, People's Republic of China

Correspondence: Zhiyuan Fan, Department of Emergency Medicine, Tongxiang First People's Hospital, Jiaxing, Zhejiang, People's Republic of China, Email fanzhiyuan19880916@126.com

**Background:** *Magnusiomyces capitatus* (*M. capitatus*) is a dimorphic opportunistic fungus that is a rare yeast and rarely reported in Asia. Owing to the absence of established clinical breakpoints, the treatment of this fungus poses challenges.

**Case Presentation:** We report a rare case of a young, non-immunocompromised man with cerebral palsy, spinal deformity, and pulmonary *M. capitatus* infection. The patient's condition improved after treatment with voriconazole and became stable.

**Conclusion:** *M. capitatus* infection is commonly associated with hematologic tumors and compromised immunity. Reports of *M. capitatus* infection in patients with non-immunocompromised host are uncommon. Insufficient understanding of these fungi may lead to underdiagnosis of fungal infection and clinical misdiagnosis, potentially resulting in delayed treatment and increased mortality.

**Keywords:** invasive fungal infection, *Magnusiomyces capitatus*, MALDI-TOF MS, ITS, cerebral palsy, spinal deformity

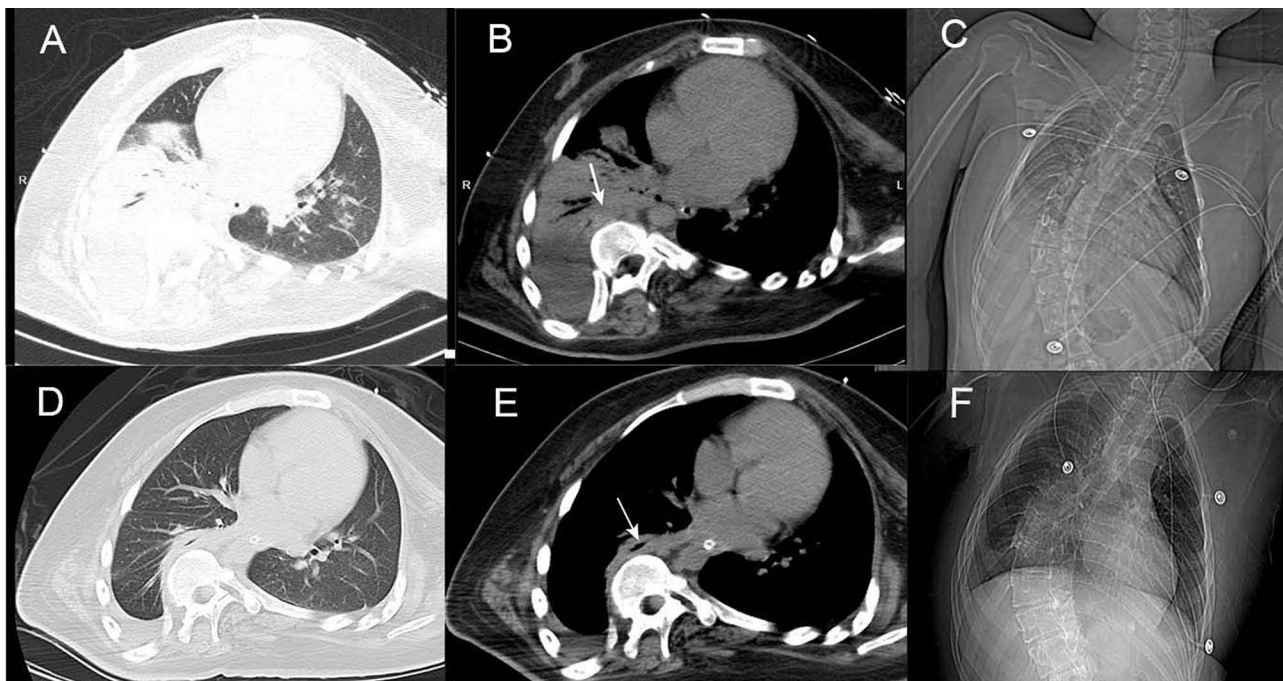
## Background

*Magnusiomyces capitatus* is a rare yeast, which has undergone several taxonomic revisions in recent decades and is classified as an Ascomycete, belonging to the Dipodidae family. *M. capitatus* is known by several names, including *Saprochaete capitata*, *Geotrichum capitatum*, *Blastoschizomyces capitatus*, *Trichosporon capitatum*, and *Dipodascus capitatus*.<sup>1</sup> *M. capitatus* may colonize the skin, digestive tract, and respiratory tract of healthy individuals; however, it remains an underestimated opportunistic pathogen.<sup>2</sup> Patients with pulmonary infection due to *M. capitatus* often present with symptoms, such as shortness of breath and cough. Common imaging findings include diffuse bilateral lung infiltration, ground-glass opacity, pleural effusion, and parenchymal nodules. When severe respiratory failure caused by *M. capitatus* infection occurs, it is common to provide intubation and mechanical ventilation. Despite timely antifungal therapy, patients with disseminated infections still have high mortality.<sup>3</sup> Therefore, bronchoalveolar lavage or thoracentesis is imperative for the etiological diagnosis and targeted treatment. Although *M. capitatus* is rarely implicated in fungemia and invasive fungal infection (IFI), it primarily affects immunocompromised patients with hematological malignancies and mortality is over 50%.<sup>4</sup> Reports of *M. capitatus* infection are exceedingly rare in non-immunocompromised patients, as in our case, the patient lacked neutropenia or an underlying malignancy. Due to its rarity and slow growth, diagnosis is challenging. Improved morphological identification, accurate culture and identification methods, and appropriate therapeutic regimens are crucial for effective treatment and ultimately reducing mortality. We report a case of pulmonary infection due to *Magnusiomyces capitatus* with improvement after effective treatment. It is approved by the Ethics Review Committee of Tongxiang First People's Hospital to publish the case details.

## Case Presentation

A 23-year-old male patient was presented to our hospital with a 7-day history of cough and 3 hours of unconsciousness. He has cerebral palsy, communication difficulties, scoliosis for 5 years, and a 2-year history of epilepsy treated with levetiracetam. No other medical condition was present. Seven days prior, he developed a cough with viscous sputum and pyrexia, reaching a maximum temperature of 38.4°C. Three days prior, his symptoms had worsened with fatigue and poor appetite, and he was admitted to a local health institution. Three hours before admission, the patient experienced sudden chest tightness, dyspnea, and a decrease in oxygenation saturation to 70%, leading to confusion and cough with copious mucus sputum, necessitating immediate endotracheal intubation. On admission, his vital signs were as follows: temperature 36.7°C, heart rate 112 beats/minute, blood pressure 139/91 mmHg, respiratory rate 20 breaths/minute, and oxygenation saturation 99%, while mechanically ventilated. The patient was sedated with sluggish reactive pupils (diameter, 2.5 mm). Auscultation revealed the presence of bilateral lung rales. Chest computed tomography (CT) on admission revealed multiple lesions in both lungs, a small left-sided pleural effusion with partial atelectasis of the left lung, and scoliosis (Figure 1). Laboratory test results were shown as follows: The white-cell count  $13.1 \times 10^9/L$  (normal range,  $3.5\text{--}9.5 \times 10^9/L$ ), neutrophil ratio 91.2%, lymphocyte count  $0.8 \times 10^9/L$ , platelet count  $343 \times 10^9/L$  (normal range,  $100\text{--}300 \times 10^9/L$ ), prothrombin time 14.8s (normal range, 9.4–12.5s), D-dimer 858ug/L (reference value, <550 ug/L), arterial blood gas analysis: PH 7.39, partial oxygen pressure 77mmHg, partial carbon dioxide pressure 52mmHg, lactic acid 1.0mmol/L, Covid-19 RNA negative, C-reactive protein (CRP) 152mg/L (reference value, <10 mg/L), procalcitonin (PCT) 0.15ng/mL (reference value, <0.05ng/mL). The serum levels of creatinine, brain natriuretic peptide (BNP), urea nitrogen, electrolytes, lipase, liver enzymes and myocardial enzyme were normal. Throughout his course of hospitalization, the lymphocyte count was mostly above  $1.0 \times 10^9/L$ , consistently with the lymphocyte count tested several months ago, indicating his non-immunocompromised state.

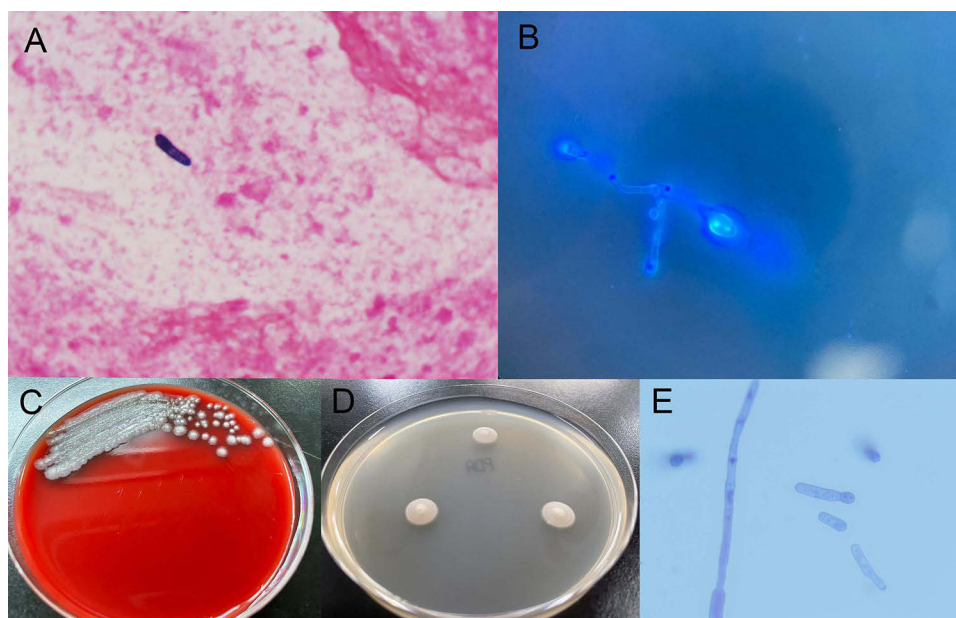
On admission, the score of APACHE II and SOFA were 18 and 10, respectively, and the patient was diagnosed with severe community-acquired pneumonia and acute respiratory failure. Bronchoscopy and alveolar lavage were performed



**Figure 1** Chest imaging before and after treatment. (A) Lung window: Pre-treatment computed tomography (CT) scan showing right lower lobe consolidation with air bronchogram; (B) Mediastinal window: white arrow indicating right inferior lobar bronchus compressed by curved spine in pre-treatment CT. (C) X-ray positioning film showing right lower lobe high density shadow with right costophrenic angle disappeared. (D) Lung window: Follow-up CT scan after antifungal treatment for 14 days showing right lower lobe consolidation absorbed and a small amount exudates in the right thoracic cavity. (E) Mediastinal window: white arrow indicating right inferior lobar bronchus still compressed by curved spine in follow-up CT. (F) Follow-up X-ray positioning film showing increased opacity of right lower lobe with right costophrenic angle appeared.

promptly to ameliorate oxygenation and to identify the etiological agent. According to the local guidelines of CAP, piperacillin and sulbactam were administered intravenously covering gram-negative bacteria and anaerobe.

Broncho alveolar lavage fluid (BALF) centrifuge gram staining observed that squamous epithelial cells accounted for less than 1% of all cells. No other bacterial morphology except fungal spore was seen under microscope, indicating that the specimen was qualified and was not contaminated by upper respiratory tract secretion.<sup>5</sup> BALF 10 $\mu$ L is inoculated onto a Blood Agar plate, Potato Dextrose Agar Plate (PDA), and direct smear Gram staining of the sample (Figure 2A). Fungal fluorescent-stained smears showed enlarged segmented spores at both ends, or a single large spore (Figure 2B). After 48 hours of BALF culture, multiple white villous colonies grew on the Blood Agar plate (Figure 2C), whereas after 72 hours of cultivation on PDA, a white, dry, button-like colony with a raised center grew (Figure 2D). Fungal culture count  $>10^4$  CFU/mL indicates clinical significance.<sup>5</sup> Microscopically, the culture displayed fragmented mycelia, pseudomycelia, spores, and linked conidia following methylene blue staining (Figure 2E). Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS, Bruker BioTyper3.1) was used to identify *M. capitatus* with a score of 2.3. The sequencing results were compared with those from the NCBI database with 100% similarity to *M. capitatus* (Sequence ID: KX376252.1). In vitro antifungal tests using ATB FUNGUS 3 (Meriette, France) showed minimum inhibitory concentration (MIC) values (mg/L) for amphotericin B  $<0.5$  mg/L, fluconazole 4 mg/L, itraconazole 0.125 mg/L, 5-fluorocytosine  $<4$  mg/L, and voriconazole 0.25 mg/L. However, owing to the lack of established breakpoints for antifungal agents against *M. capitatus*, susceptibility cannot be determined. Amphotericin B liposomes are preferred as the first-line treatment according to global Guidelines for the Diagnosis and Management of rare yeast infections. During the 20-day hospitalization period, alveolar lavage was performed six times, and every time *M. capitatus* was detected by culture, together with fungal spores. The concurrent serological G ((1 $\rightarrow$ 3)- $\beta$ -D-glucan, BDG) tests were negative twice, as were bilateral blood culture. After antibiotic treatment, the patient's condition, including the inflammatory marker levels, pulmonary function, and imaging findings, did not improve. Therefore, lung infection with *M. capitatus* was confirmed. Owing to the lack of amphotericin B liposomes, intravenous voriconazole 0.25 g bid was administered as a first-line treatment alternative for the patient. After initiation of antifungal treatment, the patient's inflammatory marker decreased. A follow-up CT scan after antifungal treatment for 14 days was performed and compared with the pre-treatment CT scan (Figure 1). Owing to the patient's weak ability to expectorate, tracheotomy was



**Figure 2** (A) BALF direct gram staining shows fungal spores  $\times 1000$ ; (B) BALF direct fungi fluorescent dye shows fungal hyphae  $\times 1000$ ; (C) Colony morphology observed on blood agar plate after 48 hours culture; (D) Colony morphology of PDA cultured for 72 hours; (E) Detection of fungal structure by methylene blue staining on colony smear (fungal mycelium and fungal spore)  $\times 1000$ .

performed on day 23, followed by high-flow oxygen (FiO<sub>2</sub> 40%) on day 25, and the patient was transferred to the general ward for treatment on day 31.

## Discussion and Conclusion

Our case report focuses on the omission of diagnosis, misdiagnosis of *M. capitatus*, and the outcome of clinical treatment. This report describes a young male patient with cerebral palsy and spinal deformity presented to our hospital due to a pulmonary infection and acute respiratory failure. During hospitalization, bronchoscopy and alveolar lavage were performed and *M. capitatus* was cultured in BALF several times. Ultimately, his condition improved after antifungal treatment. Most reported Magnusiomyces infections originated in Mediterranean Europe, with increasing cases noted in Central Europe, possibly linked to global warming.<sup>6</sup> However, relatively few such cases have been reported in Asian countries.<sup>7,8</sup> However, there is insufficient evidence to confirm this relationship definitively. Forster et al found that the prevalence of invasive *M. capitatus* infection may be underestimated in presumed non- and low-risk areas.<sup>9</sup> The slow growth of this organism at the initial stage of culture, coupled with the potential for error and missed detection when mixed with other bacteria, emphasizes the importance of accurate morphological recognition for early diagnosis through direct microscopic examination.<sup>10</sup> MALDI-TOF MS Bruker BioType r3.1 mass spectrometers and ITS sequencing are excellent and reliable tools for identifying *M. capitatus*.<sup>3</sup>

To date, there is no high-quality evidence pertaining to the effectiveness of antifungal treatment for invasive Magnusiomyces spp as per guidelines,<sup>11</sup> mainly because of the rarity of the strain, diagnostic challenges of conventional methods, and lack of antifungal breakpoints.<sup>6</sup> The antifungal regimen and duration of administration reported in the literature for the treatment of *M. capitatus* infections are generally sparse. Global guidelines for the diagnosis and management of rare yeast infections: an initiative of the ECMM in cooperation with ISHAM and ASM released in 2021,<sup>11</sup> and summarizes consensus recommendations regarding diagnosis and treatment options for patients with rare yeast infections, including *M. capitatus*. The guidelines recommend the use of amphotericin B, either alone or in combination with fluorocytosine, as a first-line treatment based on clinical evidence.<sup>11</sup> Voriconazole is recommended as the first-line alternative, consistently with the susceptibility to 5-fluorocytosine and amphotericin B observed in this case, whereas fluconazole and itraconazole exhibit some degree of resistance; hence, they are not recommended. Biofilm formation may also contribute to the development of systemic infections. In vitro biofilm experiments by Mei ElGindi et al on catheter materials showed that *M. capitatus* and *C. albicans* could produce biofilms; however, there were some obvious differences. The *M. capitatus* biofilm had visible extensions protruding from the silicone square covered by the biofilm, similar to mycelium extension.<sup>12</sup> Guidelines also strongly recommend CVC catheter removal in such cases.

It is uncommon to find *M. capitatus* infection in a non-immunocompromised patient. To date, there are only 15 documented cases of *M. capitatus* lung infection in immunocompetent patients, according to literature review.<sup>13</sup> Most reported cases have pre-existing lung pathology, but the exact physiopathologic mechanism has not been understood yet.<sup>13</sup> Wu et al<sup>14</sup> reported a young patient with cerebral palsy developed severe pyopneumothorax, then coinfection by *M. capitatus* and *Trichomonas tenax* were identified. Similarly, the patient mentioned above is also a non-immunocompromised patient with no medical history except for cerebral palsy. However, no discussion regarding the relationship between cerebral palsy and *M. capitatus* infection was mentioned in the literature. The following reasons could be interpreted. Firstly, cerebral palsy is a group of conditions affecting whole body muscles and movement. Therefore, weakness of breath muscles could lead to difficulty in sputum excretion, which could contribute to pneumonia. Secondly, Scoliosis, which is a common complication of cerebral palsy, could lead to breathing difficulty. As the CT scan shows (Figure 1), the bronchus of inferior lobe of right lung is compressed by curved spine, leading to difficulty in draining the secretions. Taken together, weakness to expectorate the secretions and difficulty in draining lead to accumulation of secretions, providing the conditions for *M. capitatus* to grow and invade the host.

In conclusion, the incidence of *M. capitatus* infection may be underestimated, particularly in non-immunocompromised individuals. Timely microscopic smear staining is vital for prompt detection of rare fungi. The accuracy of MALDI-TOF is consistent with ITS sequencing. Combining in vitro antimicrobial susceptibility testing with the recommendations of the guidelines enables a timely, individualized anti-infection treatment, which is crucial for the

precise management of *M. capitatus* infections. It is also essential for increasing awareness among health professionals about *M. capitatus* infections in non-immunocompromised patients, especially with cerebral palsy.

## Ethics Approval and Informed Consent

The study was approved by the ethics committee of Tongxiang First People's Hospital (2024-187-01). The consent for publication has been obtained from the patient's parent since the patient has cerebral palsy and cannot sign his own name.

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## Disclosure

The authors report no conflicts of interest in this work.

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