PULMONARY GEOTRICHOSIS IN CHRONIC GRANULOMATOUS DISEASE

Deborah Palacios-Reyes, Marco Antonio Yamazaki-Nakashimada, Lina Castaño-Jaramillo, Carla M Roman-Montes, María F González-Lara, Selma Scheffler-Mendoza, Ángeles Costta-Michuy, Jacinta Bustamante, Lizbeth Blancas-Galicia.

[1]Institut National de la Santé et Mycology Department, National Institute of Pediatrics, Mexico City, Mexico.
Immunology Department, National Institute of Pediatrics, Mexico City, Mexico.
Clinical Microbiology Laboratory, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico.
Infectious Diseases Department, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico.
Infectious Diseases Department, National Institute of Pediatrics, Mexico City, Mexico
St. Giles Laboratory of Human Genetics of Infectious Disease, Rockefeller Branch, Rockefeller University, New York, NK, United States.
Laboratory of Human Genetics of Infectious Diseases, Necker Branch, INSERM UMR 1163, Paris, France
Imagine Institute, University of Paris, Paris, France.
Study Center for Immunodeficiencies, Necker Hospital for Sick Children, AP-HP, Paris, France.
Immunodeficiencies Research Unit, National Institute of Pediatrics, Mexico City, Mexico.

Introduction: Chronic granulomatous disease (CGD) is an inborn error of immunity (IEI). The *CYBB* gene is responsible for the most frequent genetic forms of the CGD. The affected cells have an impaired ability to generate reactive oxygen species (ROS), thus failing to kill intracellular bacteria and fungi, and excessive granulomatous inflammation. Fungal pathogens include, notably, the *Aspergillus fumigatus* complex, *Aspergillus nidulans* and *Candida* spp.; however, other genders have also been described. We describe two unrelated CGD patients with pulmonary infections due to *Geotrichum* spp., an emerging and opportunistic pathogen.

CASE 1. A 9-year-old male at 5-years-of age, he suffered a cervical abscess and received intravenous antibiotics. His admission to the hospital was necessary due to a history of cough, fever, and dyspnea with progressive respiratory failure, which required mechanical ventilation and admission to the ICU.

Chest X-ray and CT scan images showed diffuse interstitial thickening in the lung parenchyma, multiple intrathoracic lymph node enlargements, pneumomediastinum, and subcutaneous emphysema, which suggested a fungal etiology; therefore, liposomal amphotericin B (L-AmB) was added empirically

(Figure). Pseudohyphae and arthroconidia were detected in cultures of bronchoalveolar lavage (BAL) samples (Figure), and *Geotrichum capitatum* was identified with MALDI-TOF Mass Spectrometry. A mutation was found in the *CYBB* through next-generation sequencing (p.P383L/y), confirming CGD diagnosis. L-AmB was suspended after six weeks due to a good clinical response, and itraconazole was changed to a prophylactic dose.

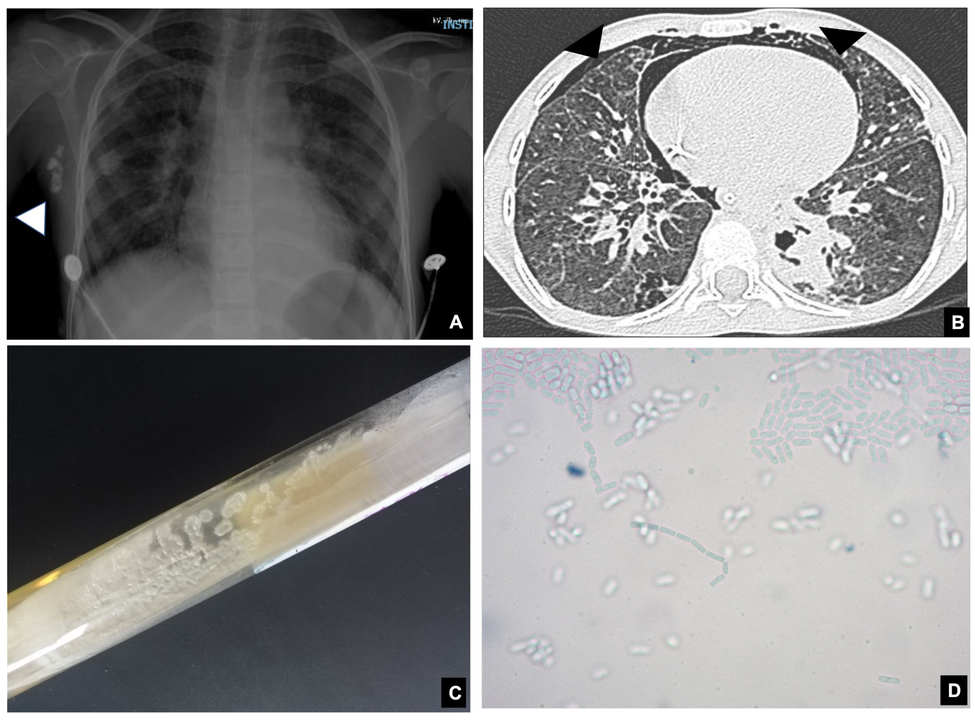

Figure . A. Chest X-ray (case-1) with hiliar and parenchyma interstitial infiltrates, multiple calcifications in axillar right region (arrowhead). **B.** Thorax CT scan (case-1) with bronchiectasis, parenchyma infiltrates, pneumomediastinum (arrowhead), and subcutaneous emphysema (arrowhead). **C.** Cream-colored, dry, and wrinkled yeast colonies of *Geotrichum capitatum* on Sabouraud agar **D.** Microscopic examination of bronchoalveolar lavage culture showing the presence of arthroconidia, lactophenol cotton blue stain, 40 X magnification

CASE 2. The second case is a 19-year-old male urban resident who was previously diagnosed with CGD secondary to a pathogenic variant in the *CYBB* gene (p.H115Q/y) at 14 years old .

He had a history of inflammatory bowel disease and multiple pneumonia, one of which was diagnosed as tuberculosis. The young patient had poor adherence to prophylactic antimicrobial treatment.

He arrived at the emergency room with myalgia, malaise, and dyspnoea. The physical examination revealed fever, tachycardia, and tachypnoea, and the oxygen saturation was low (SpO2 70%).

Parenchymal nodules suggestive of pneumonia were visualized through thorax CT scan, and the administration of meropenem and vancomycin was initiated. In the first 24 hours, the patient required mechanical ventilation due to refractory hypoxemia; during the bronchoscopy sample-BAL culture was collected.

On the 6th day, in the absence of pneumonia improvement (Figure 2), empirical amphotericin B (AmB) was initiated On the 28th day, *Geotrichum* spp. grew from the admission BAL culture; AmB was replaced with voriconazole and administered for 12 weeks with a favourable response (Figure 2). Two years later, he continued to be monitored at the hospital as an outpatient with prophylactic treatment.

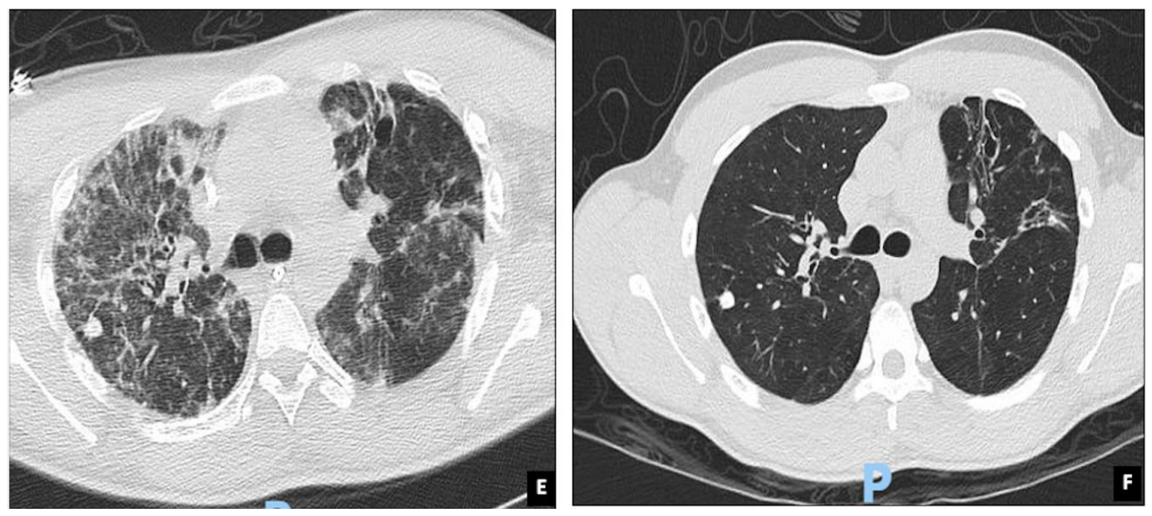

Figure 2: **E.** Thorax CT scan (case-2) showing bronchiectasis and parenchyma interstitial infiltrates. **F.** Thorax CT scan (case-2). Evident changes images accord to clinical improvement pneumonia.

Conclusion: *Geotrichum capitatum,* (also known as *Magnusiomyces capitatus*) is known to cause disseminated opportunistic infections, especially in neutropenic patients with haematologic malignancies. *G. capitatum*, however, is rarely reported as a pathogen in the literature. Erman *et al.* reported an adolescent with CARD 9 deficiency (an IEI) who presented with *G. capitatum* cholangitis. *Geotrichum* spp. have not been previously reported in CGD patients. The occurrence of geotrichosis should raise the suspicion of an underlying IEI; We described two patients with CGD presenting with geotrichosis, an emerging and opportunistic pathogen associated in this disease.