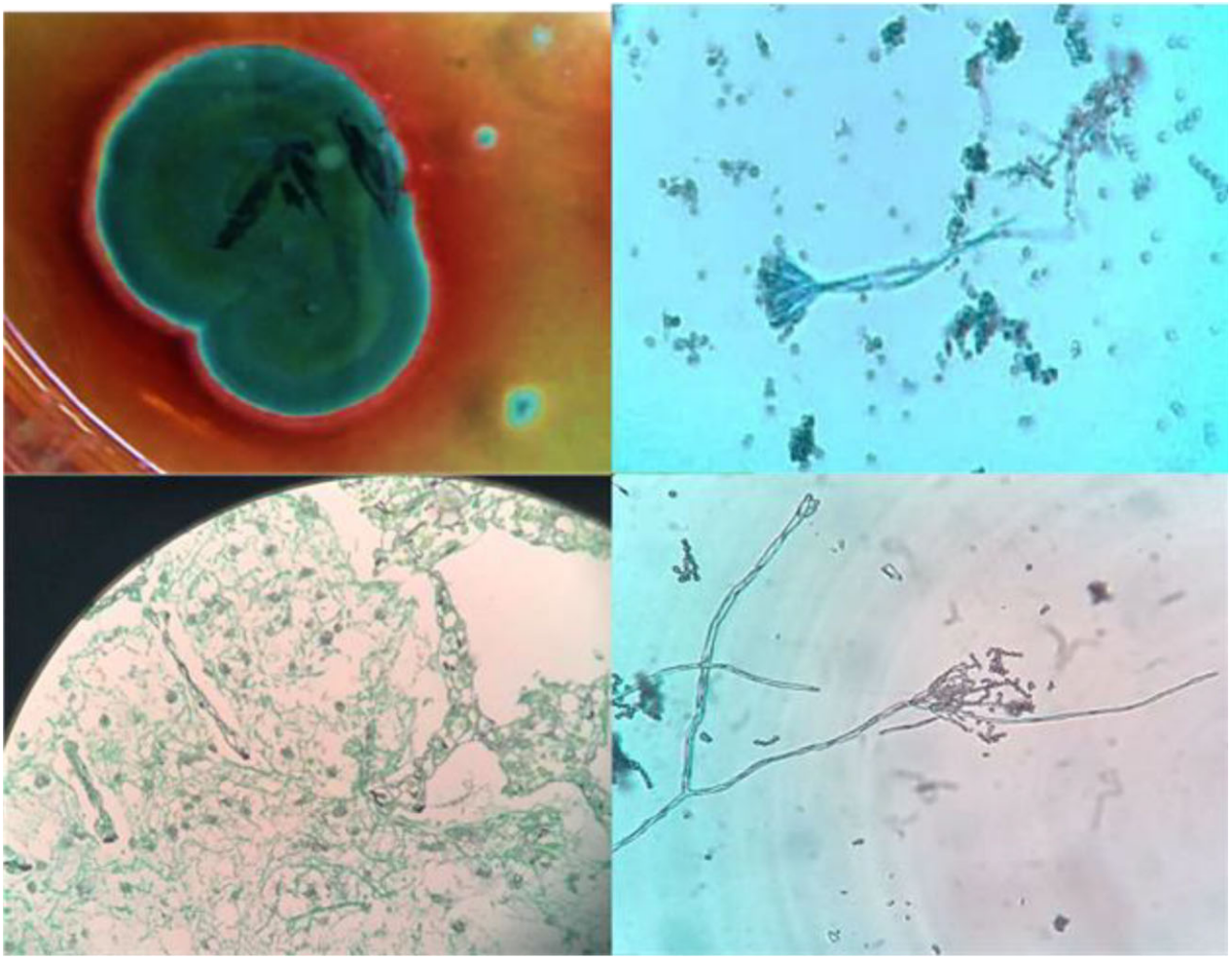

Figure 2.

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Fungal osteomyelitis in patients with chronic granulomatous disease: a case series from a tertiary care medical centre.

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Poster session 2, September 22, 2022, 12:30 PM - 1:30 PM

Objectives: To present details of a case series of fungal osteomyelitis initially misdiagnosed as disseminated tuberculosis, in pediatric patients with chronic granulomatous disease.

Method: Informed consent was obtained from the parents of three children (known cases of chronic granulomatous disease) with clinical features suggestive of chronic osteomyelitis. Clinical history was collected by interview and chart review. Samples were sent to the mycology laboratory for direct microscopy and fungal culture. Following a diagnosis of fungal osteomyelitis, antifungal therapy was administered and patients were monitored till discharge.

Results:

First case:

The first patient presented with fever, cough and progressive painful swelling over the left lower chest, and a past history of recurrent pneumonia and cervical lymphadenopathy, which were previously empirically treated with anti-tubercular therapy (ATT) and broad-spectrum antibiotics. Imaging revealed a soft tissue abscess with underlying rib osteomyelitis and pulmonary consolidation. Pus samples showed hyaline septate hyphae in direct microscopy and growth of *Aspergillus nidulans* in culture. The patient was successfully treated with intravenous voriconazole, which was switched to oral formulation on discharge.

Second case:

The second patient presented with fever and post-auricular swelling with multiple discharging sinuses, and a past history of fever and hilar lymphadenopathy, which were previously empirically treated with ATT and broad-spectrum antibiotics. Imaging revealed osteomyelitis involving mandible, temporal bone and skull base, with underlying sigmoid sinus thrombosis. Pus and tissue samples showed hyaline septate hyphae in direct microscopy and growth of *Aspergillus fumigatus* in culture. The patient was successfully treated with a combination of intravenous voriconazole and liposomal amphotericin B, and discharged on oral posaconazole.

Third case:

The third patient presented with progressive painful swelling over the right upper chest, and a past history of pneumonia, hemoptysis, and mediastinal lymphadenopathy, which were previously empirically treated with ATT and broad-spectrum antibiotics. During a previous hospitalization, imaging showed features suggestive of fungal pneumonia; BAL showed hyaline septate hyphae in direct microscopy and growth of *Aspergillus fumigatus* and *Aspergillus flavus* in culture, providing a diagnosis of fungal pneumonia which was treated with voriconazole and liposomal amphotericin B. During the present admission, imaging of the chest lesion revealed pus collection with underlying rib osteomyelitis, communicating with a cavity in the middle lobe of the right lung. FNAC from the lesion showed hyaline septate hyphae in direct microscopy but no growth in culture (probably due to previous antifungal therapy). The patient was successfully treated with a combination of intravenous voriconazole and liposomal amphotericin B, and discharged on oral posaconazole.

Conclusions: Fungal pneumonia and fungal osteomyelitis are often misdiagnosed as tuberculosis or bacterial infections, leading to unnecessary and ineffective ATT or broad-spectrum antibiotics. A high index of suspicion for fungal osteomyelitis is required in pediatric patients with a history of recurrent/chronic soft tissue infections, preceded by febrile episodes and/or pneumonia, especially if a diagnosis of chronic granulomatous disease (CGD) has already been established; if not, this characteristic clinical picture should in fact warrant evaluation for CGD.

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Emerging and cryptic *Aspergillus* species isolated from hospitalized patients with underlying primary immunodeficiencies

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Objectives: Although *Aspergillus fumigatus* is the most common etiologic agent of invasive aspergillosis, multiple poorly recognized non-*fumigatus* species have been reported from patients with iatrogenic immunosuppression and individuals with underlying primary immunodeficiencies (PIDs). The species-level identification of causative agents and the determination of antifungal susceptibility patterns can play significant roles in the outcome of aspergillosis. In the current study, we aimed to investigate the frequency of non-*fumigatus Aspergillus* species isolated from hospitalized patients with PIDs at National Institutes of Health (NIH) Clinical Center, Bethesda, MD, USA.

Methods: In a prospective study between January 2019 and December 2021, a total of 279 *Aspergillus* species were isolated from NIH hospitalized patients with underlying PIDs. The species-level identification of each isolate was attempted by colony morphology, microscopic characteristics, matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF), and PCR-sequencing of the internal transcribed spacer (ITS) region of ribosomal DNA, the β-tubulin and Calmodulin (CaM) genes.

Results: Overall, members of *Aspergillus* section *Fumigati* were the most common group (71%), followed by section *Veriscolores* (7%), section *Usti* (4%), section *Tanneri* (4%), section *Terrei* (3%), section *Nigri* (3%) and section *Nidulantes* (3%). *Aspergillus* species belong to sections *Falvi, Clavati, Flavipedes*, and *Circumdati* were less frequent, and each counted for only 1% of the total isolates identified.

Notably, cryptic, and non-*fumigatus* members of section *Fumigati* comprised only 12% of the isolates, including *A. felis, A. udagawae, A. lentulus, A. thermomutatus, A. viridinutans,* and *A. pseudoviridinutans*, while *A. fumigatus* was the dominant species (88%).

MALDI-TOF assay was able to properly differentiate sections of *Aspergillus* from each other. However, PCR-sequencing of the β-tubulin gene was the most reliable target to separate the cryptic species of each section.

Conclusion: Our study shows that frequency of rare and cryptic *Aspergillus* species that primarily affect patients with PIDs may significantly differ from those with acquired immunodeficiencies.

Due to their lower susceptibility to available antifungal agents than *A. fumigatus*, correct and prompt identification at the species level is critical for appropriate therapy to improve patient outcomes.

In addition, DNA sequence-based species identification targeting β-tubulin gene is more accurate than ITS and CaM genes and using MALDI-TOF to differentiate the emerging and cryptic *Aspergillus* species.