

Adjunctive interferon- γ immunotherapy in a pediatric case of *Aspergillus terreus* infection.

Assendorp EL, Gresnigt MS, Sprengeler EGG, Meis JF, Dors N, van der Linden JWM, Henriët SSV (2018) Adjunctive interferon- γ immunotherapy in a pediatric case of *Aspergillus terreus* infection. *Eur J Clin Microbiol Infect Dis* 37(10), 1915-1922.

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Abstract

Aspergillus terreus causes invasive aspergillosis (IA) in immunocompromised patients. Treatment is complicated by intrinsic resistance to amphotericin B and thereby contributing to a high mortality. Therefore, we conducted in vitro studies to investigate the effectivity of adjunctive recombinant interferon- γ immunotherapy. We describe a pediatric patient with *A. terreus* IA who received adjunctive recombinant interferon- γ (rIFN γ) immunotherapy. In vitro studies were conducted to investigate the capacity of rIFN γ to improve antifungal host defense in terms of fungal killing ability and the release of pro-inflammatory cytokines in cells of the patient as well as healthy controls. An 8-year-old female pediatric patient with leukemia developed *A. terreus* IA. She clinically deteriorated and had high serum galactomannan levels despite broad antifungal therapy. Therefore, adjunctive immune stimulatory therapy with rIFN γ was initiated. After 3 weeks of treatment, galactomannan levels decreased and the patient clinically showed improvement. Addition of rIFN γ boosted the capacity of monocytes of healthy volunteers to mount TNF α and IL-1 β cytokine responses to *Escherichia coli* LPS, and increased TNF α response to both *A.*

terreus and *Aspergillus fumigatus*. Monocytes isolated from the patient's blood demonstrated a similar augmented cytokine induction in response to rIFN γ . In addition, rIFN γ increased the capacity of monocytes from healthy volunteers as well as monocytes from the patient to kill *A. terreus* spores. Adjuvant immunotherapy with rIFN γ might be a promising additional treatment strategy that could be used to improve outcome in patients with refractory invasive *A. terreus* infections or other resistant invasive *Aspergillus* infections.

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