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SCIENTIFIC LETTER

Role of MDA5 Deficiency in Pathogenesis of Fungal Infections

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To the Editor: Multiple molecules which sense viruses and trigger IFN1 secretion include toll-like receptors, Retinoic acid-inducible gene I (RIG-I) and Melanoma Differentiation-Associated protein 5 (MDA5), collectively known as the RIG-I-like receptors (RLRs). They sense viral double-stranded RNA motifs to induce expression of IFN1 and other pro-inflammatory cytokines during the early stage of viral infection [1]. MDA5 is encoded by interferon induced with helicase C domain - containing protein 1 (IFIH1) gene located on chromosome 2q24.2 of human gene. The loss of function mutations of IFIH1 gene lead to MDA5 deficiency leading to recurrent viral infections [2].

A 2 mo 20 d old boy presented with fever, cough and lethargy. He had recurrent pneumonia since 10th day of life for which he had two previous admissions. During hospitalization, he developed blackish discoloration over his nose, that extended into the hard palate with perforation. Contrast computed tomography of head, neck and orbit showed extensive rhino-cerebro-ocular mucormycosis. Immunodeficiency work-up revealed normal immunoglobulins. Dihydrorhodamine (DHR) test was normal. Whole genome sequencing showed an autosomal dominant mutation in IFIH1 gene on chr2:163124025 A>C. General condition of the patient worsened. He had septic shock and disseminated intravascular coagulation (DIC). He finally succumbed to death.

Jaeger et al. conducted a study in MDA5 knockout mice and humans to show that the cytosolic RIG-I-like receptor MDA5 has an important role in defence against *C. albicans*. IFIH1 expression in macrophages is specifically induced by invasive *C. albicans* and chronic mucocutaneous candidiasis (CMC) expresses lower levels of MDA5 than controls [3]. In an another study by Wang et al., it was demonstrated that MDA5 signalling is essential for host resistance against pulmonary *Aspergillus fumigatus* [4]. It was critical for antifungal neutrophil killing of *A. fumigatus* spores. This case report suggests the role of MDA5 against candida and aspergillus infection.

Declarations

Conflict of Interest None.

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