Pattern recognition receptor expression is not impaired in patients with chronic mucocutaneous candidiasis with or without autoimmune polyendocrinopathy candidiasis ectodermal dystrophy.


Source

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Abstract

Patients with chronic mucocutaneous candidiasis (CMC) have an unknown primary immune defect and are unable to clear infections with the yeast Candida. CMC includes patients with AIRE gene mutations who have autoimmune polyendocrinopathy candidiasis ectodermal dystrophy (APECED), and patients without known mutations. CMC patients have dysregulated cytokine production, suggesting that defective expression of pattern recognition receptors (PRRs) may underlie disease pathogenesis. In 29 patients with CMC (13 with APECED) and controls, we assessed dendritic cell (DC) subsets and monocyte Toll-like receptor (TLR) expression in blood. We generated and stimulated monocyte-derived (mo)DCs with Candida albicans, TLR-2/6 ligand and lipopolysaccharide and assessed PRR mRNA expression by polymerase chain reaction [TLR-1-10, Dectin-1 and -2, spleen tyrosine kinase (Syk) and caspase recruitment domain (CARD) 9] in immature and mature moDCs. We demonstrate for the first time that CMC patients, with or without APECED, have normal blood levels of plasmacytoid and myeloid DCs and monocyte TLR-2/TLR-6 expression. We showed that in immature moDCs, expression levels of all PRRs involved in anti-Candida responses (TLR-1, -2, -4, -6, Dectin-1, Syk, CARD9) were comparable to controls, implying that defects in PRR expression are not responsible for the increased susceptibility to Candida infections seen in CMC patients. However, as opposed to healthy controls, both groups of CMC patients failed to down-regulate PRR mRNA expression in response to Candida, consistent with defective DC maturation, as we reported recently. Thus, impaired DC maturation and consequent altered regulation of PRR signalling pathways rather than defects in PRR expression may be responsible for inadequate Candida handling in CMC patients.

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