AUTOIMMUNE CONNECTIVE TISSUE DISEASES

AZITHROMYCIN PROMOTES ALTERNATIVE ACTIVATION OF MACROPHAGES IN SYSTEMATIC LUPUS ERYTHEMATOSUS VIA PI3K/AKT SIGNALING PATHWAY

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Introduction: Alternatively activated macrophages have been reported to be helpful to alleviate systematic lupus erythematosus (SLE), and azithromycin could serve as an immunomodulator by promoting alternatively activated macrophage phenotype. However, the effect of azithromycin in SLE and the involved mechanism remain undetermined.

Objective: To characterize azithromycin and the underlying mechanism contributing to SLE therapy.

Materials and Methods: Monocytes from SLE patients and matched healthy donors were compared by phenotypes and functions, followed by differentiated into macrophages and azithromycin treatment. Activated lymphocyte derived-DNA was used to imitate SLE macrophages in vitro to investigate the possible mechanism involved.

Results: Monocytes from SLE patients exhibited more CD14+CD86+ cells, impaired phagocytic activity, elevated interleukin (IL)-1β, IL-6 and tumor necrosis factor (TNF)-α (the classical activated phenotype), which could be blocked by azithromycin. On the contrary, there were fewer CD14+CD163+ cells in SLE patients, accompanied by decreased arginase (Arg)-1 and found in inflammatory zone (Fizz)-1 (the alternatively activated phenotype). And IL-10, the crucial immune regulatory factor secreted by alternatively activated monocytes/macrophages, also showed a decreased trend in SLE patients. In addition, all these markers and the phagocytic activity were up-regulated after azithromycin treatment. Azithromycin showed the same effect in imitated SLE macrophages, with distinct Akt phosphorylation at 30 min and 12 h. After inhibiting Akt phosphorylation by LY294002, the down-regulation of CD80, IL-1β, IL-6 and TNF-α caused by azithromycin raised again, meanwhile, the up-regulation of CD206, Arg-1, Fizz-1 and IL-10 due to azithromycin was abolished. Additionally, insulin-like growth factor 1 (IGF-1), the specific agonist of Akt, played a similar role to azithromycin in imitated SLE macrophages.

Conclusions: Azithromycin might play a novel role in alleviating SLE by promoting alternatively activated macrophage phenotype via PI3K/Akt signaling pathway.