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Title: Altered imbalance between Th17 and regulatory T-cells and impaired Th1 response in the recovery of multidrug-resistant tuberculosis

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Body: OBJECTIVE:Multidrug-resistant tuberculousis(MDR-TB), a lethal global threat today, requires prolonged and expensive second-line drugs of heightened toxicity. A dysregulation of $CD4^+$ T cell subsets, found in the pathogenesis of TB, is a crucial question still unsolved in MDR-TB. Insights into MDR-TB immune responses are urgent for developing new solutions. METHODS:We phenotypically examined circulating T-helper(Th)17 cells, regulatory T cells(Tregs),Th1,Th2 cells by flow cytometric detection in 26 MDR-TB patients, 26 drug-sensitive TB patients(DS-TBs) and 26 healthy subjects(HCs). The levels of circulating T cell subsets were further analyzed during before/post-treatment phases in MDR-TB patients. RESULTS:We found upregulation of circulating Th17 expression(7.45±1.54)and decreased ratio of Treg/Th17(0.42±0.01) in MDR-TBs compared to HCs and DS-TBs. More remarkble suppression of Th1 cell activation was detected in MDR-TBs(11.99±0.87) than that in DS-TBs compared to HCs. Although clinical signs of MDR-TB patients did not show obvious recovery after 7 month-chemotherapy, the circulating ratio of Treg/Th17(0.88±0.13) and level of Th1(15.1±0.90) in MDR-TB patients tended to normal compared to their previous level before treatment($P<0.05$). CONCLUSIONS:These data provided evidence for an unbalanced immune status of Treg/Th17 and inhibition of Th1 type immunity in MDR-TB infection, and suggested a specific role of these T cell-induced immunities during the evolution of MDR-TB. Further study on the immune homeostasis restoration of MDR-TB patients may aid in improving adjuvant immunotherapies and developing potential therapeutic strategies.