Abstract

The Role Of IL-17, IFN-γ, TNF-α, LTF, IL-4, IL-35, and TGF-β

As Predictor On Spectrum Of Rheumatic Valvulitis

Achmad Lefi

Background: Pro- and anti-inflammatory cytokines are important secondary signals in rheumatic valvulitis and may related with extension of valvular damage (spectrum of rheumatic valvulitis). Hence, the study aimed to determine whether serum marker of pro-Interleukin-17 (IL-17), Tumor Necrosis Factor-α (TNF-α), Interferron-γ **(**INF-γ) and lactoferrin (LTF) and anti-inflammation cytokine Interleukin-4 (IL-4), Interleukin-35 **(**IL-35) and Transforming Growth Factor-β (TGF-β) impact on the spectra (extention) of rheumatic valvulitis.

Methods: Patients were subdivided according to the extent of left-sided valvular involvement. Based on echocardiographic examination, patient with only of mitral valve disease were enrolled as on the univalvular group, while those with involvement of both mitral and aortic valves were allocated to the multivalvular group. Serum level of IL-4, IL-17, IL-35, TNF-α, TGF-β, INF-γ and LTF were determined by flow cytometri.

Results: The study included seventy-two patients with RHD (mean age 37.22±9.84 yrs, male: female 28:44) and, 36 age and sex-matched unrelated healthy volunteers (normal control). Patients were classified according to univalvular rheumatic (n=36, mean age 37.61±10.98 yrs), multivalvular rheumatic (n=36, mean age 36.83±8.70 yrs) and normal control (n=36, mean age 33.08±8.48 yrs). Serum level of pro-inflammation cytokine (IL-17, TNF-α, INF-γ and LTF) and anti-inflammation cytokine (IL-4, IL-35 and TGF-β) was significantly elevated in RHD (both univalvular and multivalvular rheumatic groups) compared with control group. Both univalvular and multivalvular groups have statistically significant association with IL-4, IL-17 and INF-γ but no significant association with TNF-α, TGF-β and LTF. IL-35 significantly increased serum level of IL-17 and INF-γ, IL-17 (b=0.253, p=0.000), INF-γ (b=0.577, p=0.000). IL-17 have greater risk for multivalvular rheumatic (OR=1.065; [95% CI: 1.027 – 1.104]; p=0.001) and univalvular rheumatic (OR=1.055; [95% CI: 1.018 – 1.094] ; p=0.003) then their matched controls. IL-4 have greater protection for univalvular rheumatic (OR=0.964; [95% CI: 0.937 – 0.992] ; p=0.011) and multivalvular rheumatic (OR=0.961; [95% CI: 0.934 – 0.989] ; p=0.007) then their matched controls. INF-γ have greater risk for multivalvular rheumatic (OR=1.070; [95% CI: 1.024 – 1.118] ; p=0.002) and univalvular rheumatic (OR=1.065; [95% CI: 1.020 - 1.112] ; p=0.004).

Conclusions: IL-17 and INF-γ were possible risk factor and IL-4 was protective factor for extension or spectrum of valvulitis rheumatic. IL-35 was possible indirect risk factor, but TNF-α, TGF-β and LTF were not predictor for extension of valvulitis rheumatic.

Keyword : IL-17, INF-γ, TNF-α, LTF, IL-4, IL-35, TGF-β, Univalvular, Multivalvular