Hubungan Ekspresi mRNA Type 1 Interferon Stimulated Genes (Isgs) dan Protein C1q dengan Perbaikan Klinis Okular pada Pasien Uveitis Idiopatik IGRA Positif pada Awal Terapi Obat Anti Tuberkulosis = Correlation of type 1 stimulated interferon gene mRNA expression and C1q protein with ocular clinical improvement in idiopathic uveitis IGRA positive patients in the early phase of anti-tuberculosis treatment

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Abstrak

Pasien uveitis tanpa etiologi yang jelas (idiopatik) dengan kriteria klinis peradangan yang tidak spesifik namun memiliki status IGRA positif kerap menyebabkan dilema dalam pengobatan. Kelompok pasien tersebut diterapi sebagai kelompok suspek ekstrapulmonari TB dan mendapatkan pengobatan Obat Anti Tuberkulosis (OAT). Berbagai penelitian menunjukan bahwa profil ekspresi transkriptomik Interferon-stimulated Genes (ISG) tipe 1 ditemukan meningkat pada pasien aktif TB dan diketahui berpotensi sebagai biomarker diagnosa dan monitoring efikasi terapi. Selain itu level protein C1q ditemukan meningkat pada pasien TB aktif dibandingkan kelompok kontrol sehat serta kadarnnya menurun signifikan seiring dengan durasi pengobatan OAT. Pada penelitian ini dilakukan pemeriksaan ekspresi mRNA menggunakan RT-qPCR terhadap Interferon Stimulated Genes (ISG) tipe 1 (MyD88, FCG1R1B, IL1B, IFIT2, GBP1, IRF7, TLR8, STAT1, SERPING1, UBE2L6) dan protein C1q menggunakan ELISA pada pasien uveitis idiopatik dengan IGRA positif dari 20 pasien dengan time-point follow up pada minggu ke-0 (M0) dan minggu ke-2 (M2). Ekspresi gen GBP1 (p=0,001), UBE2L6 (p=0,0012) dan SERPING1 (p=0,03) berbeda bermakna pada kelompok perbaikan okular, dengan 8/10 gen menunjukan tren penurunan ekspresi pada M2. Hanya GBP1 (p=0,03) yang ekspresinya berbeda bermakna pada kelompok tanpa perbaikan okular, dengan 9/10 menunjukan tren peningkatan ekspresi gen pada M2. Perubahan ekspresi gen (M0-M2) MyD88, FCGR1B, GBP1, TLR8, STAT1 berkorelasi dengan outcome okular. Perubahan ekspresi gen GBP1 dan TLR8 berbeda bermakna sebagai biomarker diagnosis dengan AUC 88,1% dan 90,5%. Pada penelitian ini, level C1q sebelum dan setelah pengobatan ditemukan tidak berbeda bermakna (p=0,87) dan tidak terdapat hubungan berbeda bermakna antara perubahan klinis okular dengan level C1q.

.....Uveitis patients without a clear etiology (idiopathic) with non-specific inflammation clinical criteria but who have a positive IGRA status often cause dilemmas in treatment. This group of patients was treated as a group of suspected extrapulmonary TB and received anti-tuberculosis drug (ATT) treatment. Various studies have shown that the transcriptomic expression profile of type 1 Interferon Stimulated Genes (ISG) was found to be increased in active TB patients and is known to have potential as a diagnostic biomarker and monitoring of therapy efficacy. In addition, the C1q protein level was found to be increased in active TB patients compared to the healthy control group and its levels decreased significantly with the duration of OAT treatment. In this study, mRNA expression was examined using RT-qPCR on Interferon Stimulated Genes (ISG) type 1 (MyD88, FCG1R1B, IL1B, IFIT2, GBP1, IRF7, TLR8, STAT1, SERPING1, UBE2L6) and C1q protein using ELISA in idiopathic uveitis patients. with positive IGRA of 20 patients with time-point follow-up at week 0 (W0) and week 2 (W2). GBP1 (p=0.001), UBE2L6 (p=0.0012), and SERPING1 (p=0.03) genes differentially expressed significantly in the group with ocular improvement, which 8/10

genes were downregulated in W2. In the non-improvement ocular group, only the GBP1 gene was significantly expressed differentially (p=0.03), with 9/10 genes expression upregulated in W2. Changes in expression of the MyD88, FCGR1B, GBP1, TLR8, and STAT1 genes correlated with ocular improvement. Changes in GBP1 and TLR8 gene expression were significantly different as a biomarker diagnosis with AUC of 88.1% and 90.5%. In this study, C1q levels before and after treatment were not significantly different (p=0.87) and there was no significant correlation between ocular clinical changes and C1q levels.