

# Plastisitas Th17 dan Respons Kemoembolisasi Transarterial pada Pasien Karsinoma Sel Hati: Kajian terhadap Th17, Th1, IL-17, IFN-Gamma, dan Rasio Neutrofil Limfosit = Plasticity of Th17 and Response of Transarterial Chemoembolization in Hepatocellular Carcinoma Patients: A Study of Th17, Th1, IL-17, IFN-Gamma, and Neutrophil-To-Lymphocyte Ratio

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## Abstrak

Peran Th17 dalam keganasan, khususnya karsinoma sel hati, masih menjadi perdebatan. Sel Th17, sel penghasil IL-17, dilaporkan berhubungan dengan efek protumor dan antitumor sekaligus. Di lain sisi, sel Th1 yang menyekresikan IFN- $\gamma$  memiliki sifat antitumor. Kemoembolisasi transarterial / transarterial chemo-embolization (TACE) diketahui dapat menyebabkan nekrosis tumor, namun peran TACE dalam memengaruhi sel Th17, Th1, IL-17, IFN- $\gamma$ , dan rasio neutrofil limfosit (RNL) masih belum diketahui. Penelitian ini bertujuan untuk menentukan perubahan Th17, Th1, IL-17, IFN- $\gamma$ , dan nilai RNL pada pasien KSH yang menjalani TACE. Penelitian ini dilakukan sepanjang Juni 2015–Januari 2019 di RSCM dan beberapa rumah sakit jejaring di Jakarta. Desain potong lintang digunakan untuk membandingkan respons imun pasien KSH dengan sirosis hati. Desain kohort prospektif diterapkan untuk menilai hubungan respons imun dengan keberhasilan TACE. Pengambilan darah dilakukan sebelum dan 30 hari setelah tindakan TACE pada pasien KSH dan satu kali pada pasien sirosis. Nilai Th17 dan Th1 dianalisis menggunakan teknik flowcytometry, sedangkan nilai IL-17 dan IFN- $\gamma$  diukur dengan teknik enzyme-linked immunosorbent assay (ELISA). Nilai RNL dihitung dari pembagian kadar neutrofil dengan limfosit yang diperoleh dari pemeriksaan hitung jenis. Respons terhadap TACE dievaluasi berdasarkan kriteria mRECIST. Sebanyak 40 pasien sirosis dan 41 pasien KSH berpartisipasi dalam penelitian ini. Sebanyak 12 pasien dan 29 pasien termasuk ke dalam kelompok respons dan nonrespons, secara berurutan. Penurunan kadar AFP dan ukuran tumor secara bermakna ditemukan pada kelompok respons. Pada kelompok ini, juga ditemukan peningkatan bermakna kadar Th1, Th17, dan sel T CD4+/IFN- $\gamma$ +/IL-17+ setelah TACE. Nilai IL-17, IFN- $\gamma$ , dan RNL tidak berhubungan dengan respons TACE. Di samping itu, didapatkan peningkatan bermakna kadar CD4+/IFN- $\gamma$ +/IL-17- pada kelompok nonrespons.

**Simpulan:** Peningkatan kadar Th1 dan Th17 dalam darah perifer yang diiringi dengan peningkatan sel T CD4+/IFN- $\gamma$ +/IL-17+ didapatkan pada pasien KSH yang berespons baik terhadap TACE.

The role of Th17 cells in malignancy, especially hepatocellular carcinoma, remains controversial. Th17 cells, IL-17 producing cells, were reported to be associated with both protumor and antitumor effects. On the other hand, Th1 cells, IFN- $\gamma$  producing cells, had antitumor properties. Transarterial chemoembolization (TACE) is known for its potency to cause tumor necrosis, but its impact on Th17, Th1, IL-17, IFN- $\gamma$ , and neutrophil-to-lymphocyte ratio (NLR) is still unclear. This study aims to determine the changes in Th17, Th1, IL-17, IFN- $\gamma$ , and NLR levels in HCC patients treated with TACE. This study was conducted from June 2015 to January 2019 at Cipto Mangunkusumo National General Hospital dan several affiliated hospitals in Jakarta. A cross-sectional study design was used to compare the immune response between HCC and liver cirrhotic patients. A prospective cohort study

design was applied to assess the relationship between immune response and tumor response to TACE. Plasma sampling was obtained from HCC and cirrhotic patients that fulfilled the inclusion and exclusion criteria. Blood samples were collected immediately before and 30 days after TACE. Th17 and Th1 levels were measured using flowcytometry technique, while IL-17 and IFN- $\hat{I}^3$  levels were quantified by using enzyme-linked immunosorbent assay (ELISA). The value of NLR was calculated by dividing the neutrophil count by the lymphocyte count. Responses to TACE were evaluated based on mRECIST.

A total of 40 cirrhotic and 41 HCC patients participated in this study. As many as 12 and 29 patients were included in the response and nonresponse group, respectively. In the response group, there were significant reduction of AFP levels and tumor size, as well as significant increase of Th1, Th17 and CD4+/IFN- $\hat{I}^3$ +/IL-17+ T cells levels after TACE. Furthermore, there was an increase of CD4+/IFN- $\hat{I}^3$ +/IL-17- levels in the non-response group. The values of IL-17, IFN- $\hat{I}^3$ , and NLR were not related to TACE response.

**Conclusion:** Patients with good response to TACE had increased levels of circulating Th1, Th17, and CD4+/IFN- $\hat{I}^3$ +/IL-17+ T cells.