# Hubungan sel T regulator, Sel T CD4+ dan CD8+ dengan agresivitas dan respons terapi kanker nasofaring = the link between regulator T Cells, CD4+ and CD8+ T cells with tumor aggressiveness and response treatment in nasopharyngeal carcinoma

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Abstrak

Latar belakang: kanker nasofaring (KNF) adalah keganasan yang umum dijumpai pada nasofaring. Cukup banyak bukti menunjukkan adanya keterkaitan KNF dengan sistem kekebalan tubuh. Tidak semua subset sel T merupakan sel T efektor. Sel T regulator (TReg) yang merupakan salah satu subset dari sel T, memiliki peran penting dalam mengatur imunitas anti tumor. Sampai saat ini belum dapat disimpulkan bahwa keberadaan sel TReg pada lokasi tumor pasti akan memicu pertumbuhan tumor. Akan tetapi, adanya sel T CD4+ dan CD8+ tentunya berpengaruh terhadap kontrol perkembangan tumor. Studi ini bertujuan untuk menilai karakterisitik CD4, CD8 dan FOXP3 pada pasien KNF dan hubungannya terhadap agresivitas tumor.
Metode: penelitian ini merupakan studi kohort prospektif. Sel TReg dinilai menggunakan marker FOXP3. Jumlah protein CD4, CD8 dan FOXP3 pada jaringan biopsi tumor dideteksi dan diukur dengan ELISA. Volume tumor primer dan volume total metastasis kelenjar getah bening regional didapatkan dari proses delineasi dengan pencitraan 3D. Spearmen-rho test digunakan untuk menilai korelasi antara CD4, CD8 dan FOXP3 dengan volume tumor primer dan volume total metastasis kelenjar getah bening regional.
Hasil: Sebanyak 23 subjek penelitian (14 pria dan 9 wanita) terkumpul berdasarkan kriteria inklusi dan eksklusi. Stadium KNF terbanyak pada studi ini adalah stadium IV (AJCC edisi ke-8). Analisis dengan uji Spearman menunjukkan korelasi kuat antara konsentrasi protein FOXP3 dan volume tumor primer (p=0.02, r=0.60), dan juga antara konsentrasi protein CD8 dan volume tumor primer (p=0.00, r=0.81). Menariknya, juga ditemukan korelasi antara konsentrasi CD8 dan FOXP3 (p=0.00, r=0.85). Tidak ditemukan korelasi antara konsentrasi protein CD4, CD8 dan FOXP3 dengan volume total metastasis kelenjar getah bening regional. Tidak ditemukan juga korelasi antara konsentrasi FOXP3 dan stadium KNF. Sayangnya, belum dapat disimpulkan hubungan antara konsentrasi FOXP3 dan respons terapi pada penelitian ini.
Kesimpulan: Keberadaan sel TReg berpengaruh terhadap agresivitias lokal tumor yang ditandai dengan peningkatan volume massa tumor primer. Korelasi antar konsentrasi CD4, CD8 dan FOXP3 memberikan gambaran interaksi dan mekanisme respons imunitas tubuh dalam menjaga keseimbangan antara sel T efektor dan sel T regulator.
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Background: nasopharyngeal cancer (NPC) is a common malignancy found in the nasopharynx area. There is quite a lot of evidence showing a link between NPC and the immune system. Regulatory T cells (TReg), a subset of T cells, have an essential role in regulating anti-tumor immunity. It has not been confirmed that TReg cells at the tumor site will trigger tumor growth. However, the presence of CD4+ and CD8+ T cells certainly affects the control of tumor growth. This study aims to assess the characteristics of CD4, CD8, and FOXP3 in NPC patients and their relationship with tumor aggressiveness.
Methods: a prospective cohort study was conducted on 23 subjects (14 men and 9 women) based on the

inclusion and exclusion criteria. TReg cells were assessed using the FOXP3 marker. The number of CD4, CD8, and FOXP3 proteins in tumor biopsy tissue was detected and measured by ELISA kit (MBS2702975, MBS165145, MBS162054). The volume of the primary tumor and the total volume of regional lymph node metastases were obtained from the delineation process based on 3D imaging. Spearmen-rho test was used to assess the correlation of CD4, CD8, and FOXP3 with primary tumor volume and total volume of regional lymph node metastases.

Results: A total of 23 study subjects (14 men and 9 women) were collected based on the inclusion and exclusion criteria. The most common NPC stage in this study was stage IV (AJCC 8th edition). Analysis by the Spearman-rho test showed a strong correlation between; concentration of FOXP3 protein and primary tumor volume ($p=0.02$, $r=0.60$) and the concentration of CD8 protein and primary tumor volume ($p=0.00$, $r=0.81$). Interestingly, a correlation was also found between the concentration of CD8 protein and FOXP3 ($p=0.00$, $r=0.85$). There was no correlation between CD4, CD8, and FOXP3 proteins and the total volume of regional lymph node metastases. There was also no correlation between FOXP3 concentration and NPC stage. Unfortunately, it is impossible to conclude the relationship between FOXP3 concentration and treatment response in this study.

Conclusions: the presence of TReg cells affects the local aggressiveness of the tumor, which is characterized by an increase in the volume of the primary tumor. The correlation between CD4, CD8, and FOXP3 concentrations provides an overview of the interactions and mechanisms of the body's immune response to maintain a balance between effector T cells and regulatory T cells.