

# Hubungan Onkoprotein Virus Epstein-barr (EBNA1 dan LMP1) terhadap Agresivitas dan Respon Terapi Pasien Kanker Nasofaring = Association between Epstein-barr Virus Oncoprotein (EBNA1 & LMP1) with Aggressivity and Treatment Response in Nasopharyngeal Cancer Patients

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## Abstrak

Latar belakang: Kanker nasofaring merupakan keganasan yang unik dimana angka kejadiannya termasuk jarang disebagian besar negara, namun endemis di wilayah tiongkok selatan, dan asia tenggara termasuk Indonesia. Histopatologi kanker nasofaring di daerah endemik biasanya merupakan karsinoma jenis tidak berkeratin tidak berdiferensiasi dan selalu terkait dengan infeksi EBV. Berbagai jenis protein virus diekspresikan pada infeksi laten EBV termasuk EBNA1 dan LMP1 mungkin berkontribusi dalam perkembangan kanker. Oleh karenanya, kami ingin menginvestigasi peran onkoprotein virus tersebut terhadap agresivitas dan respon terapi kanker nasofaring.

Metode: Spesimen biopsi jaringan dan darah yang diambil dari pasien kanker nasofaring diukur kadar EBNA1 dan LMP1 dengan menggunakan pemeriksaan ELISA kit masing-masing dari DRG® dan MyBioSource® kemudian dikorelasikan dengan volume tumor dan KGB terlibat yang dinilai berdasarkan delineasi berbasis pencitraan 3D. Pasien kemudian menjalani terapi standar, dan dilakukan penilaian 3 bulan paska terapi. Respon terapi akan dinilai hubungannya dengan kadar EBNA1 dan LMP1.

Hasil: 23 subjek dimasukkan kedalam studi, 69,5% berada pada stadium IVA keatas, dengan mayoritas laki-laki sebanyak 61%. Median volume tumor primer dan volume KGB masing masing 41,4cc (13,2-128,8) dan 40,1cc (1,2-633,5). Uji korelasi Spearman mendapatkan hubungan bermakna ( $p=0,032$ ) antara kadar LMP1 jaringan dan volume tumor sebelum terapi ( $r=0,448$ ). Tren korelasi yang moderat terlihat pada kadar EBNA1 di jaringan dengan di darah, kadar EBNA1 di jaringan dengan volume tumor primer, kadar EBNA1 di darah dengan volume KGB, serta Kadar LMP1 baik di jaringan maupun di darah dengan volume KGB, meskipun secara keseluruhan tidak bermakna secara statistik. Sementara itu, pengaruh kadar LMP1 dan EBNA1 terhadap respon terapi belum dapat disimpulkan.

Kesimpulan: Semakin tinggi kadar LMP1 di jaringan tumor akan diikuti oleh semakin besarnya volume tumor primer nasofaring. Korelasi moderat tidak signifikan pada variabel lain mungkin diakibatkan oleh jumlah sampel yang kurang. Penambahan besar sampel diperlukan untuk konfirmasi signifikansi dari korelasi tersebut.

.....Background: Nasopharyngeal cancer is an unique malignancy where the incidence is rare in most countries but endemic in Southern China and Southeast Asia, including Indonesia. The histopathology of nasopharyngeal cancer in endemic areas is usually an undifferentiated nonkeratinizing type carcinoma and is always associated with EBV infection. Various viral proteins are expressed in latent EBV infection, including EBNA1 and LMP1. These viral oncoproteins may contribute to cancer development, but they are not always be defined. Therefore, we want to investigate the role of these viral oncoproteins when it comes to the aggressivity and treatment response of nasopharyngeal cancer.

Methods: Tissue biopsy and blood specimens taken from nasopharyngeal cancer patients were measured for

EBNA1 and LMP1 using the ELISA kit examination from DRG® and MyBioSource® respectively, then correlated with primary tumor and nodal volume, which was calculated by delineation based on 3D imaging. Patients then underwent standard therapy, and was assessed 3 months post-therapy. Response to therapy will be assessed in relation to levels of EBNA1 and LMP1.

Results: 23 subjects were included in the study, 69.5% was at stage IVA and above with the majority being males (61%). The median primary tumor and lymph node volume were 41.4cc (13.2-128.8) and 40.1cc(1,2-633.5), respectively. Spearman correlation test found a significant relationship ( $p=0.032$ ) between tissue LMP1 levels and tumor volume before therapy ( $r=0.448$ ). A moderate correlation trend was seen in EBNA1 levels in tissue with blood, EBNA1 levels in tissue with primary tumor volume, EBNA1 levels in blood with lymph node volume, and LMP1 levels both in tissue and in blood with lymph node volume, although overall it was not statistically significant. Meanwhile, the effect of LMP1 and EBNA1 levels on the response to therapy cannot be concluded.

Conclusion: The higher the level of LMP1 in the tumor tissue, the larger the volume of primary nasopharyngeal tumor will be. Moderately insignificant correlation on the other variables may be caused by a small number of samples. The addition of the sample size is needed to confirm the significance of the correlation.