Pengaruh radiasi terhadap ekspresi PD-L1 intratumoral pada karsinoma sel skuamosa serviks uteri stadium lanjut lokal = Effect of radiation on intratumoral PD-L1 expression in locally advanced uterine cervical squamous cell carcinoma

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Abstrak

ABSTRAK
Latar Belakang: Kanker serviks stadium lanjut lokal (IIB-IIIB) masih menjadi beban kesehatan di Indonesia saat ini. Radiasi menjadi modalitas utama terapi pada stadium ini. Programmed Death-Ligand 1 (PD-L1) merupakan sebuah ligand yang diekspresikan pada sel tumor yang terkait dengan proses immune escape. Sampai saat ini belum diketahui karakteristik kadar PD-L1 pada karsinoma sel skuamosa (KSS) serviks stadium lanjut lokal serta pengaruh radiasi terhadap ekspresinya. Penelitian ini bertujuan untuk melihat karakteristik PD-L1 intratumoral pada kanker serviks stadium lanjut lokal serta pengaruh radiasi eksterna terhadap ekspresinya. Metode: Dilakukan pemeriksaan kadar PD-L1 pada sampel biopsi serviks dengan 2 metode, yaitu Enzyme Linked Immuno Sorbent Assay (ELISA) dan immunohistokimia (IHK). Pengambilan sampel dilakukan dua kali, yaitu preradiasi dan pascaradiasi eksterna. Dilakukan analisis statistik untuk mengetahui perbedaan kadar antara sebelum dan sesudah radiasi. Selain itu dilakukan analisis untuk melihat kesesuaian antara kadar yang ditunjukkan pada metode ELISA dengan metode IHK. Hasil: Didapatkan 29 sampel KSS serviks stadium lanjut lokal yang memenuhi kriteria inklusi dan eksklusi. Dari pemeriksaan IHK, didapatkan bahwa PD-L1 diekspresikan hampir pada seluruh subjek (96,5%). Didapatkan nilai median PD-L1 ELISA preradiasi 409,19 pg/mg protein (59,80-3011,30), pascaradiasi 444,40 pg/mg protein (27,24-3217,85). Tidak didapatkan perbedaan bermakna antara kedua kelompok tersebut (p = 0,804). Pada analisis receiver operating characteristics (ROC) didapatkan nilai ELISA >400 pg/mg protein bersifat prediktif menyebabkan terjadinya penurunan kadar ELISA pascaradiasi. Terdapat kesesuaian antara kadar PD-L1 metode ELISA dengan metode IHK, dimana nilai ELISA > 499 pg/mg protein cenderung menunjukkan nilai grade 3 pada pemeriksaan IHK. Kesimpulan: PD-L1 diekspresikan positif pada KSS serviks uteri stadium lanjut lokal. Tidak terlalu jelas efek radiasi dalam menyebabkan naik-turunnya ekspresi PD-L1. Pemeriksaan ELISA mempunyai potensi untuk dipertimbangkan mewakili hasil pemeriksaan IHK, namun perlu bukti yang lebih kuat berupa penelitian dengan jumlah sampel yang lebih banyak.
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ABSTRACT
Background: Locally advanced cervical cancer (IIB-IIIB) remains a health burden in Indonesia. Radiation is the main modality of therapy at this stage. PD-L1 is a ligand that is expressed in tumor cells associated with the immune escape process. Until now there is no clear characteristics of PD-L1 levels in locally advanced-stage cervical SCC and the effect of radiation on its expression. This study is aimed to look for the intratumoral PD-L1 characteristics in locally advanced cervical cancer and the effect of external radiation on its expression. Method: PD-L1 levels were examined on cervical biopsy samples using two methods, i.e. ELISA and IHC. Biopsy was carried out twice, preradiation and post-external radiation. Statistical analysis was performed to determine differences in levels between before and after radiation. In addition, an analysis

was conducted to see the conformity between the levels indicated in the ELISA method and the IHC method. Results: Twenty nine samples of local advanced cervical SCC were obtained that met the inclusion and exclusion criteria. From the IHC examination, it was found that PD-L1 was expressed in almost all subjects (96.5%). The median PD-L1 concentration of ELISA PD-L1 preradiation was 409.19 pg / mg protein (59.80-3011.30), post-radiation 444.40 pg / mg protein (27.24-3217.85). No significant difference was found between the two groups (p = 0.804). In the ROC analysis it was found that ELISA values > 400 pg / mg protein were predictive to cause a decrease in postradiation ELISA levels. There is a conformality between the levels of PD-L1 ELISA method with the IHC method, where the ELISA value > 499 pg/mg of protein tends to show grade 3 values on the IHC examination. Conclusion: PD-L1 was expressed positively in locally advanced cervical SCC. The effects of radiation in causing the ups and downs of the expression of PD-L1 is not very clear. ELISA examination has the potential to be considered as a representative to the results of the IHC examination, but stronger evidence is needed in the form of study with a larger number of samples.