Peran sel punca kanker, faktor apoptosis, DNA repair, dan telomerase terhadap respons terapi radiasi pada kanker serviks stadium III B: kajian khusus pada ekspresi SOX2 dan OCT4 = Role of cancer stem cell apoptotic factor DNA repair and telomerase toward radiation therapy response in stage iiib cervical cancer special study on SOX2 and OCT4 expression

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Abstrak

Radiasi merupakan terapi pilihan untuk kanker serviks stadium III B, namun permasalahan timbul karena adanya sifat radioresisten. Sel punca kanker SPK merupakan salah satu faktor yang diduga berkontribusi terhadap hal tersebut. SOX2 dan OCT4 merupakan faktor transkripsi yang mengekspresikan sifat-sifat SPK, yaitu mengontrol sifat pluripoten, self-renewal, berperan pada karsinogenesis, metastasis, resistensi terhadap terapi dan rekurensi tumor. Faktor apoptosis, DNA repair dan telomerase merupakan mekanisme yang berkaitan dengan radioresisten. Penelitian ini bertujuan untuk mempelajari hubungan antara SOX2 dan OCT4 sebagai penanda SPK terhadap respons terapi radiasi, serta kaitannya dengan faktor apoptosis caspase-3 , DNA repair Chk1 dan telomerase hTERT .Penelitian ini merupakan case control, terhadap 48 kasus karsinoma sel skuamosa serviks stadium III B yang telah menjalani terapi radiasi/kemoradiasi di RS Cipto Mangunkusumo/FKUI. Kasus dibagi dalam 2 kelompok, yaitu hasil terapi komplet 27 kasus dan hasil terapi inkomplet 21 kasus . Kasus dengan respons awal terapi radiasi baik dilakukan pemeriksaan bulan Pap smear dan HPV pada bulan ke-6 atau sampai ke-12 setelah terapi. Ekspresi SOX2, OCT4, caspase-3, Chk1 dan hTERT diperiksa secara imunohistokimia dari blok parafin biopsi awal.Ekspresi kuat SOX2 dan OCT4 dengan H-score masing-masing lebih dari 96,6 dan 61,9 mempunyai hubungan bermakna dengan respons awal terapi radiasi maupun respons akhir terapi radiasi SOX2 p = 0,017, p = 0,004 dan OCT4 p < 0,001, p < 0,001 . Ditemukan hubungan bermakna antara ekspresi Chk1 dan hTERT dengan respons awal terapi radiasi Chk1 p = 0,006, hTERT p = 0,029 . Tidak ditemukan hubungan yang bermakna antara ekspresi caspase-3, Chk1, hTERT dengan ekspresi SOX2 dan OCT4. Uji multivariat menunjukkan bahwa SOX2 dan OCT4 yang paling memengaruhi respons terapi OR = 5,12, p = 0,040 dan OR = 17,03, p < 0,001, secara berurutan . Uji probabilitas menunjukkan kemungkinan respons akhir terapi radiasi inkomplet sebesar 87,91 bila ekspresi kedua penanda SPK kuat.Ekspresi kuat SOX2 dan OCT4 dapat memprediksi hasil terapi radiasi inkomplet pada karsinoma serviks stadium III B.

.....Radiotherapy is the main choice of treatment for stage III B cervical cancer, but radioresistance becomes a difficult matter. Cancer stem cell is one of the factors suspected involving in radioresistant cancers. SOX2 and OCT4 are transcription factors which have pluripotent cell characteristics, and self renewal ability. They also involved in carcinogenesis, metastasis, tumor recurrent, and resistance toward therapy. Apoptotic, DNA repair, and telomerase factors are mechanisms that also contribute to radioresistance. This study aims to know the role of SOX2 and OCT4 as CSC markers, apoptotic factor caspase 3 , DNA repair Chk1 and telomerase hTERT toward radiotherapy.The design of this study was case control with 48 cases of stage III B cervical squamous cell carcinoma patients who had finished receiving radiation chemo radiation therapy at Cipto Mangunkusumo Hospital FMUI, Jakarta. They were classified in 2 groups based on the final

response of treatment, which were complete and incomplete one. Pap smear and DNA HPV were performed in month 6 or until month 12 after therapy for good initial therapy. Immunohistochemistry was done to analyze SOX2, OCT4, caspase 3, Chk1 and hTERT expression from the paraffin block of initial biopsy.Strong expression of SOX2 and OCT4 with each H score was higher than 96.6, and 61.9 had significant association with both initial and final therapy response SOX2 p 0.017, p 0.004 and OCT4 p 0.001, p 0.001, repectively . There was significant association between expression of Chk1 and hTERT, and initial therapy response p 0.006 for Chk1, and p 0.029 for hTERT . No significant differences were found between caspase 3, Chk1, hTERT, and SOX2 and OCT4. Multivariate analysis showed SOX2 and OCT4 were the most influenced antibodies for radiotherapy response OR 5.12, p 0.040, and OR 17.03, p 0.001, respectively . The likelihood of incomplete final therapy response was 87.91 if the expression both of CSC markers were strong.Expression of SOX2, and OCT4 could predict the incomplete radiotherapy of stage III B cervical cancer cases.