HUBUNGAN ANTARA MUTASI BRAF V600 PADA MELANOMA KULIT PRIMER TIPE NODULAR DENGAN KETEBALAN TUMOR, ULSERASI, INDEKS MITOSIS, NEKROSIS, INVASI LIMFOVASKULER, DAN INFILTRASI LIMFOSIT PADA TUMOR

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INTISARI

Latar Belakang: Melanoma merupakan keganasan kulit yang memiliki agresivitas dan mortalitas yang tinggi. Melanoma mayoritas terdiagnosis pada stadium lanjut, dan belum ada terapi yang adekuat hingga saat ini. Beberapa faktor histopatologis yang mempengaruhi prognosis melanoma adalah melanoma tipe nodular, ketebalan tumor, ulserasi, indeks mitosis, nekrosis, invasi limfovaskuler, dan infiltrasi limfosit pada tumor. Mutasi BRAF V600 pada melanoma menyebabkan proliferasi sel yang tidak terkendali, berhubungan dengan prognosis dan ketahanan hidup yang lebih buruk, namun merupakan kandidat terapi target pada melanoma. Tujuan penelitian ini adalah untuk mengetahui mutasi BRAF V600 pada melanoma kulit primer tipe nodular dan mengetahui hubungan antara mutasi BRAF V600 dengan ketebalan tumor, ulserasi, indeks mitosis, nekrosis, invasi limfovaskuler, dan infiltrasi limfosit pada tumor.

Metode: Sampel berupa 40 jaringan *formalin-fixed paraffin-embedded* (FFPE) kasus melanoma kulit primer tipe nodular dari Instalasi Patologi Anatomik RSUP Dr. Sardjito dan RSUP dr. Soeradji Tirtonegoro tahun 2011 – 2018. Mutasi BRAF V600 dinilai dengan metode *quantitative real time-PCR* (qRT-PCR). Hubungan antara mutasi BRAF V600 dengan ketebalan tumor, ulserasi, indeks mitosis, nekrosis, invasi limfovaskuler, dan infiltrasi limfosit pada tumor dianalisis dengan uji statistik *Pearson Chi-Square* dan *Fisher's exact test*.

Hasil: Mutasi BRAF V600 didapatkan pada 4 dari 40 sampel yang diteliti (10%). Terdapat hubungan yang bermakna antara mutasi BRAF V600 dengan invasi limfovaskuler (p=0,005). Namun tidak didapatkan hubungan yang bermakna antara mutasi BRAF V600 dengan ketebalan tumor, ulserasi, indeks mitosis, nekrosis, dan infiltrasi limfosit pada tumor (p=0,49, p=1,00, p=0,33, p=0,57, dan p=0,30).

Kesimpulan: Mutasi BRAF V600 positif didapatkan pada melanoma kulit primer tipe nodular sebesar 10%. Mutasi BRAF V600 pada melanoma kulit primer tipe nodular berhubungan dengan invasi limfovaskuler, namun tidak berhubungan dengan ketebalan tumor, ulserasi, indeks mitosis, nekrosis, dan infiltrasi limfosit pada tumor.

Kata kunci: Melanoma kulit primer tipe nodular, mutasi BRAF V600, faktor prognosis histopatologis.

ASSOCIATION BETWEEN BRAF V600 MUTATIONS IN PRIMARY NODULAR CUTANEOUS MELANOMA WITH TUMOR THICKNESS, ULCERATION, MITOTIC INDEX, NECROSIS, LYMPHOVASCULAR INVASION, AND TUMOR INFILTRATING LYMPHOCYTES

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ABSTRACT

Background: Melanoma is a skin malignancy that has high aggressiveness and mortality. The majority of melanoma is diagnosed at an advanced stage, and there is no adequate therapy to date. Some histopathological factors that affect the prognosis of melanoma are nodular type melanoma, tumor thickness, ulceration, mitotic index, necrosis, lymphovascular invasion, and tumor-infiltrating lymphocytes. BRAF V600 mutations in melanoma cause uncontrolled cell proliferation, associated with poorer prognosis and survival, but are candidates for targeted therapy in melanoma. The purpose of this study was to determine the BRAF V600 mutation in primary nodular cutaneous melanoma and determine the association between BRAF V600 mutations with tumor thickness, ulceration, mitotic index, necrosis, lymphovascular invasion, and tumor-infiltrating lymphocytes.

Methode: The sample was 40 formalin-fixed paraffin-embedded (FFPE) tissue of primary nodular cutaneous melanoma collected from the Anatomical Pathology Installation of RSUP Dr. Sardjito and RSUP dr. Soeradji Tirtonegoro in 2011 - 2018. BRAF V600 mutations were assessed by the quantitative real time-PCR (qRT-PCR) method. The association between BRAF V600 mutations with tumor thickness, ulceration, mitotic index, necrosis, lymphovascular invasion, and tumor-infiltrating lymphocytes was analyzed by Pearson Chi-Square statistical tests and Fisher's exact test.

Result: BRAF V600 mutations were obtained in 4 of the 40 samples studied (10%). There was a significant association between BRAF V600 mutations and lymphovascular invasion ($p = 0.005$). However, there was no significant association between BRAF V600 mutations with tumor thickness, ulceration, mitotic index, necrosis, and tumor-infiltrating lymphocytes ($p = 0.49$, $p = 1.00$, $p = 0.33$, $p = 0.57$, and $p = 0.30$).

Conclusion: A positive BRAF V600 mutation was found in primary nodular cutaneous melanoma of 10%. BRAF V600 mutations in primary nodular cutaneous melanoma are associated with lymphovascular invasion, but are not related to tumor thickness, ulceration, mitotic index, necrosis, and tumor-infiltrating lymphocytes.

Keywords: Nodular type primary skin melanoma, BRAF V600 mutation, histopathological prognosis factor.