

NRAS and BRAF mutation frequency in primary oral mucosal melanoma

Type:

Article

Abstract:

Oral mucosal melanoma (OMM) is a fatal sarcoma of unknown etiology. Histological morphology and genetic events are distinct from those of its cutaneous counterpart. Mutation and up-regulation of c-kit has been identified in OMM which may activate downstream molecules such as RAS and RAF. These molecules are involved in the mitogen-activated protein kinase (MAPK) pathway leading to tremendous cell proliferation and survival. NRAS and BRAF mutation and protein expression have been studied in other melanoma subtypes. The purpose of this study was to determine RAS protein expression and NRAS and BRAF mutation in 18 primary OMM cases using immunohistochemistry and mutation analysis. Results showed that RAS is intensely expressed in both in situ and invasive OMMs. However, NRAS mutation was only observed in 2/15 polymerase chain reaction (PCR) amplified cases both of which were silent mutations. On the other hand, BRAF missense mutations were observed only in 1/15 cases with PCR amplification. NRAS and BRAF mutations were independent from previously reported c-kit mutations. The classical V600E BRAF mutation was not found; instead a novel V600L was observed suggesting that the oncogenic event in OMM is different from that in skin melanoma. The low frequency of NRAS and BRAF mutations indicate that these genes are not common, but probable events in OMM pathogenesis, most likely independent of c-kit mutation.

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