Predictors of CNS Disease in Metastatic Melanoma: Desmoplastic Subtype Associated With Higher Risk

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Desmoplastic histologic subtype is a strong predictor of brain metastasis development and decreased 2-year BMFS in patients with metastatic melanoma. Patients with desmoplastic melanoma, particularly thick lesions involving the H&N, should be imaged frequently during the first year after the diagnosis of stage IV disease.

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INTRODUCTION: Brain metastases are a major cause of mortality in metastatic melanoma. Histologic subtype—specifically, the desmoplastic subtype and its propensity for neurotropism—has not been well studied as a predictor of central nervous system (CNS) disease. We report the largest series of brain metastases in order to better define the clinicopathologic risk factors and help guide management and surveillance.

METHODS: A prospective institutional melanoma database was used to identify patients diagnosed with metastatic melanoma between 1971 and 2013. Patient age and sex; primary tumor location, thickness, ulceration, and histology; and types of recurrence and treatment were analyzed. Primary endpoints were development of brain metastases and 2-year brain metastases–free survival (BMFS). The secondary endpoint was overall survival (OS) from the date of stage IV diagnosis.

RESULTS: Among 3,756 patients with metastatic melanoma, 711 (18.9%) developed brain metastases. Histology was available for 2,132 patients, 397 (18.6%) of whom developed brain metastases (32 [8.1%] brain only, 38 [9.6%] brain as the first site of stage IV disease). Head and neck (H&N) location (P = .01), presence of ulceration (P = .04), and desmoplastic variant (P = .04) were associated with a higher risk of CNS disease. Multivariable analysis identified presence of ulceration (hazard ratio [HR] = 1.49; P < .01), primary location (upper extremity vs H&N: HR = 0.55, P < .01; lower extremity vs H&N: HR = 0.63, P = .01; mucosal vs H&N: HR = 0.42, P = .04; ocular vs H&N: HR = 0.29, P = .04), and histologic subtype (desmoplastic vs superficial spreading; HR = 2.38; P = .01) as independent predictors of 2-year BMFS. Improved 2-year OS was seen with female sex, younger age, upper extremity location, lack of ulceration, and ipilimumab therapy. Of the 25 patients diagnosed with desmoplastic melanoma, 9 (36%) were found to have brain metastases, all within the first year after the diagnosis of another systemic disease. Thick lesions (> 4 mm) of the H&N region were at greatest risk.

CONCLUSIONS: Desmoplastic histologic subtype is a strong predictor of brain metastasis development and decreased 2-year BMFS in patients with metastatic melanoma. Patients with desmoplastic melanoma, particularly thick lesions involving the H&N, should be imaged frequently during the first year after the diagnosis of stage IV disease.

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