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Importance of universal mismatch repair protein immunohistochemistry in patients with sebaceous neoplasia as an initial screening tool for Muir-Torre syndrome☆,☆☆

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Summary Muir-Torre syndrome, a Lynch syndrome variant, is characterized by sebaceous neoplasia plus one or more malignancies, typically colon cancer. The significance of DNA mismatch repair (MMR) deficiency detection by immunohistochemistry (IHC) in colorectal carcinomas is well established and is recommended as a screening tool for Lynch syndrome in newly diagnosed colorectal carcinomas. In comparison, literature on IHC application to detect MMR proteins (MLH1, MSH2, MSH6, and PMS2) in sebaceous neoplasia has been less studied and has been derived almost exclusively from tertiary care centers. Herein we describe the largest series to date characterizing MMR deficiency in sebaceous neoplasms, as well as the relative frequencies of each deficiency. Two hundred sixteen consecutive sebaceous neoplasms (216 patients) were analyzed from a community practice setting (133 sebaceous adenomas, 68 sebaceomas, 15 sebaceous carcinomas). One hundred forty-three were MMR deficient (66%), of which 90 were MSH2/MSH6 deficient (63%), 27 MLH1/PMS2 deficient (19%), 22 MSH6 deficient (15%), and 4 PMS2 deficient (3%). MMR deficiency was significantly associated with site, with tumors off of the head and neck more likely to be MMR deficient (specificity 96%). In contrast to prior reports, no significant trend in MMR-deficient versus -nondeficient tumors was seen in age at presentation (median age, 68 versus 66), tumor-infiltrating lymphocytes, or tumor type. Given the low sensitivity of age < 60 years (30%), location off of the head and neck (41%), or presence of tumor-infiltrating lymphocytes (29%) in MMR deficiency detection, IHC screening programs should test all sebaceous neoplasms for MMR deficiency, regardless of their clinicopathological features.

1. Introduction

Lynch syndrome (LS; hereditary nonpolyposis colorectal cancer) is caused by germ-line mutations in the DNA mismatch repair (MMR) genes MLH1, MSH2, MSH6, and PMS2. Affected individuals are predisposed to the development of

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