Sebaceous “adenoma” of an arm recurring as a carcinoma: The value of DNA mismatch repair gene expression immunohistochemistry

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INTRODUCTION

Immunohistochemistry to detect mutated mismatch repair genes is commonly performed on sebaceous neoplasms to screen for Muir-Torre syndrome.1 We report a case of the development of a sebaceous carcinoma at the same anatomic location from which a sebaceous adenoma was removed 5 years previously. Both lesions displayed the same pattern of loss of DNA mismatch repair genes.

Case

A 65-year-old woman presented with a pink, crusted papule of 3 to 4 months duration on the left deltoid area (Fig 1, A). Past medical history included thyroid disease and hypertension. Biopsy showed a symmetric neoplasm composed of circumscribed lobules of mature sebocytes centrally and a smaller component of peripheral basaloid cells, consistent with sebaceous adenoma (Fig 2). The biopsy procedure removed the entire clinical lesion; however, the lesion extended to the base of the specimen with possible transection.

Five years later, this patient presented with a pedunculated nodule on the left arm at the precise location from which the adenoma was originally removed (Fig 1, B). This nodule grew over the course of 1 year. Biopsy revealed an eroded, exophytic tumor composed of atypical epithelial cells with scattered mitoses, some ductal structures with associated squamoid keratinocytes, and foci of sebocytes (Fig 3, A and B). Most of the tumor cells expressed Ki-67 (Fig 3, C). Immunostaining revealed loss of MSH2 and MSH6 in the parenchyma of the tumor, but not in the stroma (Fig 4, C and D). MLH1 and PMS2 staining was retained.

The sebaceous adenoma removed 5 years previously showed the same pattern of immunostaining (Fig 4, A and B). A wide local excision of the site revealed no remaining tumor.

DISCUSSION

Sebaceous carcinomas most commonly occur around the eyes, occasionally at other sites of the face, and rarely at other anatomic sites.2 The documentation in the current case of a sebaceous carcinoma arising at the site of a previous adenoma supports the hypothesis that such “adenomas” may potentially be low-grade carcinomas, or may be prone to give rise to such tumors.3

The presence of sebaceous neoplasms can raise concern for the possibility of Muir-Torre syndrome, an autosomal dominant disease in which mutational loss of DNA mismatch repair genes MLH1, MSH2, MSH6, and/or PMS2 can result in the development of a variety of other skin tumors, such as keratoacanthomas, as well as visceral tumors of the gastrointestinal tract and endometrium. A suggested diagnostic criterion for Muir-Torre syndrome is the coincidence
of at least 1 visceral malignancy and 1 sebaceous neoplasm in an individual not exposed to radiation or immunosuppressive treatment. For patients older than 60 years who develop sebaceous neoplasms, and patients of at least 60 years of age who develop a sebaceous tumor on or below the neck, immunohistochemical staining for mismatch repair proteins is recommended. For those with abnormal mismatch repair protein results, visceral screenings, such as a colonoscopy and mammogram, in addition to genetic counseling are advised. Our patient’s annual mammogram and colonoscopy showed no abnormalities.

Both the sebaceous carcinoma and the previous sebaceous adenoma in the current case failed to express MSH2 and MSH6. Given the lack of any history of other neoplasms in this patient or in family members, Muir-Torre syndrome seems unlikely.

Of note was the retention of MSH2 and MSH6 staining in the stroma of the 2 neoplasms in which these stains were negative in the parenchyma. Previous studies have shown that sebaceous adenomas and carcinomas associated with Muir-Torre syndrome show negative staining in both compartments of the tumor. This discrepancy suggests that
Fig 3. Sebaceous carcinoma. Histopathology 5 years later, demonstrating an eroded, exophytic tumor composed of atypical epithelial cells with scattered mitoses and sebocytes (A and B) with prominent Ki-67 immunostaining (C).

Fig 4. Immunohistochemistry of sebaceous adenoma and carcinoma. In the sebaceous adenoma, MSH2 (A) and MSH6 (B) were expressed in the stroma, but not the parenchyma, of the tumor. Immunostaining was positive in the stroma and negative in the parenchyma of the sebaceous carcinoma for MSH2 (C) and MSH6 (D) as well.
the sebaceous neoplasms in the current case did not originate from a germline mutation, an observation which may be useful in terms of genetic counseling of affected patients.

Related findings have been observed in patients with Lynch syndrome, a hereditary disease associated with colorectal, endometrial, and other cancers related to mutated mismatch repair genes. Muir-Torre syndrome is a phenotypic variant of Lynch syndrome. In patients with Lynch syndrome, the presence of a sebaceous neoplasm led to a diagnosis of Muir-Torre syndrome in 9.2% of cases.6,9 Approximately, 3.9% of Lynch syndrome patients were found to lack germline mutations in the mismatch repair genes; however, since this finding likely does not exclude the possibility of visceral organ involvement, appropriate evaluation for visceral malignancy is still necessary. Of these cases, most had 2 somatic mutations in the DNA mismatch repair genes, similar to the findings in our case.10 The conclusion is that discrepant expression of mismatch repair genes in some, but not all, portions of a neoplasm suggests that the causative mutations were somatic rather than in the germline.

Conflicts of interest
None disclosed.

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