

Sebaceous Carcinoma and Mismatch Repair Gene Expression

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Citation

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Abstract

We present a case of an 81-year-old male with an asymptomatic skin nodule on his left upper cheek.

CASE REPORT

An 81-year-old male presents with an asymptomatic skin nodule on his left upper cheek. An excisional biopsy specimen (Fig.1) shows a well-circumscribed neoplasm in the dermis with central necrosis and peripheral chronic inflammatory cell infiltrate. The organoid neoplasm is composed of somewhat palisading or ribbon-like atypical basaloid cells and abnormal clear cells with multivesicular and vacuolated cytoplasm. The basaloid cells have enlarged hyperchromatic nuclei, prominent cherry-red nucleoli, basophilic cytoplasm, and brisk mitotic figures with scattered apoptotic bodies. The clear cells exhibit nuclear pleomorphism with prominent nucleoli with sebaceous differentiation (Fig. 2). The well-demarcated growth pattern of this sebaceous carcinoma is classified as Grade I tumor according to the WHO Classification (1).

Immunohistochemical studies show that the tumor cells

strongly positive for androgen receptor (AR) (Fig.3), a diagnostic finding in sebaceous neoplasm. The tumor cells also express mismatch repair gene MLH-1 and PMS-2 (Fig. 4), but they are non-immunoreactive to MSH-2 and MSH-6 (Fig. 5), which may indicate microsatellite instability.

Figure 1

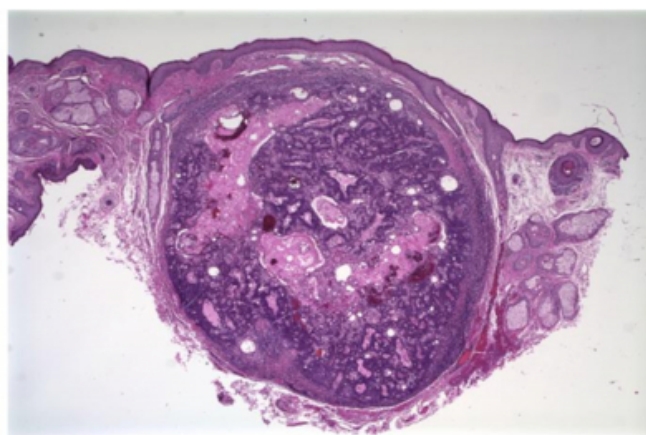


Figure 1. Skin biopsy, left upper cheek showing well-demarcated dermal nodule.

Figure 2

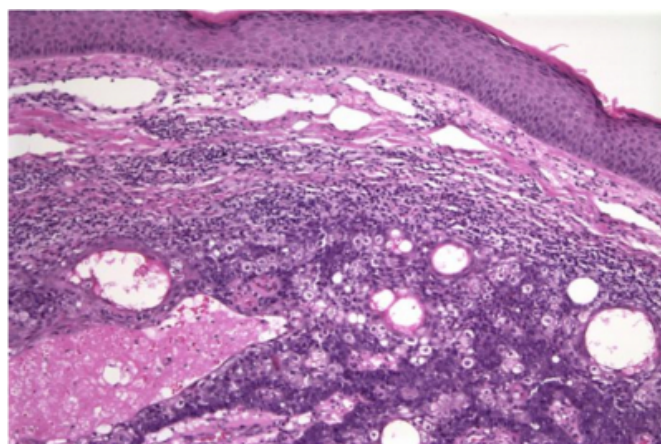


Figure 2. Higher magnification: sebaceous carcinoma with tumor necrosis.

Figure 3

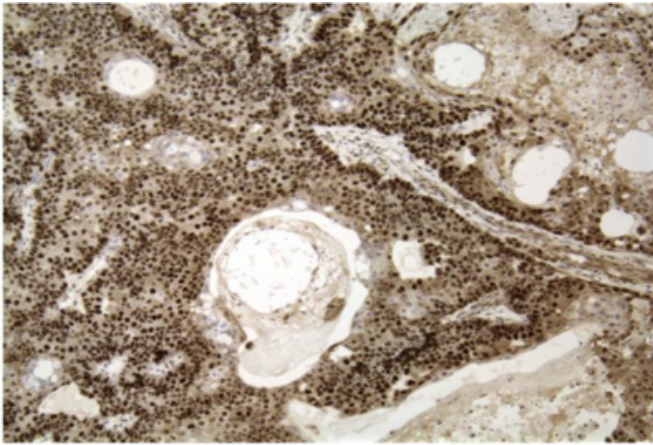


Figure 3. Androgen receptor (AR) expression in the nuclei of the neoplastic cells.

Figure 4

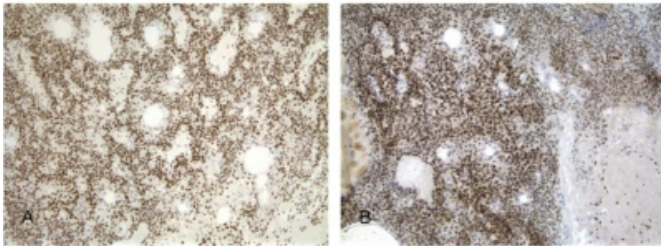


Figure 4. Normal expression of MLH-1 (A) and PMS-1 (B) in the neoplastic cells.

Figure 5

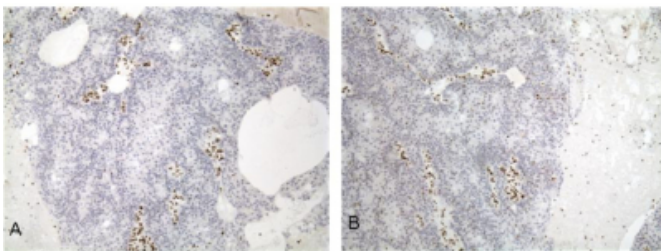


Figure 5. The neoplastic cells are non-immunoreactive for MSH-2 (A) and MSH-2 (B).

COMMENT

Sebaceous carcinoma is a rare malignant skin appendage tumor occurring in the eyelids (75%) and extraocular (25%) locations. It occurs predominantly in female (2:1 female versus male ratio) at an average age of 65 years (2). The tumor usually presents as a slowly growing, firm, and painless nodule or mass. It can be locally aggressive with 20-25% distant metastasis.

Certain sebaceous carcinomas are now known to be associated with Muir-Torre syndrome and hereditary non-polyposis colorectal cancer (HNPCC) or Lynch syndrome through sharing of germ-line mutations in Mismatch repair genes. Such tumors demonstrate microsatellite instability at DNA level (3, 4). Muir-Torre syndrome is an autosomal dominant disorder with variable penetrance that consists of at least one sebaceous gland tumor (adenoma, epithelioma, or carcinoma) and a minimum of one internal malignancy such as colorectal carcinoma, genitourinary neoplasm or breast carcinoma. In a subgroup of Muir-Torre syndrome patients, the patients have germline DNA mismatch-repair (MMR) defect(s) and microsatellite instability, which is identical to the DNA defect of hereditary non-polyposis colorectal cancer (HNPCC) or Lynch syndrome. Therefore, Muir-Torre syndrome has been postulated as a variant of HNPCC or Lynch syndrome. Approximately 80% sebaceous gland malignancies show a loss of mismatch repair proteins (either MLH-1 or MSH-2) or microsatellite instability (3, 4).

In our patient, the sebaceous carcinoma cells have lost immunoreactivity of MSH-2 and MSH-6, which may suggest microsatellite instability. MSH-2 gene defect is commonly present in sebaceous carcinoma associated with Muir-Torre syndrome. However, the loss of MSH-6 is rarely seen in this malignancy. The mismatch repair gene defect or microsatellite instability is a strong risk factor for visceral neoplasms. Additional clinical investigation may be required for appropriate management of such patients.

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