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Endocrine mucin-producing sweat gland carcinoma of the eyelid associated with invasive mucinous adenocarcinoma

Endocrine mucin-producing sweat gland carcinoma (EMPSGC), a rare, low grade neoplasm with predilection for the eyelids, has been posited as a precursor to invasive mucinous adenocarcinoma. EMPSGC and its concurrence with mucinous adenocarcinoma have received little attention in the ophthalmic literature. The combination of the 2 histologic patterns parallels endocrine ductal carcinoma in situ (eDCIS) of the breast and its transition to type B invasive mucinous carcinoma.

History A healthy 59-year-old man noted enlarging painless tumor of the right upper eyelid over 4 months. Examination showed a firm, nontender, nodular skin lesion near the lateral canthus. The mass extended to lid margin with focal madarosis and no ulceration. It measured 1 cm x 1 cm, and was fixed to underlying tissue. No lymphadenopathy or other ocular abnormalities were present. The general medical and family histories were unremarkable. A complete medical examination, including colonoscopy, was negative.
Surgical excision of a full-thickness pentagonal wedge was achieved with a #15 blade leaving a 40% defect of the upper eyelid. A lateral canthotomy and cantholysis were performed, with creation of a reverse Tenzel semicircular advancement flap. The tarsal defect was closed with buried 5-0 chromic sutures. The grey and lash lines of the lid margin defect were closed with 6-0 silk sutures. A 4-0 PDS suture anchored the deep surface of the flap to the inner aspect of lateral orbital periosteal rim. A 7-0 Vicryl suture reformed the lateral commissure. Skin closure was achieved with a running 6-0 silk suture.

Pathologic examination showed skin containing an intradermal tumor that did not violate the surgical margins. The immediate subepithelial region contained multiple nodules of tumor consisting of medium-sized, bland-appearing round to oval cells including round nuclei with stippled chromatin and inconspicuous nucleoli. There was abundant, lightly eosinophilic cytoplasm. Some areas showed moderate pleomorphism. PAS, Alcian blue, and mucicarmine stains highlighted the presence of intracellular (perinuclear) and extracellular mucin, the latter present within clefts and small cysts. Mitotic activity was low but present. This pattern was consistent with the solid and cystic patterns of EMPSGC. A second architectural pattern that occupied the majority of the lesion consisted of abundant pools of mucin within which clumps of tumor cells that resembled those in the EMPSGC appeared to "float." The latter pattern exemplified invasive mucinous carcinoma.

Immunohistochemistry showed positivity in both patterns for chromogranin, synaptophysin, CD56, estrogen, progesterone, CK7, CAM5.2, GCDFP-15, and WT1. P63 immunostain highlighted a layer of myoepithelial cells at the periphery of some EMPSGC nests but not the invasive pattern Negative stains in both patterns included CK20 and CDX2 (militating against the histologic mimic of metastatic colon cancer) and p63. Ki67 shows a low proliferative pattern (about 5%) in both patterns.

Discussion: In 2005 a landmark study of EMPSGC noted a preponderance in the lower eyelids of elderly women.[1] "Small foci" of mucinous carcinoma were present in 6 of 12 cases, unlike the overwhelming portion in the current case. The EMPSGC multinodular patterns included solid, cystic and papillary varieties. Immunohistochemical endocrine and other markers paralleled those of the current case. Observing the presence of associated eccrine ducts, some showing carcinoma in situ , the authors hypothesized that EMPSGC was a

precursor of mucinous carcinoma, a postulate first proposed in 1997 by Flieder et al[2] who noted the resemblance of cutaneous EMPSGC and endocrine ductal carcinoma in situ of the breast.[3] A more recent study supports the derivation of invasive mucinous adenocarcinoma from EMPSGC demonstrating similar immunohistochemical profiles of "pure" EMPSGC, "pure" invasive mucinous sweat gland carcinomas and tumors having mixtures of each.[4] Another study, describing WT1 expression in EMPSCG (positive in the current case) noted co-existent mucinous carcinoma in only 1 of 13 cases highlighting the variable appearances of these tumors.[5]

Primary mucinous carcinoma lacking its EMPSCG precursor is well recognized to occur on the eyelid[6] as a low grade tumor with limited capacity for metastasis. While it has been shown to express estrogen and progesterone markers, a trait of many cutaneous adnexal tumors,[7] our case is one of only a few to illustrate neuroendocrine markers chromogranin, synaptophysin and CD56 in an eyelid mucinous carcinoma. Neuroendocrine immunostains have also been demonstrated in mucinous carcinoma elsewhere on the integument.[8,9] Our case supports the contention that primary mucinous sweat gland carcinomas arise from preexisting EMPSGC even in those cases wherein an EMPSGC component cannot be identified without serial sectioning.

Complete surgical excision is the recommended treatment for EMPSGC and mucinous carcinoma, including their synchronous presentation.[1] Mohs micrographic surgery has been utilized to ensure complete tumor extirpation.[10]

Periocular sweat gland carcinomas comprise a diverse group of rare tumors and are mostly low grade with slow growth and only exceptional metastases. Among these tumors only the microcystic adnexal carcinoma subtype exhibits aggressive clinical behavior.[11] The current synchronous tumors may be expected to show a benign course.

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