Pink Papule on the Lower Eyelid

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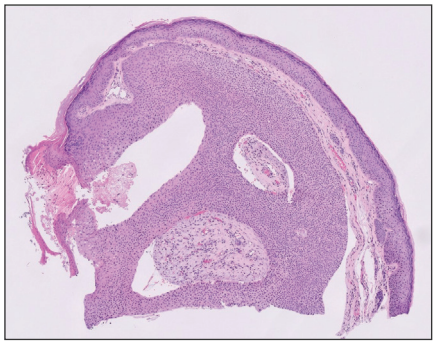

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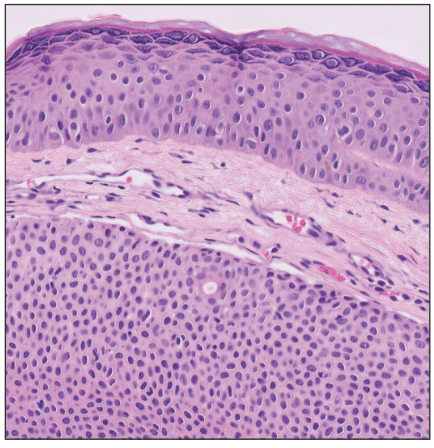

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A 57-year-old man with no notable medical history presented to the dermatology clinic for evaluation of an asymptomatic papule on the left lower eyelid. The patient reported that the lesion seemed to wax and wane in size over time. Physical examination revealed a small, pink, verrucous papule on the left lower eyelid. A shave biopsy of the lesion revealed a well-circumscribed collection of small, monomorphic, cuboidal cells with basophilic round nuclei, inconspicuous nucleoli, and compact eosinophilic cytoplasm (top) with focal areas of duct formation (bottom) that was sharply demarcated from normal keratinocytes.

THE BEST **DIAGNOSIS IS:**

a. basal cell carcinoma
b. poroma
c. spiradenoma
d. squamous cell carcinoma
e. syringoma

PLEASE TURN TO PAGE 100 FOR THE DIAGNOSIS

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The authors have no relevant financial disclosures to report.

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Cutis. 2025 March;115(3):94, 100-101. doi:10.12788/cutis.1175

THE **DIAGNOSIS:** Poroma

Poromas are benign adnexal neoplasms that often are classified into the broader category of acrospiromas. They most commonly affect areas with a high density of eccrine sweat glands, such as the palms and soles, but also can appear in any area of the body with sweat glands.[1] Poromas may have cuboidal eccrine cells with ovoid nuclei and a delicate vascularized stroma on histology or may show apocrinelike features with sebaceous cells.[2,3] Immunohistochemically, poromas stain positively for carcinoembryonic antigen, epithelial membrane antigen, and periodic acid–Schiff (PAS) with diastase sensitivity.[1,4] Cytokeratin (CK) 1 and CK-10 are expressed in the tumor nests.[1]

Poromas are the benign counterpart of porocarcinomas, which can recur and may become invasive and metastasize. Porocarcinomas have been shown to undergo malignant transformation from poromas as well as develop de novo.[5] Histologic differentiation between the 2 conditions is key in determining excisional margins for treatment and follow-up. Poromas are histologically similar to porocarcinomas, but the latter show invasion into the dermis, nuclear and cytoplasmic pleomorphism, nuclear hyperchromatism, and increased mitotic activity.[6] S-100 protein can be positive in porocarcinoma.[7] Both poromas and porocarcinomas are associated with Yes-associated protein 1 (*YAP1*), Mastermind-like protein 2 (*MAML2*), and NUT midline carcinoma family member 1 (*NUTM1*) gene fusions.[5]

Basal cell carcinoma (BCC) is the most common cutaneous malignancy. It rarely metastasizes but can be locally destructive.[8] Basal cell carcinomas typically occur on sun-exposed skin in middle-aged and elderly patients and classically manifest as pink or flesh-colored pearly papules with rolled borders and overlying telangiectasia.[9] Risk factors for BCC include a chronic sun exposure, lighter skin phenotypes, immunosuppression, and a family history of skin cancer. The 2 most common subtypes of BCC are nodular and superficial, which comprise around 85% of BCCs.[10] Histologically, nodular BCCs demonstrate nests of malignant basaloid cells with central disorganization, peripheral palisading, tumor-stroma clefting, and a mucoid stroma with spindle cells (Figure 1). Superficial BCC manifests with small islands of malignant basaloid cells with peripheral palisading that connect with the epidermis, often with a lichenoid inflammatory infiltrate.[9] Basal cell carcinomas stain positively for Ber-EP4 and are associated with patched 1 (*PTCH1*), patched 2 (*PTCH2*), and tumor protein 53 (*TP53*) gene mutations.[9,11]

Spiradenomas are benign adnexal tumors manifesting as painful, usually singular, 1- to 3-cm nodules in younger adults.[12] Histologically, spiradenomas have large clusters of small irregularly shaped aggregations of small basaloid and large polygonal cells with surrounding hyalinized

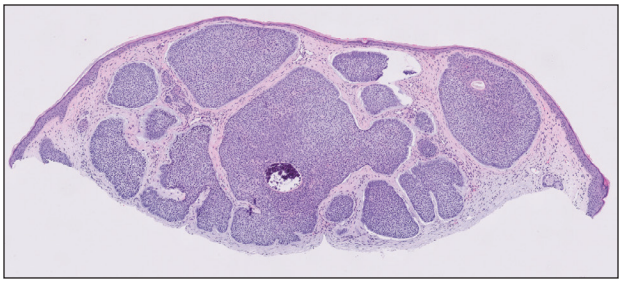

FIGURE 1. Basal cell carcinoma characterized by basaloid tumor islands with peripheral palisading and tumor-stromal retraction (H&E, original magnification ×20).

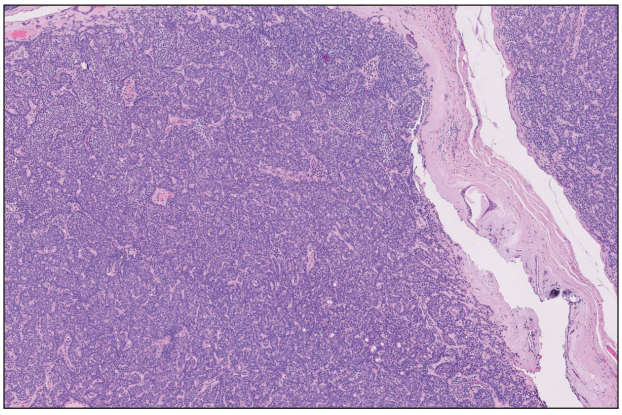

FIGURE 2. Well-circumscribed dermal basophilic tumor with ductal structures, basement membrane material arranged in trabeculae, and scattered lymphocytes throughout in the setting of spiradenoma (H&E, original magnification ×50).

basement membrane material and intratumoral lymphocytes (Figure 2).[4] Spiradenomas stain positive for p63, D2-40, and CK7 and are associated with cylindromatosis lysine 63 deubiquitinase (*CYLD*) and alpha-protein kinase 1 (*ALPK1*) gene mutations.[5]

Squamous cell carcinoma (SCC) is the second most common nonmelanoma skin cancer worldwide.[13] Lesions typically develop on sun-exposed skin and manifest as red, hyperkeratotic, and sometimes ulcerated plaques or nodules.[14] Risk factors for SCC include chronic sun exposure, lighter skin phenotypes, increased age, and immunosuppression. Histologically, there are several variants of SCC: low-risk variants include keratoacanthomas, verrucous carcinomas, and clear cell SCC, and high-risk variants include acantholytic SCC, spindle cell SCC, and adenosquamous carcinoma.[14] Generally, low-grade SCC will have well-differentiated or moderately differentiated intercellular bridges or keratin pearls with tumor cells in a solid or sheetlike pattern (Figure 3). High-grade SCC will be poorly

differentiated with the presence of infiltrating individual tumor cells.[15] Immunohistochemically, SCC stains positive for p63, p40, AE1/AE3, CK5/6, and MNF116 while Ber-Ep4 is negative.[14,15] Poorly differentiated SCCs have high rates of mutation, commonly in the tumor protein 53 (*TP53*), Cyclin-dependent kinase inhibitor 2A (*CDKN2A*), Ras pathway, and notch receptor 1 (*NOTCH-1*) genes.[13]

Syringomas are benign adnexal tumors that manifest as multiple soft, yellow to flesh-colored, 1- to 2-mm papules typically located on the lower eyelids, most commonly in women of reproductive age.[16] Syringomas are described on histology as small comma-shaped nests with cords of eosinophilic to clear cells with central ducts surrounded by a sclerotic stroma (Figure 4). They stain positively for carcinoembryonic antigen, epithelial membrane antigen, and CK-5 and are associated with genetic mutations in phosphatidylinositol-4, 5-bisphosphate 3-kinase catalytic subunit alpha (*PIK3CA*) and AKT serine/threonine kinase 1 (*ATK1*).[4]

Due to its regular exposure to sunlight, the eyelid accounts for 5% to 10% of all skin malignancies. Common eyelid lesions include squamous papilloma, seborrheic keratosis, epidermal inclusion cyst, hidrocystoma, intradermal nevus, BCC, SCC, and sebaceous carcinoma.[17] Aside from syringomas, benign sweat gland tumors like poromas, hidradenomas, and spiradenomas usually do not manifest on the eyelids but should be included in the differential diagnosis of an unidentifiable lesion due to the small risk for malignant transformation. Eyelid poromas manifest polymorphically, most commonly being clinically diagnosed as BCC, making the histologic examination key for proper diagnosis and management.[18]

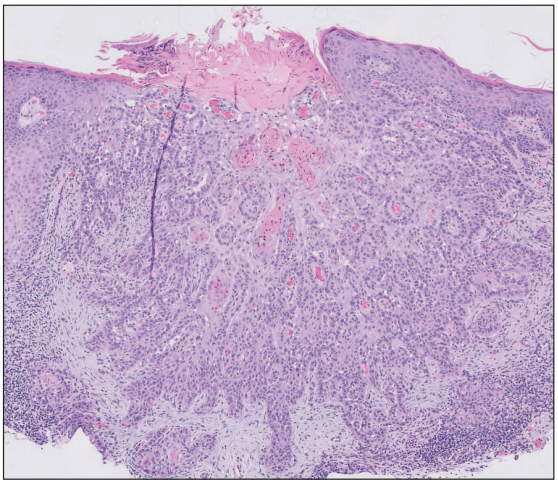

FIGURE 3. Squamous cell carcinoma manifesting with proliferation of atypical keratinocytes with abundant eosinophilic cytoplasm extending into the dermis and forming keratin pearls (H&E, original magnification ×50).

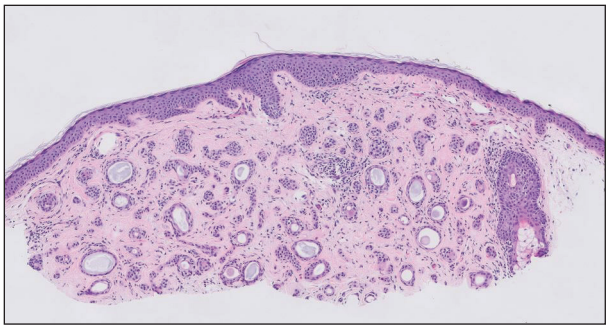

FIGURE 4. Syringoma with well-circumscribed proliferation of basaloid, cuboidal, and double-layered epithelial cells forming comma-shaped ducts as well as nests, cysts, and cords located primarily in the papillary dermis (H&E, original magnification ×50).

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