The best diagnosis is:

a. adenoid cystic carcinoma arising within a spiradenoma
b. cylindroma and spiradenoma collision tumor
c. microcystic change within a spiradenoma
d. mucinous carcinoma arising within a spiradenoma
e. trichoepithelioma and spiradenoma collision tumor
The coexistence of more than one cutaneous adnexal neoplasm in a single biopsy specimen is unusual and is most frequently recognized in the context of a nevus sebaceous or Brooke-Spiegler syndrome, an autosomal-dominant inherited disease characterized by cutaneous adnexal neoplasms, most commonly cylindromas and trichoepitheliomas.1-3 Brooke-Spiegler syndrome is caused by germline mutations in the cylindromatosis gene, CYLD, located on band 16q12; it functions as a tumor suppressor gene and has regulatory roles in development, immunity, and inflammation.1 Weyers et al3 first recognized the tendency for adnexal collision tumors to present in patients with Brooke-Spiegler syndrome; they reported a patient with Brooke-Spiegler syndrome with spiradenomas found in the immediate vicinity of trichoepitheliomas and in continuity with hair follicles.

Spiradenomas are composed of large, sharply demarcated, rounded nodules of basaloid cells with little cytoplasm (Figure 1).4 The basaloid nodules may demonstrate a trabecular architecture, and on close inspection 2 cell types—paler cells with more...
cytoplasm and darker cells with less cytoplasm—are
distinguishable (Figure 2A). Lymphocytes often are
scattered within the tumor nodules and/or stroma.
In Brooke-Spiegler syndrome, collision tumors con-
taining a spiradenomatous component in colli-
sion with trichoepithelioma are not uncommon.1
Spiradenomas in Brooke-Spiegler syndrome have
been reported to contain sebaceous differentiation
or foci with an adenoid cystic carcinoma (ACC)—
like pattern and are known to occur as hybrid lesions
of spiradenoma and cylindroma or trichoepithelioma
(as in this case).1,2

In this case, 2 distinct neoplasms (spirade-
noma and trichoepithelioma) are apparent, side by
side, with an intervening hair follicle (Figure 1). Trichoepitheliomas, also known as cribriform tricho-
blastosas,3 are characterized by lobules of basaloid
cells resembling basal cell carcinoma surrounded
by a fibroblast-rich stroma. They often contain
fingerlike projections and adopt a cribriform mor-
phology within the tumor lobules (Figure 2B).4
Numerous horn cysts may be present, but their
absence does not preclude the diagnosis. Mucin
may be present within the cribriform tumor islands
(Figure 2B) but not in the stroma. Characteristically, trichoepitheliomas are distinctly negative for
CK7 (Figure 3), and unlike spiradenomas, they lack
a myoepithelial component.6 This staining pattern
in combination with the tumor's proximity to an
adjacent hair follicle makes a diagnosis of tricho-
epithelioma and spiradenoma collision tumor
most likely and supports a clinical suspicion for
Brooke-Spiegler syndrome.

Although spiradenomas sometimes contain cys-
tic cavities (microcystic change), they typically are
filled with finely granular eosinophilic material,
not mucin, that is diastase resistant and periodic
acid–Schiff positive (Figure 4).7 Spiradenomas clas-
sically stain positive with CK7 (Figure 3), epithelial
membrane antigen, and carcinoembryonic antigen,
and have a substantial myoepithelial component, as
evidenced by the myoepithelial component staining
with p63, S-100, and smooth muscle actin (SMA).7,9
The distinct lack of staining with CK7 and SMA in
the tumor on the left in Figure 3 confirms that these
tumors are of different lineage, rather than represent-
ing cystic change within a spiradenoma.

Adenoid cystic carcinoma is a rare neoplasm that
may occur in a primary cutaneous form, as a direct
extension from an underlying salivary gland neo-
plasm, or rarely as a focal pattern within spiradeno-
mas occurring both sporadically or in the context of
Brooke-Spiegler syndrome.2,7 The tumor is composed
of variably sized cribriform islands of basaloid to
pink cells concentrically arranged around glandlike
spaces filled with mucin (Figure 5A). In contrast to
trichoepithelioma, ACC occurs in the mid to deep
dermis, often extending into subcutaneous fat with an
infiltrative border, and is not often found in close
proximity to hair follicles.7 Characteristically, hyaline
basement membrane–like material that is periodic
acid–Schiff positive is found between the tumor
cells and also surrounding the individual lobules.
Immunohistochemically, ACC has a myoepithelial
component that stains positive with SMA, S-100,
and p63; additionally, the tumor cells express
low- and high-molecular-weight keratin and dem-
onstrate variable epithelial membrane anti-
gen positivity.10 In the current case, the superficial
location, close association with a hair follicle, and
lack of staining with both CK7 (Figure 3) and SMA

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**Figure 3.** Positive staining with CK7 can be noted in the
spiradenoma (right) and negative staining is noted in the
trichoepithelioma (left) (original magnification ×3).

**Figure 4.** Cystic cavities within a spiradenoma are filled
with finely granular eosinophilic material, not mucin, that
is diastase resistant and periodic acid–Schiff positive
(H&E, original magnification ×30).
(not shown) make ACC arising within a spiradenoma a less likely diagnosis.

Cylindromas are composed of basaloid islands interconnected in a jigsaw puzzle configuration (Figure 5B).4 Similar to spiradenomas, they also are composed of 2 cell populations. Characteristically, the tumor islands are outlined by a hyalinized eosinophilic basement membrane. Hyalinized droplets of basement membrane zone material also may be noted in the islands. Unlike spiradenomas, they lack both intratumoral lymphocytes and a trabecular growth pattern. Although spiradenocylindromas (cylindroma and spiradenoma collision tumors) are perhaps the most common collision tumor associated with Brooke-Spiegler syndrome, there is no evidence suggesting the presence of a cylindroma in the current case.

Primary cutaneous mucinous carcinoma is a rare neoplasm with a predilection for the eyelids; lesions occurring outside of this facial distribution, particularly of the breast, warrant a workup for metastatic disease.7 It typically occurs in the deeper dermis with involvement of the subcutaneous fat and is characterized by delicate fibrous septa enveloping large lakes of mucin, which contain islands of tumor cells (Figure 6). It has not been reported in association with spiradenomas. In addition, the tumor cells typically are CK7 positive.

REFERENCES