MORPHOLOGY

All forms of acanthosis nigricans have similar histologic features. The epidermis and underlying enlarged dermal papillae undulate sharply to form numerous repeating peaks and valleys. Variable hyperplasia may be seen, along with hyperkeratosis and slight basal cell layer hyperpigmentation (but no melanocytic hyperplasia).

Fibroepithelial Polyp

The fibroepithelial polyp has many names (acrochordon, squamous papilloma, skin tag) and is one of the most common cutaneous lesions. It usually comes to attention in middle-aged and older individuals on the neck, trunk, face, and intertriginous areas. Rarely, fibroepithelial polyps and tumors of perifollicular mesenchyme (specialized fibroblasts associated with the hair bulb) are seen together in *Birt-Hogg-Dubé syndrome,* but the vast majority of polyps are sporadic.

MORPHOLOGY

Fibroepithelial polyps are soft, flesh-colored, bag-like tumors that are often attached to the surrounding skin by a slender stalk. On histologic examination these tumors consist of fibrovascular cores covered by benign squamous epithelium. It is not uncommon for the polyps to undergo ischemic necrosis due to torsion, which may cause pain and precipitate their removal.

Fibroepithelial polyps are usually inconsequential, but can occasionally be associated with diabetes, obesity, and intestinal polyposis. Of interest, like melanocytic nevi and hemangiomas, they often become more numerous or prominent during pregnancy, presumably related to hormonal stimulation.

Epithelial or Follicular Inclusion Cyst (Wen)

Epithelial cysts are common lesions formed by the invagination and cystic expansion of the epidermis or, perhaps more commonly, a hair follicle. The lay term, *wen,* derives from the Anglo-Saxon *wenn*, meaning a lump or tumor. When large they may be subject to traumatic rupture, which can spill keratin into the dermis and lead to an extensive and often painful granulomatous inflammatory response.

Adnexal (Appendage) Tumors

There are literally hundreds of neoplasms arising from or showing differentiation toward cutaneous appendages. Their significance varies according to type and clinical context.

- Some are entirely benign, but may be confused with cutaneous cancers such as basal cell carcinoma.
- Other appendage tumors are associated with mendelian patterns of inheritance and occur as multiple disfiguring lesions.
- In some instances, these lesions warn of a predisposition for internal malignancy; such is the relationship between multiple *trichilemmomas* and *Cowden syndrome*, a disorder caused by germline loss of function mutations in the tumor suppressor gene *PTEN* that is associated with an increased risk of endometrial cancer, breast cancer, and many other tumors.

Appendage tumors are often nondescript, flesh-colored solitary or multiple papules and nodules. Some have a predisposition to occur on specific body surfaces. Selected examples are provided here to illustrate neoplasms of hair follicles and sebaceous, eccrine, and apocrine glands.

- *Eccrine poroma* occurs predominantly on the palms and soles where sweat glands are numerous.
- *Cylindroma*, an appendage tumor with ductal (apocrine or eccrine) differentiation, usually occurs on the forehead and scalp (Fig. 25-10*A*), where coalescence of nodules with time may produce a hatlike growth, hence the name *turban tumor.* These lesions may be dominantly inherited; in such cases they appear early in life and are associated with inactivating mutations in the tumor suppressor gene *CYLD*, which encodes a deubiquitinating enzyme that negatively regulates the oncogenic transcription factor NF-κB and other factors that contribute to cell cycle progression. In addition to familial cylindromatosis, germline mutations in *CYLD* are associated with two other genetic syndromes marked by the occurrence of multiple adnexal tumors, multiple *familial trichoepithelioma* (a follicular tumor) and *Brooke-Spiegler syndrome* (associated with both trichoepithelioma and cylindroma).
- *Syringomas,* lesions with eccrine differentiation, usually occur as multiple, small, tan papules in the vicinity of the lower eyelids.
- *Sebaceous adenomas* can be associated with internal malignancy in the *Muir-Torre syndrome,* a subset of the hereditary nonpolyposis colorectal carcinoma syndrome (Chapter 17) associated with germline deficits in DNA mismatch repair proteins.
- *Pilomatricomas,* showing follicular differentiation, are associated with activating mutations in *CTNNB1*, the gene encoding β-catenin. Mutations in this gene are seen in numerous neoplasms but are of interest here since Wnt signaling through β-catenin is critical for early hair development and regulates hair growth and maintenance.
- Adnexal tumors can also show primarily apocrine differentiation; these usually arise in body areas where apocrine glands are most prevalent, such as the axilla and scalp. Some skin adnexal tumors may arise from multipotent cutaneous stem cells, which are believed to reside in a specialized niche associated with hair follicles.

MORPHOLOGY

The **cylindroma** is composed of islands of cells resembling those of the normal epidermal or adnexal basal cell layer (basaloid cells). These islands fit together like pieces of a jigsaw puzzle within a fibrous dermal matrix (Fig. 25-10*B*).