frequent causes of SIADH are the secretion of ectopic ADH by malignant neoplasms (particularly small-cell carcinoma of the lung), drugs that increase ADH secretion, and a variety of central nervous system disorders, including infections and trauma. The clinical manifestations of SIADH are dominated by hyponatremia, cerebral edema, and resultant neurologic dysfunction. Although total body water is increased, blood volume remains normal, and peripheral edema does not develop.

Hypothalamic Suprasellar Tumors

Neoplasms in this location may induce hypofunction or hyperfunction of the anterior pituitary, diabetes insipidus, or combinations of these manifestations. The most commonly implicated tumors are *gliomas* (sometimes arising in the chiasm; Chapter 28) and *craniopharyngiomas*. The craniopharyngioma is thought to arise from vestigial remnants of Rathke pouch. These slow-growing tumors account for 1% to 5% of intracranial tumors. A small minority of these lesions occurs within the sella, but most are suprasellar, with or without intrasellar extension. A bimodal age distribution is observed, with one peak in childhood (5 to 15 years) and a second peak in adults 65 years or older. Patients usually come to attention because of headaches and visual disturbances, while children sometimes present with growth retardation due to pituitary hypofunction and GH deficiency. Abnormalities of the *WNT signaling pathway*, including activating mutations of the gene encoding β-catenin, have been reported in craniopharyngiomas.

MORPHOLOGY

Craniopharyngiomas average 3 to 4 cm in diameter; they may be encapsulated and solid, but more commonly they are cystic and sometimes multiloculated. They often encroach on the optic chiasm or cranial nerves, and not infrequently they bulge into the floor of the third ventricle and base of the brain. Two distinct histologic variants are recognized: **adamantinomatous craniopharyngioma** (most often observed in children) and **papillary craniopharyngioma** (most often observed in adults). The adamantinomatous type frequently contains radiologically demonstrable calcifications; the papillary variant calcifies only rarely.

Adamantinomatous craniopharyngioma consists of nests or cords of stratified squamous epithelium embedded in a spongy "reticulum" that becomes more prominent in the internal layers. "Palisading" of the squamous epithelium is frequently observed at the periphery. Compact, lamellar keratin formation ("wet keratin") is a diagnostic feature of this tumor (Fig. 24-7). As mentioned earlier, **dystrophic calcification** is a frequent finding. Additional features include cyst formation, fibrosis, and chronic inflammation. The cysts of adamantinomatous craniopharyngiomas often contain a cholesterol-rich, thick brownish-yellow fluid that has been compared to "machine oil." These tumors extend fingerlets of epithelium into adjacent brain, where they elicit a brisk glial reaction.

Papillary craniopharyngiomas contain both solid sheets and papillae lined by well-differentiated squamous epithelium. These tumors usually lack keratin, calcification, and cysts. The squamous cells of the solid sections of the tumor lack the peripheral palisading and do not typically generate a spongy reticulum in the internal layers.

Patients with craniopharyngiomas, especially those less than 5 cm in diameter, have an excellent recurrence-free and overall survival. Larger lesions are more invasive but this does not impact on the prognosis. Malignant transformation of craniopharyngiomas into squamous carcinomas is exceptionally rare and usually occurs after irradiation.

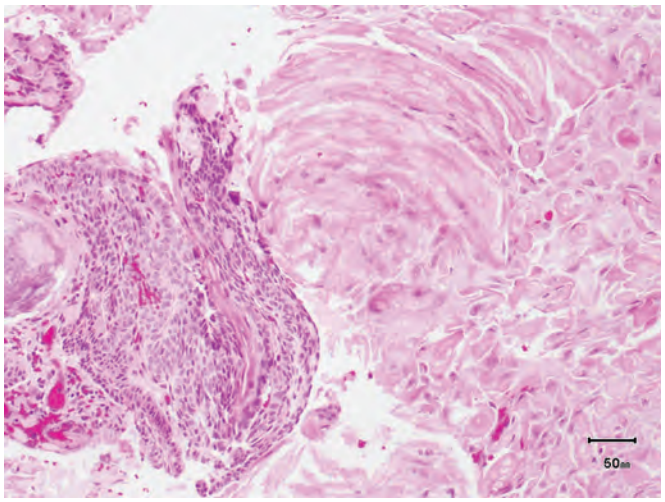

Figure 24-7 Adamantinomatous craniopharyngioma, demonstrating characteristic compact, lamellar "wet" keratin (right half of photomicrograph) and cords of squamous epithelium with peripheral palisading on the left. (Courtesy Dr. Charles Eberhart, Department of Pathology, Johns Hopkins University, Baltimore, Md.)

THYROID GLAND

The thyroid gland, usually located below and anterior to the larynx, consists of two bulky lateral lobes connected by a relatively thin isthmus. The thyroid is divided by thin fibrous septae into lobules composed of about 20 to 40 evenly dispersed follicles, lined by a cuboidal to low columnar epithelium, and filled with PAS-positive thyroglobulin. In response to hypothalamic factors, TSH *(thyrotropin)* is released by thyrotrophs in the anterior pituitary into the circulation. The binding of TSH to its receptor on the thyroid follicular epithelium results in activation of the receptor, allowing it to associate with a G_s protein (Fig. 24-8). Activation of the G protein stimulates downstream