Tumors of the Nose, Sinuses, and Nasopharynx

Tumors in the nose, sinuses, and nasopharynx are infrequent but include the wide spectrum of mesenchymal and epithelial neoplasms. Distinctive types are described here.

Nasopharyngeal Angiofibroma. **Nasopharyngeal angiofibroma is a benign, highly vascular tumor that occurs almost exclusively in adolescent males who are often fair-skinned and red headed.** There is also an association with familial adenomatous polyps. It is believed to arise within the fibrovascular stroma of the posterolateral wall of the roof of the nasal cavity. Surgical removal is the treatment of choice. However, because of its locally aggressive nature and intracranial extension, recurrence rates can be as high as 20%. In about 9% of cases it is fatal, with death being caused by hemorrhage and intracranial extension.

Sinonasal (Schneiderian) Papilloma. **Sinonasal papilloma is a benign neoplasm arising from the respiratory or schneiderian mucosa lining the nasal cavity and paranasal sinuses.** These lesions occur in three forms: *exophytic* (most common), endophytic (*inverted*; most important biologically), and *cylindrical*. HPV DNA, often types 6 and 11, has been identified in the exophytic and endophytic lesions, but not the cylindrical type. Sinonasal papillomas are observed most commonly in adult males between the ages of 30 and 60. Because of its uniquely aggressive biologic behavior, only the endophytic form is discussed here. Endophytic sinonasal papillomas are benign but locally aggressive neoplasms occurring in both the nose and the paranasal sinuses. As the name implies, the papillomatous proliferation of squamous epithelium, instead of producing an exophytic growth, invaginates into the underlying stroma (Fig. 16-9). It has a high rate of recurrence if not adequately excised, with the potentially serious complication of invasion of the orbit or cranial vault. Furthermore, malignant transformation is observed in approximately 10% of cases.

Olfactory Neuroblastoma (Esthesioneuroblastoma). **Olfactory neuroblastomas arise from the neuroectodermal olfactory cells present within the mucosa, particularly in the superior aspect of the nasal cavity.** There is a bimodal age distribution with peaks at 15 and 50 years of age. The patients typically present with nasal obstruction and/or epistaxis. Histologically, olfactory neuroblastomas are one of the small, blue, round cell neoplasms that include lymphoma, small cell carcinoma, Ewing sarcoma/peripheral neuroectodermal tumor, rhabdomyosarcoma, melanoma, and sinonasal undifferentiated carcinoma. Typically, olfactory neuroblastomas are composed of nests and lobules of well-circumscribed cells that are separated by a fibrovascular stroma. Many of the tumors also contain a fibrillary matrix that ultrastructurally corresponds to tangles of neuronal cell processes. Because these neoplasms are of neuroendocrine origin, the tumor cells contain membrane-bound secretory granules on electron microscopy and express neuron-specific enolase, synaptophysin, CD56, and chromogranin by immunohistochemistry. Depending on the stage and grade of a particular neoplasm, combinations of surgery, radiation therapy, and chemotherapy yield 5-year survival rates of 40% to 90%.

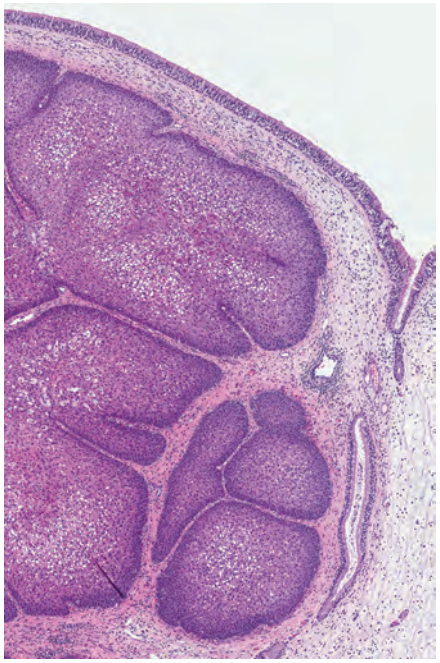

Figure 16-9 Inverted papilloma. The masses of squamous epithelium are growing inward; hence, the term *inverted*.

NUT Midline Carcinoma. This is an uncommon tumor that may occur in the nasopharynx, the salivary gland, or in other midline structures in the thorax or abdomen. It can occur at any age, from infancy to late adulthood. Its true incidence is not known, as it easily mistaken for squamous cell carcinoma, which it resembles morphologically. It is extremely aggressive and resistant to conventional therapy; as a result, most patients survive for less than a year following diagnosis.

Although rare, NUT midline carcinoma is pathogenically interesting. It is uniformly associated with translocations that create fusion genes encoding chimeric proteins comprised of most of NUT, a chromatin regulator, and a portion of a "chromatin reader" protein, usually BRD4. Drugs that displace BRD4-NUT from chromatin induce NUT midline carcinoma cells to terminally differentiate, a mechanism of oncogenesis that is common in acute leukemias but unusual for epithelial cancers. Targeted therapy with BRD4-NUT inhibitors is now being tested in the clinic and offers hope for those with this lethal form of cancer.

Nasopharyngeal Carcinoma. **Nasopharyngeal carcinoma is characterized by a distinctive geographic distribution, a close anatomic relationship to lymphoid tissue, and an association with EBV infection.** The nomenclature for nasopharyngeal carcinomas is in constant flux. However, at present the disease is thought to take one of three patterns: (1) keratinizing squamous cell carcinomas, (2) nonkeratinizing squamous cell carcinomas, and (3) undifferentiated/basaloid carcinomas that have an abundant non-neoplastic, lymphocytic infiltrate. The last pattern has often been called *lymphoepithelioma.* While widely used in clinical practice, this descriptive term should be avoided.