# Glandular Neoplasia of the Sinonasal Tract

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**KEYWORDS**

• Adenocarcinoma • Nasal • Papillary • Intestinal • Respiratory epithelial adenomatoid hamartoma • Seromucinous hamartoma • Sinonasal • Sinus

**Key Features**

- A few well-described glandular lesions have been described that occur within the sinonasal tract. These include so-called hamartomas as well as adenocarcinomas.
- The pathologist must be able to distinguish these lesions from one another and from other sinonasal lesions owing to the vastly different prognoses and treatments for these lesions.

## ABSTRACT

Glandular lesions that cannot be diagnosed readily as salivary gland tumors occur uncommonly in the upper aerodigestive tract. They occur only with some frequency within the sinonasal tract. Well-characterized lesions at this site include the respiratory epithelial adenomatoid hamartoma, seromucinous hamartoma, and intestinal and non–intestinal-type adenocarcinomas. This article reviews the clinicopathologic features of these fascinating lesions.

## OVERVIEW

As with the mouth, the sinonasal tract forms during embryogenesis from the ectoderm, although true skin appendageal structures extend only into the distal nares.[1] The majority of the remaining tract is covered with a ciliated columnar or respiratory-type epithelium with occasional goblet cells and underlying seromucinous glands. Squamous and mucinous metaplasia can be present in varying quantities and degrees throughout the tract, usually as a response to injury. Focally, usually at the very apex of the tract, the mucosa is lined by olfactory mucosa. This layer is a specialized mucosa composed of tall, eosinophilic supporting cells, elongated, ciliated olfactory neurons, and small, basally located cells.

As with other sites of the upper aerodigestive tract, squamous cell carcinoma is the most common malignancy and even neoplasm of the sinonasal tract. At this site, however, squamous cell carcinoma accounts for a lesser percentage of overall neoplasia and malignancy than it does throughout other components of the upper aerodigestive tract. Not surprising, salivary gland–type neoplasia account for the second most frequent neoplasia seen here and the majority of the array of named salivary gland tumors have been identified at this site.

After excluding squamous cell carcinoma and salivary gland–type neoplasia, things get quite interesting, however. Within the sinonasal tract, a variety of distinct and less distinct glandular neoplasms occur, lesions that are almost unheard of within the remainder of the tract. This article explores the fascinating array of benign and malignant glandular tumors that have described primary to the sinonasal tract.

## BENIGN TUMORS

Benign glandular tumors unique to the sinonasal tract have, for better or worse, been generally termed "hamartomas." These include the respiratory epithelial adenomatoid hamartoma (REAH) and the seromucinous hamartoma (SMH).

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Surgical Pathology 10 (2017) 89–102
http://dx.doi.org/10.1016/j.path.2016.10.004

## RESPIRATORY EPITHELIAL ADENOMATOID HAMARTOMA

The term "hamartoma" has been used to describe a number of disparate lesions of the nasopharynx and sinonasal tract throughout the years. The first major synthesis and potential identification of a unique entity was made by Wenig and Heffner.[2] They identified 31 lesions with consistent histologic features that they named REAH.

Nearly 90% of patients with REAHs are men and the reported patient ages have ranged from 27 to 81 years (median, 58).[2–6] Symptoms include obstruction, stuffiness, epistaxis, postnasal drainage, and chronic rhinosinusitis. Sites of occurrence include the nasal septum, lateral nasal wall, ethmoid sinus, maxillary sinus, frontal sinus, and nasopharynx. Approximately 70% of REAHs occur in the nasal cavity, usually along the posterior nasal septum–olfactory cleft.[7,8]

REAHs are circumscribed and polypoid, and have been reported to measure up to 5 cm in size. A stalk has sometimes been noted. On cut surface, lesions are firm, tan-white, and solid with occasional cystic foci. The surfaces are covered by ciliated respiratory epithelium, which is in direct continuity with well-developed, branching glands lined chiefly with ciliated respiratory epithelial cells (**Fig. 1**).[2,6] Sometimes, the epithelium is cuboidal or flat and mucous gland metaplasia may also be present (see **Fig. 1**). Numerous glands with mucinous luminal contents may be observed, and these are sometimes dilated. A seromucinous gland hyperplasia is sometimes seen and there may be stromal hyalinization. Other nonspecific changes include stromal edema, increased vascularity, and a mixed acute and chronic inflammatory infiltrate. Noted conditions found coincidentally have included inverted papilloma and solitary fibrous tumor. Lymphangiomatous proliferation and osseous metaplasia have been seen rarely within the REAH. Foci of squamous metaplasia may be present. The fibrovascular stroma sometimes has foci of metaplastic bone or lymphoid follicles.[5] When bone is present, some have referred to such lesions as chondroosseous respiratory epithelial hamartomas.[5]

As mentioned, there is some controversy as to whether these lesions are hyperplastic or neoplastic. The distribution of disease and association with chronic rhinosinusitis suggest a reactive process, but an early study by Ozolek and Hunt[9] showed REAHs to have increased fractional allelic loss (31%) when compared with polypoid sinusitis. The most loss occurred on 9p and 18q near the p16 and SMAD4 genes, respectively.

The typical REAH should be distinguished from an inflammatory polyp and Schneiderian papilloma. Unlike inflammatory polyps, REAHs occur as single lesions and are usually present on the posterior nasal septum. Other features that favor a diagnosis of REAH over inflammatory polyp include a greater quantity of glandular proliferation, basement membrane material enveloping the glands, and atrophic epithelial changes. Schneiderian papillomas have a thickened, proliferating epithelium with intraepithelial mucous cysts and acute inflammation. Another very important consideration in the differential diagnosis is chondromesenchymal hamartoma.[10] These lesions frequently have a REAH-like glandular proliferation associated with nests of differentiated chondroid material and loose stromal elements (**Fig. 2**). These lesions typically occur in children and may be a manifestation of a germline

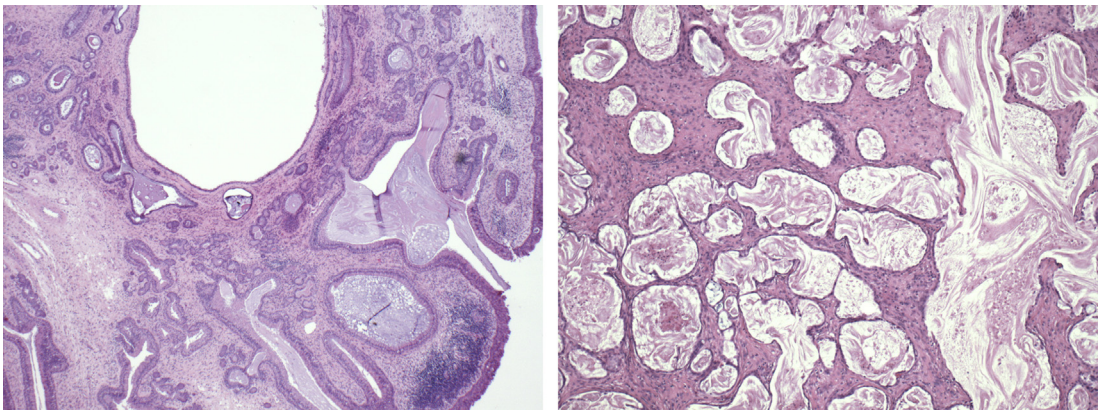

*Fig. 1.* Respiratory epithelial adenomatoid hamartoma (REAH). (*Left*) Typical low-power image of REAH with numerous dilated glands lined by a respiratory-type epithelium (H&E, ×40). (*Right*) Mucinous change may be prominent (H&E, ×100).