

A Rare and Unique Sinonasal Entity, Respiratory Epithelial Adenomatoid Hamartoma - Report of Two Cases from a Single Institute

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Abstract: Respiratory epithelial adenomatoid hamartoma (REAH) is a very rare benign lesion characterized by an adenomatoid proliferation of respiratory ciliated cells occurring in the nasal cavity, paranasal sinuses, and nasopharynx. It is important to distinguish REAH from other neoplastic processes that may lead to overly aggressive treatment. We present two cases of REAH reported in our institution.

Keywords: Respiratory epithelial adenomatoid hamartoma, benign lesion, nasal cavity, rhinorrhea.

INTRODUCTION

Respiratory epithelial adenomatoid hamartoma (REAH) is a very rare benign lesion characterized by an adenomatoid proliferation of respiratory ciliated cells occurring in the nasal cavity, paranasal sinuses, and nasopharynx [1]. It is important to distinguish REAH from other neoplastic processes that may lead to overly aggressive treatment [2].

Case 1:

A 29 year old male presented with difficulty in breathing of 2 months duration. He had past history of recurrent sinusitis. Anterior rhinoscopy showed a polypoidal mass in the right nasal cavity. CT imaging revealed deviated nasal septum to left side and ill defined soft tissue mass in right nasal cavity and maxillary sinus. There were no destructive bone changes. A clinical diagnosis of AC polyp was made. Patient underwent functional endoscopic sinus surgery under general anaesthesia. A large polypoidal mass was seen occupying most of the right nasal cavity and maxillary sinus and it was completely removed.

Grossly mass was polypoidal, measuring 5x3x2cm with mucoid, glistening surface. Cut section showed solid uniform grey white appearance. Histological examination revealed unencapsulated lesion composed of well-formed, tubular, glandular and cystic glandular elements of various sizes lined with cuboidal to columnar epithelial cells. The surface of the lesion was lined with ciliated respiratory epithelium in a

direct continuity with some of the glands. Cystic glands containing mucus material were present. There was stromal hyalinization, stromal oedema, sero mucinous glands proliferation, increased vascularity and a mixed inflammatory infiltrates. There was no cellular pleomorphism or atypical mitosis. A histological diagnosis of Respiratory Epithelial Adenomatoid Hamartoma (REAH) was made.

Case 2:

A 50 year old male patient presented with rhinorrhea and nasal obstruction. Chest X-ray, electrocardiogram, complete blood picture, blood urea and serum creatinine were all within normal limits. Clinical examination revealed polypoid mass in the olfactory region. CT scan findings suggested bilateral sinonasal polyposis. The mass was removed and sent for histopathological examination.

On Gross, it was a polypoid greyish glistening mass measuring 1x0.8 cm. On microscopy, sections showed round to oval glandular structures lined by ciliated columnar respiratory type of epithelium. These epithelial structures are surrounded by dense eosinophilic hyaline basement membrane. Gland lumen showed amorphous material. Stroma is fibrous with scant inflammatory infiltrate. (Fig: 1) Based on these histological features, a diagnosis of Respiratory Epithelial Adenomatoid Hamartoma (REAH) was made.

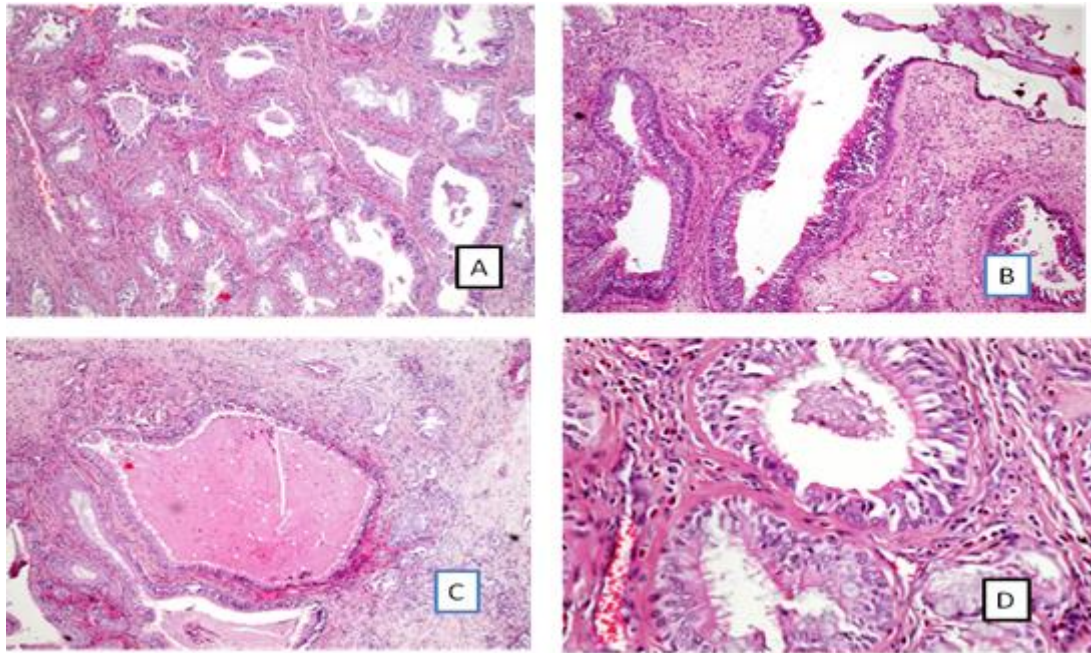


Fig 1: A: Glandular proliferation separated by stromal tissue composed of multilayered ciliated pseudo stratified epithelium. B: Glands arising in direct continuity with surface epithelium. C: Glandular dilatation distended with mucus. D: stromal hyalinisation with envelopment of glands by thickened eosinophilic basement membrane.

DISCUSSION:

Respiratory epithelial adenomatoid hamartoma (REAH) was first described by Wenig and Heffner in 1995 as a benign overgrowth of ciliated respiratory lined glands in submucosa, forming a polypoid mass lesion [3, 4]. Around 60 cases have been reported in the literature till 2008, confirming the uncommon nature of this proliferation [5].

REAH occurs in adult patients, the median age of diagnosis being situated in the sixth decade, with predominance in males. Age ranges from 27 to 81 years with a median age of 58 years. [3] Patients present with nasal obstruction, nasal stuffiness, epistaxis, chronic (recurrent) rhino sinusitis, cacosmia with posterior rhinorrhea [6, 7].

The lesion appears as a polypoid mass most commonly arising in the posterior septum. The majority occur in the nasal cavity, in particular the posterior nasal septum, nasopharynx, olfactory recesses, ethmoid sinus and frontal sinus. Most are unilateral, but some may be bilateral [1, 6].

Radiologically, the most common finding of REAH is an opacification of the affected sinus and connection to the nasal septum. [5] It has been recognized that the computed tomography scans of bilateral disease display a characteristic widening of the olfactory clefts, trait that is essential in distinguishing REAH from sinonasal polyps [2].

Grossly these lesions are typically polypoid or exophytic with a rubbery consistency, tan white to red-

brown appearance, measuring up to 6 cm in greatest dimension.[6] Microscopically characterized by a benign proliferation of round to oval, hamartomatous glandular structures composed of multilayered ciliated respiratory epithelium often with admixed mucocytes, surrounded by a thick, eosinophilic, hyalinized basement membrane. [1, 6] The glandular lumina contain mucinous or amorphous material. The surface of the lesion is lined with ciliated respiratory epithelium in a direct continuity with some of the glands, creating a tubular appearance with elongated invaginations into the underlying loose myxoid lamina propria [7]. Small mucoserous (salivary) glands are also occasionally seen. Whether they are part of the hamartoma or just a reactive hyperplastic response to the inflammation is uncertain, although the latter is favoured [6, 8].

REAHs are most often confused with ordinary Sinonasal polyps, Inverted papillomas, Seromucinous hamartoma and low grade adenocarcinomas [3, 9]. Sinonasal polyps inflammatory do not have florid adenomatoid proliferation and stromal hyalinization which, when present, favor REAH.[5] Inverted papilloma, has characteristic multistratified epithelium as opposed to the pseudo stratified ciliated columnar epithelium seen in REAH. In addition, the intraepithelial neutrophil infiltrate seen in inverted papilloma is absent in REAH and inverted papilloma lacks the thick basement membrane characteristic to REAH [10]. Seromucinous hamartoma is a tubular proliferation reminiscent of normal serous glands, which may be associated with REAH. Weinreb et al consider REAH and sero mucinous hamartoma represent different stages of a spectrum of progression

rather than distinct entities [4,10]. Sinonasal Adenocarcinoma is characterized by back to back arrangement of their glands, occasional nuclear pleomorphism, prominent mitotic activity, and a desmoplastic response to stromal invasion. These features are not seen in REAH [8]. The distinction of REAH with florid mucinous metaplasia from low-grade adenocarcinoma can be challenging particularly in the setting of small biopsy sample [11].

Immunohistochemistry is not used for diagnosis, but could be useful in differential diagnosis. The p63 and 34bE12 basal layer are seen in REAH and the overlying respiratory epithelium.[4] Benign lesions; REAH, Chronic Sinusitis and Inverted papilloma, share similar immunoprofiles (CK7+, CK20-, and CDX-2-) contrasting with Sinonasal Adenocarcinomas (CK7+, CK20+/-, CDX-2-/+) [1,5,12].

Recent molecular genetic studies have also challenged REAH's original classification as a hamartoma. Genetic profile of REAH, fractional allelic loss of 31%. High loss of heterozygosity rate (chromosome 9p and 18 q) raises the possibility that REAHs may represent a benign neoplasm instead of a developmental malformation. [13] Complete surgical resection is curative, usually performed via endoscopic sinus surgery [10].

CONCLUSION:

REAH is a rare and unique entity with distinctive morphologic features. Histologic diagnosis can be challenging, especially if the biopsy specimens are small and REAH can be easily mistaken for other more common and more aggressive entities that arise in the sinonasal tract.

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