Huge Respiratory Epithelial Adenomatoid Hamartoma Originating from the Inferior Nasal Turbinate: A Case Report

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Abstract Respiratory epithelial adenomatoid hamartoma (REAH) is a recently described entity consisted of benign glandular proliferations lined by pseudostratified respiratory epithelium. We report a case of a 22-year-old male patient with 7-year history of nasal obstruction and headache resulting from a huge left-sided nasal lesion. Computed tomography, magnetic resonance and biopsy were performed to make a provisional diagnosis of REAH originating from the left-sided inferior turbinate. The definitive diagnosis of REAH was made by histopathological examination of the removed mass. We also discuss the origin and differential diagnosis of these rare lesions.

Keywords Respiratory epithelial adenomatoid hamartoma · Inferior turbinate · Surgical treatment · Histopathological analysis

Introduction

Hamartomas can be defined as non-neoplastic developmental malformations characterized by an admixture of tissues indigenous to a part of the body with an excess of one or more of the cellular components. Respiratory

epithelial adenomatoid hamartoma (REAH) was first described in 1995 by Wenig and Heffner [1], as prominent benign glandular proliferations lined by ciliated respiratory epithelium originating from the surface epithelium forming a polypoid mass lesion. The etiology of REAH is unknown. The most accepted hypothesis suggests that REAH is a result of chronic inflammation of the nasal mucosa and frequently associated with chronic rhinosinusitis with or without nasal polyps, allergic rhinitis and bronchial asthma [2]. On the other hand, molecular genetic findings, as presented by Ozolek and Hunt, suggest that REAH may in fact be a benign neoplasm and not a hamartoma, as it was originally believed [3]. About 70 % of REAHs occur in the nasal cavity, most often originated from the posterior part of the nasal septum [2]. Bilaterality has also been reported, along with involvement of the paranasal sinuses and olfactory clefts [1, 4]. An imaging evidence of olfactory cleft expansion associated with REAHs has been demonstrated by Lima et al. [5], implicating the olfactory cleft as a potential site of origin rather than nasal septum. We describe a case of a huge REAH arising from the posterior portion of the inferior nasal turbinate which was radiologically also characterized by enlargement of the olfactory cleft.

Case Report

A 22-year-old male patient presented to our Ear, Nose and Throat Department with a 7-year history of progressive nasal obstruction, nasal discharge, headache, posterior rhinorrhea and foetor ex ore. The nasal obstruction was firstly left-sided and, during the time, became bilateral. He had smoked for 5 years. The patient denied any past history including chronic sinonasal inflammation, allergic rhinitis and surgical treatment of the diseases of the nose and

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paranasal sinuses. Anterior rhinoscopy and endoscopic examination showed a huge polypoid mass obstructing the left nasal cavity. The right nasal cavity was narrowed by dislocated and deformed nasal septum. Computed tomography (CT) scan showed the presence of a large soft-tissue mass in the left nasal cavity pushing the nasal septum to the right lateral nasal wall and left-sided middle turbinate to the left lateral nasal wall, and an enlargement of the left olfactory cleft. We also found the complete opacification of the left ethmoid sinus and partial opacification of the left maxillary sinus. There was no evidence for bony destruction (Fig. 1a, b). Magnetic resonance imaging (MRI) showed low intensity in the central part of the lesion and high intensity around its circumference. A preoperative punch biopsy of the mass suggested the diagnosis of benign glandular lesion. Left lateral rhinotomy was performed under general anesthesia and the mass was completely excised. The tumor was found to have arisen from the posterior part of the left inferior turbinate, extending from the left nasal cavity and pushing the nasal septum to the right nasal wall. We performed an endoscopic examination of upper nasal cavity and we found the left lamina cribrosa was complete after the surgery. In the left middle meatus we found no polypoid lesions. The resected mass was smooth, hard and elastic, yellow-to-pink in color and it measured $9 \times 6 \times 3$ cm in size. Histopathological examination revealed that the mass was covered with pseudostratified respiratory ciliated epithelium and composed of proliferated medium sized glands resulting from an invagination of the surface respiratory epithelium (Fig. 2a). The glands consisted of columnar epithelial cells, sheltering mucus secreting cells, and there was no evidence of metaplasia or cellular atypia. The stroma was edematous and consisted of an inflammatory infiltrate, composed of diffusely spread lymphocytes, plasma cells and eosinophils (Fig. 2b). We diagnosed the lesion as a REAH. The post-operative period was uneventful and there was no evidence of recurrence 5 years after surgery.

Discussion

Hamartomas do not clearly represent either neoplastic or inflammatory disorders. In contrast to neoplasms, hamartomas have no capacity for continuous unimpeded growth and their proliferation is self-limiting. Hamartomas have no malignant potential and no tendency to regress spontaneously. The mechanisms that induce hamartoma growth remain unknown, but it has been speculated that they arise as a result of an underlying inflammatory process [6]. It is very interesting a frequent association between nasal polyposis and bilateral REAH of the olfactory cleft. Nguyen et al. [7] found that the development of REAH in

Fig. 1 Coronal (a) and axial (b) CT scan showed the presence of a huge soft-tissue mass in the left nasal cavity pushing the nasal septum to the right lateral nasal wall and left-sided middle turbinate to the left lateral nasal wall, and an enlargement of the left olfactory cleft. We also found the complete opacification of the left ethmoid sinus and partial opacification of the left maxillary sinus. There was no evidence for bony destruction

patients with nasal polyposis is induced by a long-lasting and/or severe inflammation of the nasal mucosa in the olfactory cleft region. A subtype of REAH, chondro-osseous respiratory epithelial adenomatoid hamartoma (COREAH) is an extremely rare entity that contains islands of cartilage and mature bone interspersed throughout the lesion [8].

The differential diagnosis of REAH includes nasal polyposis, inverted papilloma, and sinonasal adenocarcinoma. In contrast to REAH, which more commonly originate from the nasal septum and olfactory cleft, inflammatory nasal polyps usually arise from the ethmoid and maxillary sinus mucosa [2]. Macroscopic examination showed REAH to have a yellow-to-pink color and cerebriform surface, in contrast with smooth and translucent appearance of nasal polyps. REAH is characterized by a submucosal proliferation of small to medium-sized round

Fig. 2 Microphotographs of REAH. **a** Continuity between the surface respiratory epithelium and submucosal glands. The glands were also lined by ciliated respiratory epithelium and mucus secreting cells (Hematoxylin & Eosin staining, magnification $\times 100$). **b** Submucosal round to oval glands are situated in an edematous stroma containing a mixture of inflammatory cells including lymphocytes, plasma cells and rare eosinophils (Hematoxylin & Eosin staining, magnification $\times 200$)

to oval glands lined by ciliated respiratory epithelium, often admixed with mucin-secreting cells. Inflammatory nasal polyps show stromal edema, epithelial and fibroblast proliferation, and numerous epithelial and subepithelial inflammatory cells, especially eosinophils and lymphocytes. Glandular proliferation is generally seen in inflammatory polyps, but abnormal submucosal proliferation of the surface ciliated respiratory epithelium is more typically seen in REAH [4]. CT scan is very important for differential diagnosis between REAH and nasal polyposis. REAH of the olfactory cleft is characterized by opacity of the olfactory cleft which appears enlarged due to suppression of middle and superior turbinate to the exterior, in contrast to the situation with nasal polyposis where the middle turbinate can be compressed against the septum from outside [5]. In our case, we found the enlargement of the left

olfactory cleft in lesion which originate from inferior turbinate, not from olfactory cleft. Intra ethmoid opacities indicate either simple ethmoid mucus retention or association with sinonasal polyposis [9], to be differentiated on endoscopy of the middle meatus and ethmoid region. Inverted papillomas are characterized by infoldings and invaginations of the mucosal epithelium, not associated with glandular proliferations. Low-grade adenocarcinomas show crowded glandular proliferations, pleomorphism, mitoses and varying degrees of cellular atypia and those histological characteristics were not seen in REAH [2, 4].

In the world English literature, Kaneko et al. [10] reported a case of a patient with history of 10 year left-sided nasal obstruction. This tumor was diagnosed histologically as a combination between respiratory epithelial hamartoma and inverted papilloma. The maximum size of this lesion was $8 \times 5 \times 2.5$ cm. The tumor growth resulted in defect in the skull base in the region of left lamina cribrosa. Our patient had a histologically clear REAH, minimally larger than that previously reported, but without the evidence of bony destruction in the skull base. The treatment of choice for REAH is endoscopic sinus surgery. However, although such minimally invasive procedures are recommended as treatment for REAH, a wide surgical field is necessary for complete removal to prevent recurrence of a huge lesion.

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