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Caso clínico

Respiratory epithelial adenomatoid hamartoma – case report and literature review

Hamartoma adenomatóide epitelial respiratório – caso clínico e revisão da literatura

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Abstract

The Respiratory Epithelial Adenomatoid Hamartoma (REAH) is a distinct kind of hamartoma found in the nasal cavity and paranasal sinuses. REAH is rare and it has a benign behavior. The etiology of this lesion remains unclear. REAH usually presents with nasal obstruction, rhinorrhea, hyposmia/anosmia or epistaxis. The histological observation shows a well-differentiated glandular proliferation limited by pseudostratified ciliated epithelium, with a self-limited growth. Complete resection of the lesion is curative and the recurrence is unexpected. We report a case of a 63-year-old man, with history of long-lasting nasal obstruction. Computed tomography (CT) scans demonstrated a bilateral polypoid mass arising from olfactory recess. The lesion was removed through endoscopic sinus surgery. The histopathologic analysis confirmed REAH. Follow-up after six months showed no evidence of recurrence. This entity must be considered in the differ-

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ential diagnosis of sinonasal lesions and distinguished from nasal polyposis, inverted papilloma and adenocarcinoma. The correct identification of REAH is important to avoid more aggressive treatments.

Keywords: Respiratory epithelial adenomatoid hamartoma, hamartoma, nasal obstruction.

Resumo

O Hamartoma Adenomatóide Epitelial Respiratório (REAH) é um tipo distinto de hamartoma encontrado na cavidade nasal e seios perinasais. O REAH é raro e tem um comportamento benigno. A etiologia desta lesão permanece por esclarecer. O REAH apresenta-se habitualmente com obstrução nasal, rinorreia, hiposmia/anosmia ou epistáxis. A observação histológica mostra uma proliferação glandular bem diferenciada limitada por epitélio pseudoestratificado ciliado, com um crescimento auto-limitado. A ressecção completa da lesão é curativa e a recorrência inesperada. Apresentamos um caso clínico de um homem de 63 anos de idade com história de obstrução nasal de longa duração. A tomografia computadorizada demonstrou uma neoformação polipóide bilateral surgindo da fenda olfactiva. A lesão foi removida por cirurgia endoscópica nasossinusal. A análise histopatológica confirmou REAH. O seguimento de seis meses não mostrou evidência de recorrência. Esta entidade deve ser considerada no diagnóstico diferencial de lesões nasossinusais e distinguida de polipose nasal, papiloma invertido e adenocarcinoma. A identificação correcta do REAH é importante para evitar tratamentos mais agressivos.

Palavras chave: Hamartoma adenomatóide epitelial respiratório, hamartoma, obstrução nasal.

Introduction

Hamartomas are malformations composed of an excessive but localized overgrowth in the cells and tissues of an organ, firstly described by Albrecht in 1904[1]. They are composed of mature elements without ability to grow continuously and without malignant potential. Hamartomas may arise in anywhere in the body, most frequently originating from the lung, liver, spleen, kidney and bowel. The involvement of the head and neck is extremely uncommon [2,3]. The first case of a hamartoma in the upper aerodigestive tract was reported in 1995 by Birt and Knight-Jones [4]. In the same year, Wening and Heffner described a particular subset of hamartoma in a series of 31 cases and they introduced the term respiratory epithelial adenomatoid hamartoma (REAH) [5]. In the sinonasal region, hamartomas have been designed as epithelial, mesenchymal and mixed. They include the chondromesenchymal hamartoma, the REAH and the seromucinous hamartoma [5-7]. The REAH is a rare, unknown and undiagnosed lesion with a benign behavior. These lesions preferential appear in the nasal cavity, especially in the posterior septum, but may also occur in the nasopharynx and paranasal sinuses [8-10]. In the differential diagnosis, it is mainly important consider nasal polyps, inverted papilloma and adenocarcinoma. The histological features found in the REAH are proliferation and accumulation of glands covered by pseudostratified ciliated epithelium [5, 11]. It is essential to distinguish REAH from more aggressive neoplasms because this entity can be cured by surgical resection,

without other complementary treatments.

In this study, we present a case report of a REAH localized in the nasal cavity. We review the clinical features, differential diagnosis and typical imaging, histological and immunohistochemically characteristics of this interesting lesion.

Case report

A 63-year-old Caucasian man presented with bilateral nasal obstruction for 8 months, without other associated sinonasal symptoms. The patient had no nasal discharge, epistaxis, altered sense of smell or headaches. He also denied past history of allergic rhinitis or chronic rhinosinusitis. The patient had no ear complains and he did not present systemic features. Nasal fiber-optic endoscopy disclosed a bilateral polypoid mass, covered by normal mucosa, in both nasal cavities but more involvement on the right. CT-scan showed a soft-tissue mass, involving both olfactory recesses and causing enlargement of its most anterior part (Fig. 1). There was bone demineralization and erosion of the upper and middle turbinates. There was no adjacent structures invasion. Frontal and ethmoidal right sinuses were partially opacified. The nasal mass was completely excised by endoscopic sinus surgery, under general anesthesia. The lesion measured approximately 24 mm x 10 mm. The pathologic analysis revealed a glandular proliferation, lined by ciliated pseudostratified epithelium. The glands were well differentiated. There was no evidence of atypical cells or metaplastic changes. These histological findings confirmed the diagnosis of RAEH. There were no surgical complications. During postoperative period, the patient evolved well and became asymptomatic. Six months later, he repeated the imaging study which showed no evidence of recurrence (Fig. 2).

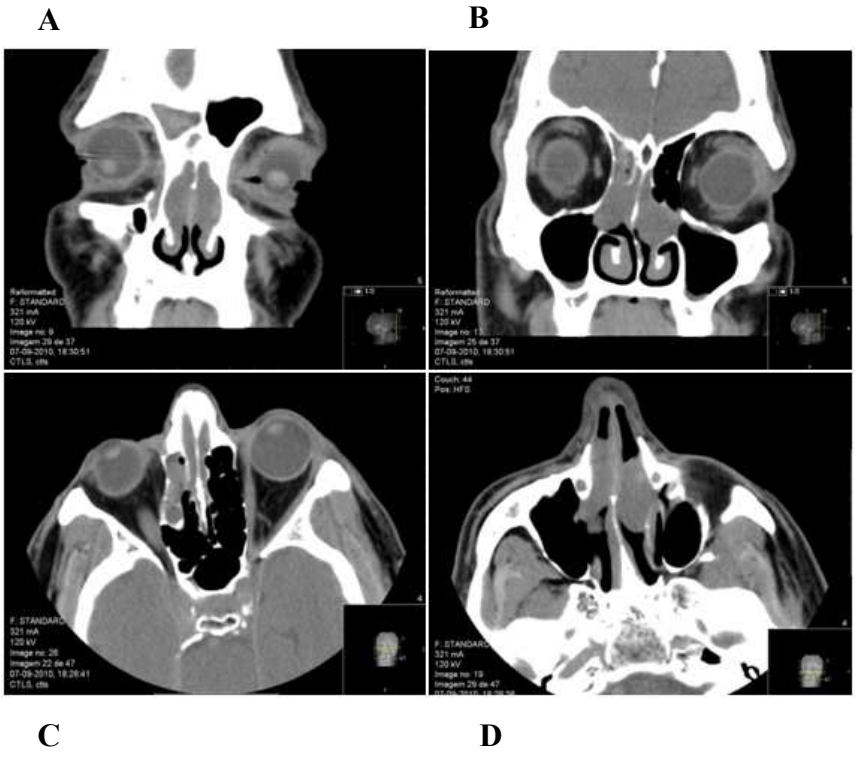
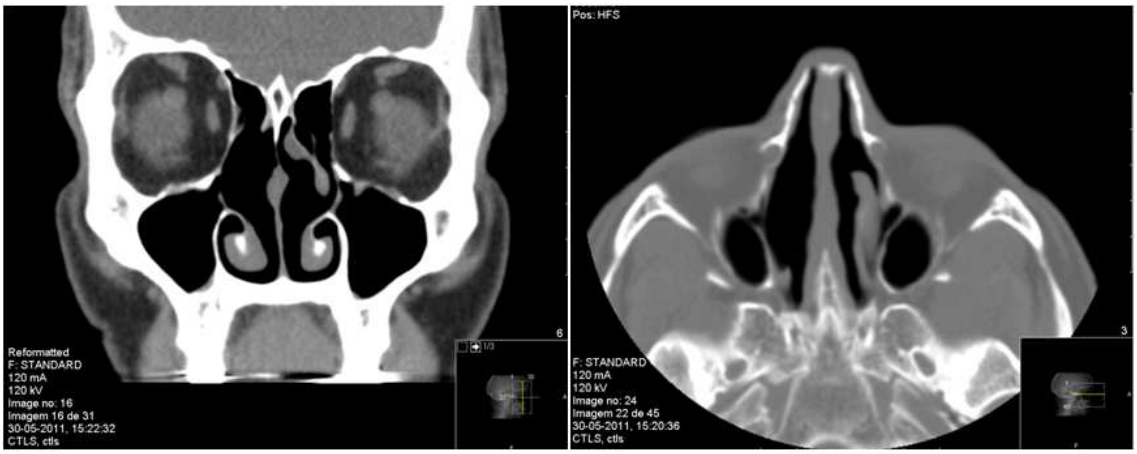


Figure 1 - CT-scan of paranasal sinuses: coronal (A and B) and axial (C and D) views. Sections A and B show a soft-tissue mass arising from both olfactory recesses and occupying the space between the middle turbinates and the nasal septum of both nasal cavities. A, B and C also exhibit the characteristic widening of the olfactory clefts manly in its most anterior part. B and C demonstrate opacity of the right ethmoidal sinus. D reveals bilateral nasal obstruction. There was loss of definition of the cortical bone of the upper and middle turbinates with bone demineralization. There was no adjacent structures invasion.



A **B**

Figure 2 - CT-scan of paranasal sinuses: coronal (A) and axial (B) views six months after surgery. These sections show good permeability of nasal cavity and paranasal sinuses without recurrence of the disease.

Discussion

Clinical features

REAH is a distinct and rare type of hamartoma occurring in the sinonasal tract. This benign lesion predominantly affects adult men with a male-to-female ratio of 7:1 and a mean age of 58 years [12, 13]. About 70% of REAHs occur in the nasal cavity, frequently localized in the posterior part of the nasal septum. There is no right or left side predilection and often involves both nasal cavities. These lesions can also appear in nasopharynx, ethmoid, frontal and maxillary sinuses [9, 13]. The etiology of REAH remains unknown. However, two theories have been considered. The first one defends a congenital origin. More recent considerations suggest that the development of REAH is secondarily induced by an inflammatory process [14-15]. This idea is supported by the concomitant diagnosis of REAH and nasal polyposis in some cases [14]. Environmental or occupational factors were not identified as etiological agents [5, 10]. REAH is associated with multiple symptoms, depending on the location of the lesion. According literature, nasal obstruction is the more frequent presenting complaint followed by rhinorrhea and anosmia/hyposmia. Epistaxis, headache, facial pain and proptosis were also reported [5, 9-10, 12].

CT-scan

Imaging studies are an essential tool in the evaluation of patients with a nasal polypoid growth. In patients with REAH localized in the nasal cavity, the CT-scan commonly shows an expansive mass connected to the nasal septum, most often involving the posterior area. REAH tends to growth slowly with bony expansion rather than erosion. In patients with bilateral disease, CT-scan shows an enlargement of the olfactory clefts, particularly in its most anterior part, displacing the turbinate wall of the ethmoidal labyrinth laterally. This feature is important in the differential diagnosis with nasal polyposis. Opacification of adjacent sinuses is also a very common finding in REAH [12, 16]. Despite clinical and imaging features, the definitive diagnosis is always histological.

Pathologic findings

Macroscopically, REAH appears as an edematous polypoid mass of varying sizes resembling an inflammatory polyp. The polyps can be fleshy or firm with yellow to white appearance [11]. Histological sections revealed a glandular proliferation and accumulation, with a polypoid form. In shape, the glands are round to oval, surrounded by an edematous stroma. The proliferation of glands tends to be submucosal, connected to the surface, and it is lined by pseudostratified ciliated epithelium. There is a thick basal membrane. Acute and chronic inflammation can be present with neutrophils, eosinophils, lymphocytes and vascular and fibroblastic proliferation. The glands are well differentiated and the epithelial cells do not show atypical, metaplastic or dysplasic changes [5, 17]. Distinguishing between REAH and other sinonasal lesions is often challenging, particularly on small biopsies. The immunohistochemically features can be helpful. Ozolek et al. studied the imunoprofile of REAH and verified that it was positive for cytokeratin (CK) 7 and negative for CK 20 and caudal type homeobox 2 (CDX-2). p63 and Ki-67 proteins staining showed a low proliferative index in this entity [14]. The molecular genetics of REAH is poorly known. Ozolek and Hunt tried to analyze genes on chromosomes 9p (p16 protein), 11p (Harvey rat sarcoma viral oncogene homolog - H-ras), 17p (p53 protein) and 18q (deleted in colorectal carcinoma/deleted in pancreatic carcinoma 4 - DCC/DPC4) by capillary electrophoresis. They concluded that the allelic loss was unusually high for a non-neoplasic lesion. However, more studies are necessary in this area to clarify these results [18].

Differential diagnosis

The differential diagnosis of REAH is difficult due to its unspecific clinical presentation. The misdiagnosis can occur because of the overlap of the clinical and morphological features among several pathologies. The imaging study can be helpful in the localization and characterization of the lesion. However, the histological analysis is always needed. The diagnosis should consider some entities as nasal polyposis, antrochoanal polyps, inverted papilloma and adenocarcinoma [11].

The nasal polyposis is a very common entity. However, the polyps frequently appear in the middle meatus and prolapse into the nasal cavity. They rarely show septal involvement. Polyps are edematous and they have an infiltration of inflammatory cells, mainly eosinophils, with swelling of basal membrane. Inflammatory polyps do not have adenomatoid proliferation. They have an increased expression of MMP-2 [10-11, 15, 19].

Antrochoanal polyps arise from the maxillary sinus, emerging through the middle meatus and growing to the choana and nasopharynx [20]. The histological findings are similar to observed in nasal polyposis.

Inverted papillomas appear from the endophytic growth of stratified squamous epithelium. There is a marked thickening of the epithelial layers and the squamous cells usually present with atypia. Inverted papillomas commonly occur in the lateral wall of the nasal cavity. They have a locally aggressive clinical behavior with the ability to destroy bone and invade the adjacent structures. They can be recurrent and they also have the potential for malignant transformation. These neoplasms require more extensive surgical excision [11].

Sinonasal adenocarcinoma is another important differential diagnosis, mainly the low grade type. This tumor preferentially occurs in the nasal cavity, ethmoid or maxillary sinuses. However, sinonasal adenocarcinoma presents cellular atypia, dysplasia and an increased mitotic rate. A cribriform architecture can be

present [11, 15]. The low grade adenocarcinoma is well differentiated but also has an aggressive behavior.

Treatment

The definitive diagnosis of REAH is important to decide the appropriated treatment. Conservative resection by endoscopic sinus surgery, under general anesthesia, is the treatment of choice. No malignant potential is recognized to REAH [18]. The complete excision is curative, leading to an excellent prognosis. There is no evidence of recurrence in the literature, despite a short follow-up period reported [8-9].

Conclusion

REAH is a rare, poorly known and underdiagnosed lesion of the sinonasal tract. The otolaryngologist should know the existence of this entity and consider it in the differential diagnosis of sinonasal masses. A correct diagnosis is important to avoid a more aggressive surgical excision. The documentation of these cases is necessary to improve our knowledge about the true incidence, etiology and risk factors. It is also important to have a longer follow-up period of these patients.

Conflicts of Interest: No conflict of interest was declared by the authors.

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