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RESPIRATORY EPITHELIAL ADENOMATOID HAMARTOMA OF THE MIDDLE MEATUS MASQUERADING AS A SINONASAL MALIGNANCY: A CASE REPORT

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ABSTRACT

Introduction: Respiratory Epithelial Adenomatoid Hamartoma (REAH) is a rare, benign lesion of the upper respiratory tract that primarily affects the nasal cavity and paranasal sinuses. What makes REAH particularly unique and what it adds to the scientific literature is its tendency to be misdiagnosed as an inflammatory polyp, an inverted papilloma, or a frank sinonasal malignancy due to its gross, radiological, and histological resemblances to these pathologies.

Main Symptoms and Clinical Findings: A 55-year-old male presented with a 6-month history of right-sided nasal obstruction. Nasal endoscopy revealed a large, well-circumscribed, whitish polypoidal lesion arising from the middle meatus, accompanied by foul-smelling and mucopurulent discharge.

Main Diagnoses, Therapeutic Interventions, and Outcomes: Pre-operative contrast-enhanced computed tomography (CECT) imaging suggested a neoplastic etiology due to bone sclerosis and pressure erosions. An initial biopsy suggested an inflammatory polyp. The patient underwent endoscopic sinus surgery for definitive excision. Final histopathological examination confirmed a diagnosis of REAH.

Conclusion: REAH is a benign malformation that is frequently misdiagnosed as a malignant tumor due to clinical and radiological similarities. Accurate recognition through histopathological evaluation is essential to avoid unnecessarily aggressive and mutilating surgical treatments or adjuvant therapies.

KEYWORDS: Respiratory Epithelial Adenomatoid Hamartoma, Sinonasal Neoplasm, Endoscopic Sinus Surgery, Misdiagnosis.

1. INTRODUCTION

The term "hamartoma" is derived from the Greek word hamartia, meaning fault or defect, and describes a malformation presenting as a benign, non-neoplastic overgrowth of disorganized tissue indigenous to the area of its occurrence.[1][2] Hamartomas are common in the lung, kidney, liver, and intestine, but they are extremely rare in the upper aerodigestive tract.[2] In 1995, Wenig and Heffner first described a specific subgroup of hamartomas involving the nasal cavity and nasopharynx, which they termed Respiratory Epithelial Adenomatoid Hamartoma (REAH).[2][3] REAH originates from the schneiderian respiratory epithelium (pseudostratified respiratory epithelium) and is characterized by a prominent glandular proliferation of surface epithelial cells.[4][5] It is presently categorized as a non-neoplastic hamartomatous lesion in the World Health Organization (WHO) 5th edition classification.[6] This case report details a unique and highly deceptive presentation of REAH. While approximately 70% of REAH cases originate from the posterior nasal septum,[6-8] this case involved a lesion originating from the middle meatus with maxillary sinus involvement, a presentation that is exceptionally rare in the literature. Furthermore, typical REAH lesions present as soft tissue masses,[9] but the patient in this case demonstrated a mass with radiological evidence of pressure erosions and bony sclerosis, heavily suggesting a malignant neoplastic etiology. The discrepancy between the sinister radiological presentation, the initial benign biopsy of an "inflammatory polyp," and the final diagnosis of REAH highlights the critical diagnostic challenges associated with this entity.

Patient Information

De-identified Patient Specific Information: The patient is a 55-year-old male.

Primary Concerns and Symptoms: The primary chief complaint was right-sided nasal obstruction that had been progressively worsening over a period of 6 months.

Medical, Family, and Psycho-social History: The patient had no other specific genetic history of nasal pathologies or known relevant prior interventions mentioned at the time of consultation.

Clinical Findings

During the physical examination, diagnostic nasal endoscopy was performed. The examination revealed a large, well-circumscribed, whitish lesion with a polypoidal component. The mass was observed to be arising from the right middle meatus and was associated with a foul-smelling, mucopurulent discharge. The presence of discharge raised suspicion of an obstructive mechanism leading to secondary sinus infection or necrosis.

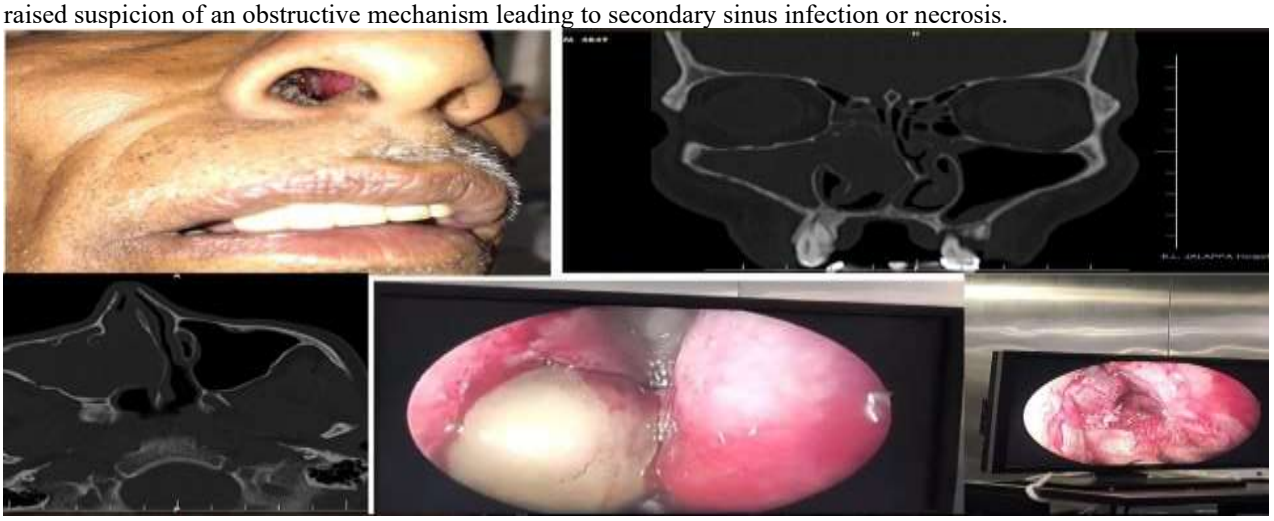

Figure 1:

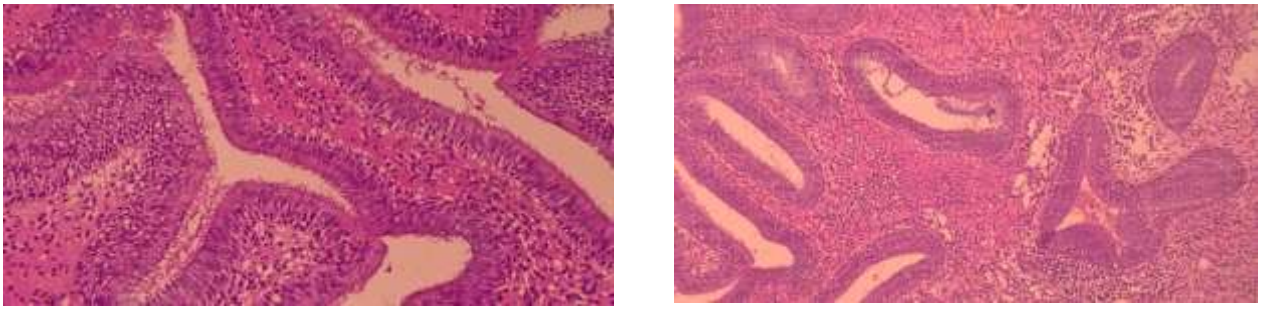

Figure 2A&2B:

Timeline

To facilitate a clearer understanding of the patient's presentation and clinical course, both past and current details are summarized in the timeline below.

Table 1: Patient care timeline

Timeframe	Clinical Event & Intervention	Outcome / Finding
6 Months Prior	Onset of patient's symptoms.	Gradual worsening of right-sided nasal obstruction.
Initial Visit	Diagnostic nasal endoscopy performed.	Large, whitish, polypoidal mass found arising from the right middle meatus, with foul-smelling discharge.
Pre-operative Phase	Contrast-Enhanced CT (CECT) of Paranasal Sinuses.	Diffuse soft tissue density with peripheral enhancement in the right maxillary sinus and nasal cavity, showing mass effect, pressure erosions, and bony sclerosis.
Pre-operative Phase	Outpatient incisional tissue biopsy.	Preliminary histopathology suggested features consistent with a benign inflammatory polyp.
Surgical Phase	Endoscopic Sinus Surgery (ESS).	Complete excision of the mass from the middle meatus.
Post-operative Phase	Definitive Histopathological Examination.	The excised mass was confirmed to be a Respiratory Epithelial Adenomatoid Hamartoma (REAH).

Diagnstic Assessment

Diagnostic Testing: CECT of the paranasal sinuses demonstrated a diffuse soft tissue density with peripheral enhancement involving the right maxillary sinus and the right nasal cavity. Notably, the imaging revealed a mass effect accompanied by pressure erosions and bony sclerosis.

Diagnostic Challenges: The primary diagnostic challenge in this case was the profound clinico-radiologic-pathologic discrepancy. The CECT findings of mass effect, pressure erosions, and sclerosis were highly suggestive of an aggressive neoplastic etiology, such as a sinonasal malignancy. However, the initial pre-operative biopsy returned features consistent merely with an inflammatory polyp. This is a common pitfall, as superficial biopsies may fail to capture the deep, diagnostic glandular invaginations of REAH.

Diagnosis: Following complete surgical excision, the definitive histopathological evaluation established the final diagnosis of REAH. It is critical to differentiate REAH from other sinonasal masses. The table below outlines the key differential diagnoses considered in such presentations.

Table 2: Differential Diagnosis of Polypoidal Sinonasal Masses

Pathology	Key Clinical/Radiological Features	Key Histopathological Features
Inflammatory Polyp	Soft tissue density, often bilateral, history of allergies/asthma.	Edematous stroma, inflammatory infiltrate, thickened basement membrane, lack of glandular proliferation.
REAH	Widened olfactory cleft (>10mm) on CT, commonly septal (70%), firm/gritty feel.	Proliferation of round/oval glands, thick eosinophilic basement membrane, stromal hyalinization, no atypia.
Inverted Papilloma (IP)	Unilateral, lateral nasal wall origin, bone erosion possible.	Hyperplastic squamous/respiratory epithelia invaginating into stroma, thin/intact basement membrane, sparse seromucinous glands.
Adenocarcinoma (Low-Grade)	Bone destruction, aggressive local invasion, unilateral.	Cribriform pattern (back-to-back fused glands), cellular pleomorphism, atypical mitoses, lack of intervening stroma.

Prognosis: The prognosis for REAH is excellent, as it is a benign, self-limiting growth with no malignant potential. Recurrence following complete local excision is exceptionally rare.

Therapeutic Intervention

The patient was managed surgically. The patient underwent endoscopic sinus surgery. During the procedure, the mass located in the right middle meatus and right maxillary sinus was completely excised and sent for final histopathological examination. Complete local excision is the gold standard and curative treatment for REAH.

Follow-up and Outcomes

Clinician and Patient-assessed Outcomes: Following the endoscopic sinus surgery, the patient's nasal obstruction and foul-smelling discharge were resolved by the removal of the mass.

Adverse and Unanticipated Events: No adverse events or post-operative complications were noted. The definitive histopathology successfully downgraded the initial radiological suspicion of malignancy, sparing the patient from further aggressive treatments such as mutilating surgeries or adjuvant therapies.

To summarize the clinical paradox encountered in this patient, Table 3 compares the conflicting initial impressions against the final diagnosis.

Table 3: Comparison of Initial Impressions vs. Final Diagnosis

Assessment Modality	Findings in this Case	Initial Interpretation	Final Definitive Diagnosis
Endoscopy	Large, whitish polypoidal lesion, foul discharge.	Inflammatory or neoplastic.	REAH.
CECT Imaging	Diffuse density, peripheral enhancement, bone sclerosis, pressure erosions.	High suspicion of malignancy / neoplasm.	Benign hamartoma mimicking malignancy.
Pre-operative Biopsy	Superficial edematous tissue.	Inflammatory polyp.	Sampling error missed deep REAH glands.
Post-operative Pathology	Whole specimen evaluation.	N/A	**REAH** (Curative).

DISCUSSION

While approximately 70% of REAH cases originate from the posterior nasal septum, our case involved the middle meatus and maxillary sinus. Maxillary sinus involvement alone is quite rare, with very few cases having been reported in the literature. Because of its unusual location, a middle meatus or maxillary sinus REAH can easily obscure the clinical picture, leading to an initial impression of hypertrophic chronic sinusitis, an antrochoanal polyp, or a malignant tumor.

Radiologically, differentiating REAH from other sinonasal lesions is notoriously difficult. While a widened olfactory cleft greater than 10 mm on a CT scan has been documented as a highly characteristic feature of REAH[10], many cases simply present as nonspecific soft-tissue opacification.[11] In our patient, the presence of bone erosion and sclerosis raised immediate red flags for malignancy. Malignancies such as nasopharyngeal carcinoma (NPC) or low-grade sinonasal adenocarcinoma, as well as locally aggressive benign tumors like juvenile nasopharyngeal angiofibroma (JNA) and inverted papilloma (IP), frequently exhibit bone erosion and remodeling. Consequently, REAH must be included in the differential diagnosis of erosive sinonasal masses to prevent overtreatment.[1][9]

Discussion of the Relevant Medical Literature: Since Wenig and Heffner's initial analysis of 31 cases in 1995, REAH has been recognized as a distinct clinical and histological entity.[12] The epidemiology of REAH shows a significant male preponderance (over 80% of patients), with ages ranging from 30 to 90 years and a median age in the sixth decade of life. [4][11]This demographic data aligns perfectly with our 55-year-old male patient.

Strengths and Limitations: A major strength of this case report is its emphasis on the diagnostic masquerade of REAH. By presenting a case with significant bony sclerosis and pressure erosions on imaging, this report underscores the necessity of maintaining REAH in the differential diagnosis even when imaging suggests malignancy. A limitation of this report is the lack of detailed long-term follow-up data or advanced immunohistochemical profiling to further characterize the lesion's molecular signature.

Scientific Rationale for Conclusions: Because clinical and radiological findings can be highly deceptive, the definitive diagnosis of REAH relies entirely on histopathological features, which serve as the gold standard. Microscopically, REAH is characterized by the prominent proliferation of small- to medium-sized round or oval glands lined by a multi-layered ciliated respiratory epithelium, often with an admixture of goblet cells. These glandular elements arise in direct continuity with the surface epithelium and invaginate into the submucosa. A defining hallmark of REAH which helps differentiate it from inflammatory polyps is the presence of stromal hyalinization with a notably thick, eosinophilic basement membrane enveloping the glands. Furthermore, unlike adenocarcinomas, REAH exhibits no cellular atypia, nuclear stratification, or increased mitotic rates.
Distinguishing REAH from an inverted papilloma (IP) is equally critical. IPs are composed of hyperplastic squamous or respiratory epithelia that invaginate with a thin, intact basement membrane, whereas REAH features adenomatoid structures with thickened basement membranes. Furthermore, an initial incisional biopsy might capture only the superficial edematous stroma without the deeper characteristic glandular invaginations, leading to a misdiagnosis of a simple inflammatory polyp precisely the diagnostic trap encountered initially in this case. Should histopathology remain ambiguous, immunohistochemistry can be employed. REAH is typically positive for CK7 and p63, but negative for CDX-2 and CK20.

Primary "Take-away" Lessons: The primary take-away from this case is that Respiratory Epithelial Adenomatoid Hamartoma is a rare, benign malformation that can completely mimic an aggressive sinonasal malignancy both clinically and radiologically. Because REAH lacks malignant potential and has an extremely low recurrence rate following complete local excision, achieving an accurate histopathological diagnosis is paramount. Recognizing this entity prevents patients from undergoing unnecessarily morbid, aggressive, and mutilating surgical procedures or unwarranted adjuvant therapies.

Patient Perspective
Following the definitive histopathological diagnosis of Respiratory Epithelial Adenomatoid Hamartoma, the patient expressed profound relief. Having initially been informed that the preoperative CT scan was highly suggestive of a neoplastic or malignant etiology due to the presence of bony destruction, the confirmation of a benign, self-limiting tumor alleviated significant psychological distress regarding the need for further aggressive therapies.

Informed Consent: Informed consent was obtained from the patient for the publication of this case report and any accompanying non-identifying images or clinical details.

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