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Oncocytic Chondro-Osseous Respiratory Epithelial Hamartoma: Expanding the Histological Variants of CORE Hamartoma and Literature Review

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1. Abstract

Chondro-osseous respiratory epithelial (CORE) hamartoma is a rare sinonasal lesion and is considered a benign tumor-like lesion. However, a growing body of evidence suggests that CORE hamartoma may represent a benign neoplasm which could potentially undergo malignant transformation. An oncocytic variant of CORE hamartoma has not yet been described. Herein, we present the first case of oncocytic CORE hamartoma in an 85-year-old patient. We summarize the current state of knowledge on CORE hamartoma, including epidemiological/clinical, histopathological and immunohistochemical findings, and discuss potential diagnostic pitfalls that may lead to erroneous diagnosis.

2. Introduction

Epithelial hamartomas, namely respiratory epithelial adenomatoid hamartomas (REAH) are the most common type of sinonasal / nasopharyngeal hamartomas. REAH is defined as a tumor originating from the surface mucosa characterized by excessive proliferation of glandular elements. Chondro-osseous respiratory epithelial (CORE) hamartoma is similar to REAH, but with additional cartilaginous and / or osseous elements [1,2]. To date, only 16 cases of CORE hamartomas have been reported in literature. To the best of our knowledge, an oncocytic variant has not been documented. We present a case of oncocytic CORE hamartoma with literature review. Our aim is to clearly identify clinical and histopathological features of this lesion, in order to avoid diagnostic misinterpretations leading to over aggressive treatment.

3. Case Presentation

An 85-year-old man presented with worsening nasal obstruction for several months. His history was significant for right-sided epistaxis and chronic sinusitis. Nasal endoscopy identified a large tan, lobulated mass within the right nasal cavity with attachments on the surface of the right nasal septum. Computer tomography (CT) imaging of the paranasal sinuses demonstrated a 6.7^{cm} right nasopharyngeal mass which was lobulated and partially calcified. The mass obstructed the choanae and extended to the oropharynx (Figure 1). No associated bony erosion was seen. Magnetic resonance angiogram confirmed lack of hypervascularity. The radiological findings were suggestive of antrochoanal polyp (Figure 1). The mass was endoscopically excised. Intraoperatively, a large smooth polypoid lesion was found, attached to the posterior septum. It was easily excised with no postoperative complications. The resected specimen was polypoid with a fleshy edematous cut surface (Figure 2). Microscopically, it was composed of dilated oncocytic cysts and tubuloglandular proliferations covered by an oncocytic surface epithelium. Chondro-osseous differentiation surrounded by small glands was centrally present. The cysts and glands contained abundant luminal mucinous secretion. The glands were diffusely lined by bilayered to multilayered oncocytic epithelium. The epithelial cells were cuboidal to polygonal with moderate eosinophilic cytoplasm and round nuclei. Nuclear atypia, mitoses and necrosis were absent. A spectrum of the submucosal glands arose in continuity with the surface epithelium. Respiratory-type ciliated cells lined entrapped tubules and areas of the surface epithelium. Both surface epithelium and glandular proliferation showed extensive goblet cell metaplasia. Serous budding from surface epithelium was identified only focally. Inflammatory cells were scattered throughout the fibromyxoid stroma with periglandular condensation. There was no thickened basement membrane (Figure 3). Immunohistochemically, tubuloglandular proliferations were diffusely positive for CK7. Surface epithelium displayed variable discontinuous positivity for CK7. Surface epithelium and glandular basal cells expressed p63 protein. DOG1 and CK20 were completely negative. S100 protein expression was only focally present in serous budding (Figure 4). Ki-67 proliferation index was low (3%). Given the absence of complex glandular architecture, atypia, and mitosis, the case was diagnosed as oncocytic CORE hamartoma.

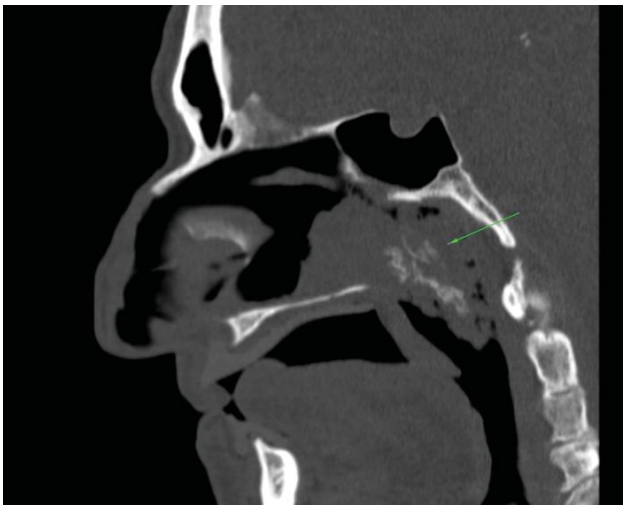

Figure 1: Axial images of sinus CT scan showing large lobulated mass with partial calcification within the posterior half of the right nasal passageway with extension to nasopharyngeal airway.

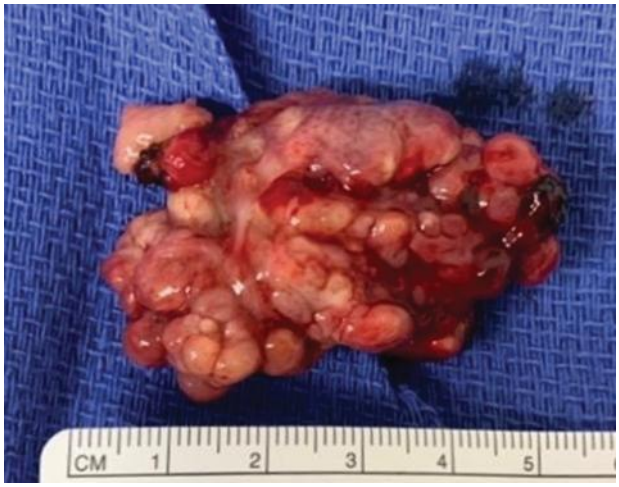

Figure 2: Macroscopical evaluation showed a polypoid fleshy mass with glistening surface.

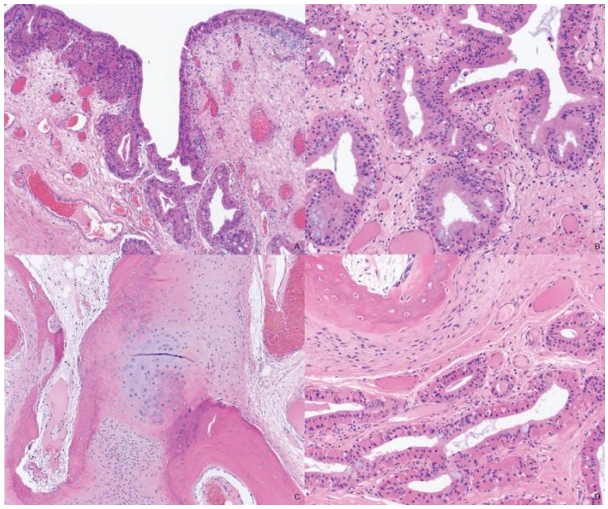

Figure 3: Microscopical evaluation demonstrated an oncocytic surface epithelium with underlying cystic and tubuloglandular proliferations consist of bilayered to multilayered oncocytic epithelium (A-B). Areas with chondro-osseous differentiation surrounded by small oncocytic glands (C-D). Note goblet cell metaplasia involving surface and glandular proliferation.

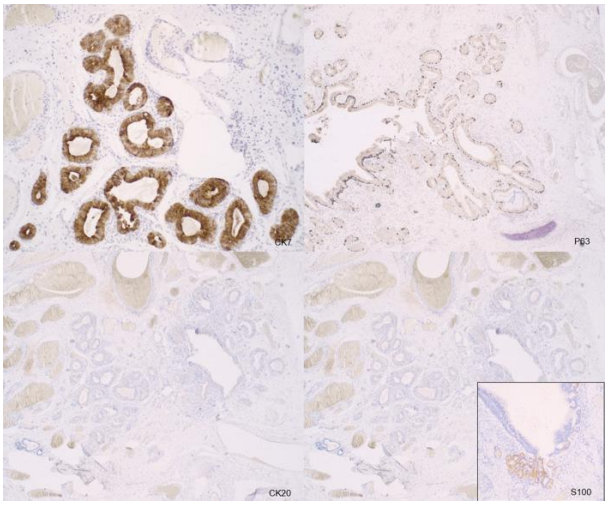

Figure 4. Immunohistochemical studies revealed diffuse CK7 expression in tubuloglandular proliferation, and p63 protein expression by surface epithelium and glandular basal cells. CK20 was completely negative. S100 protein was negative except for focal positivity in serous budding.

4. Methods

An extensive review of the PubMed and Google Scholar databases was carried out for studies published until March 2025. The inclusion criteria were as follows: final diagnosis of CORE hamartoma and articles published in English and availability of data. The exclusion criteria were as follows: unclear diagnosis after pathological analysis. The search included 16 publications after excluding the posters with limited information. There is no access to the primary reported data [1,2].

5. Results

We reviewed 16 cases from 1995 to 2025 and the review ultimately included 17 cases including our current case. The mean patient age is 48.6 years, ranging from 3-85 years old. The female-to-male ratio was 2.4:1. CORE hamartoma occurs in both adults and children, with 17.64% (3/17) of the reported cases in children. The evolution time was several weeks to 5 years. In 82.3% of patients, the tumor was associated with nasal obstruction. Half of the CORE hamartomas originated from lateral wall and turbinate, 25% arose from nasal septum. The average tumor size was 5.3 cm (3.5-7.2 cm). All patients were treated with surgery/endoscopic approach. The mean follow-up period was 9.3 months (range 3-18 months). None of the cases reported malignant transformation. Recurrence occurred in one case at 1-year follow-up.

6. Discussion

Hamartoma is defined as a non-neoplastic, tumor-like growth of specialized cell types indigenous to a particular body site. Wenig and Heffner first described surface epithelial adenomatoid hamartomas of the sinonasal tract in 1995. Their series included one case with osseous metaplasia [1]. A year later Adair et al. designated the sinonasal hamartoma with chondro-osseous metaplasia as CORE hamartoma [2]. The World Health Organization of head and neck tumors sub-classifies CORE hamartoma as a rare subtype of REAH [18]. CORE hamartomas occur in the nasal cavity; commonly originating from the lateral nasal wall followed by septum, olfactory clefts and ethmoid sinus. It occurs mostly in adults, but it also can be seen in children; there is a wide age range of 3–85 years old. Our patient was 85 years old; to date he is the oldest reported patient with CORE hamartoma. Unlike prior reviews with no clear sex predilection, our literature review showed a female preponderance. In distinction, REAH has a male preponderance [10,15]. We observed that nasal obstruction is the most common clinical presentation. Review of the reported cases reveals that there are no characteristic features on CT imaging that can distinguish CORE hamartoma from other benign, nasal paranasal sinuses entities. Similar to malignancies, CORE hamartoma may cause bony erosions [15]. Surgical intervention is curative. If limited to the nasal cavity, local resection through endoscopic sinus surgery is recommended. Recurrence is rare after complete removal. One reported patient did develop recurrence, which may have been due to various factors limiting feasibility of complete surgical excision [7]. Macroscopically, these lesions are smooth and polypoid. The cut surface ranges from fleshy edematous-cystic to firm, ranging in size from 3.5 cm to 7.2 cm. Histologically, all reported cases were composed of surface respiratory epithelium, submucosal glandular proliferation, fibromyxoid stroma and chondro and/or osseous mesenchymal components. Surface epithelium is a ciliated respiratory type that may contain goblet cells. Focal oncocytic metaplasia and squamous metaplasia are reported [8,14]. The submucosal glands are variably sized and shaped and may exhibit focal mucinous metaplasia. Some cases reported thickened basement membrane surrounding glandular proliferation [6,10]. The stroma is hypocellular, myxoid to fibrous commonly containing bland cells. Chatzopoulos et al. reported a case with stromal bizarre and multinucleated cells [10]. Stroma

Table 1: ND No data available, CT Computerized Tomography Scan.

Case	Reference	Age	Sex	Site	Presentation	Symptoms	Imaging	Size	Pathology	Follow-up
1	Flavin, 2005 [3]	11	M	Lateral nasal wall middle turbinate	Nasal obstruction	6 months	CT: Soft tissue mass. No bony destruction.	4 cm	Abundant glands, some cystically dilated, covered by squamous, respiratory, and transitional zone epithelium.	NED 6 months
2	Roffman 2006 [4]	59	M	Posterior nasal septum	Nasal obstruction Occasional headaches	3 years	CT: Partially ossified mass. No bony destruction	ND	REAH and bony trabeculae enveloped in fibromyxoid stroma.	NED 1 year
3	Choi 2006 [5]	34	F	Ethmoid	Facial pain, hyposmia, poor sense of taste	Weeks	MRI: Mass with bony and cystic components	6.8 cm	Fibrotic, polypoid, retention cysts, ossification, mature bony trabeculae focally rimmed by osteoblasts.	NED 9 months
4	Fedda 2013 [6]	38	F	Nasopharynx	Nasal obstruction	Few months	CT: Isodense mass, focal enhancement, calcification. No bony erosion.	4.0 cm	Respiratory epithelium, submucosal glands, focal mucinous metaplasia, hypocellular fibromyxoid stroma, mature bone.	ND
5	Nomura 2014 [7]	7	F	Lateral nasal wall, bilateral superior turbinates	Nasal obstruction	1.5 years	CT: Soft tissue mass of olfactory fossae and ethmoids. No bony destruction.	ND	Pseudostratified respiratory epithelium, proliferating cystically dilated glands, fibromyxoid stroma with fibroblasts, inflammatory cells, cartilage.	Recurred 1 year after excision
6	Perić 2015 [8]	68	F	Middle turbinate	Nasal obstruction	2 years	CT: Soft-tissue mass extending into nasopharynx	3.5 cm	Pseudostratified respiratory epithelium, squamous metaplasia, inflammatory cells, fibromyxoid stroma with dilated glands, cartilage and mature bone.	NED 3 years
7	Fang 2016 [9]	3	M	Nasal cavity roof, posterior olfactory cleft	Nasal obstruction, rhinorrhea	6 months	CT: heterogeneous mass. No bony destruction	7.2 cm	Prominent glandular proliferation with respiratory epithelium, stromal edema. Immature hyaline cartilage, no osseous metaplasia or atypia. No basement membrane thickening.	NED 6 months
8	Chatzopoulos 2017 [10]	64	F	Olfactory cleft	Nasal obstruction	1 year	CT: Mixed density mass	5.0 cm	Proliferating hamartomatous respiratory glands, fibrous stroma, chondroid tissue, numerous bizarre stromal cells, some multinucleated. No mitotic activity	NED 1 year
9	Idris 2018 [11]	46	F	Lateral wall	Nasal obstruction, rhinorrhea, anosmia	3 years	CT: Soft tissue mass with calcification. No bony erosion.	6.5 cm	Respiratory epithelium with fibrous stroma, multiple aggregates of tubular respiratory glands, cystic dilated glands, mature bony tissue.	ND
10	Daniel 2019 [12]	83	F	Posterior nasal septum	Headache, perioral paresthesia	3 years	CT: Irregular mass, calcified core.	5.2 cm	Respiratory epithelium, no dysplasia, central bone, edematous submucosa, connective tissue, inflammatory cells	NED 6 months
11	Nikolopoulos 2019 [13]	66	F	Middle turbinate extends to posterior nasal cavity	Headache, nasal obstruction, mid-facial pain	3 years	CT/MRI: Soft tissue mass, calcification. No bony erosion.	5.0 cm	Polypoid, respiratory epithelium invaginating into lamina propria. Myxoid stroma, cystic dilated spaces lined by mucinous cells, immature bony and fibrocartilaginous tissue.	ND
12	Yu 2021 [14]	54	F	Posterior nasal septum	Nasal obstruction	Several months	CT: Polypoid lesion, internal calcification, No bony erosion.	4.5 cm	Respiratory epithelium with invaginated glands lined by ciliated columnar cells, goblet cells. Osseous trabeculae. Focal chondroid metaplasia.	NED 1 year

13	Yu 2021 [14]	57	M	Lateral wall, superior turbinate	Nasal obstruction, bloody mucus	6 months	CT: Polypoid mass with internal calcifications. No bony erosion.	5.0 cm	Cystic glands lined by ciliated epithelium, focal oncocytic metaplasia, in continuity with surface epithelium, trabecular bone, edematous stroma.	NED 8 months
14	Li 2022 [15]	49	F	Lateral wall, superior turbinate	Nasal congestion, obstruction	3 years	CT: Heterogenous mass,focal bony erosion of the cribriform plate, concerning for malignancy.	6.5 cm	Intimately mixed glandular and mesenchymal components. Epithelial component had both REAH-like and small serous glands. Mesenchymal component, from immature appearing chondromyxoid areas to well-developed bone trabeculae.	NED 3 months
15	Nayani, 2024 [16]	55	F	Lateral wall	Nasal obstruction, smell disturbances, sporadic bleeding	2 years	CT: Opacified mass with bilateral sphenoid sinusitis.	ND	Polypoidal mass, respiratory epithelium. Proliferating seromucinous glands, focal adenomatous change, inflammatory cells, bony lamellae, chondro-osseous proliferation	NED 6 months
16	Hachemi 2024 [17]	58	F	Roof of nasal cavity and ethmoid	Nasal obstruction	5 years	CT?MRI: Bony destruction of anterior ethmoid with meningeal imprint on nasal septum	3 cm	Submucosal glands between bone trabeculae.	NED 12 months
17	Samankan 2024	85	M	Posterior nasal septum	Epistaxis, chronic sinusitis	Several months	CT: Partially calcified, lobulated mass extending from posterior choanae to nasopharynx	6.7 cm	Polypoidal mass, tubular glandular proliferation, oncocytic epithelium. Central bony trabeculae and cartilage, small oncocytic glands. Submucosal glands in continuity with surface epithelium. Fibromyxoid stroma with inflammatory cells	NED 18 months

may contain inflammatory infiltrate similar to, but less than that of inflammatory polyps. The chondro-osseous components are varied, ranging from immature-appearing mesenchyme to well-developed cartilaginous and bony trabeculae. Cellular pleomorphism, mitotic figures, and necrosis are absent. The overall pathological features in this case are similar to those reported in the literature. However, this tumor is unique due to the diffuse, pronounced, surface and glandular oncocytic metaplasia. A thickened basement membrane was absent in our case. Both surface epithelium and glandular proliferation were composed of oncocytic cells with prominent goblet cell proliferation. Only focal budding serous acini was present, confirmed by weak S100 staining. The remaining oncocytic glands and surface epithelium were negative for S100. The etiology of CORE hamartoma is not yet clearly understood [6,9,11,12,14]. REAH and CORE hamartoma were historically thought to be non-neoplastic. Although molecular studies are not reported on CORE hamartoma, studies by Ozolek and Hunt have shown an increased fractional allelic loss in REAH [19]. Baneckova and colleagues identified EGFR-ZNF267 gene fusion in one case of REAH/ seromucinous hamartoma [20]. Moreover, in one study REAH was associated with low-grade non-intestinal sinonasal adenocarcinomas (non-ITAC) [21]. These recent data suggest a possible neoplastic etiology for REAH and CORE hamartoma.

CORE hamartoma may histologically resemble sinonasal polyp, low-grade sinonasal adenocarcinoma, and low-grade salivary adenocarcinoma. Both CORE hamartoma and low-grade adenocarcinoma can cause bony erosion with overlapping radiologic findings. Radiological assessment of the CORE hamartoma reported by Li et al. [15]. Showed bony erosion concerning for malignancy [15]. Low-grade oncocytic non-ITAC should be in the differential diagnosis of any cytologically bland gland forming sinonasal tumor with oncocytic and mucinous differentiation. It should be noted that it is not uncommon to have uniform nuclei, absent mitotic figures and necrosis in low-grade non-ITAC. Four cases of low-grade tubulopapillary adenocarcinomas reported by Banecková et al. [20], showed overlapping morphological and immunohistochemical features with REAH and seromucinous hamartoma [20]. CORE hamartoma with mucus containing cysts should also be differentiated from low-grade mucoepidermoid carcinoma [5]. Inflammatory polyp is a benign mimicker that may contain focal condo-osseous metaplasia; however, it lacks prominent submucosal glandular proliferation. Unlike nasal polyps, CORE hamartoma lacks stromal edema and excessive inflammatory cells. In this case, the diffuse oncocytic nature, and prominent goblet cell population, raised the possibility of other oncocytic neoplasms of the sinonasal tract. However, lack of crowded, back-to-back, and confluent tubules and identifying chondro-osseous components helped in separating oncocytic CORE hamartoma from low-grade oncocytic non-intestinal-type sinonasal adenocarcinoma or oncocytic mucoepidermoid carcinoma.

7. Conclusion

Oncocytic CORE hamartoma is a rare lesion that can mimic other benign and malignant tumors. The sinonasal tract can give rise to a diverse range of oncocytic and mucinous gland-forming neoplasms. The oncocytic appearance of the CORE hamartoma can present a diagnostic challenge to the surgical pathologist. Detailed histopathological examination is necessary to recognize and distinguish it from more ominous nasal lesions and avoid aggressive surgical intervention. Therefore, oncocytic CORE hamartoma should be considered as a differential diagnosis in oncocytic seromucinous lesions of the sinonasal tract.

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