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Seromucinous Hamartoma of the Nasal Cavity

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Abstract
Seromucinous hamartoma (SMH) is a rare benign epithelial proliferation occurring in the sinonasal tract. The clinical, radiographic, and histologic appearance of SMH may mimic several benign and malignant entities. Presented is a novel case, with a review of the literature focused on potential histologic diagnostic pitfalls.

Keywords Seromucinous hamartoma · Epithelial hamartoma · Glandular hamartoma · Nasal · Nasal cavity · Sinonasal · Radiology

History

A 56 year-old female with a history of migraine headaches was referred to Otolaryngology for an incidental finding of a nasopharyngeal mass on brain magnetic resonance imaging (MRI). The patient had a history of chronic migraines and new facial headaches for a year. She also reported a history of decreased airflow through her right nasal passage, but denied bothersome obstruction, rhinitis, post-nasal drip, epistaxis or allergies. On examination, she had an obstructing right septal spur and a lobulated mass that appeared to extend from the posterior right nasal cavity into the nasopharynx (Fig. 1).

She underwent an endoscopic incisional biopsy, which was interpreted as an inflammatory polyp, via an approach through the left naris. She was then taken to the operating room for formal surgical excision. An uncomplicated endoscopic excision of the mass was performed, in conjunction with septoplasty for improved right sided access. Operatively, the mass was pedicled from the posterior superior nasal septum, adjacent to the middle turbinate.

Radiographic Features

The right posterior nasal mass was an incidental finding on noncontrast brain MRI performed for chronic refractory migraines. It revealed an elongated lobulated mass arising from the right posterior nasal septum and extending posteriorly into the right nasopharynx (Fig. 2) that measured approximately 2.5 cm in the long or anteroposterior axis, and 0.9 cm in the short or transverse axis. It was isointense to muscle on T1-weighted images and peripherally hyperintense on T2-weighted images.

A contrast-enhanced computed tomography (CT) scan was also performed (Fig. 3). It confirmed an elongated lobulated mass in the right posterior nasal cavity extending to the nasopharynx, similar in attenuation and density to muscle and without any significant contrast enhancement, indicating relative hypovascularity.

The radiologic differential diagnosis included inflammatory polyp (most common) and rare nasal cavity tumors (e.g. carcinoma, hamartoma, papilloma). There were no aggressive or suspicious features, such as destruction or invasion of local structures.

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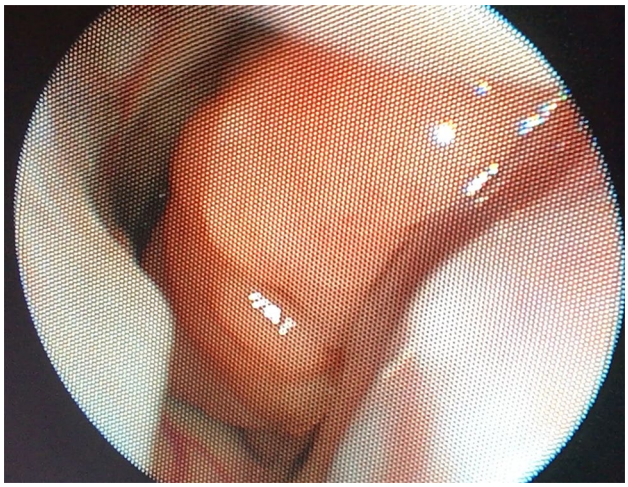

Fig. 1 Endoscopic view of lobulated mass extending from the posterior right nasal cavity into the nasopharynx

Diagnosis

The initial incisional biopsy (material unavailable for review) of the mass had been interpreted at a separate institution as an inflammatory polyp. The subsequent resection specimen grossly consisted of an elongated, polyp-like, gray-tan soft tissue mass measuring 2.5 cm in length. Microscopic examination revealed polypoid portions of fibromyxoid stroma surfaced by ciliated respiratory epithelium. Numerous compact seromucinous glands with simple cuboidal cell lined ducts and mixed acinar structures were distributed throughout the stroma. Larger, invaginated glandular structures were present at varying intervals along the surface. These ciliated epithelium lined glands were reminiscent of those seen in respiratory epithelial adenomatoid hamartomas (REAH) and typically terminated in proliferative or budding seromucinous glands (Fig. 4). The ratio of gland to stroma varied considerably between different areas of the lesion and foci of closely aggregated glands were evident in some fields (Fig. 5). Basement membrane thickening was present in areas but was not conspicuous. Several prominent, enlarged mucous cysts were also present. A few inflammatory polyp-like myxoid areas were noted at the periphery

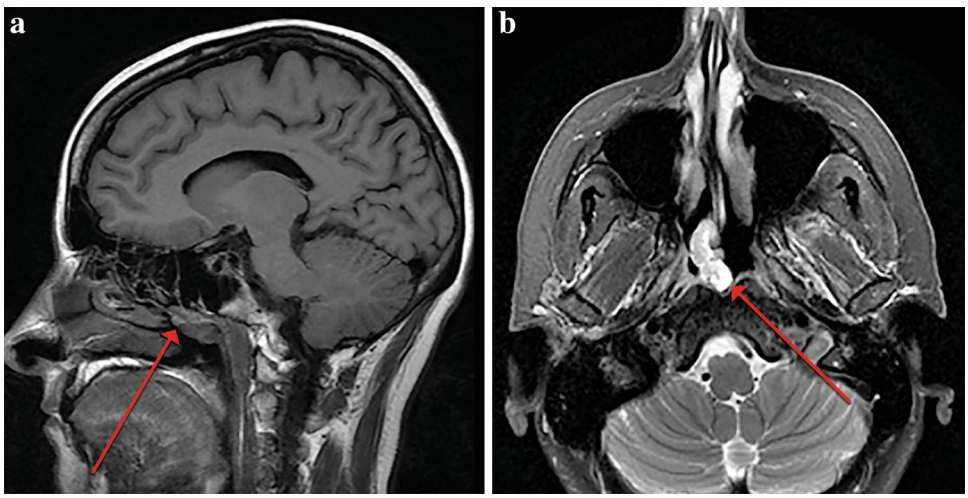

Fig. 2 Sagittal T1-weighted (**a**) and axial T2-weighted (**b**) MRI images show similar signal intensity to muscle on T1 ("isointense") and brighter signal intensity on T2 ("hyperintense"), especially at the periphery of the mass (red arrows)

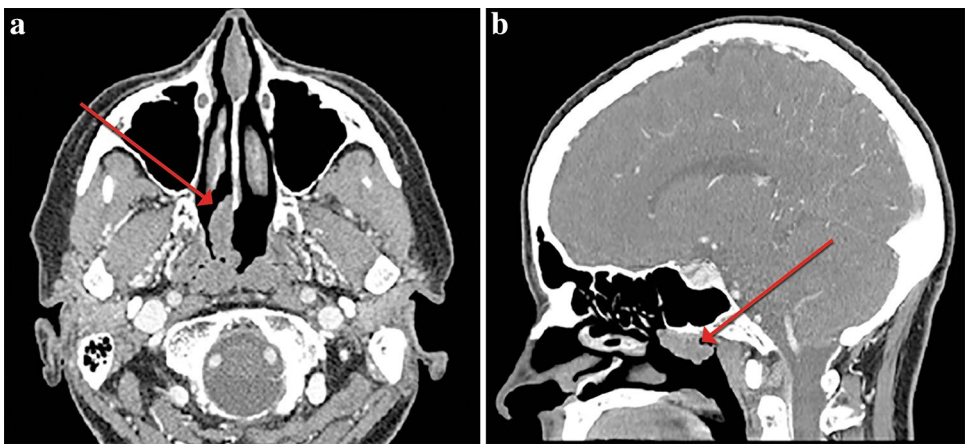

Fig. 3 Contrast-enhanced axial (**a**) and sagittal (**b**) images in soft tissue window CT reveal a lobulated mass (red arrows) arising from the right posterior nasal septum and extending posteriorly into the right nasopharynx that is similar in attenuation to muscle ("isodense") and hypovascular, without any significant contrast enhancement

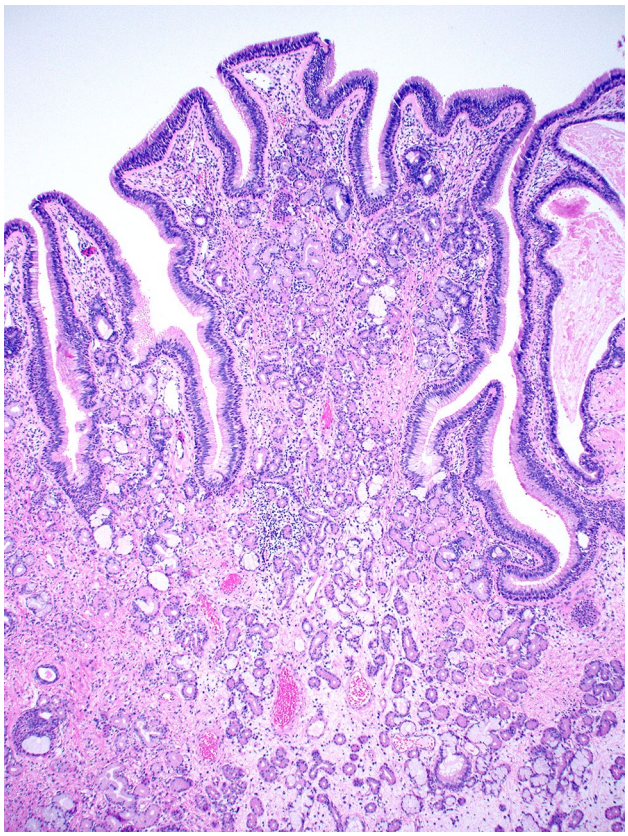

Fig. 4 Invaginations of the surface respiratory epithelium terminate in proliferative seromucinous glands

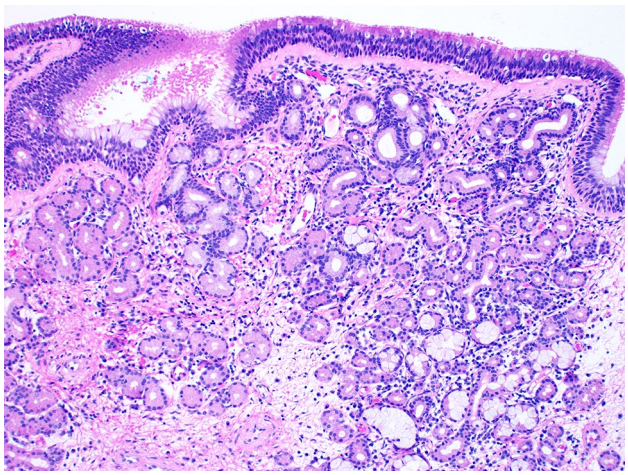

Fig. 5 Proliferation of compact seromucinous glands with simple cuboidal cell lined ducts and mixed acinar structures comprise the lesion

of the lesion, but were not a dominant feature of the lesion. Background inflammation consisted of scattered plasma cells and lymphocytes. No atypia or features of malignancy were identified. Overall, the characteristic microscopic features of seromucinous hamartoma were well represented.

Discussion

The seromucinous hamartoma (SMH), also known as epithelial hamartoma, glandular hamartoma, or microglandular adenosis of nose, is a benign epithelial proliferation of the sinonasal tract [1]. To date, approximately 25 examples have been reported. The entity was first described in 1974 simply as an overgrowth of an admixture of seromucinous glands within a fibrous stroma [2]. Since then, several additional clinical and histologic features, along with potential diagnostic pitfalls, have been described. SMH has morphologic features that overlap with other sinonasal tract epithelial lesions, most notably respiratory epithelial adenomatoid hamartoma (REAH) and low-grade non-intestinal adenocarcinoma (LGNIA) [1, 3–6]. It is reasonable to also include the recently described olfactory epithelial hamartoma in this group of lesions [7]. The distinction between SMH and LGNIA in particular, is important to make as the diagnosis can alter treatment significantly [8]. However, due to overlapping features, diagnosis of small biopsies can prove to be a challenge [9].

Clinically, SMH are polypoid soft tissue masses that range in size from 0.6 to 6.0 cm. SMH are most commonly found in the posterior nasal cavity, often arising from the posterior septum. The most common symptom is unilateral nasal obstruction. SMH has a female predilection (F:M = 1.5:1) and is seen most often in middle-aged to elderly patients. Simple surgical removal appears to be curative in the majority of cases with only one reported recurrence [4, 10].

Histologically, SMH is composed of a lobular growth of small, bland seromucinous gland tubules set in a fibrous to myxoid background stroma. Chronic lymphoplasmacytic inflammation is usually present. The serous gland tubules are typically composed of a single layer of cuboidal to columnar epithelium with little variation in size and shape compared to pre-existing normal acini. These tubules often appear to bud off of larger respiratory elements. Invaginations of the superficial ciliated respiratory epithelium can result in larger gland-like structures mimicking respiratory epithelial adenomatoid hamartoma (REAH), even demonstrating the periglandular hyalinization often seen in REAH [3, 8, 11]. In fact, it is not uncommon for areas of both SMH and REAH to be present in the same lesion, suggesting a spectrum of lesions [1, 3].

In addition to REAH, other benign and malignant lesions may be considered in the microscopic differential diagnosis of SMH. As initially diagnosed in the reported case, inflammatory polyp is a consideration. Inflammatory polyps lack proliferative epithelium but may contain an occasional

glandular component. In addition, inflammatory polyp background stroma is typically loose and edematous with a mixed inflammatory cell infiltrate including abundant eosinophils. This is in contrast to SMH, which usually has a denser fibrocellular background devoid of eosinophils and is defined by a characteristic glandular proliferation. This distinction may be significant, as inflammatory polyps are prone to recurrence with rates described from 10 to 30%, whereas SMH typically do not recur [8].

Malignant differential diagnostic considerations include low grade non-intestinal type adenocarcinoma (LGNIA) and intestinal type adenocarcinoma (ITAC). Both of these entities require more aggressive intervention [4, 5].

LGNIA are of presumed seromucous gland origin and share an almost identical immunophenotype with SMH. In contrast to normal glands, virtually all tubules in SMH and LGNIA are devoid of myoepithelial cells, as indicated by absent or minimal p63 staining. This is in contrast to REAH, in which the glandular elements include a layer of p63 positive basal cells [4]. In addition, a recent study by Purgina et al. found that all SMH expressed the seromucinous markers S100, DOG1, and SOX10 while the majority of non-intestinal adenocarcinomas (non-ITAC) also expressed at least one of these markers. LGNIA tended to show stronger and more diffuse staining than intermediate or high grade non-intestinal adenocarcinoma. Not unexpectedly, both entities stain with CK 7 and CK 19. Purgina et al. also found that areas of squamous morular metaplasia may be present in both non-intestinal adenocarcinoma and SMH. These squamous morules often demonstrate focal CDX2 reactivity that can suggest a diagnosis of ITAC, however CDX staining is restricted to the morular areas of SMH [5].

There is little utility in applying IHC staining to distinguish SMH from LGNIA [3]. LGNIA is best differentiated through routine examination and identification of a complex, back-to-back epithelial proliferation with evidence of at least focal invasion; both of which should be absent in SMH [6]. SMH can be difficult to distinguish from LGNIA if tubular architecture appears crowded. Although the glands can sometimes appear prominent and haphazard in SMH, the absence of papillae, tufting, and cribriforming and the lack of infiltrative growth or confluent, back-to-back architecture should serve to steer the diagnosis in a benign direction. Absence of cellular atypia and mitoses would also assist with establishing benignancy [8]. ITAC has a tendency to mimic colonic mucosa outright, making a striking appearance on light microscopy. However, low grade ITAC can have cellular morphology and architecture very similar to LGNIA and hence possibly similar to SMH. While staining with p63 would not be helpful, as ITAC and non-ITAC are p63 negative and SMH is largely p63 negative, positive immunostaining with intestinal markers such as CK20 and CDX2 is useful in distinguishing ITAC from other low-grade sinonasal tubular lesions [3, 5].

While SMH is a rare entity, awareness of its existence is important to avoid overcalling malignancy especially in equivocal low grade sinonasal tubular lesions. Radiographic imaging findings are nonspecific with the clinical differential diagnosis being quite broad. Direct visualization and biopsy are necessary to make the diagnosis. Routine microscopic evaluation remains the mainstay in recognizing SMH, with judicious use of IHC as an ancillary study.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

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