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Olfactory Epithelial Hamartoma

A New Subtype of Sinonasal Hamartoma

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BACKGROUND

- **Sinonasal mucosal**

✓ Vestibular region

✓ Respiratory region

✓ Olfactory region

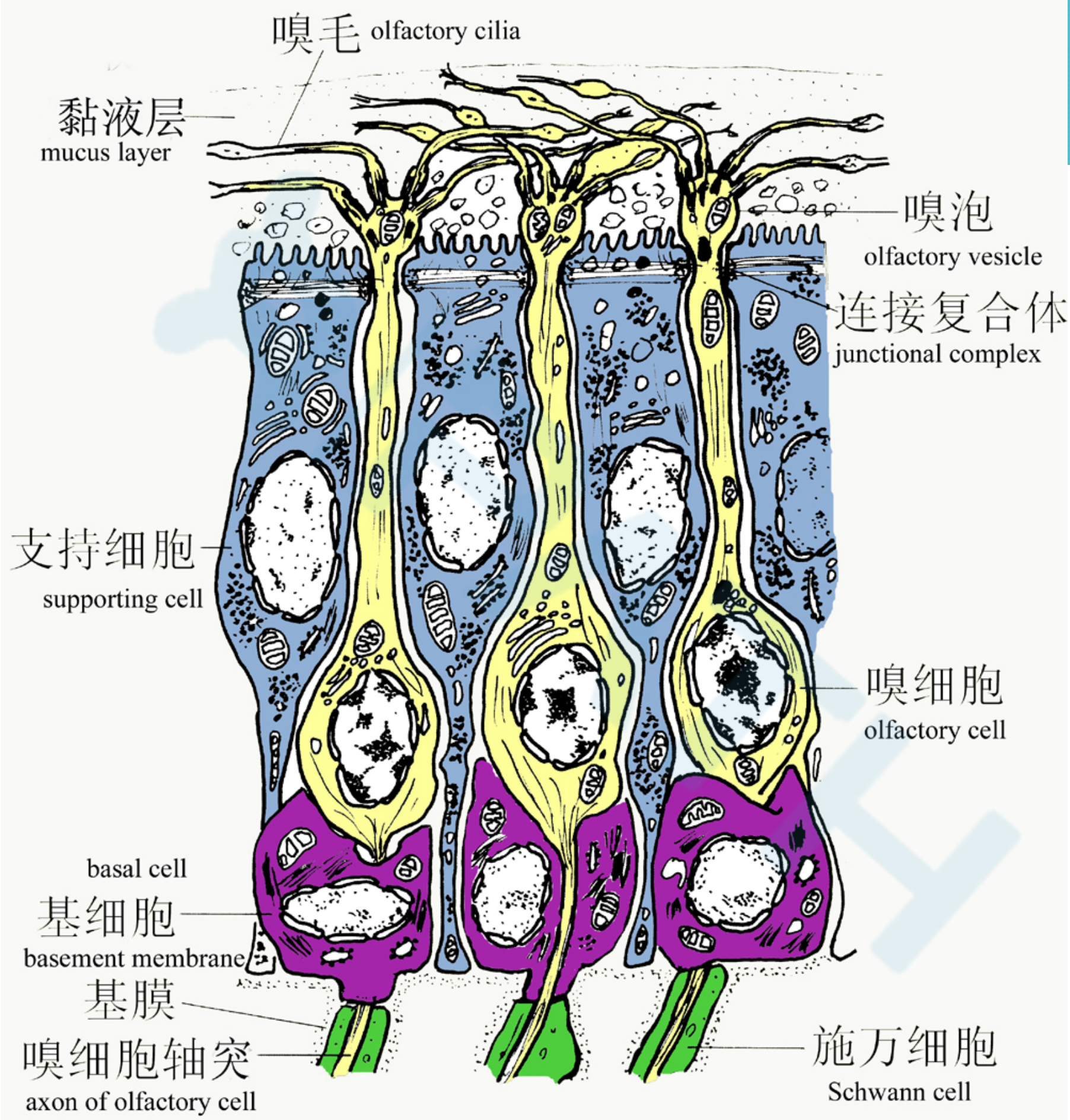
BACKGROUND

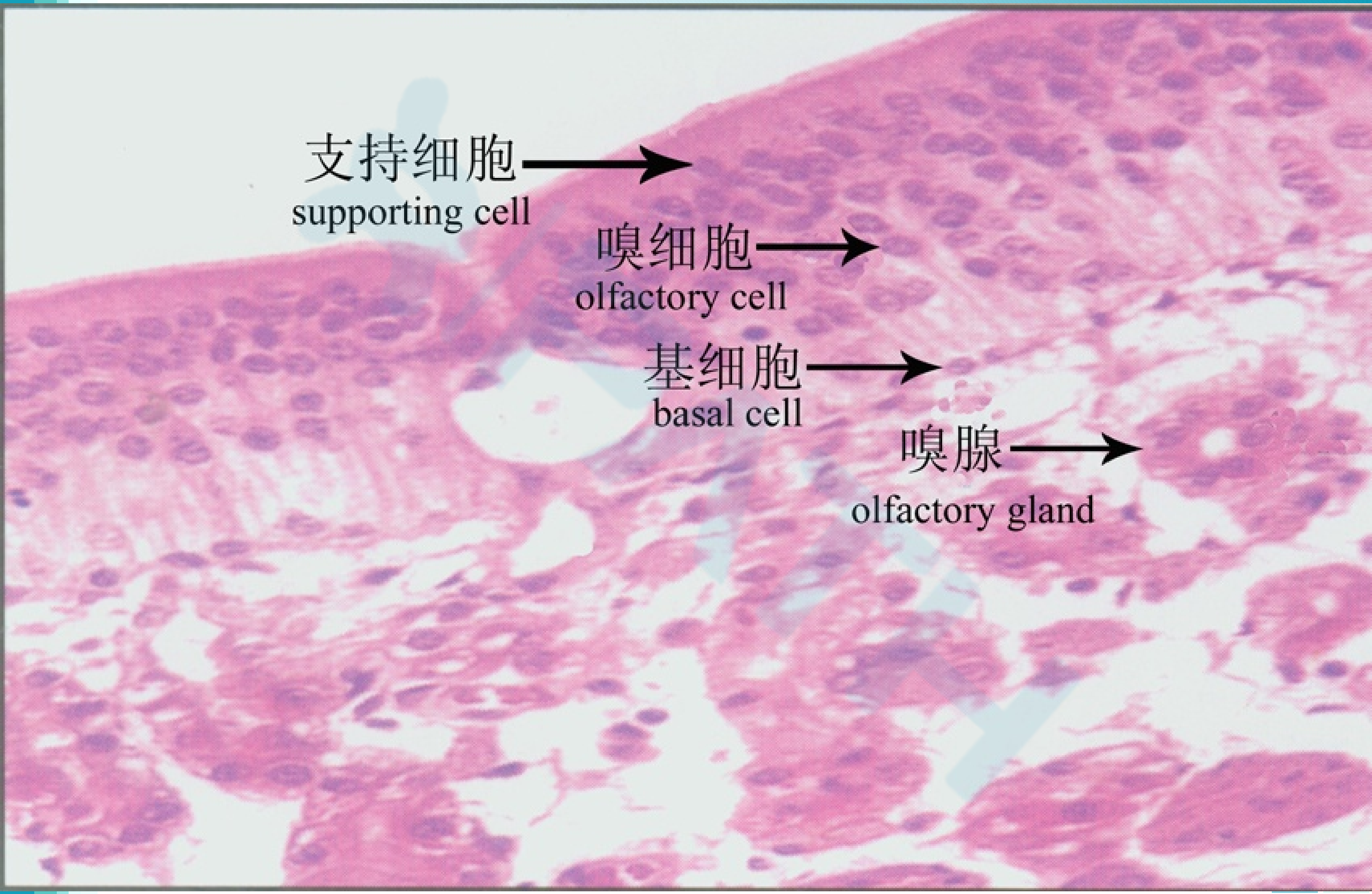
- **Olfactory mucosa**

✓ The roof of the nasal cavity, upper part of the nasal septum, and superior nasal conchae

✓ Pseudostratified neuroepithelium containing 3 types of cells— basal, sustentacular (supporting), and olfactory receptor cells

✓ Seromucinous Bowman glands


嗅毛 olfactory cilia
黏液层
mucus layer
嗅泡
olfactory vesicle
连接复合体
junctional complex
支持细胞
supporting cell
嗅细胞
olfactory cell
basal cell
基细胞
basement membrane
基膜
嗅细胞轴突
axon of olfactory cell
施万细胞
Schwann cell


支持细胞
supporting cell
嗅细胞
olfactory cell
基细胞
basal cell
嗅腺
olfactory gland

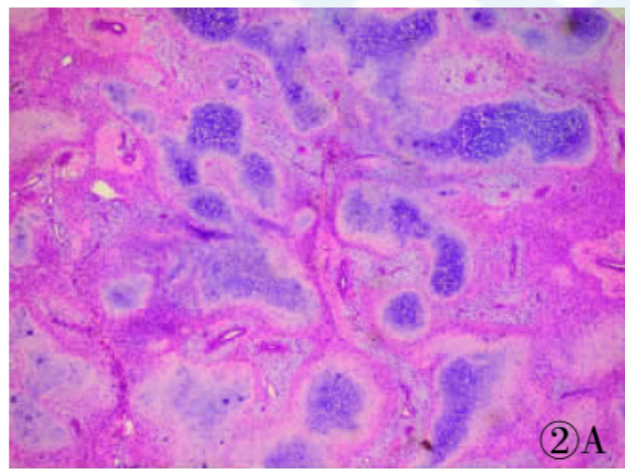
BACKGROUND

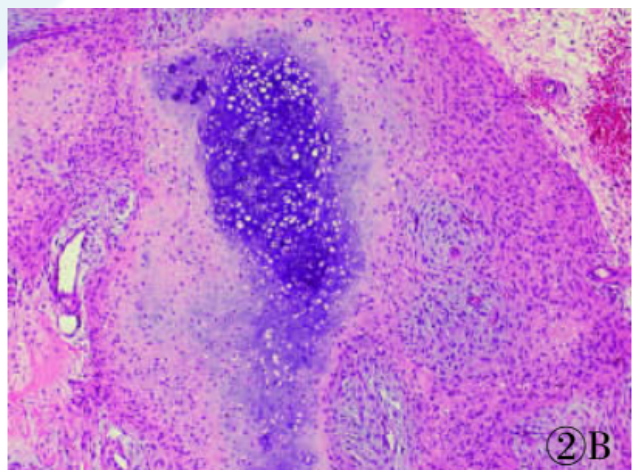
- **Sinonasal epithelial hamartomas**

✓ Seromucinous hamartoma (SMH)

✓ Respiratory epithelial adenomatoid hamartoma (REAH)

✓ Chondromesenchymal hamartomas





BACKGROUND

- **Seromucinous hamartoma (SMH)**

✓ First described in 1974 by Baillie and Batsakis

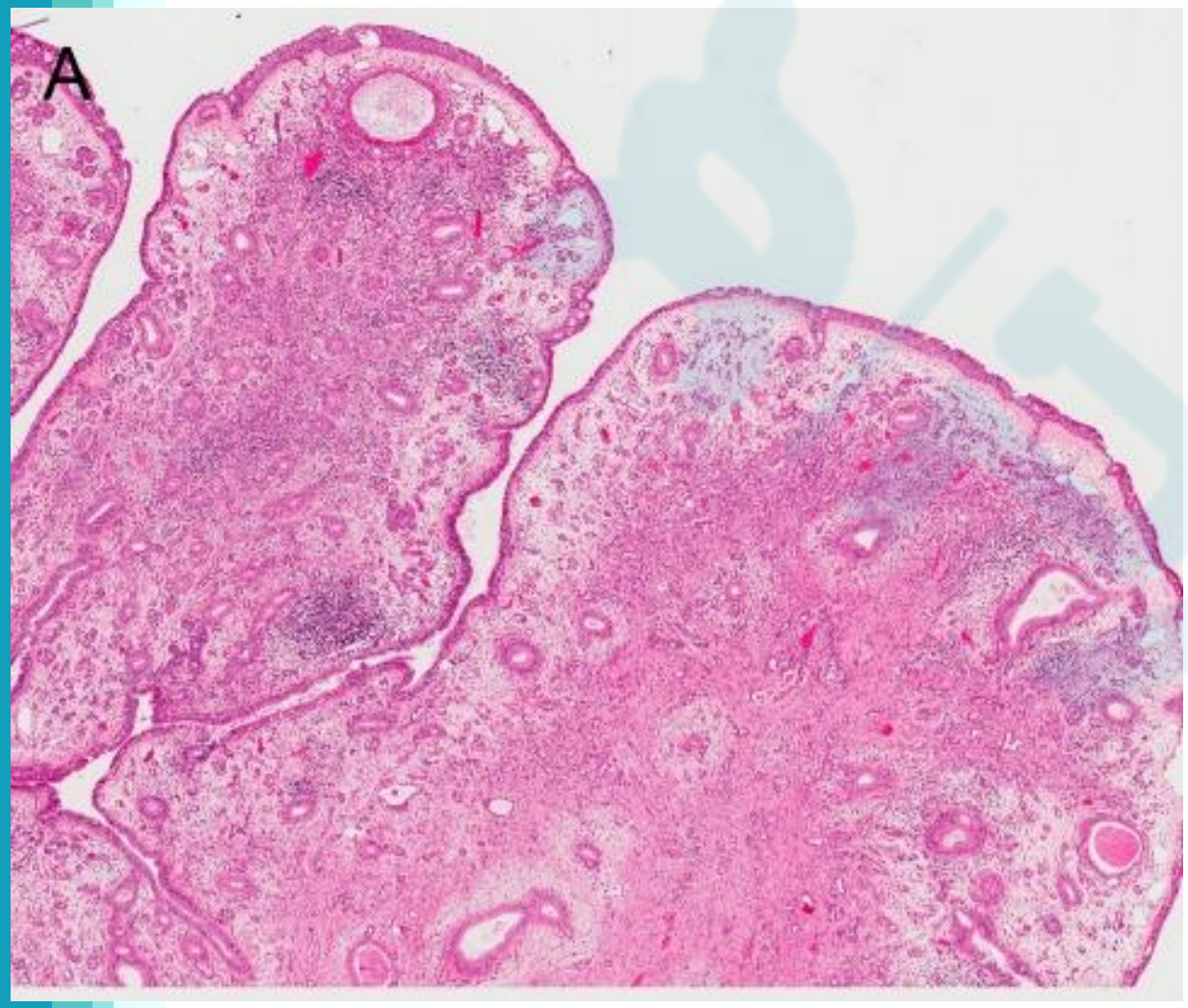
✓ Predominantly in adults（range：14-85 years，mean：56years）

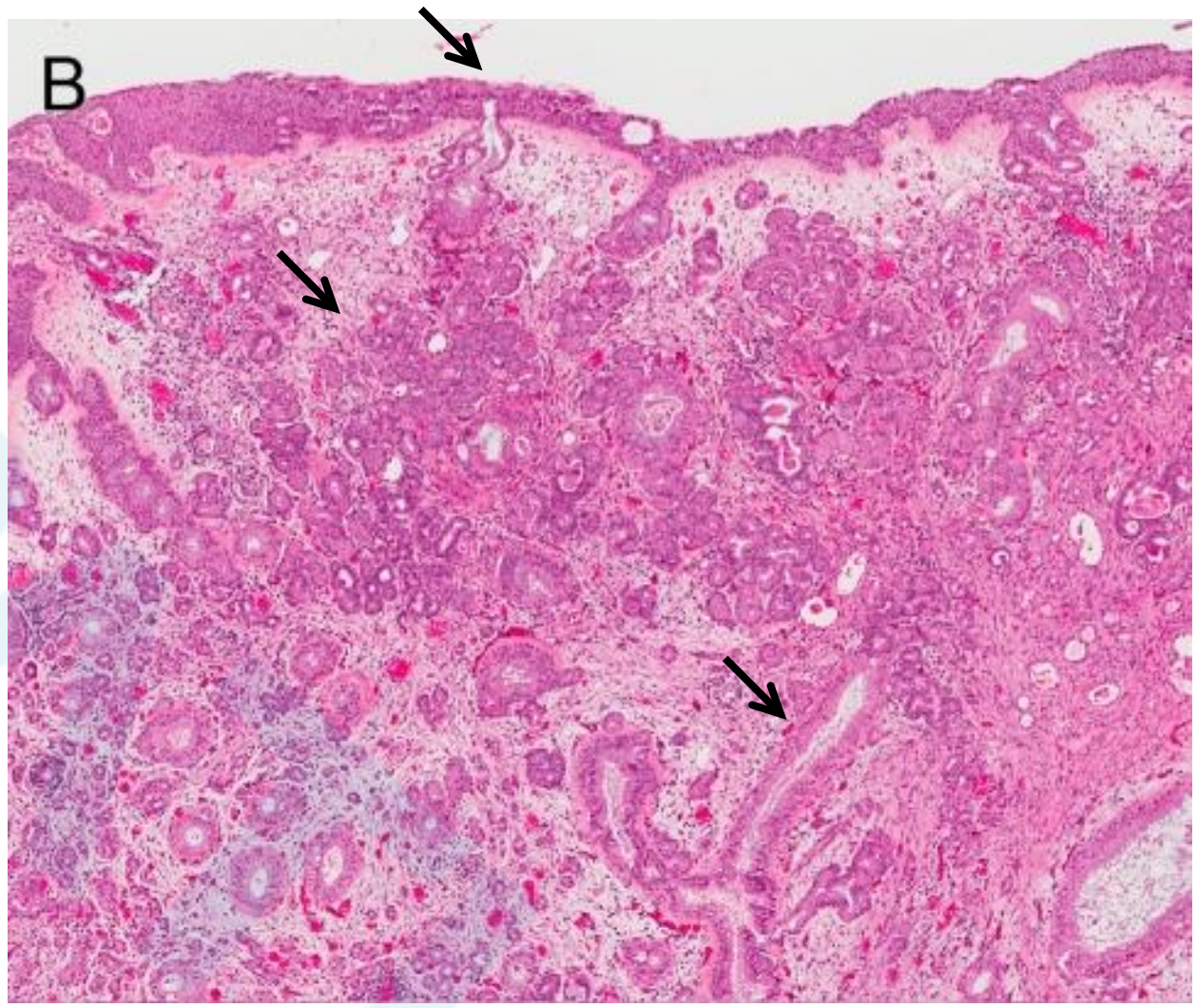
✓ Posterior nasal septum or nasopharynx

✓ Polypoid mass

BACKGROUND

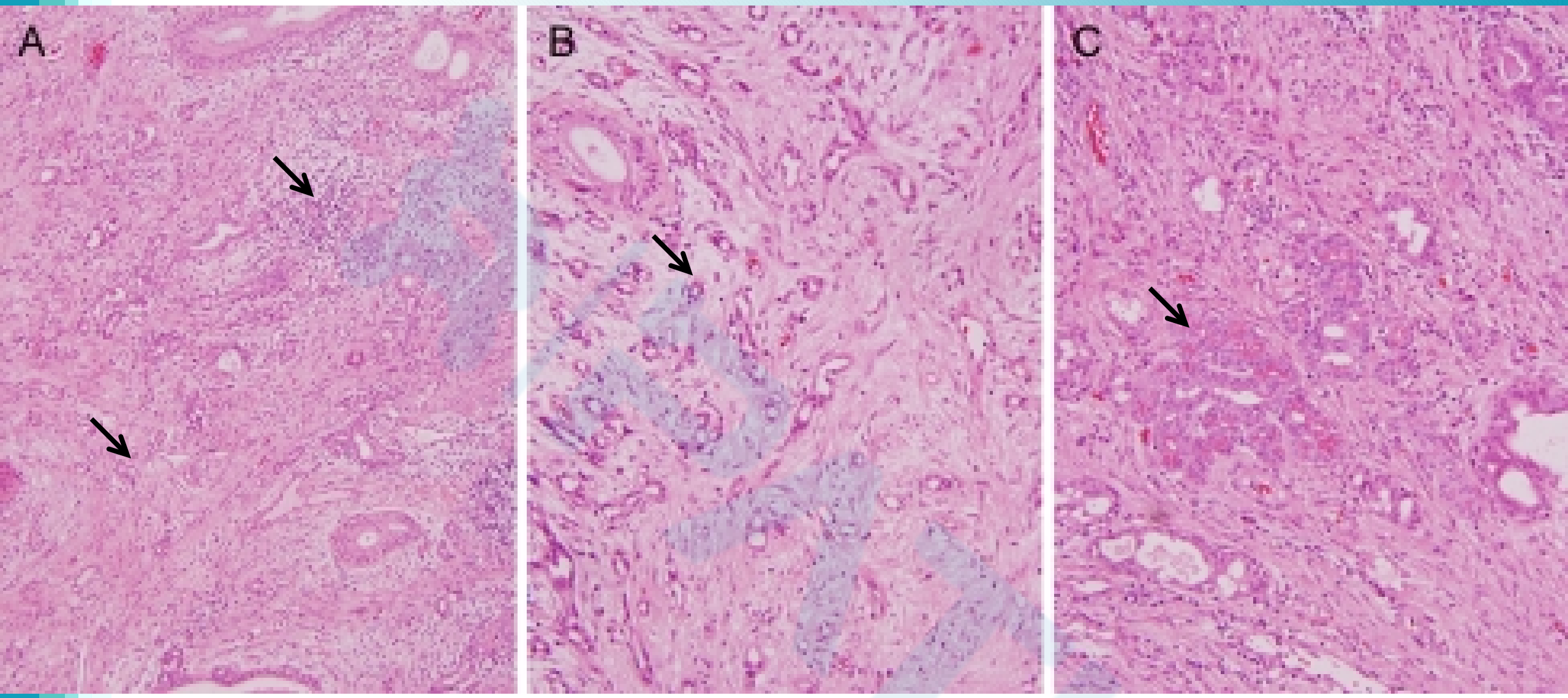
- Nonspecific respiratory surface epithelium and numerous, often disorganized, atrophic or hypertrophic seromucinous glands in the stroma
- Positivity for CK17,CK19,EMA,lysozyme,S100
- The stroma is positive for calponin，SMA and desmin
- Conservative but complete surgical excision is curative





Seromucinous hamartoma (Case 2) showing a a complex, polypoid lesion with more dense, eosinophilic submucosa (20× magnification) which has b abundant, haphazard seromucinous glands and scattered respiratory epithelial lined invaginations (40× magnification)

. *Head Neck Pathol.* 2011;5:241–247



Seromucinous hamartoma (Case 2) showing a a fibrotic submucosa with a mixture of bland seromucinous glands and slightly cellular, fibrous stroma with bland spindle cells (100× magnification). b Focally, the seromucinous glands had a more atrophic lining with cells containing less cytoplasm but still retaining bland, round, hyperchromatic nuclei (200× magnification). c The seromucinous glands retained eosinophilic cytoplasmic zymogen granules and lacked any back to back growth, epithelial tufting, papillae or destructive growth (200× magnification)

***Head Neck Pathol*. 2011;5:241–247**

BACKGROUND

- **Respiratory epithelial adenomatoid hamartoma (REAH)**

✓ First described by Wenig and Heffner in 1995

✓ Adault

✓ Polypoid or exophytic lesions

✓ Nasal cavity,in particular the posterior nasal septum

✓ Covered with ciliated pseudostratified respiratory epithelium that invaginates into the stroma, forming glandlike ducts lined by the same epithelium

BACKGROUND

- Surrounded by a thickened basement membrane or stromal hyalinization
- The glands are immunoreactive for AE1/AE3,CAM5.2,and CK7 but negative for CK20 and CDX2
- Myoepithelial/basal cells marks are typically present but may be absent
- Fractional allelic loss of 31%
- Complete surgical excision is curative

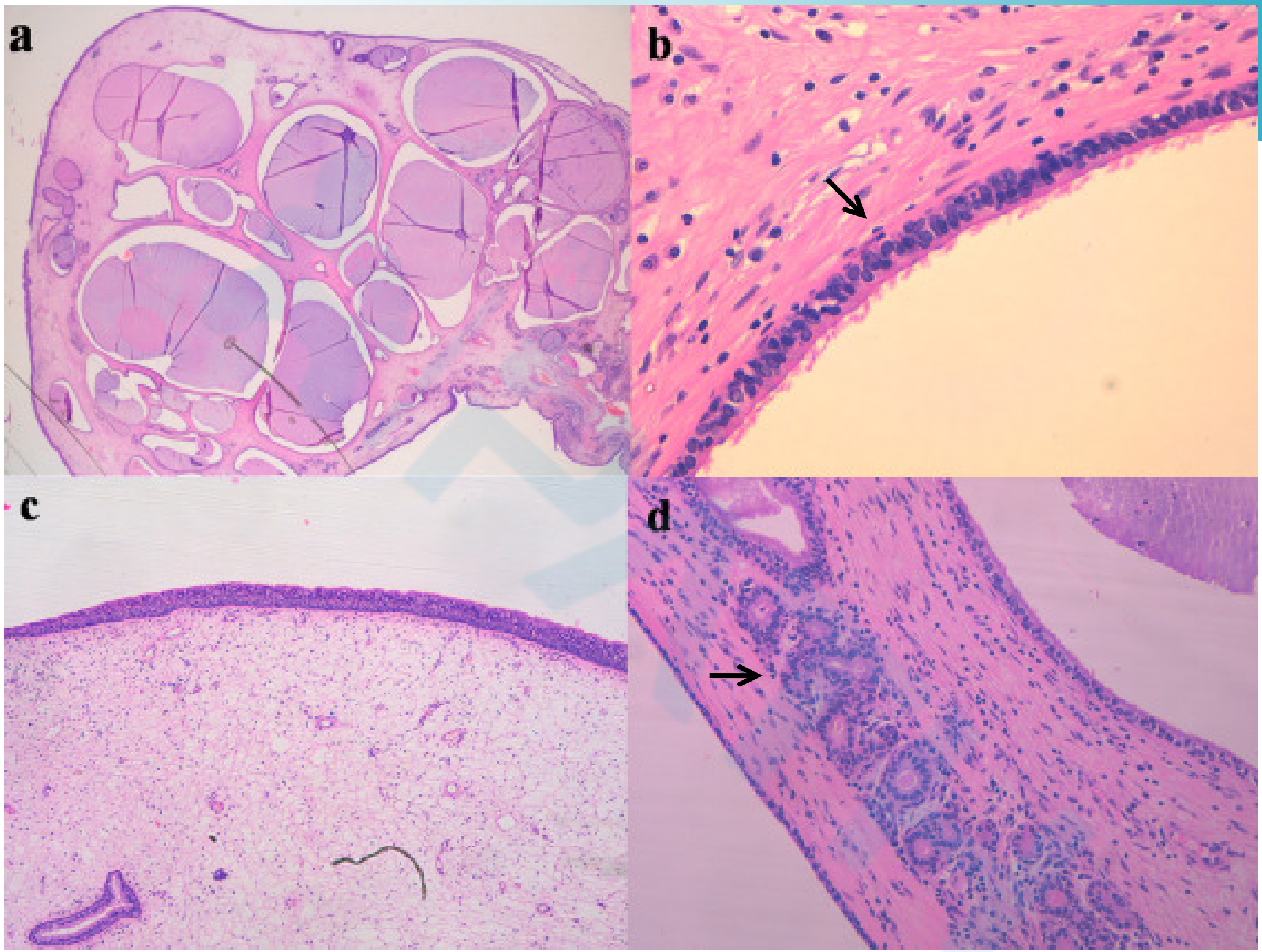


Fig. 1. a: polypoid mass composed by a proliferation of prominent dilated glands. HE staining 1.5×; b: the dilated glands are lined by ciliated respiratory epithelium. HE staining 400×; c: in some submucosal areas the appearance is indistinguishable from a sinonasal inflammatory polyp, with stromal edema and eosinophils. HE staining 100×; d: 200×.

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BACKGROUND

- According to Gauchotte et al,the presence of tissue fragments > 5 mm, containing pseudoglands lined by ciliated respiratory epithelium separated by thin bands of intervening stroma of widths less than or equal to the average mean diameter of glands, allows the differentiation of REAH from REAH-like lesions

BACKGROUND

- SMH and REAH should be considered as histologic subtypes of SEH rather than 2 distinct entities
- A third subtype of SEH that resembles SMH but contains additional areas of olfactory epithelium

MATERIALS AND METHODS

- 118 patients diagnosed with sinonasal hamartomas between 2003 and 2015

- 6 patients containing areas of olfactory epithelium

  pathology slides clinical and imaging data

TABLE 1. Immunohistochemical Profiles of Different Cell Types

Antibody	Clone (s)	Provider	E
Pankeratin	AE1/AE3, KL1	Dako	
Keratin 5/6	D5/16B4	Dako	
p63	4a4	Dako	
CD56	1B6	Novocastra	
Chromogranin A	DAK-A3	Dako	
Synaptophysin	SY38	Dako	
Neurofilament	2F11	Dako	
S100 protein	Polyclonal	Dako	

*Only cell processes and nerves in the stroma.
f indicates focal; s, scattered.

TABLE 2. Clinical Characteristics of Patients With Sinonasal Olfactory Hamartoma

Patient	Age (y)	Sex	Symptoms	Site of Insertion	Size (mm)
1	54	M	Recurring rhinosinusitis, right nasal obstruction	Right OC	50×28×20
2	30	F	NA	Left OC	80×65
3	53	F	Recurring left sinusitis and left nasal obstruction	Left OC	50×35×15
4	39	M	Bilateral nasal obstruction, ethmoidonasal polyposis	NA	NA
5	77	M	Unilateral left nasal obstruction	Left OC	40×28×12
6	67	M	Asymptomatic nasal mass, associated with sphenoid sinus retention, incidentally discovered on MRI	Right OC	38×24×10

F indicates female; M, male; NA, not available; OC, olfactory cleft.

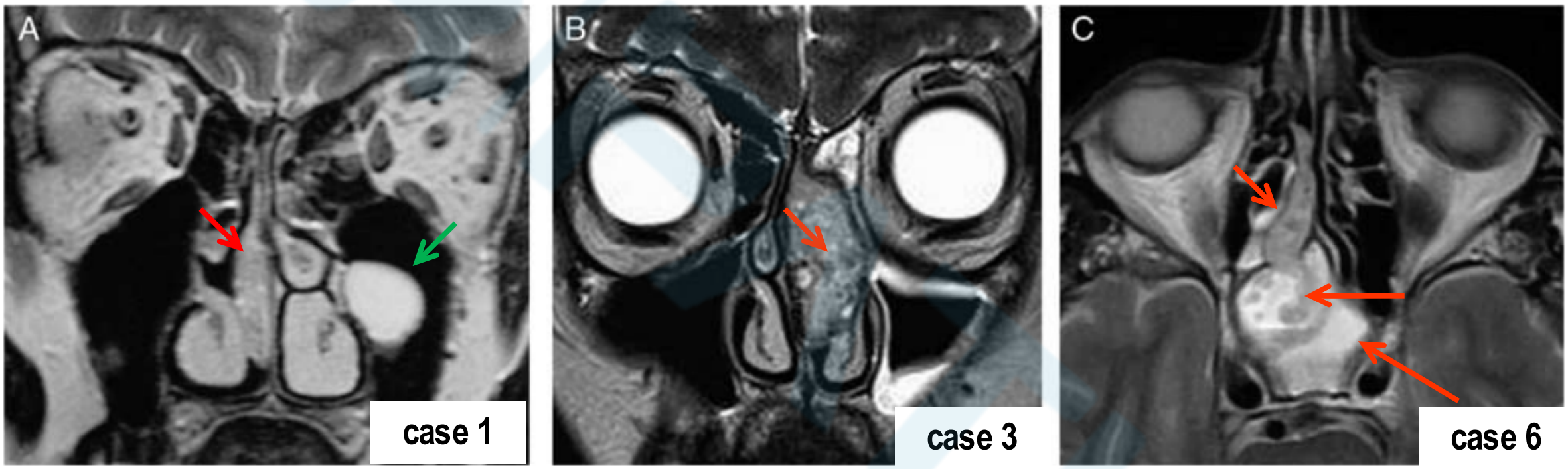

FIGURE 2. Imaging findings. A, Coronal T2-weighted MRI in patient 1. The lesion extends from the right olfactory cleft to the inferior turbinate and contains small hyperintense cysts. Note the hyperintense retention cyst in the contralateral maxillary sinus. B, Coronal T2-weighted MRI in patient 3. This large lesion exhibits a more heterogenous signal, with small foci of hypointensity and hyperintensity signals corresponding to cysts. Note the left chronic anterior sinusitis resulting from obstruction of the left middle meatus. C, Axial T2-weighted MRI in patient 6. The mass is lodged in the right sphenoethmoidal recess, partially filling the right sphenoid sinus, and is associated with mucosal thickening and obstruction of secretions.

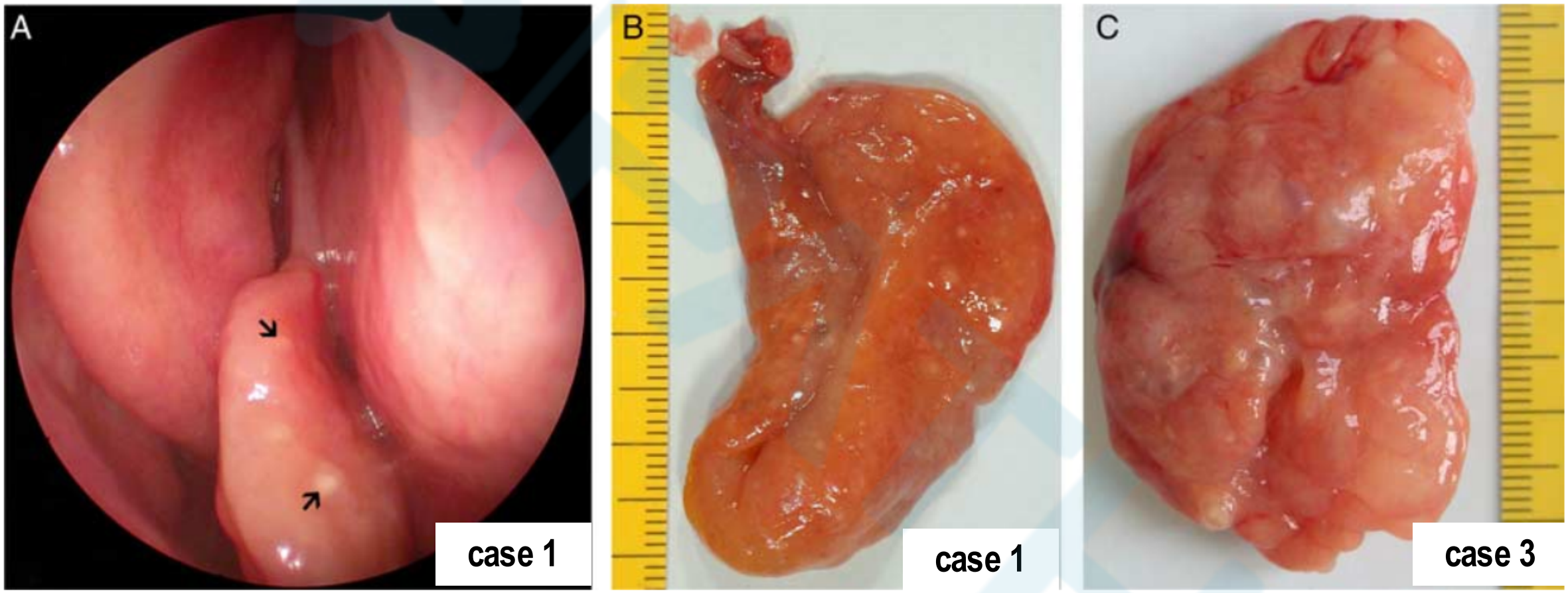

FIGURE 1. Endoscopic and gross views of the lesions. A, Endoscopic aspect of the lesion in patient 1. The lesion is pedunculate, with a stalk lodged in the olfactory cleft. Small whitish cysts are visible (arrows). B and C, Gross view of lesions in patients 1 and 3. Numerous cysts—1 to 2 mm in patient 1 and up to 5 mm in patient 3—are visible by transparency.

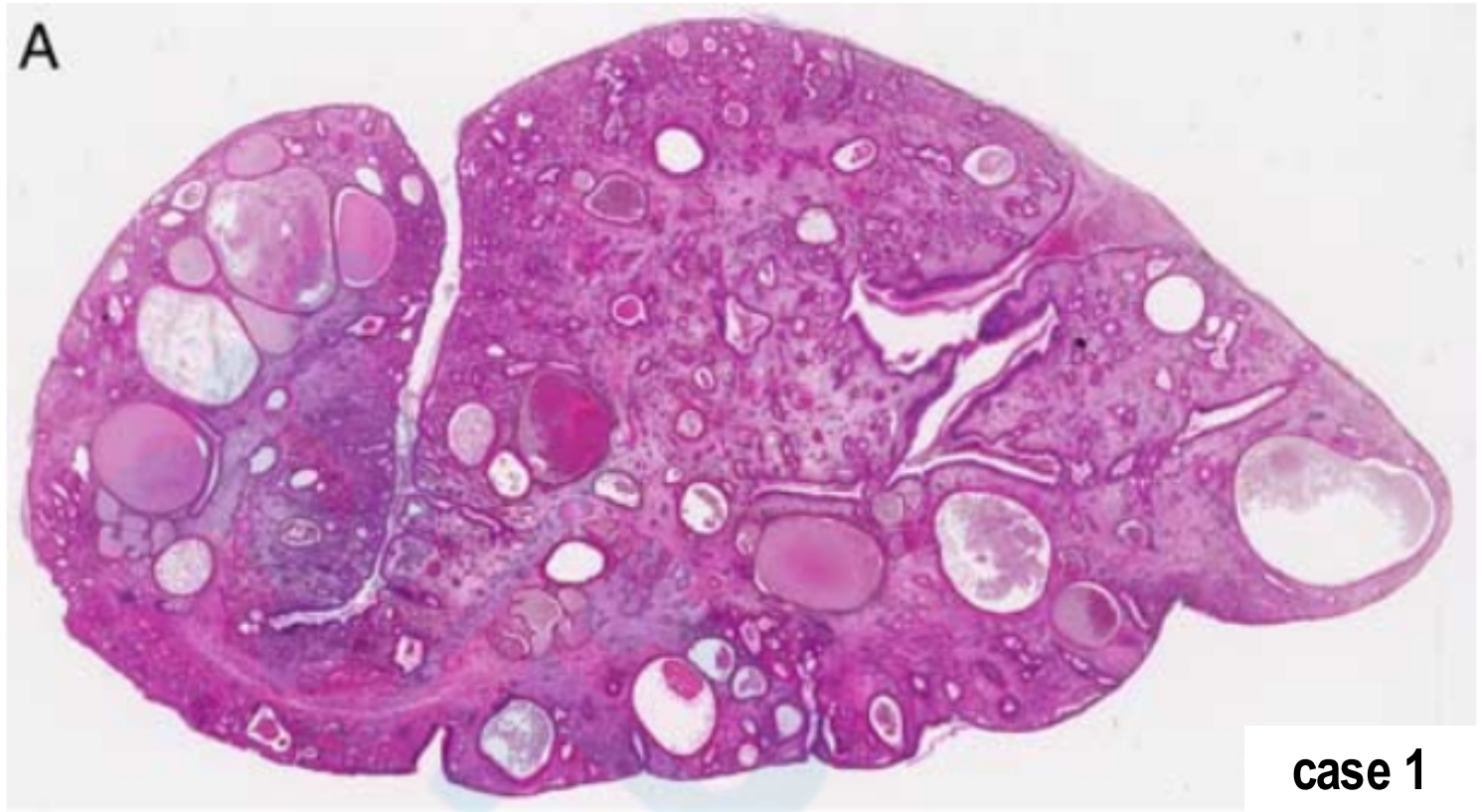

FIGURE 3. Low-magnification view of lesions in patient 1 (A) and patient 5 (B). Surface epithelium and cysts appear invaginated. Note the haphazardly distributed, poorly lobulated seromucinous glands.

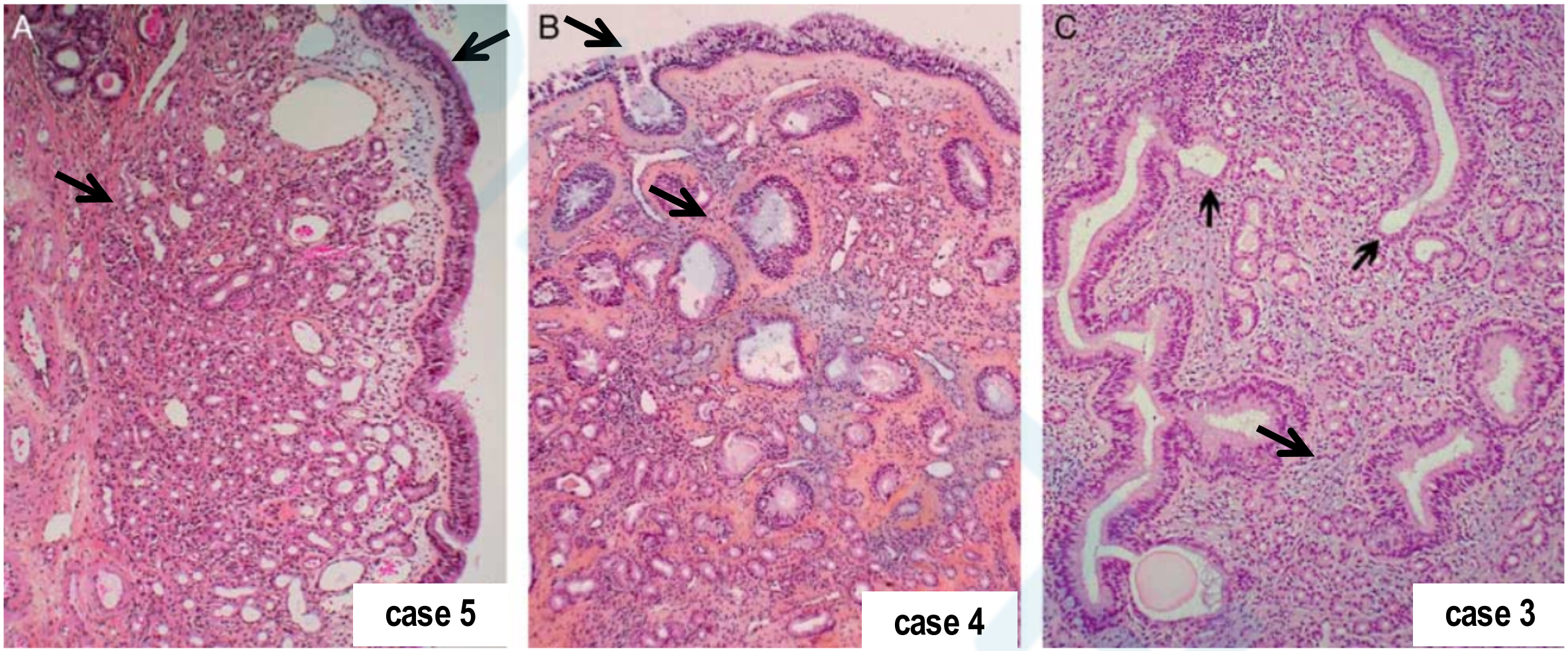

FIGURE 4. The lesions exhibit variable proportions of seromucinous glands and epithelial invaginations. Some areas mainly contain glands with ill-defined lobulation and small cystic dilatations (A, patient 5); numerous epithelial invaginations with basement membrane hyalinization, suggestive of REAH (B, patient 4); or an admixture of glands and invaginations (C, patient 3). Some of the glands open into duct-like invaginations (arrows).

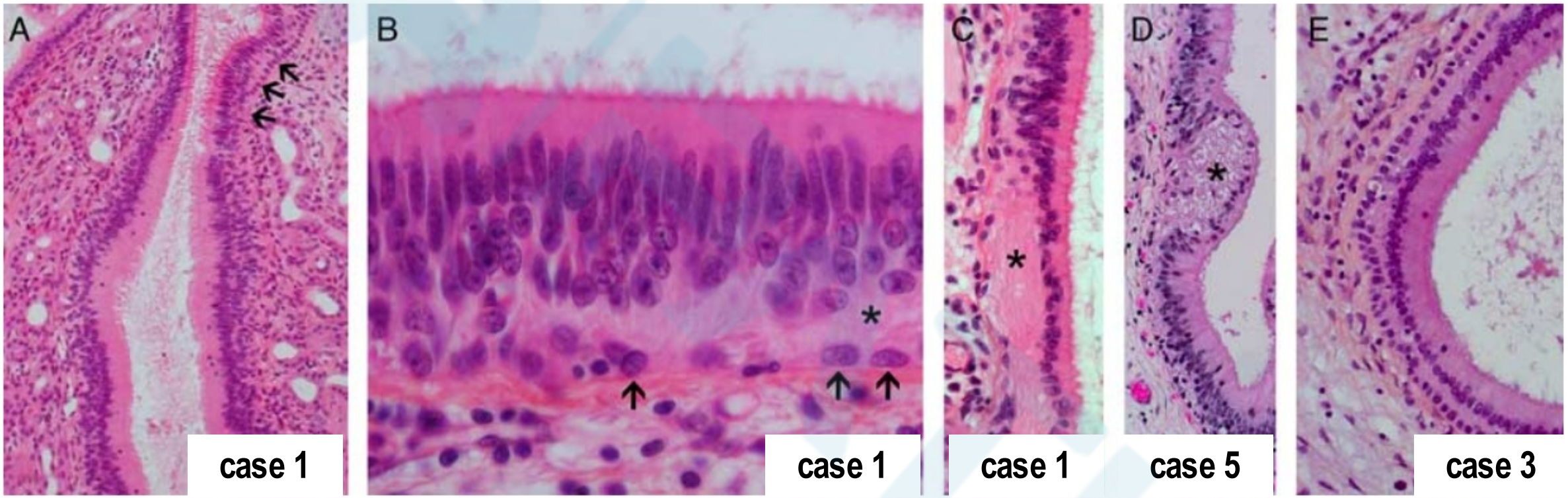

FIGURE 5. Olfactory epithelium component. A, Some of the epithelial invaginations are lined by nonciliated olfactory epithelium, generally containing dense eosinophilic apical cytoplasm continuous with respiratory epithelium (arrows; patient 1). B, This epithelium contains 3 types of cells: basal cells (arrows), sustentacular cells with superficial round or elongated nuclei, and olfactory receptors with intermediate round nucleolate nuclei. Some eosinophilic filamentous material is present above the basal cells (*) (patient 1). C and D, Elongated or globular eosinophilic aggregates of olfactory cell processes, generally basally situated, are present in olfactory epithelium (*) (patients 1 and 5). E, Some nonciliated epithelium-lined ducts only exhibit basal and sustentacular cells and, therefore, present a well-defined bilayered aspect (patient 3).

TABLE 1. Immunohistochemical Profiles of Different Cell Types

Antibody	Clone (s)	Provider	Basal Cells	Sustentacular Cells	Olfactory Cell	
					Bodies	Processes
Pankeratin	AE1/AE3, KL1	Dako	+	+	−	−
Keratin 5/6	D5/16B4	Dako	+	−	−	−
p63	4a4	Dako	+	−	−	−
CD56	1B6	Novocastra	−	−	+	+
Chromogranin A	DAK-A3	Dako	−	−	+f	+f
Synaptophysin	SY38	Dako	−	−	+f	+
Neurofilament	2F11	Dako	−	−	+s	+
S100 protein	Polyclonal	Dako	−	−	−	+*

*Only cell processes and nerves in the stroma.
f indicates focal; s, scattered.

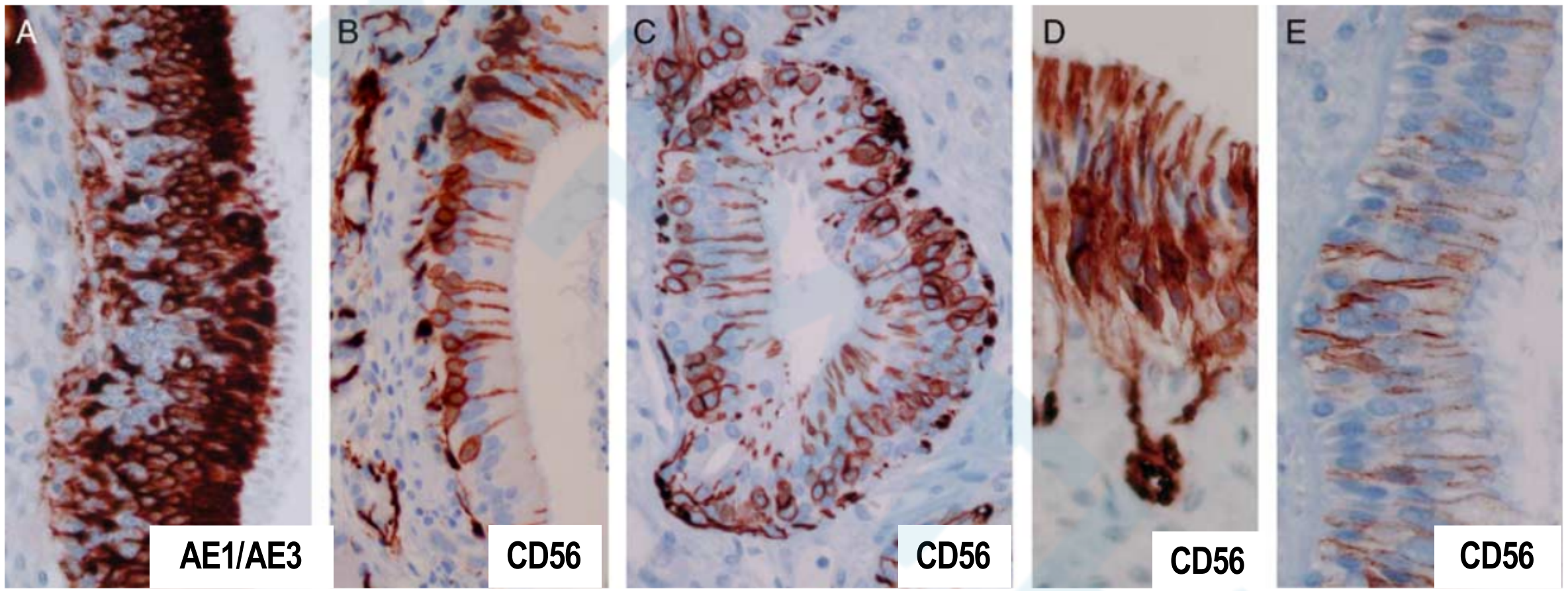

FIGURE 6. Immunohistochemistry findings. A, Basal and sustentacular cells are intensely stained by antikeratin antibodies. Olfactory receptor cells and small luminal vesicles (probably corresponding to olfactory vesicles) are not stained (patient 1). B–E, Anti-CD56 antibodies stain olfactory receptor cells and their apical and basal cell processes (B, patient 3; C, patient 2). Some of the basal cell processes penetrate the stroma and group to form small nerves (D, patient 4). Lateral membranes of mucous cells in respiratory epithelium exhibit focal staining; however, the pattern differs morphologically from that of olfactory receptor cell staining (E, patient 2).

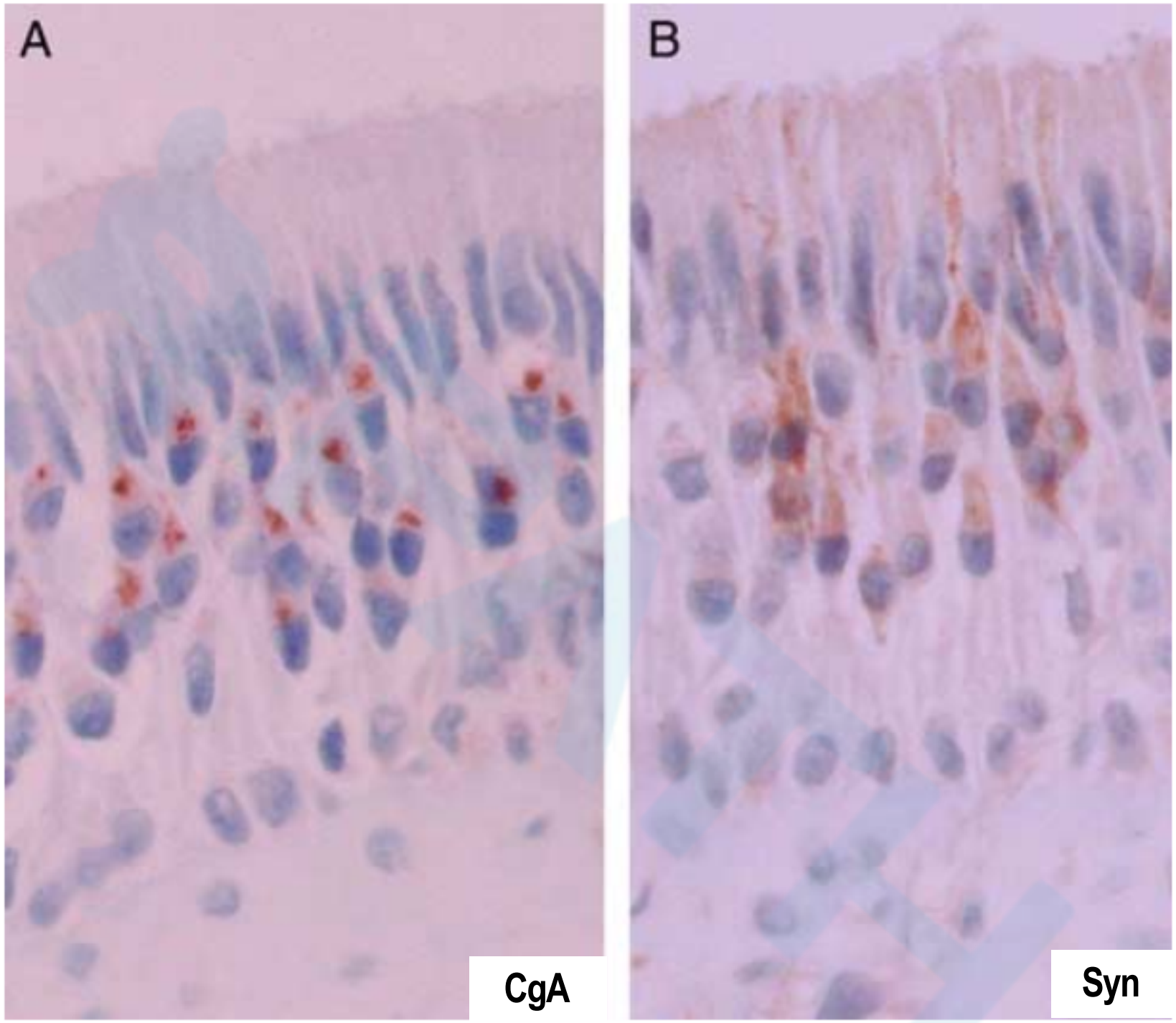

FIGURE 7. Olfactory receptor cells in a few areas express chromogranin A, with a small supranuclear dot-like aspect (A, patient 4). Synaptophysin is focally expressed in the perikaryon and cell processes of some olfactory receptors (B, patient 4).

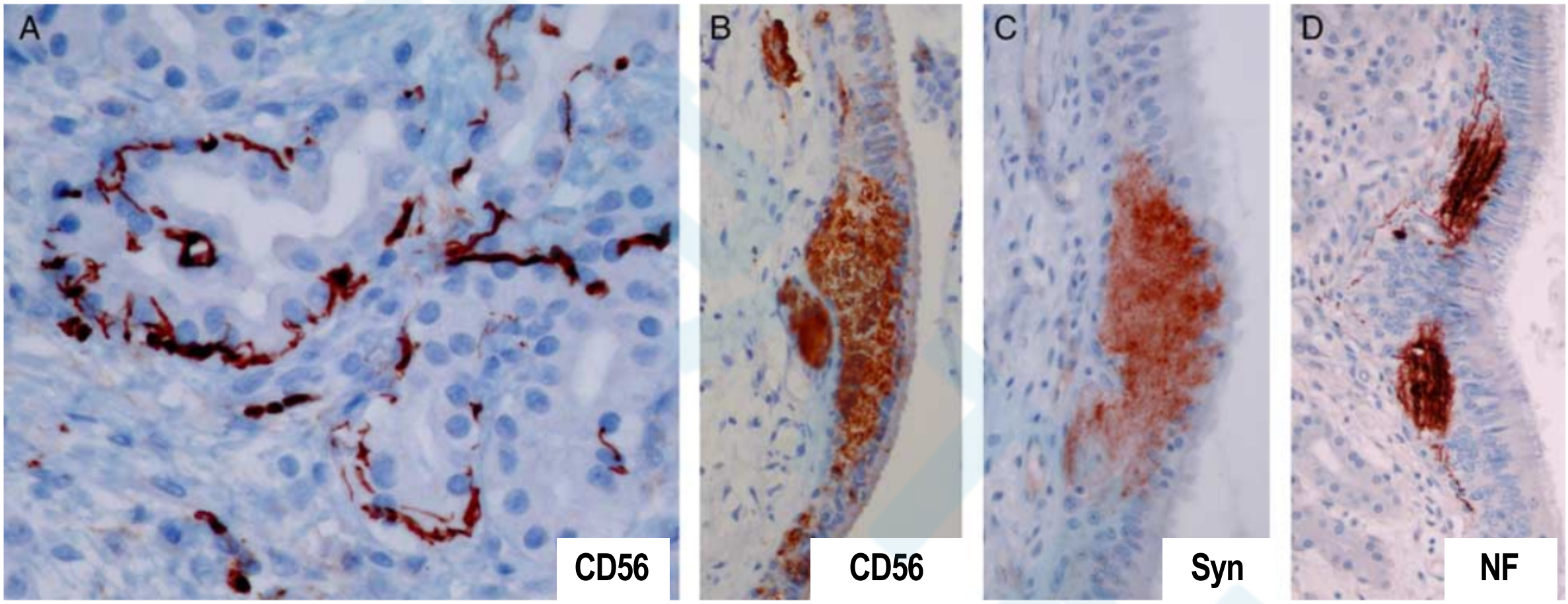

FIGURE 8. Olfactory receptor cell processes found in seromucinous glands, next to areas of olfactory epithelium (A, patient 2). The aggregates of intraepithelial cell processes express CD56 (B, patient 6), synaptophysin (C, patient 1), and neurofilaments (D, patient 1).

RESULTS

- A unique subtype of SEH, which we propose to be named sinonasal olfactory epithelial hamartoma (OEH)

✓ Adult patients (age, 30 to 77 y; mean age, 53 y)

✓ Asymptomatic or nonspecific unilateral obstructive sinonasal symptoms

✓ Five of the lesions were pedunculated and implanted in the olfactory cleft

RESULTS

- ✓ 6 SEH lesions exhibited features of SMH, with an additional olfactory epithelial component
- ✓ All patients underwent endoscopic transnasal surgery, and none experienced recurrence

DISCUSSION

- The structural abnormalities of the olfactory epithelium component

✓ Not normally present in seromucinous glands

✓ Never seen lining elongated duct-like structures or cysts

✓ Epithelium appeared thinner, with fewer cell layers relative

DISCUSSION

- Hamartomas are classically considered as developmental anomalies, composed of normal tissues at the site of occurrence, exhibiting disorganized architecture and benign appearance, and forming tumorlike masses
- Nearly all cases of SEH to date have been reported in adults, among whom developmental malformation is unlikely; this indicates that SEH is probably acquired

CONCLUSION

- SEH exhibits a broader histologic spectrum
- A third subtype in this spectrum（OEH) which resembles SMH

✓ Development from the olfactory cleft

✓ Presence of areas of olfactory epithelium

✓ Similar clinical characteristics, benign course, and imaging features as REAH and SMH

THANK YOU