Ear and Temporal Bone

7

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List of Frequently Asked Questions

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1. *What are the anatomic and histologic components of the ear?*

   The "ear" comprises the external ear, including the auricle and external auditory canal (EAC), the middle ear, the inner ear, and their components. The bony portion of the EAC, the middle, and inner ear are all enclosed in the petrous portion of the temporal bone.

   - Parts of the temporal bone that relate to the ear include the internal auditory canal (also called the internal auditory meatus) and the canals that house the internal carotid artery, internal jugular vein, and facial nerve.
   - Most structures of the ear are lined by either a single layer of squamous epithelium or a low cuboidal epithelium (middle ear mucosa). Table 7.1 summarizes the above anatomical components and their histologic composition.

   Reference: [1]

2. *What are the common congenital anomalies of the ear and temporal bone?*

   Congenital anomalies in this region generally take the form of choristomas and branchial anomalies (Table 7.2).

   - Choristomas are histologically normal tissue found in an anatomic location that is not native to that tissue type.
     - The most common type of heterotopia in the middle ear is salivary gland tissue.
     - Neuroglial tissue in the middle ear is exceedingly rare, and many believe it likely represents encephaloceles and are not true choristomas (Fig. 7.1).
       - The presence of neuroglia tissue in the middle ear should be identified as an encephalocele unless unequivocally proven otherwise. This is an important consideration as it encourages the clinician to search for, thoroughly, and definitively exclude, a connection to the central nervous system and avoid serious complications.

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- Branchial anomalies involving the ear and temporal bone are related to the first branchial arch and cleft (Fig. 7.2).
  References: [2–9]

Table 7.1 Anatomy and histology of the ear and temporal bone

Region	Structure	Anatomy/histology
External ear	Auricle	Skin Elastic cartilage
	External auditory canal	Outer 1/3: elastic cartilage and skin with sebaceous glands and deep ceruminous glands Inner 2/3: bone and flattened skin
Middle ear	Tympanic membrane	Fibrous tissue covered by flattened skin laterally and medially by middle ear mucosa
	Ossicles	Bones (stapes, incus, malleus) covered by middle ear mucosa
	Mastoid cavity and air cells	Bone and spaces connected to the middle ear and lined by middle ear mucosa
	Eustachian tube	Lined by respiratory mucosa. Connects the middle ear to the nasopharynx
Inner ear	Labyrinth: outer osseous layer and inner membranous layer	Contains the cochlear, semicircular canals, saccule, utricle, endolymphatic duct and sac
	Internal auditory canal	Bony canal that houses the vestibulocochlear nerve (CN8) and connects the inner ear with the posterior cranial fossa

CN cranial nerve

3. *What are the common keratinous lesions of the external auditory canal (EAC)?*

The EAC is lined by skin, comprising keratinizing, stratified squamous epithelium and adnexal structures. As a result, some common skin lesions can occur in this location, including seborrheic keratosis, squamous cell carcinomas, and squamous papillomas. Lesions unique to the EAC such as cholesteatomas and keratosis obturans (KO) are discussed here (Table 7.3).

- Cholesteatomas and keratosis obturans (KO) are both characterized by the accumulation of keratin within the ear.
  - Cholesteatomas are rare in the EAC but have identical histologic features with those of the middle ear and the congenital forms.
  - Acquired cholesteatomas will be detailed here to highlight the differential diagnosis with KO.
  - Middle ear cholesteatomas (Fig. 7.3) may be associated with meningiomas, middle ear adenomas, and aural polyps.
- Seborrheic keratosis of the EAC is rare and identical to those at other body sites.
  - They are plaque-like, hyperkeratotic tumors composed of a proliferation of normal-appearing squamous cells which merge with more basaloid squamous cells. Keratin cyst formation is characteristic, and cytologic atypia is absent. The lesion shows a sharp demarcation from the adjacent epidermis.
- Squamous papillomas are rare but have been reported in the auricle, EAC, and middle ear. They are identi-

Table 7.2 Congenital anomalies of ear and temporal bone region

	Choristoma		First branchial anomalies	
	Salivary tissue	Neuroglial tissue	Cyst, fistula, sinus	Accessory tragus
Age (years)	0–20	40–50	0–17 (mean 2.4)	0–20
Clinical presentation	Unilateral ear pain Hearing loss Mass behind TM	Presents with chronic otitis media History of recurrent infections or trauma	Symptoms related to infection and drainage of tract or fistula Sinuses are most common	Present with preauricular, polypoid skin lesion May be multiple or single, bilateral or unilateral
Histology	Serous and mucinous glands with ducts and fibroadipose tissue ±Chronic inflammation Covered by normal middle ear mucosa	Varying amounts of glial tissue and neurons, typically without ependymal, leptomeningeal, or choroid plexus tissue Chronic inflammation and reactive gliosis	Typically a squamous-lined tract or fistula with varying amounts of chronic and acute inflammation	Polypoid fragment of skin with adnexal structures, hair and underlying fibroadipose tissue ±Core of elastic cartilage
Other findings	May be associated with ossicular and facial nerve abnormalities	Must be considered an encephalocele until unequivocally proven otherwise	Involved areas dictate the clinical presentation: periauricular, ear, EAC, parotid region, angle of jaw Rarely associated with other anomalies	Rarely associated with other anomalies: Treacher-Collins syndrome, Townes-Brocks syndrome, VACTERL syndrome, and 4p syndrome (Wolf-Hirschhorn syndrome)

TM tympanic membrane

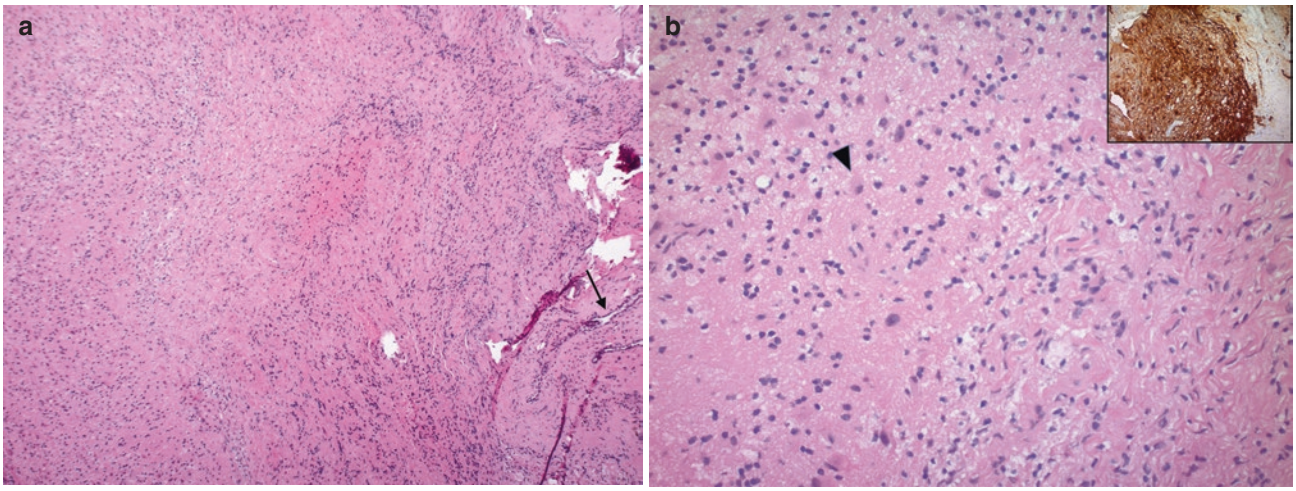

Fig. 7.1 Neuroglial tissue. (**a**) Brain tissue with underlying middle ear mucosa (arrow) and reactive fibrous changes. (**b**) Higher magnification of the glial tissue shows a fibrillary background and scattered neurons (arrowhead) which are positive for GFAP (inset)

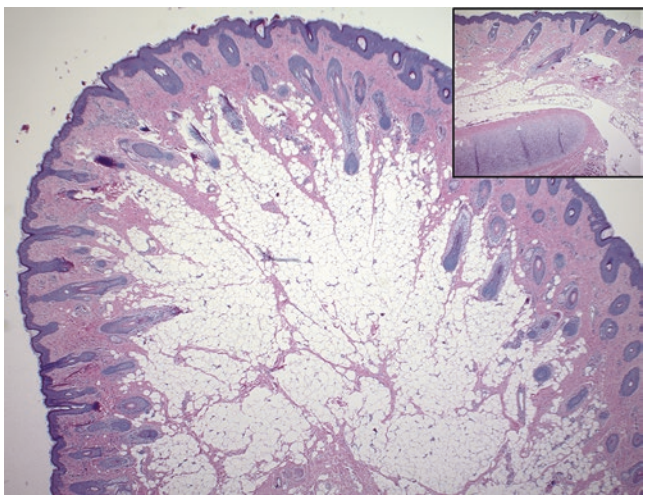

Fig. 7.2 Accessory tragus. Polypoid skin fragment with underlying fibroadipose tissue and core of elastic cartilage (inset)

cal to squamous papillomas elsewhere, described in detail in Chap. 2.

- Squamous cell carcinoma (SCC) most commonly involves the external ear including the auricle and cartilaginous EAC; rare cases involve the middle ear.
- Specifically, SCC of the temporal bone is an aggressive tumor with overall 5-year survival rates of less than 50%.
  - Patients are usually elderly and present at an advanced stage due to delayed diagnosis or misdiagnosis of otitis.
  - Morbidity and mortality are related to direct tumor extension, as lymph node metastases are a late occurrence.
  - Carcinomas of the bony canal spread out toward the cartilaginous canal or inward to involve the middle ear.
  - Middle ear tumors invade the mastoid, middle cranial fossa, Eustachian tube, and skull base.
  - Histologically, SCCs in this region is typically keratinizing and identical to those seen in other epidermal sites.

References: [1, 10–17]

4. *What are the common skin tumors of the external ear and EAC?*
   - According to the Armed Forces Institute of Pathology (AFIP), basal cell carcinomas (BCC) account for 21% of all neoplasms of the ear and temporal bone. They are the most common cutaneous tumors of the external ear and generally have an indolent clinical course.
     - Sun exposure is the most significant risk factor. Consequently, the auricle is the most common site.
     - Grossly, BCC is a pearly, white subepithelial nodule with a central ulceration.
     - BCC comprises nests of monotonous, basaloid cells with scant cytoplasm. Tumor nests show peripheral palisading of tumor cells and may demonstrate retraction from the surrounding stroma.
     - The infiltrative or morphea-like variant comprises cords and single file cells invading a desmoplastic stroma.
     - Squamous metaplasia with keratin formation can be seen and should not be confused with SCC.
     - Stromal changes include desmoplasia and mucin production.
   - Melanomas of the external ear occur most commonly on the auricle, though EAC and middle ear melanomas have been reported. Melanomas of the external ear typically occur in white males with an average age of 66 years old.

Table 7.3 Comparison of cholesteatomas and keratosis obturans

	Middle ear cholesteatoma	EAC cholesteatoma	Keratosis obturans
Patients	Adults, usually 30–40yo	Elderly	Young
Clinical	History of trauma, surgery, or chronic otitis media Associated perforated TM	Otorrhea Chronic, dull pain Rarely hearing loss Normal TM History of trauma, surgery, chronic otitis externa	Hearing loss Acute, severe pain Thickened TM
Location	Middle ear Unilateral	EAC Unilateral	EAC May be bilateral, especially in children
Histology	Cystic lesion lined by keratinizing squamous epithelium with granular cell layer Filled with layered, concentric, keratinous debris May only show keratinous debris	Cystic lesion lined by keratinizing squamous epithelium with granular cell layer Filled with keratinous debris randomly arranged May only show keratinous debris	Inflammatory lesion caused by excessive retention of exfoliated keratinocytes forming a keratin plug Keratinous debris arranged in concentric layers
Complications	Ossicles and bony canal may be eroded in chronic cases	Localized bony erosion of canal is typical Focal epithelial ulceration Osteonecrosis Abscess formation Hearing loss	Circumferential bony erosion Widening of EAC No osteonecrosis No ulceration Secondary infection
Treatment	Surgical excision, recurrences may occur	Surgical excision, recurrences may occur	Ear cleaning and removal of keratin plug

EAC external auditory canal, *TM* tympanic membrane

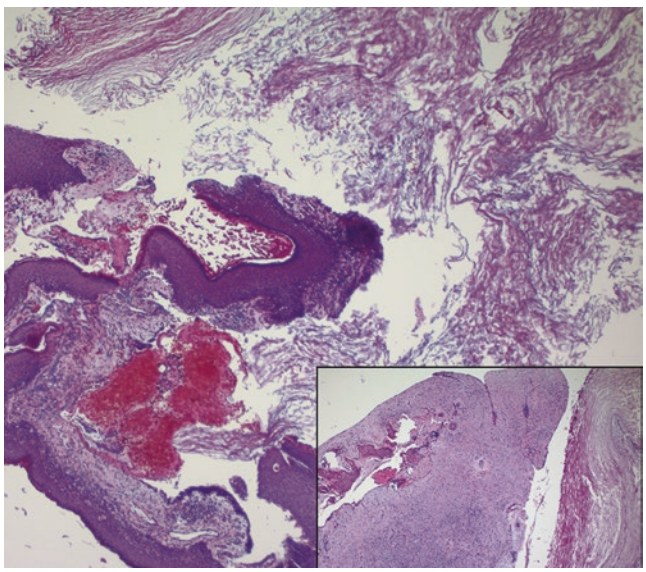

Fig. 7.3 Cholesteatoma. Strips of benign squamous epithelium associated with abundant keratinous debris. (Inset) Concentric layers of keratin and a fragment of fibrotic soft tissue with bone erosion

  - The most common growth types in decreasing frequency are superficial spreading, lentigo maligna, and nodular.
  - The most common histologic types are epithelioid and spindle types.
    - Nests, cords, and sheets of tumor cells start at the dermal-epidermal junction with eventual downward growth into the dermis.
    - The cells vary in appearance from small, nevoid cells with scant cytoplasm to larger cells with moderate amounts of eosinophilic to amphophilic cytoplasm, vesicular nuclei with prominent nucleoli or coarse chromatin.
    - Intracytoplasmic pigment is typical in the epithelioid variant.
    - Cells are keratin negative and positive for S100, HMB-45, Mart-1, Sox-10, and MiTF.
  - Stage and depth of invasion, as measured by Breslow thickness or Clark level, determine prognosis.
  - Deep et al. and Patel et al. performed large, population-based studies which show an excellent prognosis for stage 1 and 2 disease with a 5- and 10-year disease-specific survival (DSS) of 90%. Five-year DSS drops to 50% for stage 3 and 20% for stage 4.

  References: [1, 18–22]

5. *What are the common tumors of ceruminous glands, and how are they diagnosed?*

   Ceruminous glands are specialized apocrine glands found in the deep dermis of the outer half of the EAC. They are the origin of most glandular lesions in the EAC. In general, tumors arising from the adjacent parotid gland with extension into the EAC or middle ear should be excluded, as well as metastases. Ceruminous gland adenomas and carcinomas are broad terms that encompass a few different entities (Table 7.4).

- Ceruminous adenomas and adenocarcinoma, NOS, typically show prominent apocrine change. A dual-cell population of basal cells and luminal cells is present in both but may be focal in the carcinomas. The existence of true myoepithelial cells (with smooth muscle differentiation) in the adenocarcinomas is not clear. The distinction between the two tumors can be difficult (Table 7.5).
- Ceruminous gland adenoid cystic carcinoma (CG-AdCC) and mucoepidermoid carcinoma (CG-MEC) are identical to their salivary gland counterparts. Both are even rarer than the conventional ceruminous adenocarcinoma (CG-ACA, NOS). A few differences should be noted:
  - The morphologic patterns of CG-AdCC (Fig. 7.4) do not correlate with tumor grade or behavior like their salivary gland counterparts. This may be a result of its rarity and the absence of sufficient data. However, CG-AdCC behaves similarly with locally aggressive growth and a prolonged disease course plagued by multiple recurrences and distant metastases.
- The ductal cell population and apocrine differentiation may be focal.
- Cutaneous BCC is in the differential diagnosis of the solid variant of CG-AdCC and should be excluded as the prognosis is worse for the latter. CG-AdCC has frequent PNI, some cribriform architecture, and lacks palisading.
  - Ceruminous gland mucoepidermoid carcinomas have the classic three cell types: epidermoid, intermediate, and mucous cells.
- Ceruminous gland pleomorphic adenoma is the most common among the adenomas and has the classic biphasic histomorphology of pleomorphic adenomas in other sites. Sheets of myoepithelial cells and chon-

Table 7.4 Terminology of ceruminous gland tumors

Ceruminous adenomas	Ceruminous carcinomas
Ceruminous adenoma, NOS (conventional type)	Ceruminous adenocarcinoma, NOS (conventional type)
Ceruminous pleomorphic adenoma	Ceruminous adenoid cystic carcinoma
Ceruminous syringocystadenoma papilliferum	Ceruminous mucoepidermoid carcinoma

NOS not otherwise specified

Table 7.5 Clinicopathologic features of ceruminous adenoma and adenocarcinoma, NOS

	Ceruminous adenoma	Ceruminous adenocarcinoma, NOS	
		Low-grade	High-grade
Age (years)	50–60	50–60	
Presentation	Painless Subcutaneous nodule Unilateral hearing loss	Pain, otorrhea Ulceration Unilateral hearing loss	
Location	Outer, cartilaginous EAC	Cartilaginous EAC with extension into middle ear Destruction of petrous and temporal bone	
Gross findings	Circumscribed, unencapsulated, cystic Rarely ulcerated	Infiltrative with firm, solid cut surface	
Histology	Proliferation of glands and tubules Glands may be back to back Hyalinized or fibrous stroma Basal cells and myoepithelial cells present	Proliferation of glands and tubules Basal cells may be focal Invasion with desmoplasia	Irregularly shaped, infiltrative glands, sheets, cords ±Cribriform patterns Basal cells may be focal Invasive with desmoplasia Necrosis, PNI
Cytology	Inner cuboidal/columnar cells with abundant eosinophilic cytoplasm, apical snouting Golden-yellow, lipofuscin-like, cytoplasmic granules Round, bland nuclei, fine chromatin, small nucleoli No atypia, mitoses or necrosis	Glands are lined by 1–2 layers of cuboidal/columnar cells with abundant eosinophilic cytoplasm, apical snouting No golden-yellow, lipofuscin-like, cytoplasmic granules Oval, vesicular or hyperchromatic nuclei, variably prominent nucleoli None to scattered mitoses	Glands are lined by 1–2 layers of cuboidal/columnar cells with abundant eosinophilic cytoplasm May be poorly differentiated with loss of apocrine features Marked pleomorphism Brisk mitotic activity Metastases must be excluded
Positive stains	Cytoplasmic granules: PAS, Sudan black, Ziehl-Neelsen	p53: <10% – 30% of cells	
Luminal cells	CK7, CD117 (weak)	CK7, CD117 (strong), EMA, AR	
Abluminal cells	S100, CK5/6, p63	S100, CK5/6, p63	

EAC external auditory canal, *LG* low-grade, *HG* high-grade, *PNI* perineural invasion

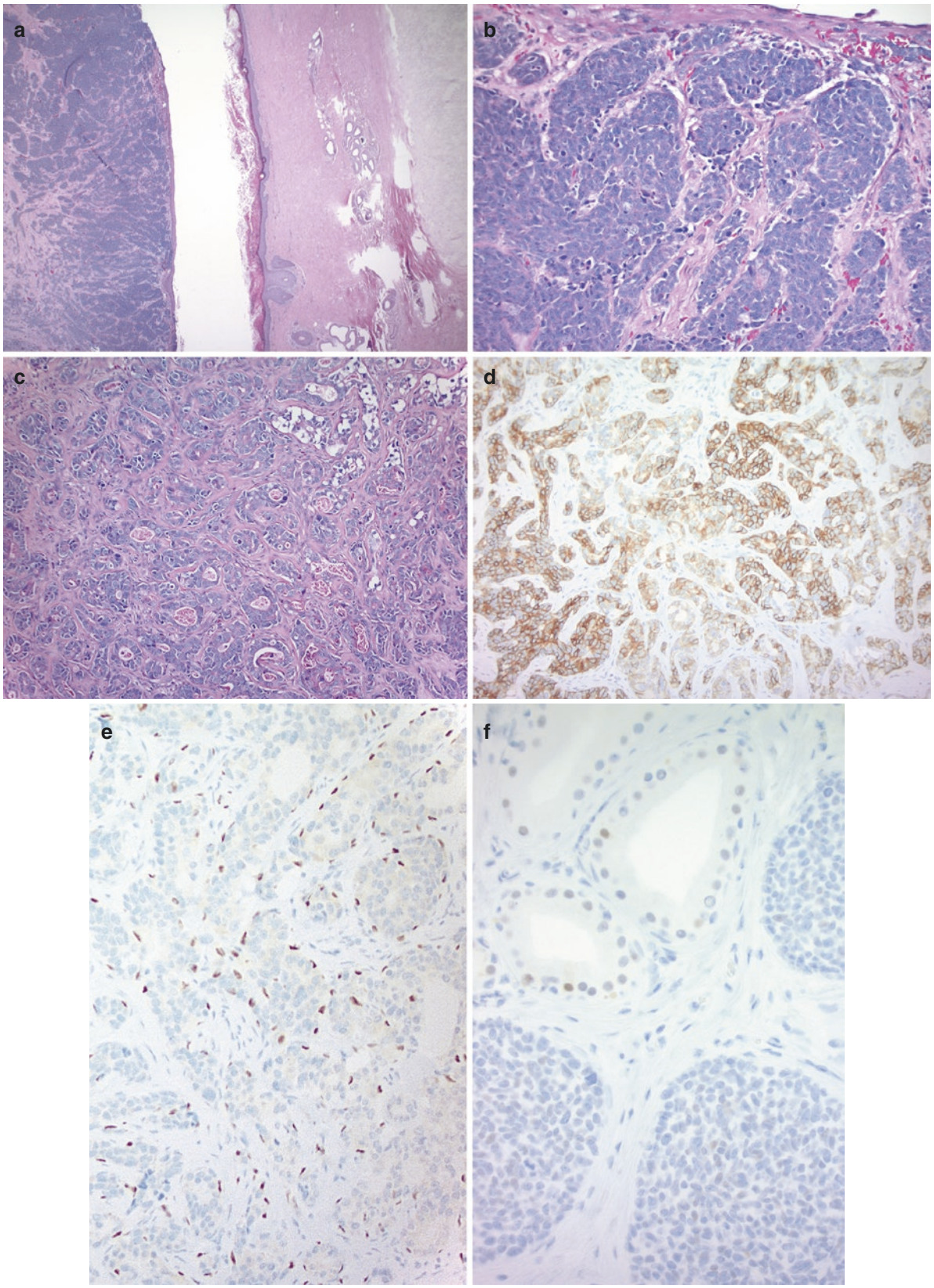

Fig. 7.4 Ceruminous gland adenoid cystic carcinoma. (**a**) Section of external auditory canal lumen shows a basaloid tumor underlying atrophic epithelium on the left. Normal epidermis lines the canal on the right with underlying normal ceruminous glands and elastic cartilage. (**b**) The tumor cells are angulated, basaloid cells with scant cytoplasm arranged in solid nests and (**c**) tubules. (**d**) The tumor cells stain strongly for CD117. (**e**) A stain for p63 highlights scattered abluminal cells. (**f**) Androgen receptor IHC shows weak nuclear staining of rare tumor cells. Normal cerumen glands are positive for AR

dromyxoid stroma aid in the distinction from CG-ACA, NOS.
  - Ductal cells will show some apocrine differentiation with apical snouting and lipofuscin-type granules.
- Ceruminous gland syringocystadenoma papilliferum is rare. It is identical to its dermal counterpart.
  - CGSCP is characterized by a cyst formed from invagination of the skin surface epithelium.
  - Numerous papillary structures protrude into a cyst and are lined by an inner layer of basal cells and an outer layer of apocrine cells.
  - The fibrovascular cores have a dense plasmacytic infiltrate.

References: [23–26]

6. *What are the inflammatory cartilaginous lesions of the ear?*
   - Idiopathic cystic chondromalacia (Fig. 7.5) and chondrodermatitis nodularis chronicus helicis (Fig. 7.6) are both idiopathic, mass-producing inflammatory lesions of the auricle (Table 7.6).
   - Relapsing polychondritis (RP) is an inflammatory disease affecting hyaline and elastic cartilage. The disease is characterized by recurrent episodic flares involving cartilage of the auricle, nose, and upper respiratory tract.
     - RP presents with bilateral chondritis of the pinna with diffuse edema and tenderness.
     - Patients may suffer from systemic manifestations including keratitis, conjunctivitis, migratory arthralgias, cardiac valve insufficiency, and kidney disease.
     - Biopsies show a marked, mixed inflammatory infiltrate of cartilage with erosion and necrosis.

   References: [27–33]

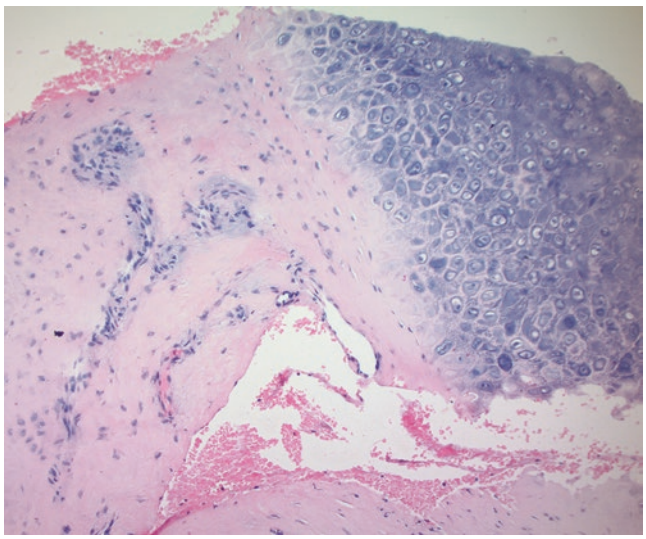

Fig. 7.5 Idiopathic chondromalacia. Pseudocyst filled with blood and serum and lined by granulation tissue with fibrosis. Elastic cartilage is noted adjacent to the lesion (right)

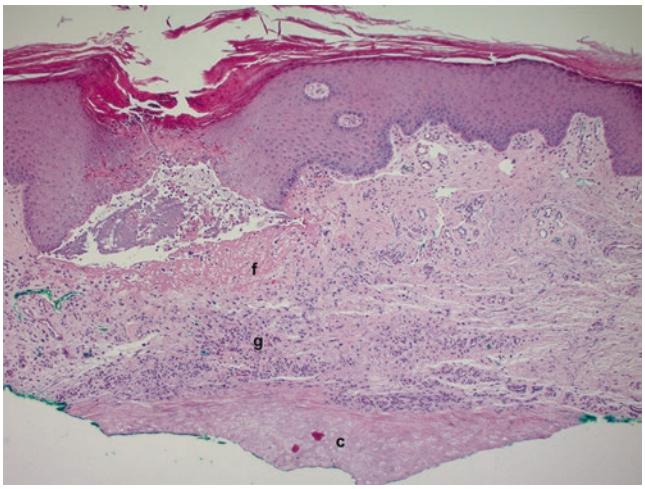

Fig. 7.6 Chondrodermatitis nodularis chronicus helicis. Acanthotic epidermis with parakeratosis and a central ulcer. The ulcer base contains (f) fibrinoid necrosis with underlying (g) granulation tissue, inflammation, and (c) degenerated cartilage

Table 7.6 Clinicopathologic features of inflammatory lesions of ear cartilage

	Chondromalacia	Chondrodermatitis nodularis chronicus helicis
Patient	Young to middle-aged, male	Middle-aged to older, male
Location	Scaphoid fossa	Superior helix
Symptoms	Painful, subcutaneous nodule	Painful, red nodule with central ulcer
Duration	Weeks to years	Sudden onset
Pathogenesis	Trauma, ischemic necrosis	Exposure to cold, actinic damage, trauma
Pathology	Fluid-filled pseudocyst caused by degeneration of cartilage Fibrous tissue or granulation tissue may line the cyst Chronic inflammation ±Reactive atypia	Epidermal changes adjacent to the ulcer: PK, HK, acanthosis, or PEH Granulation tissue in ulcer base with fibrinoid necrosis Acute and chronic inflammation Inflamed perichondrium and cartilage ±Stromal necrobiosis with palisading histiocytes
Clinical differential diagnosis	Chondrodermatitis nodularis chronicus helicis Relapsing polychondritis	Basal cell carcinoma Squamous cell carcinoma
Treatment	Surgical excision	Surgical excision, pressure relief, topical nitroglycerin

PK parakeratosis, *HK* hyperkeratosis, *PEH* pseudoepitheliomatous hyperplasia

Table 7.7 Benign osseous lesions of the ear

	Exostosis	Osteoma	Otosclerosis
Patients	Cold water swimmers, surfers Male, <50 years old	Male, <50 years old (EAC) Female > male (mastoid)	Female > male 20–30 years old
Location	Medial EAC	EAC, mastoid, rarely middle ear	Middle ear, stapes
Clinical	Bilateral, multiple	Unilateral, solitary	Bilateral (85%) Family history (50%)
Symptoms	Asymptomatic until obstructive symptoms: – Recurrent otitis externa – Conductive hearing loss – Tinnitus	Asymptomatic until obstructive symptoms: – Conductive hearing loss – Aural fullness	Conductive or mixed hearing loss ±Vestibular changes
Pathology	Broad-based, bony growth Resembles cortical bone Onion-skin layering of dense bone Periosteal and skin covering No trabeculae or marrow spaces	Pedunculated bony growth Resembles cancellous bone with trabeculae of normal, lamellar bone Marrow space filled with fibroconnective tissue May have cortical bone at periphery Periosteal and skin covering	Early phase: bone resorption with formation of perivascular spaces Increased osteoclasts Late phase: woven bone with dense sclerosis causes stapedial footplate fixation Stapes specimen may be normal*
Treatment	Medical treatment of otitis Surgery for refractory cases	Surgical excision	Surgical stapedectomy with prosthesis

EAC external auditory canal
*Otosclerosis frequently involves the bone *adjacent to* the stapes, limiting footplate motion; the excised stapes footplate may be histologically normal

7. *What are the benign bony lesions of the ear?*

The more common bony lesions in the ear and temporal bone include mass-like lesions of bone, like osteoma and exostosis, as well as reactive bone formation as seen in otosclerosis (Table 7.7).

References: [34–39]

8. *What is an aural polyp?*

An aural or otic polyp is an inflammatory polyp of the middle ear, a complication of chronic otitis media.

- Patients are usually children with complaints of otorrhea and conductive hearing loss.
- A mass presents in the middle ear with possible extension into the EAC and resultant perforation of the tympanic membrane.
- Histologic sections show polypoid granulation tissue that may be ulcerated or covered by cuboidal or respiratory epithelium (Fig. 7.7)
  - The stroma ranges from edematous to fibrous with chronic inflammation, including plasma cells. Neutrophils and eosinophils may also be present.
  - Squamous and glandular metaplasia may be seen in the stromal tissue.
  - Foreign body-type giant cells, cholesterol granulomas, and debris may be seen.
  - Langerhans cell histiocytosis and infection should be excluded.
- Chronic otitis media and cholesteatoma are frequent underlying causes.
- Bilateral aural polyps are associated with Samter's triad: aspirin intolerance, asthma, and sinonasal polyps.

References: [1, 40, 41]

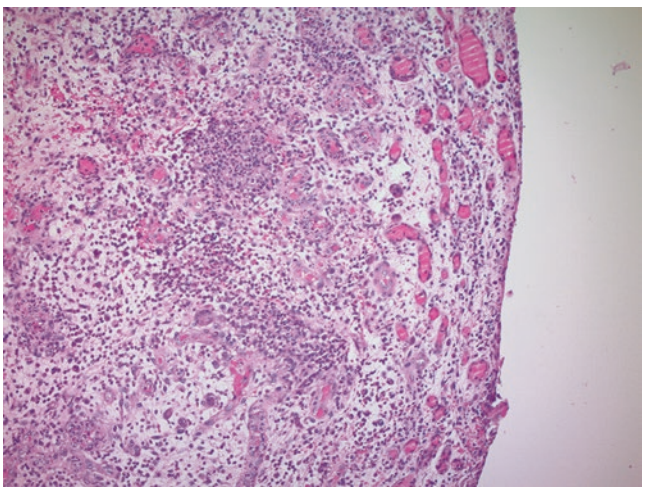

Fig. 7.7 Aural polyp. Polypoid, inflamed granulation tissue partially lined by middle ear mucosa

9. *What is the difference between middle ear adenomas and carcinoid tumors?*

Middle ear adenomas and middle ear carcinoids are currently thought to represent the same entity (Fig. 7.8). It is an epithelial tumor that demonstrates morphologic and immunophenotypic evidence of both glandular and neuroendocrine differentiation; its features are summarized in Table 7.8. There remains controversy around the appropriate terminology. The 4th edition of the WHO Classification of Head and Neck Tumors refers to these tumors as adenomas despite a handful of reported cases

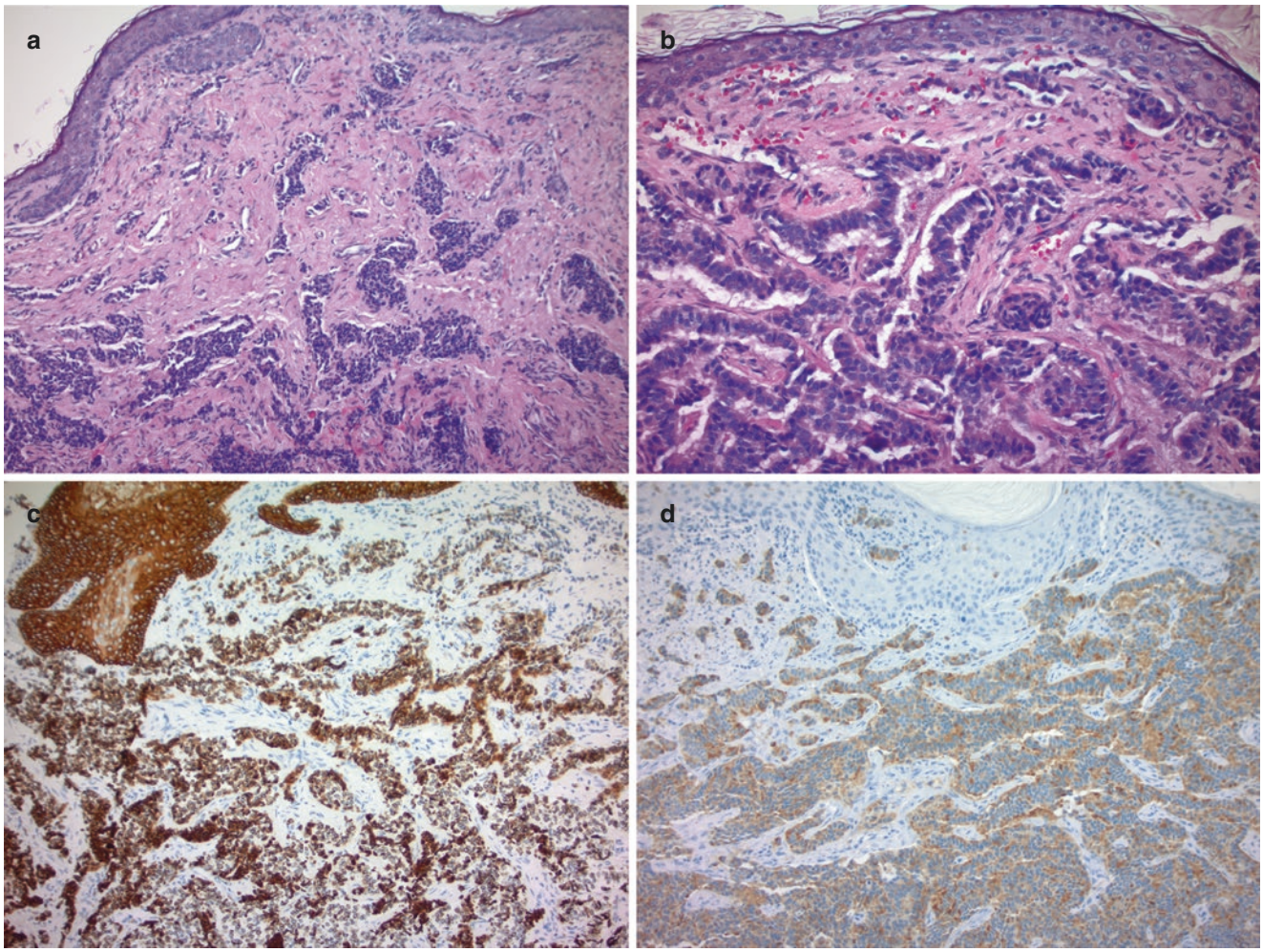

Fig. 7.8 Middle ear adenomatous neuroendocrine tumor. (**a**) Crushed nests and (**b**) trabeculae of tumor cells are present in a fibrous stroma. (**c**) The tumor stains strongly for pan-cytokeratin and (**d**) synaptophysin

which have metastasized to the bone, liver, and regional lymph nodes.

- There is an 8% metastatic rate including some disease-related deaths and a 20% recurrence rate.
- Middle ear adenomatous neuroendocrine tumor (MEANT) is one of the proposed names that embodies both its behavior and phenotype.

References: [42–46]

10. *What are the genetics associated with middle ear paragangliomas, and how are malignant ones diagnosed?*

Paragangliomas are neuroendocrine tumors that arise from paraganglia which are present throughout the body. They are the most common inherited neoplasm in humans, and their diagnosis should prompt a referral for genetic counseling.

- There are four types of head and neck paragangliomas, in order of frequency:
  1. Carotid body (60%)
  2. Middle ear (30%)
  3. Vagal (10%)
  4. Laryngeal (<1%)
- PGL syndromes 1 through 5 now represent the most common hereditary disorder.
- Genetic mutations in any one of the five subunits of the succinate dehydrogenase enzyme complex (SDHA, SDHB, SDHC, SDHD, and SDHA2) result in SDH-deficient tumor cells and loss of SDHB expression by immunohistochemistry (IHC).
- 10–20% of apparently sporadic cases of head and neck PGL may be inherited. The SDHB IHC stain can be used to screen patients for familial PGL syndromes, but genetic testing is required to confirm and identify the specific mutation.
- Approximately 2% of MEPGL are associated with familial inheritance. This is critical, as certain genetic alterations offer prognostic information on rates of metastases, clinical aggression, and association with other tumor types.

Middle ear paragangliomas (MEPGL) were historically known as glomus tympanicum or jugulotympanic

Table 7.8 Clinicopathologic features of middle ear adenomatous neuroendocrine tumor

Gender	M = F
Age (years)	Mean = 50 (range 16–80)
Clinical presentation in order of frequency	Hearing loss Aural mass/fullness Ear pain, tinnitus
Architecture	Unencapsulated, submucosal
Morphologic patterns	Glandular, trabecular, solid/plasmacytoid, organoid 80% will show more than one pattern
Cytologic features	Cuboidal cells lining duct-like structures Salt and pepper chromatin ±Focal pleomorphism Rare or no mitoses
Growth	Ossicular involvement common Nerve compression Temporal bone erosion (features are related to mass effect, not malignancy or tumor aggression) Pagetoid spread to overlying mucosa
Immunohistochemistry	Keratin+ Neuroendocrine marker expression is variable

paragangliomas. MEPGL are the most common tumors of the middle ear, affecting middle-aged patients with a 3:1 female predominance.

- Clinical presentation includes otalgia, otorrhea, and pulsatile tinnitus.
- MEPGL are slow growing but may eventually involve the bone.
- Histologic features include:
  - Solid nests of epithelioid cells with abundant eosinophilic to amphophilic cytoplasm and round nuclei with fine salt and pepper chromatin.
  - Tumor nests are surrounded by inconspicuous, spindled sustentacular cells.
- 2% of MEPGL will metastasize.
- There are no histologic features that predict behavior, despite the presence of seemingly worrisome features such as infiltrative tumor border, perineural invasion, bone involvement, and atypia.

References: [47–52]

11. *How are middle ear adenomas and paragangliomas distinguished?*

Morphology and immunohistochemical studies can aid in the distinction between MEANT and MEPGL (Table 7.9).

References: [42, 44, 47, 48]

12. *What are the clinical and histologic characteristics of temporal bone and ear schwannomas?*

Schwannomas are benign peripheral nerve sheath tumors. The most common tumor of the temporal bone is the vestibular schwannoma (VS) (acoustic neuroma). It arises from the vestibular branch of cranial nerve VIII (vestibulocochlear nerve) at the level of the internal auditory canal or the cerebellopontine angle (CPA).

Table 7.9 Comparison of middle ear adenomatous neuroendocrine tumor and paraganglioma

	MEANT	MEPGL
Gland formation	Present	Absent
Cytokeratin expression: Pan-keratin, CK7	Present	Absent
Neuroendocrine marker expression: chromogranin, synaptophysin, CD56	Present	Present
S100-positive sustentacular cells	Absent	Present

- Patients are usually middle-aged with a female predominance.
- Symptoms include progressive, unilateral sensorineural hearing loss and tinnitus.
- Histology is identical to those in other locations and shows an encapsulated, bland spindle cell proliferation with:
  - Fusiform, wavy nuclei in a fibrillary background.
  - Verocay bodies that have nuclear palisading around central eosinophilic areas.
  - Hypercellular Antoni A areas alternate with hypocellular, edematous Antoni B areas.
  - Scattered thick-walled vessels with perivascular hyalinization.
- Abrupt, degenerative nuclear atypia (enlarged, hyperchromatic) can be seen, but necrosis, increased mitoses, and nuclear pleomorphism are absent.
- VS are slow growing and may be watched clinically. Surgical excision is primarily driven by tumor growth or worsening symptoms and can be difficult given the proximity to involved structures.
- 90% of patients with neurofibromatosis type 2 (NF2) have bilateral VS.
  - NF2 patients present with VS at an earlier age (<30 years old).
  - VS in NF2 are bilateral; tend to be multicentric, more cellular, and more infiltrative with a higher likelihood of recurrence and malignant transformation.

References: [53–56]

13. *What are the clinical and histologic characteristics of temporal bone and ear (TBE) meningiomas?*

Meningiomas are benign, slow-growing tumors derived from arachnoid cap cells found in the dura of the central nervous system (CNS). Recent classification systems divide meningiomas into primary extradural and primary intracranial meningiomas. Primary extradural meningiomas (PEM) have no connection to the dura and are thought to arise from ectopic arach-

noid cap cells. TBE meningiomas can be either PEM or secondary:

- Approximately 90% of all PEM arise in the head. Primary meningiomas of the TBE region are exceedingly rare.
  - Meningiomas of the TBE account for 20–30% of all PEM of the head.
- Secondary meningiomas are the most common type seen in the TBE. They arise from the direct extension of an intracranial tumor and represent less than 2% of all intracranial meningiomas (Table 7.10). Routes of extension include:
  - Posterior petrous ridge
  - Tegmen tympani
  - Jugular bulb
  - Internal auditory meatus
- Histologic features and classification of TBE meningiomas are identical to the intracranial tumors:
  - Tumor cells are arranged in syncytial lobules and nests with a characteristic whorled pattern.
  - Cells have a moderate amount of eosinophilic cytoplasm with indistinct cell borders.
  - Nuclei are round to oval with fine chromatin and occasional intranuclear inclusions.
- Tumor growth can be infiltrative, and bone invasion is not uncommon.
- Symptomatic tumors require surgery, but complete excision is difficult given location and attempt at hearing preservation. Recurrence rates are about 20%.

References: [57–60]

14. *What is an aggressive papillary tumor of middle ear, and how does it differ from endolymphatic sac tumors?*

Table 7.10 Characteristics of temporal bone and ear meningiomas

Patient	Female predominance, mean age = 25–30 years
Symptoms	Mimics otitis media: Conductive hearing loss Otalgia Otorrhea
Location	Middle ear > temporal bone EAC
Histologic type	Meningothelial 80% Transitional ≈ Psammomatous
Grade	Benign 90% Atypical 5% Malignant 5%
IHC positive stains	Vimentin, EMA, PR, var S100 (wk), var CK, var Cam5.2
IHC negative stains	GFAP, chromogranin, synaptophysin

IHC immunohistochemical, *PR* progesterone receptors, *var* varies from case to case, *wk* weak expression, *GFAP* glial fibrillary acidic protein

There is controversy about the origins of both endolymphatic sac tumor (ELST) and aggressive papillary tumor of the middle ear (APTME). This is complicated by the interchangeable use of these terms in the literature. The WHO Classification asserts that these are distinct entities. However, there are several features of both lesions which are similar, if not identical. ELST may represent a precursor lesion of APTME. APTME tends to show extensive invasion of adjacent structures precluding an accurate assessment of tumor location. Tysome et al. noted that ELST is always associated with either bone erosion or a dilated endolymphatic sac or vestibular aqueduct. Others have not confirmed this finding. For our purposes, we will consider these tumors as the same entity for the following reasons: identical clinical presentation, immunohistochemical profile, histologic appearance, and association with von Hippel-Lindau disease (VHL).

- APTME/ELST is a rare, histologically benign, locally aggressive, slow-growing tumor possibly derived from the endolymphatic sac of the inner ear.
- There is a wide age range from adolescence to the elderly with a mean age of 30 years old and a female predominance.
- Patients present with a Meniere-like constellation of symptoms: sensorineural hearing loss, tinnitus, and vertigo. Facial nerve involvement is not uncommon.
- Duration of symptoms to diagnosis is typically several years (range 1–22 years).
- Bone invasion is common; metastases and death are rare but usually related to cranial involvement.
- APTME/ELST are associated with von Hippel-Lindau disease (VHL). Fifteen percent of VHL patients are diagnosed with APTME/ELST, and they show some features that differ from patients with sporadic cases. VHL patients are:
  - Diagnosed at an earlier age
  - More likely to be bilateral
  - Clear female predominance with a 2:1 ratio
- Histologic features include:
  - Infiltrative, hypervascular tumors with a bland cytomorphology.
  - Two growth patterns: papillary or follicular/glandular.
  - Lining cells are cuboidal to low columnar with pale pink to clear cytoplasm, arranged in a single, flattened layer. Occasional ciliated cells can be seen.
  - Nuclei are uniformly bland with rare mitoses and no atypia or necrosis.
  - Cystic glandular spaces filled with eosinophilic (PAS positive) material resembling colloid.

- Immunohistochemical stains:
  - Positive for CK19, CK7, CK5/6, EMA, NSE, CD56, vimentin
  - Negative for transthyretin, thyroglobulin, TTF-1
  - Variable staining for S100, synaptophysin, GFAP, low Ki-67 proliferative index (<1%)
- The differential diagnosis includes tumors common to the ear. Immunohistochemical stains can aid in the diagnosis for all of the following:
  - Paraganglioma
  - Middle ear adenoma
  - Metastatic renal cell carcinoma – a special consideration in VHL patients
  - Papillary thyroid carcinoma
  - Choroid plexus papillomas (CPP) – given the tendency of APTME/ELST to involve the cerebellopontine angle
- CPP are typically negative for GFAP, CK5/6, and EMA and positive for synaptophysin, S100, and transthyretin with variable expression for pan-cytokeratin.

References: [46, 61–72]

15. *What are the most common metastatic tumors to the temporal bone region?*
    - Metastases to the temporal bone and ear are primarily described as case reports and autopsy series (Table 7.11). In general, temporal bone and ear metastases are rare and generally asymptomatic. Symptomatic cases are likely a manifestation of end-stage disease.
    - Gloria-Cruz et al. performed an autopsy study of 212 patients with primary, nondisseminated malignant tumors and found 47 patients with metastases to their temporal bones. These include tumors that were either:
      1. Isolated metastases from solid or hematogenous tumors (75%)
      2. Direct extension from metastases to intracranial, leptomeningeal, or regional sites (25%)

    References: [73–77]

Table 7.11 Characteristics of metastatic tumors to the ear and temporal bone in decreasing frequency

Symptoms	Hearing loss (40%) Asymptomatic (36%)
Site of origin of the metastasis	Breast Lung Prostate
Location of temporal bone metastases	Petrous apex Mastoid
Location of ear metastases	Internal auditory canal Middle ear Eustachian tube External ear

Case Presentations

Case 1

Learning Objectives

1. To form the differential diagnosis of a middle ear mass
2. To generate a comprehensive immunohistochemical panel to diagnosis a middle ear tumor

Case History

A 51-year-old female presents with complaints of ear pain and tinnitus over several months. Physical exam reveals a bulging tympanic membrane and blood in the ear canal. CT scans show a hypervascular soft tissue mass with focal bone involvement.

Gross Findings

Multiple tan-red, bloody tissue fragments aggregating 1.0 cm.

Histologic Findings (Fig. 7.9a, b)

Nests of monotonous, epithelioid cells in a hemorrhagic, vascular stroma. Inconspicuous, small spindled cells surround the tumor nests. The tumor cells are bland and have moderate to abundant eosinophilic cytoplasm and round nuclei with finely, stippled chromatin.

Differential Diagnosis

- Middle ear adenomatous neuroendocrine tumor
- Middle ear/temporal bone meningioma
- Metastatic carcinoma, including renal cell carcinoma

IHC and Other Ancillary Studies (Fig. 7.9c, d)

- Positive: Synaptophysin, S100 (sustentacular cells), focal chromogranin
- Negative: Pan-cytokeratin, CK7

Final Diagnosis *Middle ear paraganglioma (MEPGL)*

Take-Home Messages

1. Paragangliomas are the most common tumors of the middle ear and should be at the top the differential diagnosis.
2. A negative keratin stain excludes most other tumors at this site including middle ear adenomatous neuroendocrine tumor and metastatic carcinomas. An S100 IHC

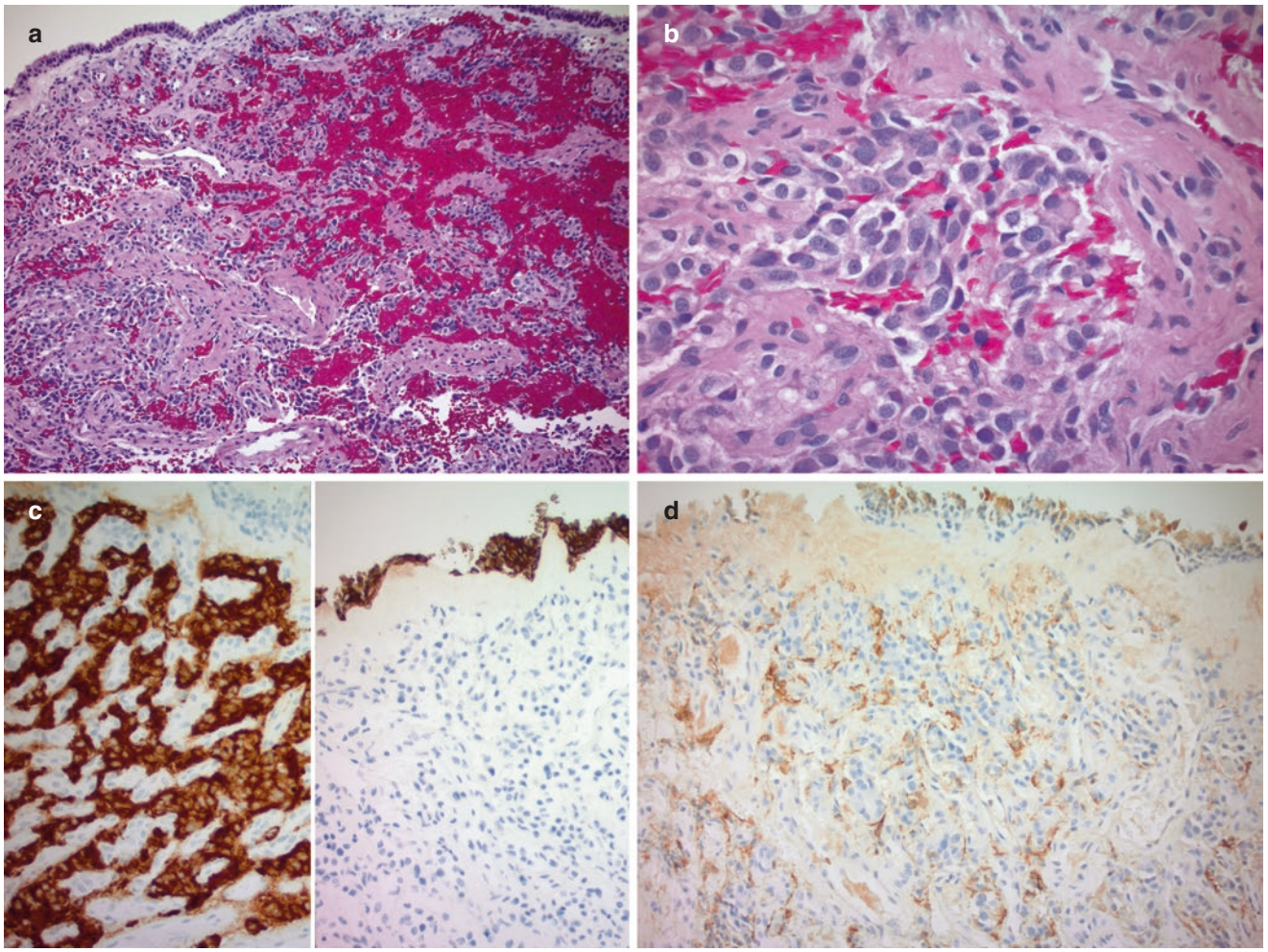

Fig. 7.9 Case 1. (**a**) Nests of cells in the middle ear submucosa with a vascular stroma. (**b**) Monotonous, epithelioid cells with amphophilic cytoplasm, round nuclei, and salt and pepper chromatin. (**c**) The tumor cells are strongly positive for synaptophysin (left) and negative for pan-cytokeratin (right) which highlights the middle ear epithelium. (**d**) An S100 stain decorates the sustentacular cells

stain highlights sustentacular cells, a unique feature of paragangliomas.

3. Paragangliomas are the most common inherited tumors in humans. A patient with this diagnosis should be referred for genetic testing.
4. Bony erosion is not an indication of malignancy. There are no histologic features to predict malignancy in paragangliomas.

References: [47, 49, 78–80]

Case 2

Learning Objectives

1. To determine the differential diagnosis of skin lesions in the ear canal
2. To become familiar with the morphologic features of being and malignant squamous tumors of the ear canal

Case History

A 73-year-old male presents with ear pain, pruritis and bloody discharge. Physical exam reveals a papillary tan-brown, keratotic lesion in the ear canal.

Gross Findings

Lobulated, epidermal lesion with a "stuck on" appearance and roughened surface.

Histologic Findings (Fig. 7.10)

A papillomatous proliferation of basal squamous cells with small, bland nuclei and a moderate amount of pink cytoplasm. Foci of hyperkeratosis are present.

Differential Diagnosis

- Squamous papilloma
- Squamous cell carcinoma
- Seborrheic keratosis
- Basal cell carcinoma (BCC)

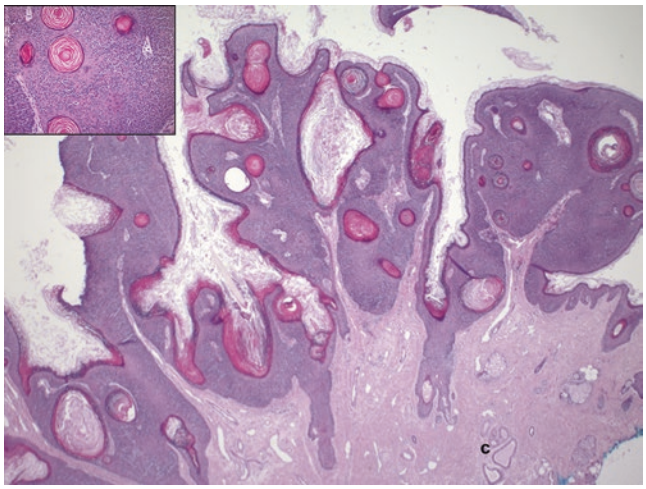

Fig. 7.10 Case 2. A papillomatous squamous lesion with characteristic horn cysts filled with laminated keratin. A proliferation of (inset) basaloid squamous cells with bland nuclei forms the acanthomatous epidermis

IHC and Other Ancillary Studies

None.

Final Diagnosis *Seborrheic keratosis*

Take-Home Messages

1. Seborrheic keratosis (SK) is a common benign, proliferative lesion of the skin that rarely occurs in the external auditory canal (EAC). Awareness of this entity is essential in avoiding a misdiagnosis of carcinoma on a small biopsy specimen.
2. Squamous cell carcinoma of the EAC has a poor prognosis and requires aggressive treatment. It must be confidently and carefully distinguished from benign squamous lesions of the EAC.
3. SK lacks atypia but may be pigmented. The downward growth of the basaloid proliferation should not be mistaken for BCC. BCC typically shows atypia, retraction artifact around the tumor nests, and a myxoid or mucoid stroma.

   References: [14, 15, 17, 19]

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