Pathology of Malignant Neoplasms of the Ear and Temporal Bone

5

Diana Bell

Introduction

The chapter is dedicated to cancers of the temporal bone; therefore, very common benign temporal bone tumors (e.g., paraganglioma, meningioma, schwannoma) will not be discussed.

Tumors of the ear can be divided into external auditory canal (EAC) and pinna tumors, middle ear tumors, and inner ear tumors. Tumors of the middle and inner ear are grouped together, as their sites of origin cannot always be determined.

Tumors of the EAC and Pinna

Basal Cell Carcinoma

Basal cell carcinoma (BCC) is a slow growing, locally infiltrative malignant neoplasm of the skin and subcutaneous adnexal tissue; BCC represents the most common cutaneous malignancy. More common in men than in women, BCC is commonly seen in the seventh decade of life. The sun-exposed areas are the most frequent sites of occurrence (e.g., pinna). BCCs of the external auditory canal although uncommon usually have extensive subcutaneous involvement, which clinically is not obvious. Initially, BCC appears as a raised papule or nodule with telangiectasia. With time, the central portion ulcerates and is surrounded by raised borders ("rodent ulcer") [1–6]. BCC may be inherited in nevoid BCC syndrome (autosomal dominant disorder caused by mutations in PTCH tumor suppressor gene on 9q22.3p31). The histology OF EAC BCC is similar to that of BCC occurring elsewhere in the body (Fig. 5.1a–c).

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Squamous Cell Carcinoma

Squamous cell carcinoma (SCC) of the EAC or pinna affects about 1 million people [7], usually between the ages of 55 and 65 years. In general, SCC has an overall predominance in women; however, pinna tumors tend to occur more frequently in men [8].

Actinic overexposure and frostbite are recognized etiologies for pinna tumors, whereas chronic inflammation and radiation are possible etiologic factors for EAC tumors [7, 9–11]. Papillomas in this region rarely transform into SCC [12].

On clinical examination, pinna tumors appear as excoriated or ulcerated masses. Usual symptoms at presentation are otitis externa, otitis media, pain, hearing changes, and cholesteatomas; nerve symptoms have later onset.

Macroscopically, EAC SCCs are warty, exophytic masses that occlude the EAC and invade the tympanic membrane. The histology of EAC SCC is similar to that of SCCs occurring elsewhere in the body, with spindle and acantholytic, but rarely verrucous variants (Fig. 5.2a, b); desmoplastic response and inflammation are frequently seen (Fig. 5.2c, d).

EAC SCC is aggressive. The disease frequently involves vital structures, often recurs locally, and can metastasize to the lymph nodes. Poor prognosis is linked to high clinical stage, tumor depth, and lymphovascular and perineural invasion [7, 9, 13–16].

Malignant Melanoma

Malignant melanoma, although relatively rare, is the third most common malignancy of the external ear, accounting for 7–16% of all head and neck melanoma [17]. Similar to the other actinically related neoplasms, there is a 2:1 male-to-female ratio with a mean age at diagnosis of 72 years [17]. Malignant melanoma can be pigmented, amelanotic, nodular, ulcerated. Histologically known as "the great mimicker," it may show a poorly differentiated epithelioid

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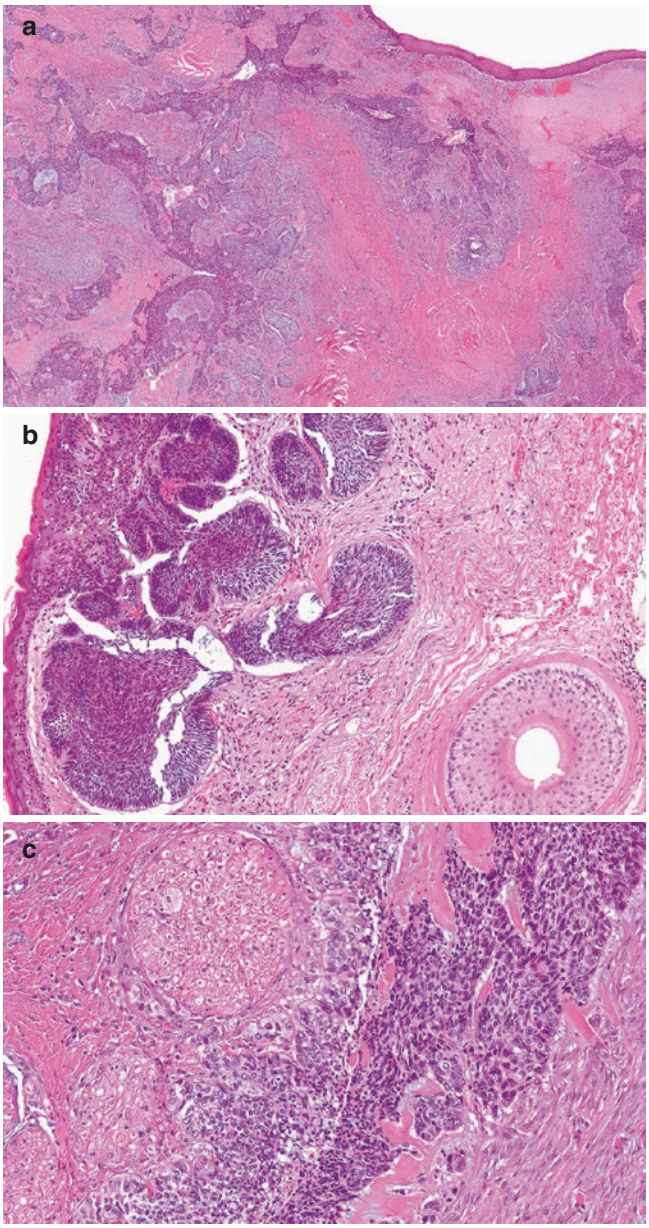

Fig. 5.1 Basal cell carcinoma (BCC). Hematoxylin and eosin stain, (**a**) low power (4×) with a deeply infiltrative growth pattern; high-power (10×) (**b**) conventional, nodular-type BCC with characteristic peripheral clefting and (**c**) BCC with perineural invasion

or sarcomatoid neoplasm, with immunoperoxidase studies paramount to the differential diagnosis (Fig. 5.3a–c). S-100, melanoma cocktail (HMB-45, tyrosinase A), MiTF5, and SOX10 are valuable and specific antibodies in the immunohistochemical work-up for melanoma. [Primary melanoma has to be distinguished from dermal and mucosal metastasis. Treatment varies according to anatomic location: melanoma of the pinna is amenable to wide local excision/amputation, while melanoma of the external ear canal may require extensive surgery including partial temporal bone resection. Similar to other cutaneous sites, the prognosis is linked to depth of invasion].

Atypical Fibroxanthoma

Atypical fibroxanthoma (AFX) is a pleomorphic, dermal mesenchymal tumor with predilection on actinic-damaged cutaneous sites of elderly individuals (75% of cases) or occasionally in younger patients (25% of cases). AFX is also known historically as low-grade malignant fibrous histiocytoma (MFH), pseudosarcoma of the skin, and pseudosarcomatous dermatofibroma. AFX presents as a solitary nodule often ulcerated, with possible bleeding, pruritus, or pain. Histology shows an unencapsulated spindle cell neoplasm centered in the dermis, with a spectrum of spindle shaped to pleomorphic cells with hyperchromatic nuclei and bizarre multinucleated cells (Fig. 5.4a, b). Foamy histiocytes, increased mitotic figures (including atypical mitoses), and a storiform pattern can be seen. The differential diagnosis includes spindle cell squamous carcinoma, melanoma spindled type, and leiomyosarcoma. Immunohistochemistry is helpful, with AFX reactivity for anti-CD68 and negative for carcinoma, melanoma, and muscle markers. Complete surgical excision is the treatment of choice, with excellent prognosis.

Ceruminous Gland Adenocarcinoma

Ceruminous gland adenocarcinomas, also known as ceruminal adenocarcinomas, cylindromas, and ceruminomas, are malignant neoplasms that arise from the apocrine ceruminous glands of the EAC. They are rare, accounting for <2.5% of EAC tumors [18–20]. Ceruminous gland adenocarcinomas can mimic adenoid cystic carcinomas, mucoepidermoid carcinomas, and adenocarcinomas not otherwise specified.

The tumors occur in the outer half of the EAC, which excludes the possibility of direct extension from the parotid [18–20], complemented by imaging studies. They occur in women and men at a ratio of 1.5:1. Patients tend to be middle-aged or older at presentation [18, 21–23] and typically present with a mass, hearing changes, drainage, pain, and neurologic deficits, such as facial nerve paralysis. Imaging studies are used to define tumor extent and exclude direct extension from the parotid or nasopharynx.

Grossly, the tumors have a polypoid appearance and are up to 3 cm in diameter. Histologically, these tumors are unencapsulated and invasive, infiltrating soft tissue and bone with various architectural patterns, such as solid, cystic, cribriform, glandular, and single-cell patterns; perineural invasion and comedonecrosis are appreciated (Fig. 5.5a). Hypercellularity, moderate to severe nuclear pleomorphism,

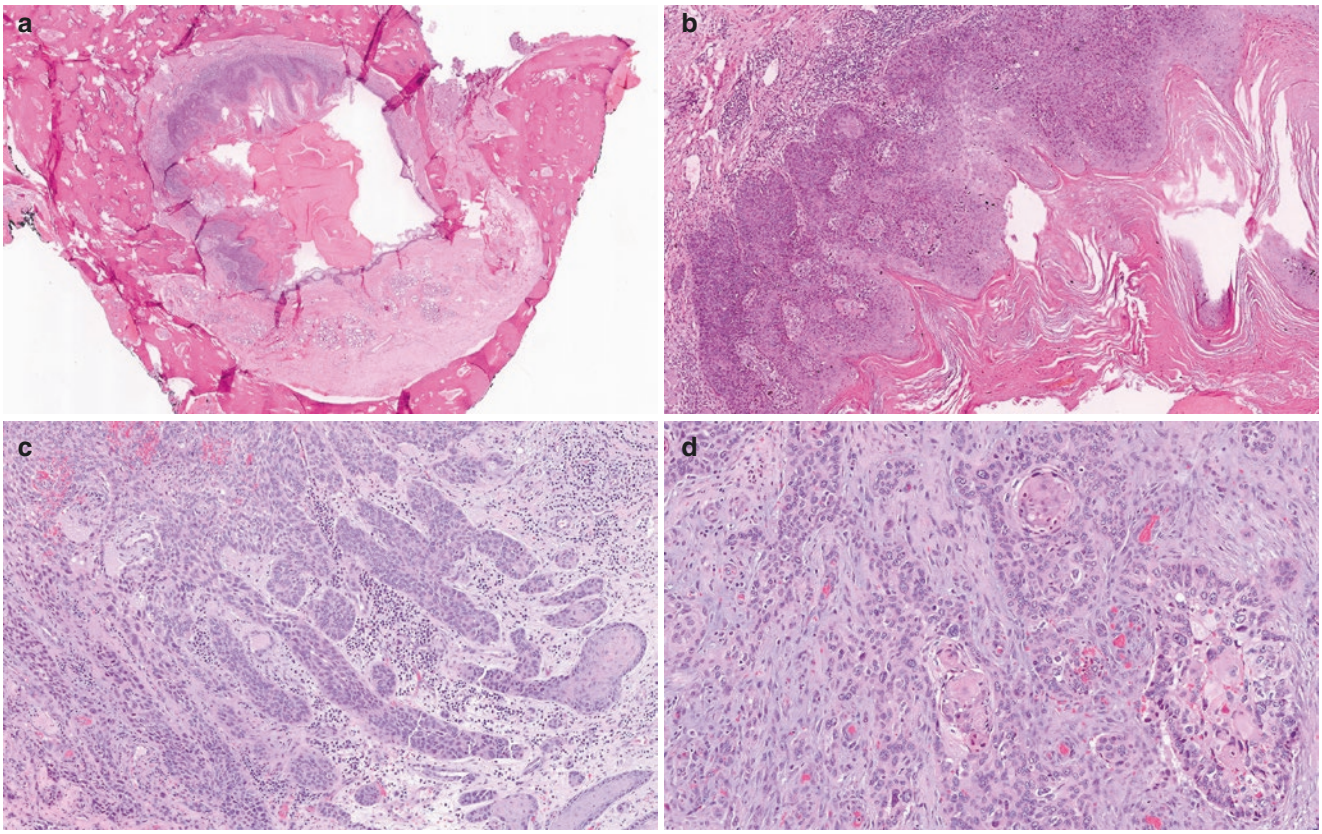

Fig. 5.2 Squamous cell carcinoma (SCC) of the ear canal. Hematoxylin and eosin stain, (**a**) low scanning power and (**b**) high power (10×) of verrucous-type carcinoma with abundant keratinization and bulbous and pushing rete pegs and (**c**) low magnification (4×) and (**d**) higher magnification (10×) of conventional-type SCC showing infiltrative cords and islands of keratinizing cells, in a background of desmoplasia and solar elastosis

and increased mitotic figures are present. Ceroid pigment is absent. Ceruminous adenocarcinomas are recognized by the eosinophilic character of their cells; apocrine-type secretions and a myoepithelial layer are less frequent in these tumors than in benign ceruminous adenomas (Fig. 5.5b). Ceruminous adenoid cystic carcinoma and ceruminous mucoepidermoid carcinoma are histologically identical to salivary gland carcinomas. Adenoid cystic carcinomas are widely infiltrative, with characteristic perineural spread (Fig. 5.6a–d). Immunohistochemistry highlights biphasic composition with CK7- and CD117-positive luminal cells and p63-, S100-, and CK14-positive abluminal cells [18, 24, 25]. Similar to salivary carcinomas, ceruminous adenoid cystic carcinomas bear the t(6;9) translocation with the MYB-NFIB fusion transcript [26, 27]. Mucoepidermoid carcinoma, myoepithelial carcinoma, and acinic cell carcinoma have been seen on rare occasions. It is very important to exclude direct invasion from a primary parotid gland and metastasis.

The prognosis is variable and depends on the extent of the disease. Recurrence, which is associated with positive surgical margins and high-grade histology, is common; patients with destruction of local vital structures or with distant metastases, which occur more commonly in the lungs than in the lymph nodes, have dismal outcomes [18–20, 28].

Rhabdomyosarcoma

Rhabdomyosarcoma (RMS) is the most common malignant tumor of the ear in children, accounting for 7% of ear tumors [21]. Common presentation is a mass in the auditory canal. Extensive bone destruction is present on imaging. RMS types are similar to those at other locations: botryoid/embryonal (frequent), alveolar, solid/pleomorphic, and spindled. On histology the malignant cells are small, dark, spindled in a loose myxoid background. Rhabdoid and striated cells can be seen occasionally and facilitate the diagnosis (Fig. 5.7a–d). The major differential diagnosis is with aural polyp (Fig. 5.7e). Immunophenotyping with lineage-specific markers (desmin, myogenin, MyoD1) is part of the work-up.

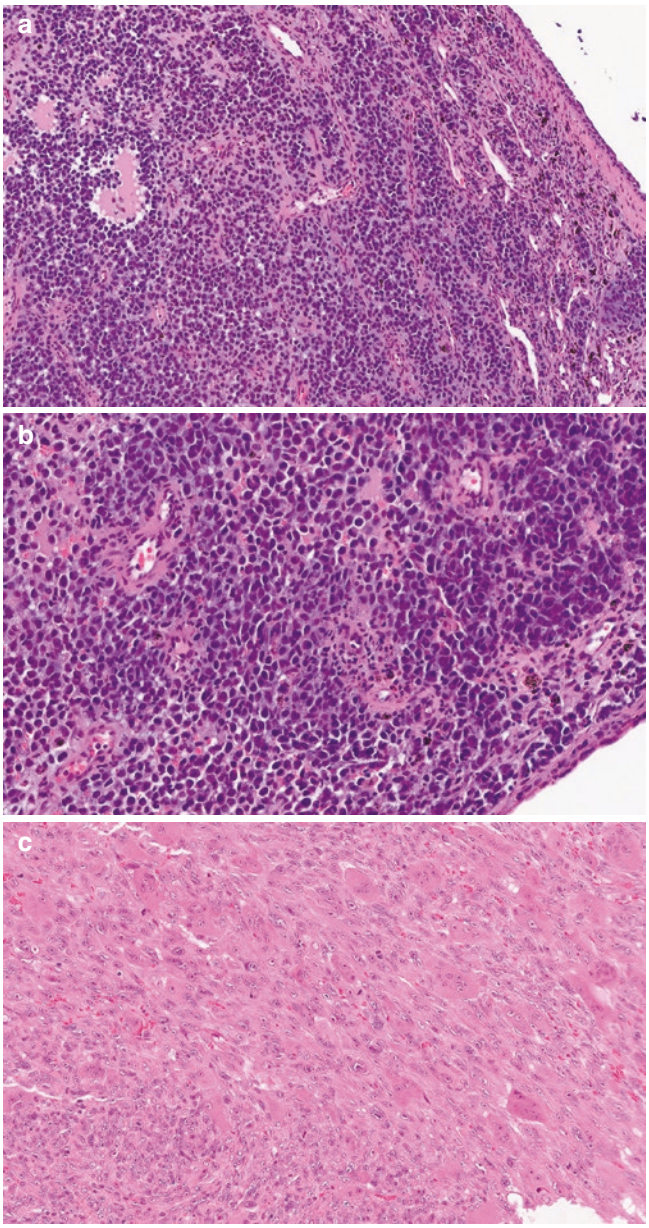

Fig. 5.3 Melanoma. Hematoxylin and eosin stain, (**a**) low (4×) and (**b**) high (10×) power—small round cell malignant morphology, with perivascular arrangement and prominent hyperchromatic, eccentric nuclei. The differential diagnosis is broad including the vast category of small round cell malignant tumors, with immunophenotyping being paramount in diagnosis. (**c**) Malignant melanoma with spindled/epithelioid morphology and associated multinucleated giant cells

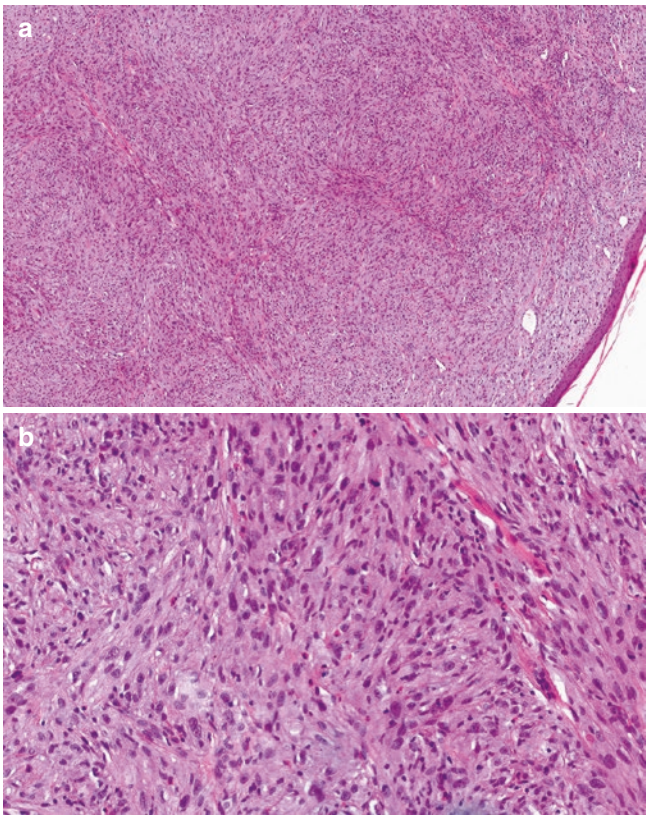

Fig. 5.4 Atypical fibroxanthoma (AFX). Histology shows an unencapsulated spindle cell neoplasm centered in the dermis (**a**), with a spectrum of spindle shaped to pleomorphic cells with hyperchromatic nuclei and bizarre multinucleated cells (**b**)

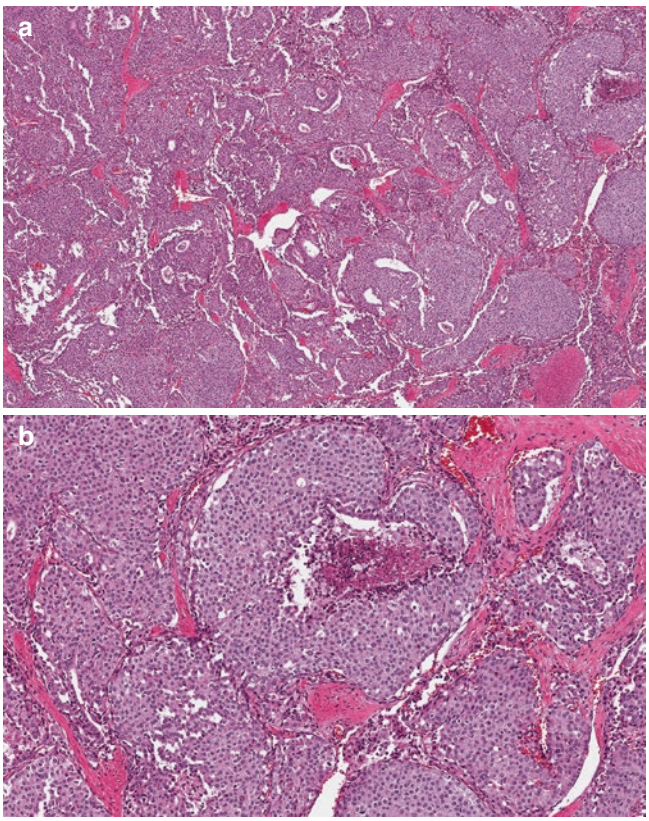

Fig. 5.5 Ceruminous gland adenocarcinoma. (**a**) Hematoxylin and eosin stain, low power (4×) morphologically; ceruminous adenocarcinomas are identical to the similar tumors arising in salivary glands, with variably irregular gland formation and significant infiltrative growth. (**b**) Hematoxylin and eosin stain, high-power (10×) cellular pleomorphism, prominent nucleoli, mitoses, and comedo-type necrosis are present in this high-grade adenocarcinoma

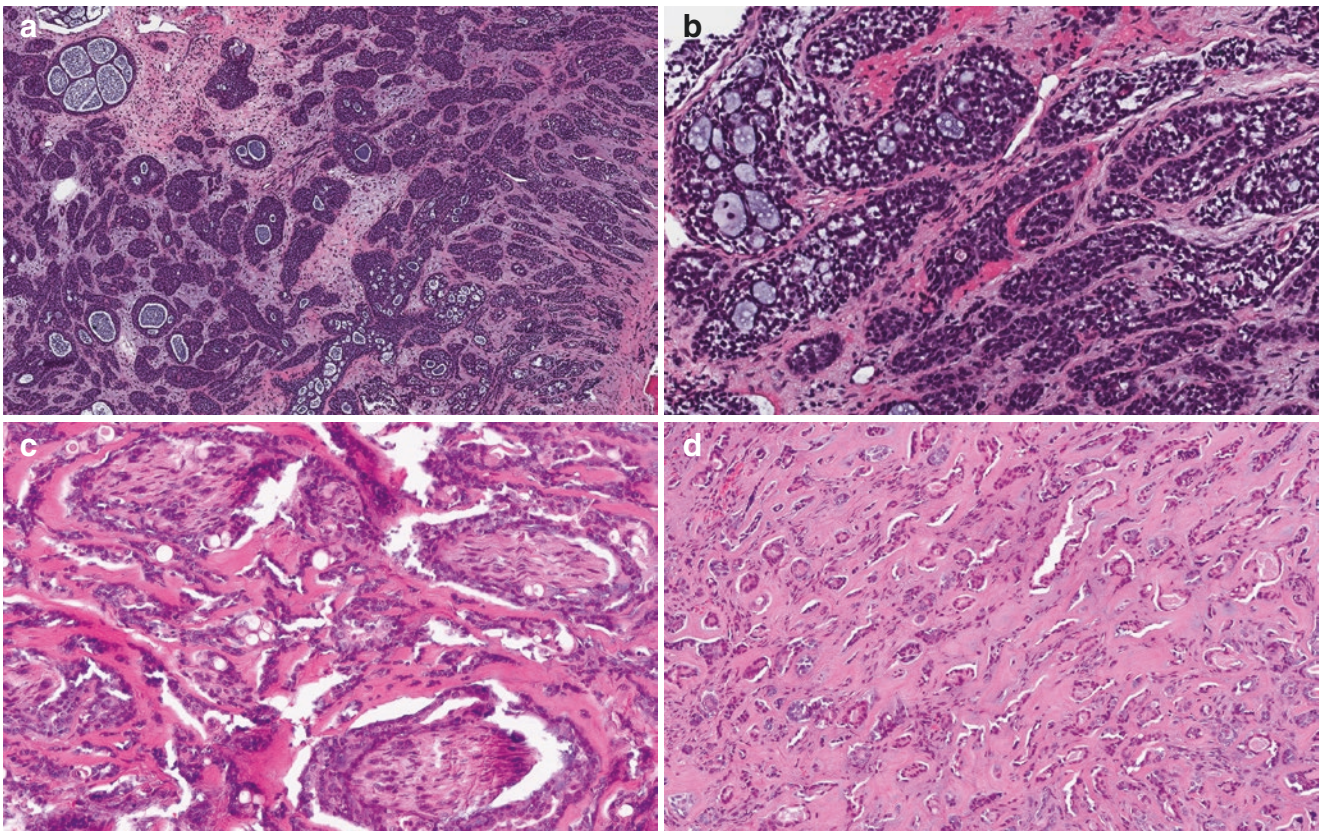

Fig. 5.6 Ceruminous adenoid cystic carcinoma (ACC). Hematoxylin and eosin. The morphology is similar to the tumors seen in major and minor salivary glands, with dual composition of epithelial and myoepithelial cells arranged in a cribriform and tubular patterns (**a**, **b**) and extensive perineural invasion (**c**). The sclerosing type ACC is rarely seen (**d**)

Tumors of the Middle and Inner Ear

Squamous Cell Carcinoma

SCC in the middle ear is rare. The mean age of patients with middle ear SCC at presentation is 60 years, and the disease has a predilection for men [29]. Chronic otitis may be a predisposing factor [30]. The tumors may originate in the middle ear or extend from SCC in the EAC. Direct spread into the inner ear, usually along cranial nerve VIII, is uncommon [31]. Prognosis is poor owing to advanced disease at presentation and delayed diagnosis. SCC of the external ear, ear canal, and middle ear is histologically identical.

Neuroendocrine adenomatoid tumor of the Middle Ear [32]

Neuroendocrine adenomatoid tumor of the middle ear is a neuroendocrine neoplasm that have been described by many names, including carcinoid tumors, middle ear adenomas, adenomatous tumors of the middle ear, adenocarcinoids, and amphicrine tumors.

These tumors are very rare, accounting for <2% of ear tumors. They have an equal gender distribution and typically occur in the fifth decade of life [33–36]. Symptoms at presentation include decreased hearing acuity, a feeling of fullness or pressure in the ear, and tinnitus. Otoscopy usually reveals an intact tympanic membrane and a brown reddish structure immediately beyond. The tumors occasionally extend into the EAC or mastoid bone. Histologically, they are unencapsulated, with variable cellularity and various architectural patterns [33, 34, 37]. The dominant glandular pattern consists of duct-like structures with "back-to-back" gland configuration; minor components include trabeculae, festooning, anastomosing cords, and solid sheets (Fig. 5.8a, b). The cytoplasm is eosinophilic, and the nuclei tend to be round to oval and plasmacytoid with minimal pleomorphism and salt-and-pepper chromatin distribution. Immunophenotypically, the tumors are positive for keratins and neuroendocrine markers, including chromogranin, synaptophysin, and neuron-specific enolase (Fig. 5.8c, d) [33, 34, 37]. The differential diagnosis

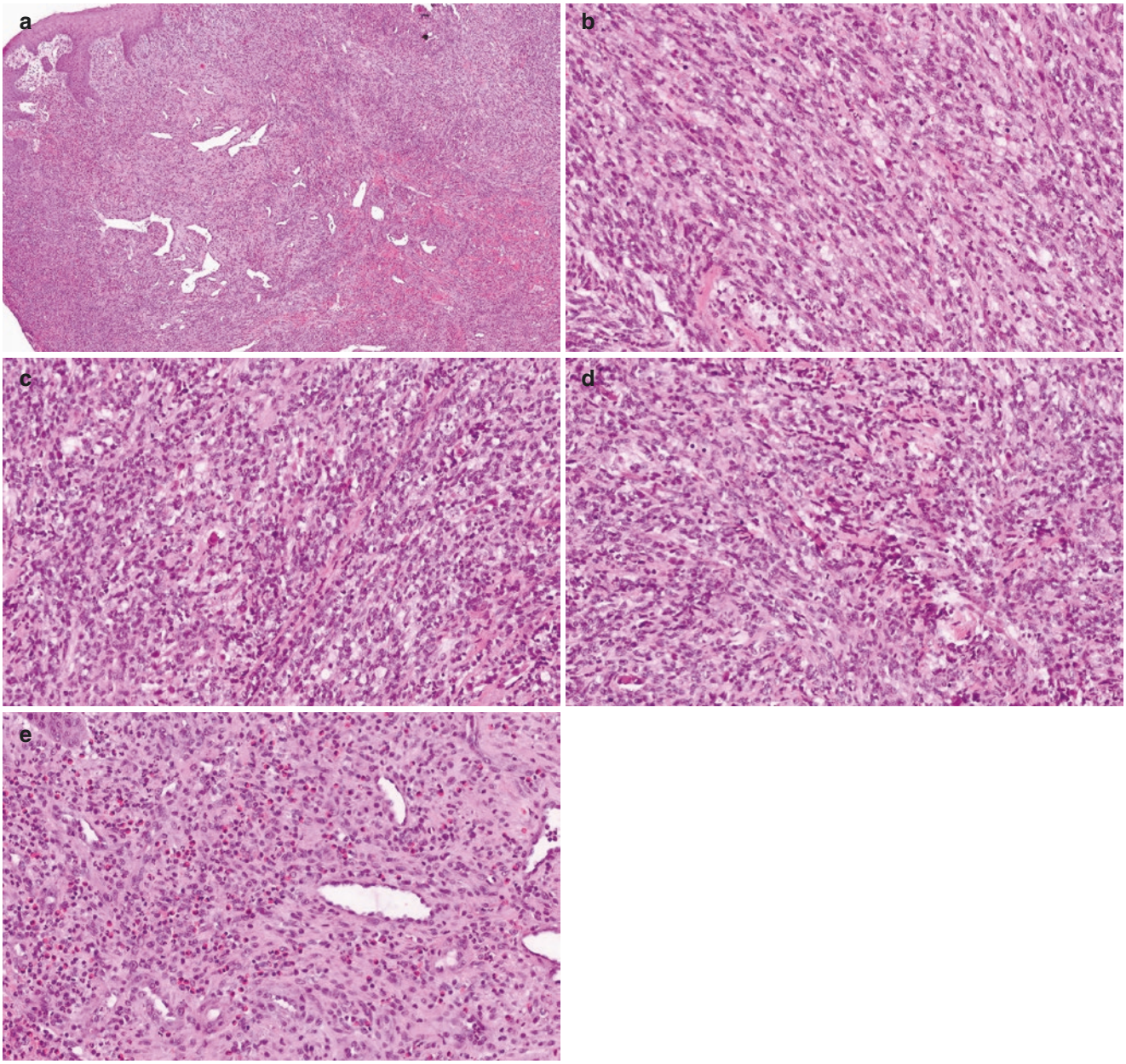

Fig. 5.7 Rhabdomyosarcoma (RMS). On histology the malignant cells are small, dark, spindled in a loose myxoid background (**a**, **b**). Rhabdoid and striated cells can be seen occasionally and facilitate the diagnosis (**c**, **d**). The major differential diagnosis is with aural polyp (**e**)

includes ceruminous adenoma, meningioma, paraganglioma, and metastatic adenocarcinoma [33, 35, 37].

The treatment of choice for middle ear adenocarcinomas with neuroendocrine features is complete surgical removal, including removal of the ossicles. Most adenocarcinomas with neuroendocrine features are excised in a piecemeal fashion (<1 cm) owing to the confined anatomic space [33, 34, 37]. About 15–20% of patients have recurrence [33, 36, 38]. Facial nerve paralysis may occur and is due to mass-related compression rather than invasion [33, 36, 38]. Unreported institutional experience (MD Anderson Cancer Center) indicates that the disease can metastasize to the lymph nodes and liver.

Aggressive Papillary Tumor (aka Endolymphatic SAC Tumor, Low-Grade Adenocarcinoma of Endolymphatic SAC Origin)

The endolymphatic sac tumor (ELST) is a rare lesion of the skull base for which an endolymphatic sac origin is supported by early manifestations of vestibular disease, radiographic evidence of a tumor in the posterior-medial petrous ridge, identification of an in situ tumor, and morpho-phenotypical similarities to normal endolymphatic sac epithelium. Historically, first series was described by Gaffey

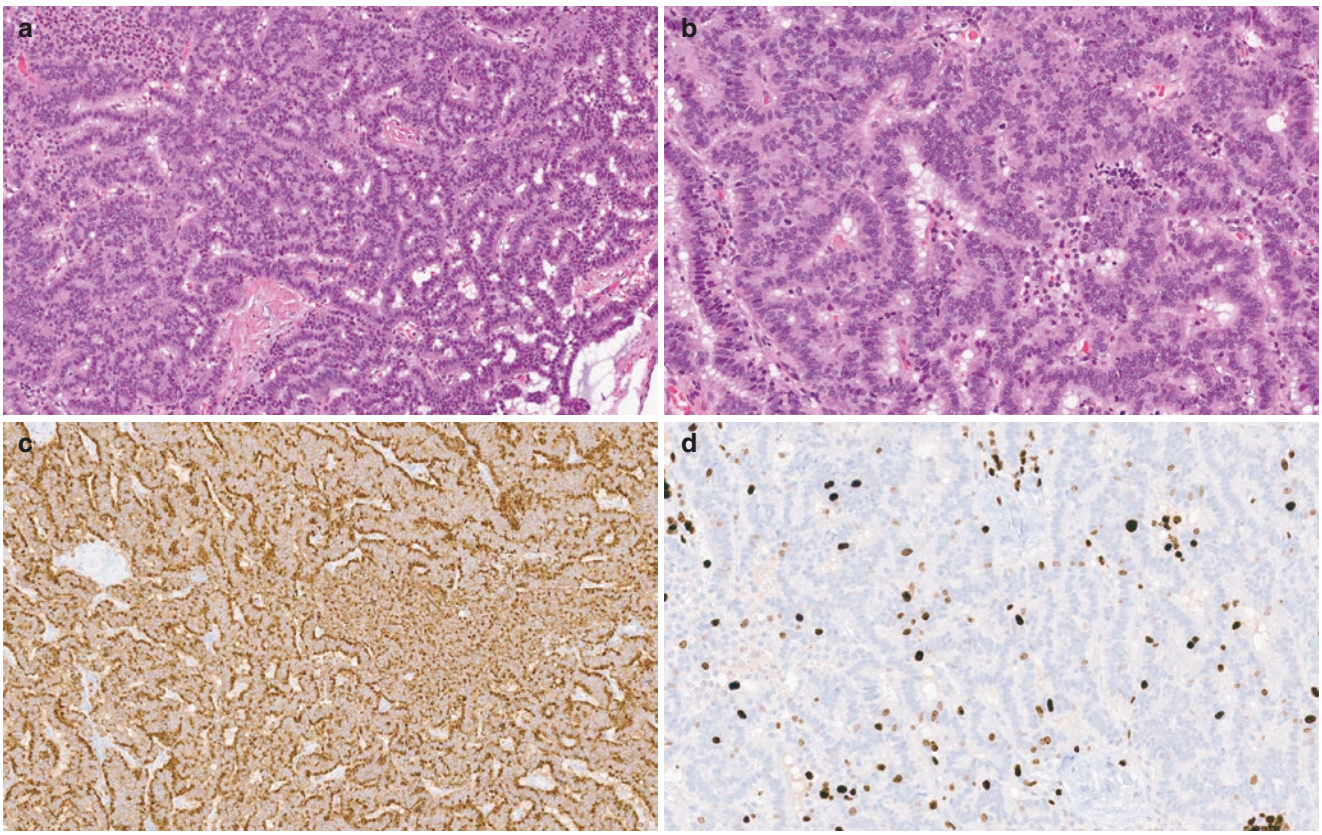

Fig. 5.8 Middle ear adenocarcinomas with neuroendocrine features. The histologic architectural patterns may be solid, glandular, or trabecular (**a**—hematoxylin and eosin stain, low power 4×); the tumor cells are uniform, with a moderate amount of acidophilic cytoplasm and nuclei with "salt-and-pepper" chromatin pattern (**b**—hematoxylin and eosin stain, high power 10×). Neuroendocrine markers are usually positive (**c**—immunoperoxidase study with anti-synaptophysin antibody, brown membranous reactivity pattern), and the proliferation rate is low to intermediate (**d**—immunoperoxidase study with anti-Ki-67 antibody, brown nuclear reactivity pattern)

et al. in 1988, reporting a series of ten cases of an aggressive papillary middle ear tumor (APMET) characterized by a locally aggressive papillary growth pattern, bone destruction, and frequent endolymphatic sac invasion, thus establishing an entity separate from middle ear adenoma [39]. A year later, Heffner reported 20 cases of an identical tumor and proposed an endolymphatic sac origin [40]. Prior to this, Hassard et al. had described intraoperatively a tumor adherent to the endolymphatic sac while performing decompression surgery for presumed Ménière's disease [41].

The endolymphatic sac is derived from neuroectoderm and is located subjacent to the posteromedial surface of the temporal bone. The distal part is ensheathed by two layers of dura mater, and the intermediate rugose part lies within the vestibular canal. It is from the latter part that ELST is suspected to originate [40, 42]. This anatomic location is important as it explains the propensity of the tumor to involve the petrous portion of the temporal bone as well as cerebellopontine angle (CPA) structures [43]. There are four potential vectors for tumor extension: posteromedially into the cerebellopontine angle, laterally toward the middle ear, superiorly toward the middle cranial fossa, and anteromedially along the petrous ridge to the cavernous and sphenoid sinuses [43]. Patients present with hearing loss, tinnitus, and vertigo; facial nerve paralysis occurs less commonly. Large tumors with growth along the posteromedial vector may cause symptoms secondary to cerebellopontine angle extension. An indolent clinical course and long-standing symptom history is typical. A diagnosis of ELST should prompt the clinician to consider the possibility of von Hippel-Lindau (VHL) disease, but this is not a prerequisite for diagnosis as these tumors also occur sporadically. Patients with VHL disease are more likely to have bilateral ELSTs. The histopathological appearance of ELST is that of a papillary, cystic, and glandular neoplasm. Interdigitating complex papillary processes are embedded in sheets of dense fibrous stroma. The papillary processes are lined with a single layer of low columnar-to-cuboidal epithelial cells, resembling those of the normal endolymphatic sac, middle ear, and mastoid sinuses (Fig. 5.9a–c). Nuclear pleomorphism and mitotic figures are inconspicuous. The histopathologic differential diagnosis includes metastatic carcinomas from the thyroid, lung, kidney and breast; paraganglioma; choroid plexus papilloma; meningioma; and middle ear adenoma. The precise location of the tumor as defined by preoperative imaging studies and intraoperative surgical observation, together with

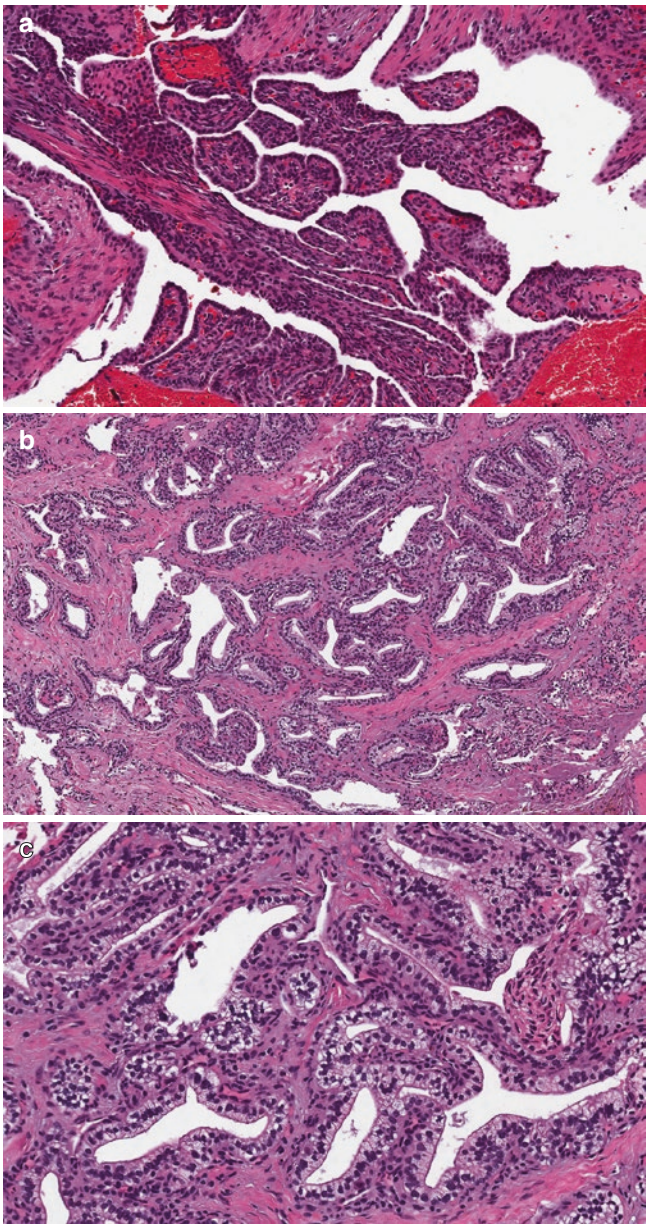

Fig. 5.9 Endolymphatic sac tumor (ELST). The histopathological appearance of ELST is that of a papillary, cystic, and glandular neoplasm. Interdigitating complex papillary processes are embedded in sheets of dense fibrous stroma (**a**, **b**—hematoxylin and eosin stain, low power 4×). The papillary processes are lined with a single layer of low columnar-to-cuboidal epithelial cells, resembling those of the normal endolymphatic sac, middle ear, and mastoid sinuses (**c**—hematoxylin and eosin stain, high power 10×)

the use of immunohistochemical markers (Table 5.1), helps to differentiate ELST from mimics [43]. Choroid plexus papillomas (CPPs) typically express transthyretin (prealbumin), which is not characteristic of the ELST immunophenotype. Of note, other differentiation markers, such as glial fibrillary acidic protein (GFAP) and synaptophysin (associated with central nervous system tumors), may also be expressed by ELSTs, in keeping with the embryonic origin of the endolymphatic sac from the neural crest. A history of VHL disease or other tumors associated with the VHL disease spectrum, or of bilateral ELST, facilitates correct diagnosis [39, 44]. Metastatic renal clear cell carcinoma can still be a diagnostic consideration since it occurs in patients with VHL disease, and both ELSTs and clear cell carcinomas of the kidney may occur in the same patient. The imaging hallmark of ELST is the presence of a retrolabyrinthine mass associated with osseous erosion. ELST presents a diagnostic challenge at all levels of presentation. Clinically, patients often initially receive a misdiagnosis of Ménière's disease. Metastases from ELST have rarely been reported in the literature [45, 46]. The following ELST grading system was proposed by Bambakidis et al. [47]: grade I lesions are confined to the temporal bone, middle ear, and external auditory meatus; grade II lesions have extension into the posterior fossa; grade III lesions involve the posterior and middle cranial fossae; and grade IV lesions (very rare, 2–4% ELSTs) extend to the clivus or sphenoid wing. Surgery is the treatment of choice for small ELST [38]. Remission may last for years, but local recurrence after surgery, likely secondary to incomplete resection, can occur. Radiotherapy has a 50% success rate with large or residual tumors.

A mouse model for ELST has been described recently [48]; the tumors also expressed mutant EGFR and downstream targets Akt, mTOR, and ERK1/2. The good response to EGFR inhibitors cetuximab and erlotinib suggests that EGFR inhibitors may be potential alternatives in the treatment of ELST [48].

Other Malignant Tumors of the Middle Ear and Temporal Bone

Osteosarcoma

Osteosarcomas of the skull (including temporal bone) are exceedingly rare (1% of all osteosarcomas) [49–51]. Paget disease of the bone, fibrous dysplasia, and postradiation therapy are the usual setting for osteosarcomas in this location. New osteoid matrix production (Fig. 5.10a) is mandatory for the diagnosis in all histological types of osteosarcoma: osteoblastic (Fig. 5.10b), chondroblastic, fibroblastic, telangiectatic, and small cell type. Osteosarcomas of the skull are aggressive, with lung and brain metastasis and with a dismal 5-year survival [52–54].

Chondrosarcoma

The region of the spheno-petrous synchondrosis is the most commonly reported site for chondrosarcoma of temporal bone [55]. Similar to other locations, chondrosarcomas are morphologically classified as conventional (most common) (Fig. 5.11a, b) [55], mesenchymal, clear cell, dedifferentiated. Grading according to a three-tier system (I, II, III

Table 5.1 Immunophenotype of middle ear and temporal bone glandular neoplasms

	Neuroendocrine (synapto/chromo/NSE)	Keratins	S100	Mucin	Prealbumin (transthyretin)	PSA	TTF-1 and thyroglobulin	Vimentin and RCC	GFAP
NAME	+	+	−	+	−	−	−	−	−
ELST	+/−	+	+/−	−	−	−	−	−	+
Choroid plexus papilloma	−	+	+	−	+	−	−	−	−
Metastatic thyroid carcinoma		+	−	−	−	−	+	−	−
Metastatic renal cell carcinoma		+	−	−	−	−	−	−	−
Metastatic prostate carcinoma		+	−	−	−	+	−	+	−

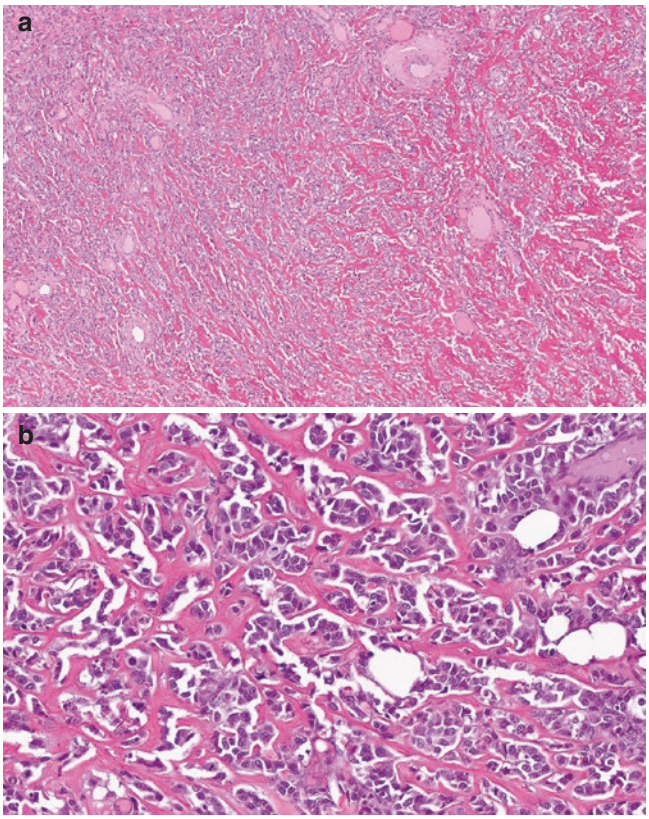

Fig. 5.10 Osteosarcoma. New osteoid matrix production (**a**) is mandatory for the diagnosis in all histological types of osteosarcoma. (**b**) Osteosarcoma, osteoblastic type

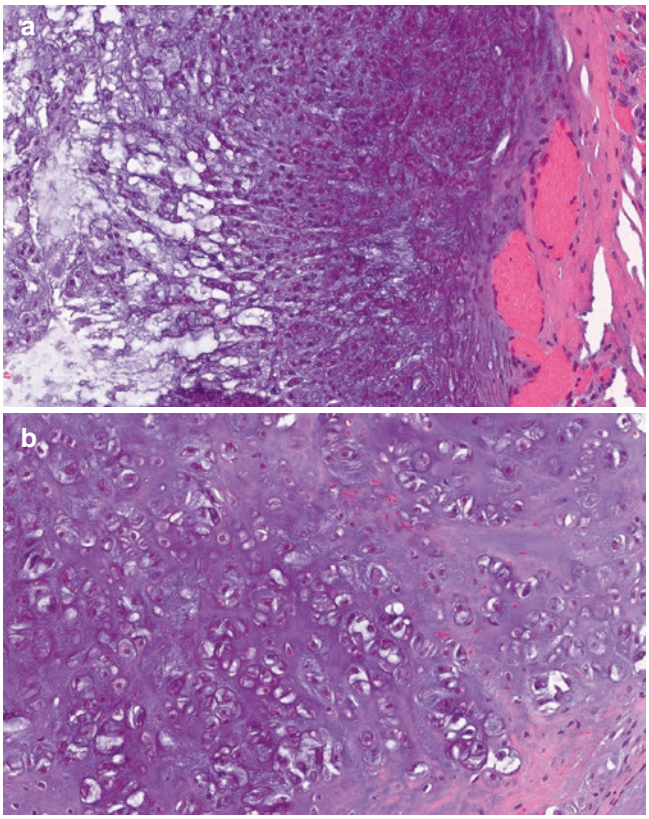

Fig. 5.11 Chondrosarcoma, conventional type (**a**) and low grade (**b**) showing disorganized chondrocytic architecture, increased cellularity and cellular pleomorphism, and scattered hyperchromatic nuclei

corresponding to well/moderately/poorly differentiated) is an important prognosticator. Surgery with radiotherapy is the treatment of choice.

Ewing Sarcoma

Ewing sarcoma (ES) is the second most common primary malignant bone tumor in children and adolescents, following osteosarcoma. The majority of ES arise in the bone and up to 30% in soft tissue [56]. Six cases have been reported in the literature, with a primary ES of the petrous temporal bone [57–59].

ES is a histologically diverse group of tumors with varying degrees of neural differentiation. Traditionally, ES is divided into three major histologic subtypes: classical ES, primitive neuroectodermal tumor (PNET), and atypical ES [56]. Classical ES is comprised of solid sheets or vague lobules of uniform small cells; majority of ES show classical morphology. Tumors with evidence of neural differentiation are classified as primitive neuroectodermal tumors (PNET); rosettes and neural differentiation highlighted on phenotyping are supporting the diagnosis. Atypical ES (large cell ES) category describes tumors that deviate from classical ES;

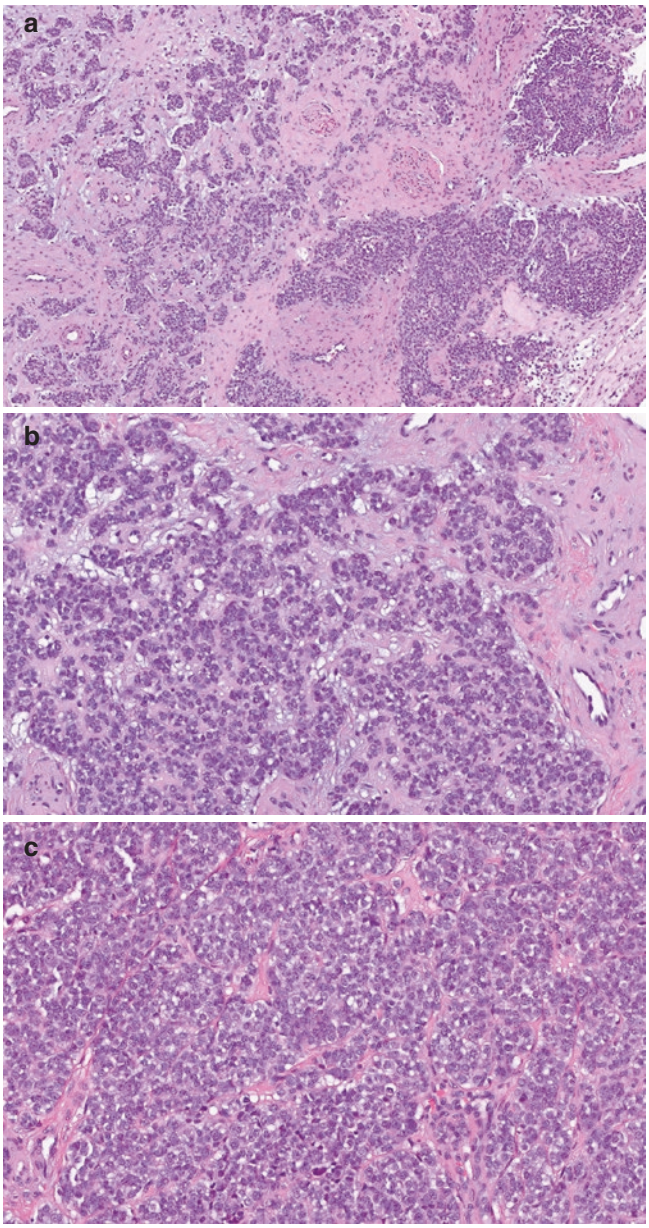

Fig. 5.12 Ewing sarcoma (ES). Classical ES is comprised of solid sheets or vague lobules of uniform small cells. Low (4×) (**a**) and high power (10×) (**b**, **c**)

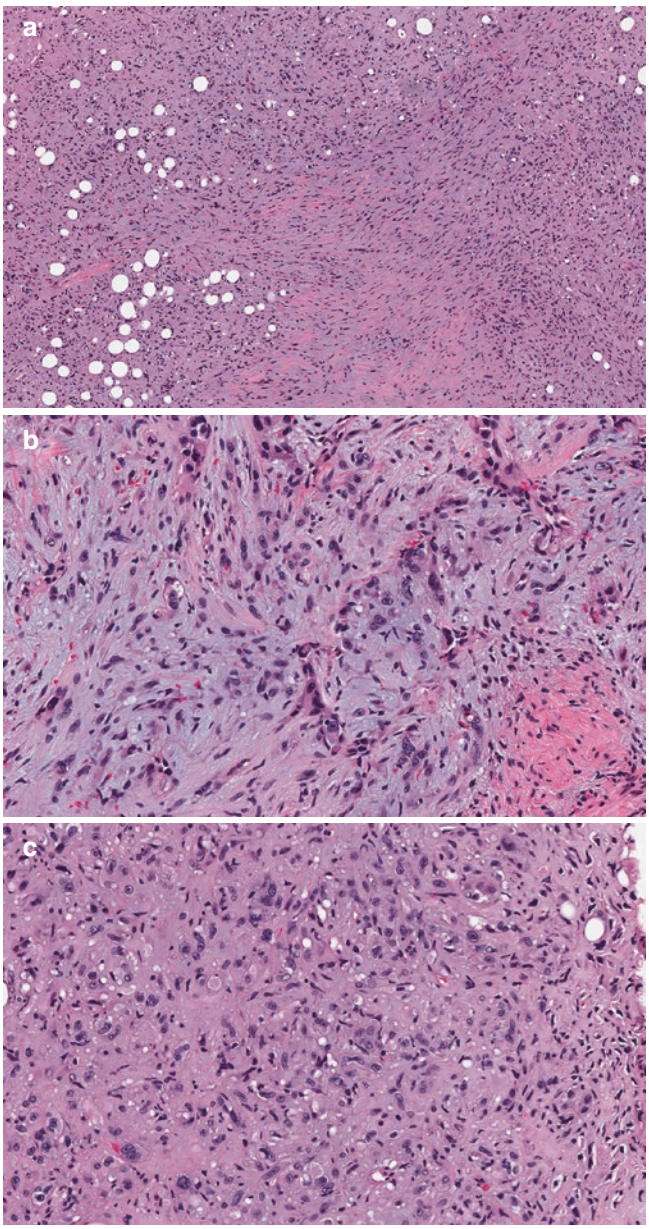

Fig. 5.13 Epithelioid hemangioendothelioma (EHE). Low-to-intermediate-grade mesenchymal neoplasm characterized by short cords and nests of epithelioid tumor cells with endothelial differentiation set in a myxohyaline matrix (**a**, **b**, **c**)

adamantinoma-like ES is a relatively newer described entity. ES is genetically defined by a balanced translocation that involves the *EWSR1* gene (locus22q12) and a member of the *ETS* family of transcription factors, most frequently *FLI1* or *ERG*. Eighty-five percent of ES harbor a t(11;22)(q24;q12) resulting in *EWSR1-FLI1* gene fusion [56]. [Diana, where do you want to place Fig. 5.12a–c?]

Hemangioendothelioma/Epithelioid Hemangioendothelioma

Epithelioid hemangioendothelioma (EHE) is a rare low-to-intermediate-grade mesenchymal neoplasm (Fig. 5.13a) characterized by short cords and nests of epithelioid tumor cells with endothelial differentiation set in a myxohyaline matrix (Fig. 5.13b, c) [60]. Primary sites include the skin, superficial and deep soft tissues, visceral organs, and bone [60]. Anecdotal cases of primary hemangioendothelioma of the temporal bone have been described [61–64]. Although the majority behave in an indolent fashion, there is about 20% risk of widespread metastasis and death from disease [60]. The diagnosis of EHE may be challenging particularly on limited biopsy, with several mimickers such as metastatic carcinoma and myoepithelial and chondroid neoplasms.

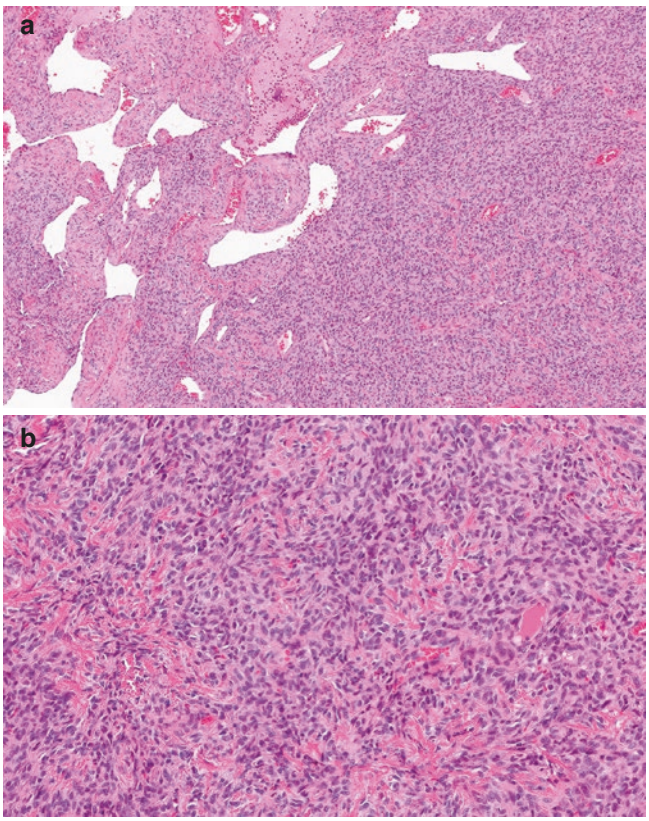

Fig. 5.14 Hemangiopericytoma/solitary fibrous tumor. The tumors are uniformly cellular with numerous thin branching vessels with gaping sinusoidal spaces (staghorn configuration) (**a**); hyalinization, myxoid changes, and fibrosis can be present (**b**)

EHE of the bone and extra-skeletal sites has a highly specific recurrent translocation, t(1;3)(p36.3;q23–25), resulting in a *WWTR1-CAMTA1* fusion transcript [60].

Hemangiopericytoma/Solitary Fibrous Tumor

Hemangiopericytoma (HPC) coined in 1924 by Stout and Murray was described as a distinctive soft tissue neoplasm, presumably of pericytic origin, exhibiting a characteristic "staghorn" branching vascular pattern [65]. Over the years, it became more obvious that this growth pattern is shared by several unrelated benign and malignant lesions and that HPC was better considered as a diagnosis of exclusion. Up to 15% of soft tissue neoplasms show HPC-like features, at least focally [65]. Solitary fibrous tumors (SFT) can be allocated to the group of HPC-like neoplasms [65]. Solitary fibrous tumor is considered by many to form a spectrum with hemangiopericytoma. Microscopically, the tumors are uniformly cellular with numerous thin branching vessels with gaping sinusoidal spaces (staghorn configuration) (Fig. 5.14a); hyalinization, myxoid changes, and fibrosis can be present (Fig. 5.14b). Molecular studies have discovered a NAB2-STAT6 fusion gene in up to 100% of HPC/SFT. Recent studies demonstrated that STAT6 immunohistochemistry is a reliable surrogate for the detection of the fusion gene. Nuclear STAT6 immunoreactivity is highly sensitive and specific marker of SFTs and can be helpful when diagnosis is inconclusive by conventional methods [66]. HPC/SFT has been reported to involve the temporal bone and temporal fossa [67–74].

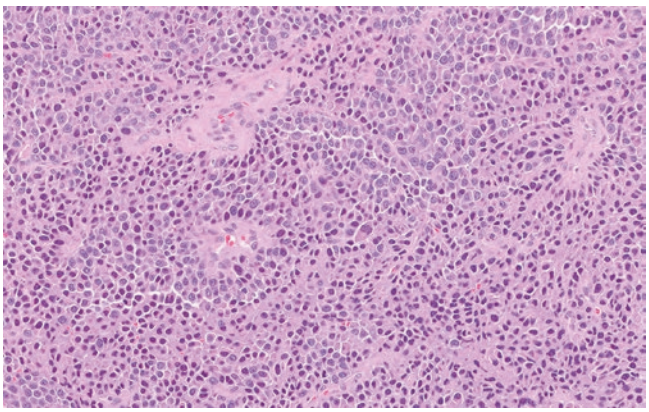

Fig. 5.15 Extramedullary plasmacytoma. Monotonous (clonal) proliferation of plasma cells with eccentric nuclei (hematoxylin and eosin)

Hematolymphoid Neoplasms

Non-Hodgkin and Hodgkin lymphomas, leukemias, and plasma cell dyscrasias (Fig. 5.15) can secondary involve the middle ear and temporal bone in the setting of primary disease elsewhere [55].

Metastatic Tumors to the Middle Ear and Temporal Bone (Secondary Tumors)

Metastasis to the middle ear and temporal bone may originate from virtually every site, most frequently of breast, head and neck, lungs, and prostate origin [75–78]. Beside hematogenous spread, direct extension from nearby primary tumors (squamous cell carcinoma) and leptomeningeal extension from intracranial tumors and meningeal carcinomatosis are other possible routes of middle ear/temporal bone involvement.

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