Ear and Temporal Bone: Cartilaginous and Osseous Pathologies

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Abstract

Although the majority of conditions involving the ear and temporal bone are inflammatory or epithelial based, cartilage and osseous entities will also be encountered. The pathologic examination of these underlying cartilaginous and osseous structures and their histologic findings and associated differential diagnoses will be discussed. Correlation with clinical and imaging findings are also critical for accurate determination of the pathologic entity.

Keywords Ear · Temporal bone · Idiopathic cystic chondromalacia · Protuberant fibro-osseous lesion of temporal bone · Chondromyxoid lesions · Synovial chondromatosis

Cartilaginous Lesions of the Ear and Temporal Bone

The pinna of the external ear is composed of folded elastin cartilage forming the helix, anti-helix, conchal bowl and tragus. Elastin cartilage also forms the lateral one-third of the external auditory canal (eustachian tube). The composition of elastin cartilage is chondrocytes surrounded by elastin (elastic fibers) which allow the cartilage to be flexible and bend, in contrast to hyaline cartilage which is rigid. The inner 2/3rds of the eustachian tube is surrounded by an osseous canal formed within the temporal bone. Lying immediately anterior to the eustachian tube, the temporomandibular joint (TMJ) abuts the temporal bone articular surface (anterior/inferior). The TMJ develops from hyaline cartilage with enchondrosis and ossification. The adult TMJ is composed of a synovial lining with an articular disc. The proximity of the TMJ to the external ear canal can lead to ear symptoms and pathologies and at times involve both structures.

Thereby understanding the cartilaginous and osseous framework of the external ear and ear canal aids in developing a differential diagnosis in these structures.

External Ear

Beginning with the external ear, conditions affecting the auricular cartilage can be acute or chronic and range from reactive to autoimmune. Understanding each condition, the presenting symptoms or associations, and histologic findings will allow for enhanced diagnosis in this area. Specifically, idiopathic cystic chondromalacia, relapsing polychondritis and chondrodermatitis nodularis helicis will be discussed.

Idiopathic Cystic Chondromalacia

Idiopathic cystic chondromalacia was first described by Engel in a Chinese population [1]. As the name implies, idiopathic cystic chondromalacia is a swelling of unknown etiology that affects the auricular cartilage. While the etiology of idiopathic cystic chondromalacia is currently unknown, various theories ranging from developmental and inflammatory to traumatic origin have been proposed [2]. Clinically, idiopathic cystic chondromalacia commonly presents as a unilateral, non-tender swelling involving the scaphoid fossa of the ear. The pseudocystic swelling is slow growing and the overlying skin is unremarkable on clinical examination [3]. The pathologic swelling is located within the plates of auricular cartilage that demonstrates degenerative features. Histologically, idiopathic

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cystic chondromalacia shows an intracartilagenous cleft which is the most consistent finding. The presence of additional microscopic features varies depending on the age of the lesion. There may be scant fibrous connective tissue and mucinous contents within the cleft and some cases will show areas of hemorrhage, hemosiderin and mixed inflammatory infiltrate. The lining of the pseudocystic space is seen in cartilage early on, but granulation and fibrous connective tissue may develop [4] (Fig. 1). Clinical and histological differential diagnosis of idiopathic cystic chondromalacia include; relapsing polychondritis, chondrodermatitis nodularis chronica helices and traumatic perichondritis.

Relapsing Polychondritis

Relapsing polychondritis is an autoimmune disorder that affects cartilaginous and proteoglycan-rich tissues due to autoantibodies against type II collagen [5, 6]. In about one-third of the cases, relapsing polychondritis presents with another autoimmune disorder such as rheumatoid arthritis, Hashimoto thyroiditis and systemic lupus erythematosus [7, 8]. Auricular cartilage is the most commonly involved site in relapsing polychondritis. Presenting clinical symptoms vary depending on if it is in the acute or chronic phase. In acute phase, the external ear is tender and edematous with a red–purple discoloration. Characteristically, the non-cartilaginous part of the ear lobule is spared from the disease process [6]. After repeated acute exacerbations, the ear morphology is altered and demonstrates a floppy/collapsed appearance [6]. Histologically, relapsing polychondritis demonstrates loss of basophilia of the cartilaginous tissue with perichondrial infiltration by mixed inflammatory infiltrate and blurring of the cartilage–soft tissue interface. In progressing lesions, the inflammatory infiltrate can extend from the perichondrium into the cartilaginous matrix. The damaged cartilage has a moth-eaten appearance and is replaced by granulation tissue and eventually undergoes fibrosis [9]. On immunofluorescence, granular immunoglobulin and C3 deposits are noted at the cartilage–fibrous tissue interface [10]. Depending on the sites and extent of involvement, relapsing polychondritis needs to be differentiated from diseases including granulomatosis with

polyangitis and extranodal NK/T-cell lymphoma. However, for localized involvement of the ear by relapsing polychondritis, gout, and idiopathic cystic chondromalacia may be considered in the differential diagnosis [8].

Chondrodermatitis Nodularis Helicis

Chondrodermatitis nodularis helicis is an inflammatory and degenerative process affecting the auricle and is thought to be caused by localized injury and/or chronic actinic damage [11]. Clinically, chondrodermatitis nodularis helicis often presents in older white males and involves the helix of the external ear. Interestingly, in females, the antihelix is more commonly involved [11, 12]. Chondrodermatitis nodularis helicis presents as a painful nodule usually less than 1 cm with raised or rolled edges, a central ulceration or depression with keratinaceous plug [11, 12]. Microscopically, squamous hyperplasia, fibrinoid necrosis and solar elastosis of the overlying epidermis is noted. The epidermis surrounds an inverted funnel-shaped defect that contains keratinaceous debris, mixed inflammatory infiltrate and extends to the underlying cartilaginous tissues. The cartilage demonstrates features of degeneration and the perichondrium may exhibit fibrosis and an inflammatory infiltrate (Fig. 2). In addition, neural hyperplasia in the connective tissue stroma may also be noted [11–13]. The ulcerated appearance of the lesion in sun damaged skin of an older male will likely lead to clinical consideration of squamous cell carcinoma. Epidermal hyperplasia, keratinous plug and solar elastosis present on microscopic examination could lead to misinterpretation as a hypertrophic actinic keratosis and/or well differentiated squamous carcinoma, a pitfall to be avoided. Other diagnostic considerations during evaluation of the case include idiopathic cystic chondromalacia, and relapsing polychondritis [11, 12].

Temporomandibular Joint (TMJ)

As an articular joint the recognition of synovium and the associated entity of chondromatosis although rare should be considered in cartilaginous lesions of this area and not mistaken for a cartilaginous malignancy. Imaging findings

Fig. 1 Idiopathic cystic chondromalacia. **a** Low magnification of cystic cleft within auricular cartilage (Hematoxylin and eosin [H&E], $\times 50$). **b** Higher magnification of transition between cystic cleft and surrounding cartilage. (H&E, $\times 200$)

Fig. 2 Chondrodermatitis nodularis helices. **a** Low magnification of this helical skin shave biopsy shows marked hyperkeratosis within a slight epithelial depression (H&E, $\times 20$). **b** At higher magnification, epithelial hyperplasia is present over solar elastosis; a deeper biopsy would be required to see the cartilaginous changes (H&E, $\times 200$)

are valuable to correlate with both site of the lesion and the characteristics of the process for the differential diagnostic considerations [14]. Knowing the site of biopsy tissue and awareness of a mass associated with the TMJ is critical information. Additionally, awareness of the spectrum of histologic findings that may be found in chondromatosis will assist with the correct pathologic interpretation.

Synovial Chondromatosis

Synovial chondromatosis is characterized by formation of multiple cartilaginous nodules in the TMJ space, probably through metaplasia of synovial membrane connective tissue [15]. Although synovial chondromatosis is primarily a pathology of the TMJ, it can produce swelling in the preauricular region and in the external auditory meatus [16, 17]. Additionally, limited motion of the TMJ and deviation of mandible are important clinical features that aid in diagnosis [16, 17]. Imaging of the joint space is vital to the diagnosis as CT scans demonstrate characteristic multiple, small, rounded radiopacities superior to the condylar head [14]. When cartilaginous nodules are not adequately calcified, MRI yields better visualization of the TMJ space and may aid in diagnosis as an MRI of chondromatosis shows numerous chondroid nodules with increased joint effusion within an expanded joint space and capsule [14, 18]. Histologically, multiple nodules of mature cartilage are noted and may exhibit atypical features. Specifically, the cartilaginous nodules often show hypercellular, hyperchromatic nuclei, interspersed with binucleated chondrocytes and possible increased mitotic activity. A looser myxoid collection of chondrocytes may also be present. In addition, foci of endochondral ossification may also be seen [19] (Fig. 3). Due to the aforementioned atypical features which may be seen in synovial chondromatosis, chondrosarcoma may be considered as a histological differential diagnosis however requires direct correlation with imaging to avoid overcalling a malignancy [19].

Neoplasms of the Temporal Bone and Middle Ear

True neoplasms arising from chondrocytes have been reported in the ear and temporal bone region, including such entities of chondroblastoma, chondromyxoid fibroma, chordoma, and chondrosarcoma. As all of these entities in this region are rare, adequate tissue and radiographic correlation of the biologic behavior and extent of the process is important for rendering the diagnosis.

Chondroblastoma

Chondroblastoma is another benign cartilaginous tumor which may arise in the temporal bone. Compared to other cartilaginous entities described a key finding in chondroblastoma is the presence of giant cells (Fig. 4). As such, this entity is covered in the companion article in this special edition on giant cell rich lesions by Dr. Martinez et al. entitled “Selected Giant cell rich Lesions of the Ear and Temporal Bone”.

Chondromyxoid Fibroma

Chondromyxoid fibroma is a benign cartilaginous tumor first described in 1948 by Jaffe and Lichtenstein [20]. Chondromyxoid fibroma is perhaps the rarest of chondroid bone tumors at <1% overall, making involvement of the skull base and temporal bone very rare [21]. About ten cases of chondromyxoid fibromas have been reported arising in the temporal bone. They occurred in patients 20–67 years of age with a male predominance of 3:1 [22]. Presenting symptoms when associated with the temporal bone have included aural fullness and tinnitus, headaches, pain, hearing loss, vertigo and visual disturbance [22]. Imaging findings show a lytic lesion that has well-defined sclerotic and scalloped borders. Cortical expansion may be present. Though most of the imaging findings are based on the most common site within the metaphysis of the long bones. Tarhan et al. reported radiographic findings of a temporal bone chondromyxoid fibroma showing a lytic temporal bone mass

Fig. 3 Synovial chondromatosis of the temporomandibular joint. **a** A coronal CT image shows marked punctate cartilage abutting the ear canal (arrow). **b** On sagittal CT this radiographic abnormality is noted anterior to the external auditory canal in the region of the temporal mandibular joint (TMJ). **c** Low power evaluation is important to appreciate the lobular nature of the cartilaginous proliferation (H&E, $\times 20$). **d** The cartilaginous proliferations may vary from more matured matrix and chondrocytes in lacunae (right side) to hypercellular small spindled chondrocytes more loosely arranged (H&E, $\times 100$). **e** Although cellular, the spindled chondrocytes are uniform and bland, though occasional mitoses may be encountered (H&E, $\times 200$). **f** High cellularity and atypical forms with large nucleoli or binucleation should not be mistaken for chondrosarcoma/malignancy when the radiographic and otherwise nodular background of chondromatosis is present (H&E, $\times 200$)

Fig. 4 Chondroblastoma **a** At low magnification, irregular bony matrix is noted to be surrounded by hypercellularity (H&E, $\times 20$). **b** At higher magnification uniform polygonal cells are present in

sheets association with giant cells. Focal matrix is suggested in the upper left corner, though the characteristic chickenwire matrix around single cells is not evident (H&E, $\times 200$)

with well delineated borders. Central calcification was present with MRI having a hypointense mass on T1 and heterogeneous hyperintense mass on T2-weighted images [21].

Histologically a lobulated proliferation is seen with a smooth boundary if the edge of the lesion is sampled. Uniform spindled or stellate cells with prominent eosinophilic cytoplasm

are present within a myxoid background. Centrally chondromyxoid fibroma may be hypocellular (Fig. 5). Calcifications may occur in 1/3rd of cases. Rarely is true hyaline cartilage identified in which case other entities should be considered in the differential diagnosis. While the cells are often monotonous occasional atypical forms may be present. Pleomorphism or high-grade features are not identified and should raise the possibility of a malignant entity. The histologic differential diagnosis includes consideration of

synovial chondromatosis, chordoma, pleomorphic adenoma, and chondrosarcoma. Table 1 compares growth pattern and histologic features in chondroid-like neoplasms.

Chordoma

Chordoma is a slow growing neoplasm that arises from remnant notochord. The majority of tumors thereby arise along the midline with one-third of chordomas arising in

Fig. 5 Chondromyxoid fibroma. **a** At low magnification, variability in cellularity is noted (H&E, $\times 20$). **b** At higher power the stellate to spindled cells are eosinophilic, monotonous, and hyperchromatic (H&E, $\times 200$). **c** Variable cellularity of the uniform stellate cells is common, as well as, variability in the background chondromyxoid matrix quality (H&E, $\times 200$). **d** Cytologically there is more nuclear atypia in this example, though the cells remain dispersed and without overt mitotic activity (H&E, $\times 200$)

Table 1 Comparison of chondroid-like lesions

Entity	Growth	Cytologic features
Chondromyxoid fibroma	<ul style="list-style-type: none"> • Lobular • Circumscribed border to bone • Increased cellularity peripherally 	<ul style="list-style-type: none"> • Eosinophilic spindled cells in chondromyxoid matrix • Essentially no mature cartilage • Fibrous bands with vessels and +/- osteoclast-like giant cells
Synovial chondromatosis	<ul style="list-style-type: none"> • Multiple nodules • Mature hyaline cartilage or myxoid 	<ul style="list-style-type: none"> • Mature cartilage +/- mild atypia • Hypercellular; hyperchromatic • +/- Binucleated chondrocytes
Chordoma ^a	<ul style="list-style-type: none"> • Infiltrative 	<ul style="list-style-type: none"> • Eosinophilic or vacuolated • Epithelioid or spindled cells in cords and nests • Round nuclei
Chondrosarcoma ^b	<ul style="list-style-type: none"> • Encases normal bone trabeculae 	<ul style="list-style-type: none"> • Peripheral lobularity • Typically, low or moderate cellularity • Mildly pleomorphic • Binucleated • Mitoses and necrosis in higher grade
Chondroblastic osteosarcoma	<ul style="list-style-type: none"> • Invasive mixed with malignant osteoid 	<ul style="list-style-type: none"> • Highly cellular, pleomorphic cells, may be lobular, spindled peripherally, look for epithelioid component with osteoid (lace-like/filigree, or trabecular)

^aChondroid chordoma will show a hyaline like matrix, immunohistochemical evaluation is used to differentiated from true cartilage neoplasms

^bChondrosarcomas are graded I–III, low to high grade representing a range of corresponding cytologic features

the skull base. Chordomas overall are rare, representing 3% of all bone tumors. Despite the high-frequency in the skull base, only a few case reports document an association of chordoma arising in the petrous temporal bone [23, 24]. In 1973 Heffelfinger et al. described a chondroid variant of chordoma leading to the recognition of significant histologic overlap between chordoma and chondrosarcoma [25]. MRI features are also similar between chordoma and chondrosarcoma making tissue biopsy essential for diagnosis [26].

Histologically, chordomas show lobulated growth with thin fibrous stroma. Tumor cells grow in strands and cords within a myxoid or chondroid matrix. The tumor cells often contain characteristic vacuoles leading to the characteristic ‘physaliphorous cells’ which represent the accumulation of mucopolysaccharides. Cytoplasm is also often prominently eosinophilic. The nuclei are round and uniform with low mitotic activity; occasional pleomorphic cells may be present. While epithelioid cells are more common, tumors with predominant spindled cells are well documented (Fig. 6).

Chondroid chordoma is a rare variant almost exclusively of the skull base that was delineated by Dr. Heffelfinger [25]. For this subtype, cartilaginous differentiation must be a part of the tumor that also shows typical chordoma features. The cartilaginous component is most often hyaline cartilage matrix with lacunae formation and is typically cytologically bland. Chondroid chordoma must be differentiated from chondrosarcoma where these both occur particularly in the head and neck and sella region. Biologically, these two tumors are distinct. Bohman et al. utilizing the SEER database from 1983 to 2009, showed patients with skull base chordomas had a markedly lower overall 10 year survival compared to chondrosarcoma in this area, 32% versus 50% [27].

Along with assessment of morphology on an adequate sized sample, immunohistochemical findings allow for the differentiation of these entities. Chordoma is positive for

cytokeratin AE1/3 and EMA with a sensitivity and specificity of 90 and 100% compared to chondrosarcoma [28]. S100 and SOX9 will be expressed in the majority of chordomas and chondrosarcomas and are not useful in the differentiation of these entities. Brachyury, a transcription factor involved in regulating development of notochord is expressed in > 80% of chordoma [29, 30]. Adding brachyury to AE1/3 increases the sensitivity to identify chordoma to 98% [28]. Importantly EMA may react in a subset (8%) of chondrosarcomas, and should be coupled with a panel of immunostudies when used as support for a particular diagnosis. Other diagnostic considerations on small biopsies may include chondroid meningioma, myoepithelial carcinoma and metastatic clear cell carcinoma which would also be reactive with cytokeratin and possibly s100.

Chondrosarcoma

Chondrosarcoma is a malignant tumor composed of chondrocytes where 5% occur in the head and neck region. In the skull base, a median age of 42–46 years was identified though a broad age range for this diagnosis has been documented (0–92 years). Chondrosarcomas showed a similar incidence in men and women [27, 31]. It is important to recognize chondrosarcomas are much more common than their benign counterparts. As slow growing tumors, chondrosarcomas present with non-specific symptoms of headaches, hearing reduction or tinnitus, and/or facial nerve dysfunction. MRI shows a low signal intensity mass on T1 weighted images with T2 high-signal intensity [32]. Imaging findings for chondrosarcoma notably overlap with chordoma, thereby requiring tissue sampling for diagnosis [26, 33]. Utilizing the SEER database, outcomes for chondrosarcomas of the skull base were 12.6–22 year median survival and a 10 year 50–62% overall survival [27, 31]. The lower median survival noted in Jones et al. SEER

Fig. 6 Chordoma. **a** Low magnification shows a lobular proliferation with a myxoid to cartilaginous background (H&E, $\times 40$). **b** High-magnification demonstrates a predominance of round eosinophilic cells growing in cords. Rare cell ‘physaliphorous’ forms are noted (cen-

tral to upper left). The nuclei are round though may show atypia with variable size. Immunostudies are helpful in distinguishing chordoma from other cartilaginous and skull base tumors (H&E, $\times 200$)

study may be secondary to the inclusion of older SEER data and the potential of mistaken chondroid chordomas included as chondrosarcomas in this region.

Grossly, chondrosarcomas are lobulated firm to gelatinous, gray-white lobulated tissue. Histologically chondrosarcomas vary from well-differentiated (grade I, II) trying to recapitulate hyaline cartilage to less commonly high-grade tumors (grade III) composed of clearly malignant chondrocytes in a myxoid or cartilaginous stroma. Grade I chondrosarcomas show slight increase in chondrocytes, nuclear hyperchromasia and binucleation may be encountered and must be differentiated from chondromas. Chondromas are likely encountered at the junctions with adjacent bones (petrosphenoidal, petroclival, sphenoccipital) [34, 35]. A clinical history of Ollier disease and Maffucci syndrome may also be present when chondroma is being considered. While cartilage signals by imaging will be similar between entities, CT may show ring-like chondroid matrix calcification [34]. Grade II Chondrosarcomas show higher cellularity, increased pleomorphism and possible mitoses (Fig. 7). Grade III chondrosarcomas are high-grade with increased frequency of multinucleation, mitoses and necrosis. When high-grade features are present, chondroblastic osteosarcoma must be included in the differential diagnosis. Evaluation of osteoid matrix histologically and reviewing the imaging for characteristics of osteosarcoma is essential to aid in the correct diagnosis on biopsy material. Surgery remains the primary modality for treatment of these tumors.

Bone Lesions of the Ear and Temporal Bone

Bone abnormalities may involve the middle ear ossicles as in otosclerosis or directly involve the temporal bone. The temporal bone is a complex 3-dimensional bone composed of mastoid portion (posterior), external acoustic meatus (inferior central) with the squamous portion and zygomatic process (superior/anterior). The petrous apex extends medial to form part of the skull base. The temporal bone may be altered by adjuvant therapies for advanced skin cancers (osteoradionecrosis) or show benign bony diseases as occurs in other bones including osteoma, exostosis or develop malignancies, including osteosarcoma. Evaluation of the architecture, cytologic features and presence of matrix are all combined with radiographic features for classification of osseous lesions. Considerations for the differential diagnosis and imaging findings are discussed.

Otosclerosis (Middle Ear)

Otosclerosis is an acquired abnormality with genetic linkages that affects bones derived from the otic capsule [36]. In otosclerosis, there is disturbed bone remodeling that results in fixation of the stapes or the lateral ossicular chain [36]. Symptoms of otosclerosis include tinnitus, vertigo and hearing loss that may be sensorineural, conductive or mixed [37, 38]. On otoscopy, a faint pink hue may be noted (Schwartz sign) and is indicative of otospongiosis [39]. High resolution cone beam CT is both highly sensitive and specific for diagnosing otosclerosis (Fig. 8). On radiological examination,

Fig. 7 Chondrosarcoma. **a** Imaging shows characteristic features of cartilage with low signal on T1 axial MRI with contrast in the mass approximating the right ear canal compared to **b** the bright signal seen on T2 axial MRI. **c** On a sagittal T1 the mass is compressing the external auditory canal and shows heterogeneous composition. **d** Low magnification shows scalloping of the underlying bone trabecular with a moderately cellular possible cartilaginous matrix (H&E, $\times 40$). **e** At higher magnification single cells with variable enlarged nuclear size and occasional binucleation are present. The growth is disorganized and not corded as in chordoma. The matrix varies from loose to more mature (H&E, $\times 200$)

Fig. 8 Otosclerosis axial high resolution CT image of right temporal bone in an adult with otosclerosis. A hypodense demineralized focus (arrow) is noted. Reproduced with permission from image courtesy of Esther X. Vivas MD, Emory University, Atlanta, GA

depending on extent of involvement, otosclerotic changes can be either solely fenestral or cochlear with or without fenestral changes [40]. Histologically, the spectrum of changes can range from spongiotic to a fibrotic-sclerotic presentation. In spongiosis, perivascular bone resorption creates dilated vascular spaces which is then replaced by hypercellular and hypervascular fibrous tissue. Additionally, osseous changes range from production of immature bone to mature woven bone with irregular osteon structure and arrangement [41]. Osteogenesis imperfecta, osteoporosis and Paget disease may be considered in the differential diagnosis of otosclerosis however would not be isolated to the middle ear and other sites of involvement by imaging would aid in these considerations [42].

Osteonecrosis/Osteomyelitis of Temporal Bone

Complications of adjuvant radiotherapy in the head and neck include osteonecrosis. The temporal bone, like the jaw bones is susceptible to this condition though it was not

recognized in this region until the 1960s [43]. Skin cancers with adverse features including perineural invasion and/or secondary regional metastasis in the neck and periparotid region may benefit from adjuvant radiotherapy placing the temporal bone at risk for necrosis. Similarly, radiation therapy for salivary gland tumors of the parotid and treatment for nasopharyngeal carcinomas may also lead to osteoradionecrosis here [44]. Presenting symptoms include ulceration of the skin and exposed temporal bone with drainage (otorrhea) from the wound or ear canal in the majority of patients. Hearing loss is also common and pain is present in approximately half of patients. This constellation of presenting symptoms can be difficult to discern osteonecrosis from recurrent tumor, leading to repeat biopsies. The presence of an open wound is then secondarily exposed to skin flora leading to an osteomyelitis clinical scenario. Studies have shown the onset of osteoradionecrosis varied from 1 to 22 years with a mean of 8 years [44, 45]. CT findings identified erosions of the external auditory canal and mastoid effusions in nearly all patients. Other CT features included soft tissue enhancement mimicking tumor recurrence, and soft tissue air/abscess formation. The TMJ may also be involved with erosions of the condylar bone concurrently present with temporal bone osteoradionecrosis [45]. In cases where osteonecrosis is identified in the absence of prior radiation therapy, medication-related osteonecrosis may be a consideration but requires clinical correlation to identify a prior history of anti-resorptive type medications such as bisphosphonates and/or denosumab. Medication-related osteonecrosis is well documented in the jaw bones and can also occur in the temporal bone but is reported far less frequently [46, 47].

Histologically the temporal bone affected by osteomyelitis shows irregular bony cortex and trabeculae ('moth-eaten') with open/empty lacunae. Osteocytes are lost and variable degree of bone resorption is present. Irregular cement lines may also be seen. The marrow space is replaced by mixed acute and chronic inflammation and fibrosis (Fig. 9). Overlying squamous epithelium may show pseudoepitheliomatous hyperplasia and should be differentiated from recurrent carcinoma. Special stains may be used to evaluate for fungal and/or bacterial elements though often broad-spectrum

Fig. 9 Osteomyelitis of temporal bone. **a** Low power evaluation shows irregular 'moth-eaten' bone trabeculae. The marrow is replaced by fibrosis and non-bone marrow elements (H&E, $\times 20$). **b** At higher magnification the bone shows empty lacunae consistent with osteonecrosis. The marrow is replaced by mixed inflammation and granulation tissue. (H&E, $\times 200$)

antibiotics and fungal ear drops may already be implemented. The histologic features of medication-related osteonecrosis of the temporal bone are not well-described [46, 47]. Conservative management is advised though in severe cases surgery may be warranted.

Exostosis

Exostosis of the external auditory canal is a benign bony outgrowth that is often noted in young males with history of prolonged exposure of cold water (swimmers, surfers and divers) [48]. Exostosis is almost always bilateral and usually presents medial to the isthmus of the external auditory canal. Patients may experience conductive hearing loss, tinnitus, inflammation and pain in the ear [49, 50]. Otoscopic examination shows circumferential narrowing of the external auditory canal with unremarkable overlying soft tissue [49]. Imaging shows bilateral, broad-based, circumferential bony outgrowths around the external auditory canals [51]. Histological examination on low power shows a dome-shaped configuration composed of lamellar bone that may be surfaced with an overlying cartilaginous cap [52]. In the external auditory canal, the layers of compact bone are often arranged in an onion-skin configuration, without trabecular bone formation or developed marrow spaces. The obvious histological differential diagnosis is an osteoma which would require clinico-radiologic correlation (i.e. unilateral versus bilateral and potentially circumferential) to separate it from an exostosis of the external auditory canal [52, 53]. In general, osteoma is regarded as a pedunculated bone lesion in contrast to the broad-based nature of an exostosis. While true osteoma of the external auditory canal is uncommon in comparison to canal exostoses, they are known to occur along the outer cortical surface of the skull. In the latter, the compact, or ‘ivory’ osteoma would appear microscopically similar to exostoses of the auditory canal [54]. The true auditory canal osteoma would be more likely to exhibit microscopic trabecular bone formation and marrow spaces (Fig. 10).

Protuberant Fibro-Osseous Lesion of the Temporal Bone

In 1999, a unique solitary exophytic bone lesion appearing along the outer cortex of the temporal bone was described by Selesnick et al. and termed protuberant fibro-osseous lesion of the temporal bone [55]. Though the description of the initial two cases shared remarkable similarity in the clinical, radiographic and microscopic findings, it would be > 10 years before additional cases were described [56]. In the second publication dedicated to protuberant fibro-osseous lesion (FOL) of the temporal bone, the radiographic and histologic description of the predominantly right sided retroauricular lesion overlying the mastoid bone remained

essentially identical to the original description [56]. The investigators proposed the term, ‘Bullough lesion’ or ‘Bullough bump’ to credit Dr. Peter Bullough as the pathologist participating in the original 1999 report. In the interval since 2010, an additional five cases have been described, predominantly in females, across a wide age range (10–71 years, average age 41) [57–59]. As the name suggests, the lesion is composed of bone and fibrous connective tissue, and while most cases are located along the temporal bone, specifically postauricular region, occipital bone involvement was recently reported [58]. Radiographically, CT demonstrates a broad based, well-delineated, solitary lesion along the surface of the bone, without intramedullary bone involvement or intracranial extension [56]. Radiographic mineralized matrix has been documented within the lesion in all cases [55–59]. Some cases had been present for multiple years prior to excision with little or no radiographic change documented [57]. Speculation regarding the etiopathogenesis of protuberant FOL of temporal bone includes reactive and/or an embryologic abnormality in view of the association with suture lines of the skull and multiple muscle attachments in the area [56]. Thus far, no evidence of common clinical or historical data such as radiation exposure, postural, occupational, or history of prior trauma has been identified and the etiopathogenesis of protuberant FOL lesion of temporal bone remains unknown.

At low power magnification, multiple small round-to-oval profiles of bone varying in size are distributed within dense fibrous stroma consistent with the appearance of a FOL [55]. Light microscopy and polarized light exam reveals rounded bony islands may be composed of woven bone, lamellar bone or a mixed woven and coarse lamellar pattern [55–58]. Islands of bone are with or without osteoblastic rimming [58]. Small spindle shaped cells show even distribution within the relatively hypocellular dense fibrous connective tissue stroma present between bone islands. The fibrous stroma appears interwoven, with short, subtle haphazard fascicles and without prominent vascularity [56] (Fig. 11). No evidence of hyperchromatism, nuclear atypia or mitotic activity is seen. Immunohistochemical stains including cytokeratins, EMA, s100, desmin, CD34 and nuclear beta catenin staining have all been reported as negative in protuberant FOL of the temporal bone [56–58].

The differential diagnosis of a bone-forming lesion localized to the outer surface of skull cortex includes reactive lesions, and neoplasms such as osteoma (discussed in previous section) and parosteal osteosarcoma. While a reactive proliferation cannot be entirely excluded as an underlying cause of the Bullough lesion, expected reactive changes such as formation of granulation tissue, xanthomatous inflammation, hemosiderin deposition or zones of bone deposition have not been reported [56, 57]. Juxtacortical osteosarcoma, also known as parosteal osteosarcoma could appear as a

Fig. 10 Exostoses/osteoma. **a** and **b** Axial view of CT demonstrating bilateral external auditory canal exostoses (courtesy of Amy F. Juliano MD, Massachusetts Eye and Ear Infirmary, Boston, MA). **c** An exostosis of dense bone with peripheral onion skinning pattern (H&E, $\times 50$). **d** Higher magnification of osseous layering (H&E, $\times 110$). **e** Imaging of pedunculated osteoma within external canal (courtesy of Esther X. Vivas MD, Emory University, Atlanta, GA). **f** Woven and lamellar bone surfaced by skin of the external auditory canal. Lesion best considered osteoma (H&E, $\times 20$). **g** Axial view of CT demonstrating osteoma of parietal bone. **h** Scanning magnification reveals nodule of dense viable bone, consistent with osteoma (H&E, $\times 40$). **i** Higher magnification of osteoma (H&E, $\times 100$)

Fig. 11 Protuberant fibro-osseous lesion of temporal bone. **a** Scanning magnification of the fibro-osseous lesion fragments (H&E, $\times 3$). **b** Rounded and ovoid islands of lamellar/woven bone within dense fibrous stroma (H&E, $\times 40$). **c** Higher magnification of ovoid and stellate cells within dense fibrous stroma (H&E, $\times 200$). Reproduced with permission from Case courtesy of Mark A. Edgar MD, Emory University, Atlanta, GA

surface FOL due to its origin from the outer layer of periosteum [60, 61]. Parosteal osteosarcoma is rare, slow-growing and similar to protuberant FOL of the temporal bone, lacks an associated intraosseous component [56]. In contrast to the rounded osseous islands of the Bullough lesion however, bony trabeculae of parosteal osteosarcoma are often arranged in parallel within the bland fibrous stroma. Mitotic figures are rare and minimal cytological atypia is seen [60, 62, 63].

However, without knowledge of the clinicoradiographic features of the case, FOL such as fibrous dysplasia and ossifying fibroma may enter the microscopic differential diagnosis. Microscopically, fibrous dysplasia is characterized by numerous immature bony trabeculae with irregular shapes set within a well-vascularized fibrous stroma [55]. The molecular underpinnings of the Bullough lesion are suspected to be distinct from fibrous dysplasia. The latter is most often associated with GNAS mutation, which has not been detected in the Bullough lesion thus far [57]. Microscopic examination of ossifying fibroma reveals irregular and rounded trabeculae and/or bone islands haphazardly distributed within fibrous but well-vascularized stroma. Ossifying fibroma and monostotic fibrous dysplasia occur uncommonly within the temporal bone [64–66]. Importantly, fibrous dysplasia including the very rare example of exophytic fibrous dysplasia, and ossifying fibroma would be expected to be centered within an intraosseous location, in contrast to the outer cortex-based location of the Bullough lesion, making radiographic correlation essential [64–67].

Treatment of protuberant FOL of the temporal bone has most frequently included local excision with an osteotome followed by recontouring of the bony attachment point by rotary instrumentation [55]. Several cases have documented a long presurgical clinical history, and this, along with overall low rate of recurrence after excision and bland histologic

features support the perception of a benign lesion. On balance, the lesion is rare and in at least one case there remains a question of clinical recurrence [58]. For these reasons, clinical and radiographic follow up appears prudent.

Osteosarcoma

Osteosarcoma is a malignancy of osteocytes for which matrix, specifically osteoid, is usually a component recognized both microscopically and by radiographic imaging. Primary osteosarcoma of the jaws and skull bones represent 6–13% of all osteosarcomas [68]. The age of onset is 10–20 years later than in long bones with patients often presenting in the 3rd to 4th decade of life. There is a similar male to female occurrence [69]. Osteosarcomas may also be encountered as a post radiation associated sarcoma, where the tumor arises in the radiation field from a prior cancer treatment. Post-radiation sarcomas have a median onset of 10 years after radiation and show a wide range of morphologies. Post-radiation osteosarcoma may represent up to 5% of all osteosarcoma. These radiation associated osteosarcomas are high-grade, often with an aggressive clinical course [70].

The wide range of histologic features that may be encountered in osteosarcomas must be appreciated to avoid misclassification as another tumor type. Particularly challenging is chondroblastic osteosarcoma, for as the name implies it produces both malignant cartilage and osteoid. Typically, this entity is high-grade including the cartilaginous component which is a clue to consider osteosarcoma over chondrosarcoma. The malignant cartilaginous component may still be lobulated though often surrounded by more hypercellular spindled and or polygonal cells with mitoses and variable osteoid matrix. Chondroblastic osteosarcoma is the most common subtype in the head and neck making up to one-half of osteosarcomas of the jaw. In comparison,

chondrosarcomas of the head and neck are typically well-differentiated (Grade 1 or II); radiographic findings suggesting bone formation may also aid the differential diagnosis. Imaging correlation is therefore advised in all potential bone tumors.

Osteosarcoma may be predominantly fibroblastic, composed of malignant spindled cells. The fibroblastic variant is seen less frequently, with osteoblastic and chondroblastic variants occurring most commonly [68] (Fig. 12). As the fibroblastic areas show low to absent osteoid matrix, caution is recommended in calling a soft tissue sarcoma in the head and neck, when the mass is associated with an underlying bone. Other variants include osteoblastic, telangiectatic, periosteal, parosteal (discussed in prior section), post-radiation which is often high-grade with variable to minimal osteoid matrix, and others.

Grossly tumors are often solid, gritty white and dense. Histologically, osteoid may be purplish on small biopsies when not decalcified versus the pink post-decalcification appearance. Osteoid may be partially forming trabeculae albeit irregular with lacunae, lace-like or filigree with fine delicate osteoid wrapping around individual tumor cells. High-grade tumors may show pleomorphism, giant cells and a paucity of identifiable osteoid. Immunohistochemistry does not add to the diagnosis, though is important to

exclude possible metastases to the bone (high-grade carcinomas, melanomas, etc.) that enter the differential diagnosis.

Surgery is the primary treatment with margin status critical to aid in local control in head and neck osteosarcomas [68]. The role of adjuvant chemotherapy is not as clear in the head and neck as it is in long bone osteosarcomas. The differences for these observations remain unclear [71]. Adjuvant radiation therapy appears to impact local control and survival [72]. Five-year disease specific survival is 62–67% for head and neck osteosarcomas [69, 72].

Key Points

The ear and temporal bone manifest a variety of cartilaginous and bone pathologies. The complexity of this region combined with the rarity of biopsies from this site lead to challenges distinguishing disease processes in this area. Creating a differential diagnosis based on location and clinicopathologic and imaging findings will aid in establishing the correct diagnosis. Particularly challenging are the cartilaginous and cartilage-like entities of the temporal bone on small biopsies. The findings of myxoid or chondroid features leads to a broad differential diagnosis including chondromyxoid fibroma, chondroid chordoma/chordoma,

Fig. 12 Osteosarcoma. **a** Low magnification of an osteoblastic osteosarcoma with filigree osteoid surrounding cellular areas of malignant cells (H&E, $\times 40$). **b** At higher power there is marked pleomorphism, and crowding. The filigree ‘hook-like’ osteoid is better appreciated (H&E, $\times 200$). **c** This fibroblastic osteosarcoma is composed of highly cellular spindled areas with intermittent areas of osteoid (bottom

right corner) that confirm the morphologic diagnosis as osteosarcoma (H&E, $\times 40$). **d** Chondroblastic osteosarcoma must also be considered in the head and neck region when malignant, cellular cartilage is encountered; imaging may elucidate bone matrix aiding the differential diagnosis on small biopsies. Spindled malignant cells are noted at the periphery. (H&E, $\times 200$)

pleomorphic adenoma, and consideration of TMJ synovial chondromatosis. (Table 1). A frankly malignant chondroid component raises the possibility of chondrosarcoma and chondroblastic osteosarcoma. Review of the imaging is essential to the diagnostic process and should be coupled with the biopsy in diagnosis and triaging for patient care. Additionally, the imaging may aid in identifying the epicenter of the process, delineate more benign features and/or highlight potential osteoid in order to expand the differential to include osseous lesions. Thus, caution is critical when approaching matrix producing tumors on small biopsies in the temporal bone region.

Compliance with Ethical Standards

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

Research Involving Human and Animal Rights This article does not contain any studies with human participants or animals performed by any of the authors.

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