Article:
Hankinson, P. orcid.org/0000-0002-7213-5380, Brierley, C. and Brierley, D. orcid.org/0000-0003-0152-2372 (2024) A review of oral pathology in orthodontics. part 2: pathology of the jaw bones. American Journal of Orthodontics and Dentofacial Orthopedics, 165 (2). pp. 131-142. ISSN: 0889-5406

https://doi.org/10.1016/j.ajodo.2023.09.015

A review of oral pathology in orthodontics. Part 2: Pathology of the jaw bones

Paul Hankinson,[a] Catherine Brierley,[b,c] and Daniel Brierley[a]
Sheffield and Chesterfield, United Kingdom

For many patients, their first full jaw imagining will be requested and reported by an orthodontist. This may lead to the discovery of unexpected pathology in the jaws. In this review article, we discuss the clinical and radiological appearance as well as the pathologic features and treatment of the more common entities of the jaws. In addition, we will discuss the less common lesions which carry important consequences for the patient. Through the identification of these lesions, appropriate referral and management can be pursued. (Am J Orthod Dentofacial Orthop 2024;165:131-42)

Many children and young adults will receive their first full jaw imagining from an orthodontist. Approximately 6% of radiographs for orthodontic treatment planning will reveal other abnormalities, some of which may require surgical management or have implications for a patient's general health.[1] Though many patients treated by orthodontists in the United Kingdom are children,[2] an increasing number of adults are also having orthodontic treatment.[3] In either case, there is significant scope for an orthodontist to be the first clinician to encounter disease of the jaws and other bones of the head and neck. This review aims to describe common hard tissue pathology an orthodontist may encounter as well as less common but important diseases that present in children, young adults, and adults (Table I). The first publication of this series, published in this issue, described the pathology of soft tissues.[4]

[a]Unit of Oral and Maxillofacial Pathology, School of Clinical Dentistry, University of Sheffield, Sheffield, United Kingdom.
[b]Orthodontic Department, Charles Clifford Dental Hospital, Sheffield, United Kingdom.
[c]Orthodontic Department, Chesterfield Royal Hospital, Chesterfield, United Kingdom.
All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest, and none were reported.
Address correspondence to: Paul Hankinson, Unit of Oral and Maxillofacial Pathology, School of Clinical Dentistry, University of Sheffield, 19 Claremont Crescent, Sheffield S10 2TA, United Kingdom; e-mail, p.hankinson@sheffield.ac.uk.
Submitted, May 2023; revised and accepted, September 2023.
0889-5406

https://doi.org/10.1016/j.ajodo.2023.09.015

COMMON ENTITIES

Odontogenic cysts are the most commonly encountered pathology of the jaws in children and adults.[5-7] In addition, pathology related to the teeth is also very common (eg, periapical granulomas[6,7] and other odontogenic lesions such as odontomas[6]). In descending frequency, we will discuss periapical granuloma, radicular cysts, dentigerous cysts, odontomas, odontogenic keratocysts, bone exostoses, peripheral/central giant cell granulomas, inflammatory collateral cysts and nasopalatine cysts.[6]

Periapical granuloma

Of all specimens originating in the jaws submitted to oral pathology laboratories, periapical granulomas are the most frequently encountered.[6,7] They are commonly asymptomatic but may present with pain.[8] The lesions will be associated with a nonvital tooth and appear as a well-defined radiolucency associated with the apex of a tooth.[8] The lamina dura of the associated tooth will be disrupted.[8] Distinguishing a radicular cyst from a periapical granuloma is difficult radiologically, though larger lesions are more likely to be cysts, so histologic assessment is valuable.[9] A periapical granuloma, when assessed microscopically, comprises granulation tissue with an associated inflammatory infiltrate that may include variable lymphocytes, macrophages, polymorphonuclear leukocytes, and plasma cells.[8] Removal of the nonvital tooth or successful endodontic treatment will typically resolve the lesion.

Radicular cyst

Radicular cysts are the most common odontogenic cysts in both children and adults,[6,7] accounting for

Table I. Summary of the pathologic entities discussed in this review separated into the categories reactive/inflammatory, developmental/hamartomas, benign neoplasms, and malignant neoplasms

Reactive/inflammatory	*Developmental/hamartomas*	*Benign neoplasms*	*Malignant neoplasms*
Periapical granuloma	Dentigerous cyst	Ameloblastoma	Langerhans cell histiocytosis
Radicular cyst	Odontoma	Adenomatoid odontogenic tumor	Osteosarcoma
Giant cell granuloma	Odontogenic keratocyst	Ameloblastic fibroma	Ewing sarcoma
Inflammatory collateral cyst	Exostoses	Cemento-ossifying fibroma	
MRONJ	Nasopalatine cyst		
	Fibrous dysplasia		

52% of odontogenic cysts.[5] These cysts are caused by chronic inflammation from the apex of a nonvital tooth,[10] which can be a primary or secondary tooth.[11] Most are asymptomatic but may cause pain where infection has occurred, and occasionally, cysts can grow large enough to cause expansion of the jaws.[12] They appear as well-defined, often corticated round radiolucencies on radiographs, with continuation between the lamina dura of the affected tooth and the cyst.[12] They may cause root resorption.[13] Microscopic examination shows an inflamed fibrous cyst wall lined by a nonkeratinized stratified squamous epithelium.[12] Cholesterol clefts may also be seen.[12] Treatment is through a combination of enucleating the cyst and treating the tooth causing the inflammation, whether through root canal treatment, if possible, or extraction.

Dentigerous cyst

Dentigerous cysts are developmental cysts that surround the crown of an unerupted tooth, with a lining derived from the reduced enamel epithelium, and have an uncertain pathogenesis.[12] They are the most common developmental cyst of the jaws in all age groups.[5-7,10,12] The mandibular third molars are the most commonly affected tooth, followed by the maxillary third molars.[12] This is followed by the canines and then the second premolars in a distribution that matches the general pattern for unerupted teeth.[12] Often, these lesions are asymptomatic, but they may present with swelling, pain, or infection when large.[14] On radiological examination, they appear as well-defined, corticated, unilocular radiolucencies associated with the crown of an unerupted tooth.[12,14] They may cause both displacements of teeth[14] or root resorption.[13] Histologic examination of the cyst will show a thin, nonkeratinized epithelial lining and fibrous cyst wall, though these cysts may become inflamed, giving the lining similar qualities to a radicular cyst.[12] As such, either radiographically or at the macroscopic pathologic examination, a relationship between the cyst and tooth crown must be established to make a diagnosis of a dentigerous cyst. Treatment is by enucleation of the cyst with removal of the associated tooth in most cases. However, marsupialization may be used if keeping the associated tooth is important for orthodontic treatment.[15,16]

Odontomas

Odontomas are hamartomas that comprise all forms of dental tissue, including enamel, dentine, cementum, and dental pulp.[17] They come in 2 forms: compound and complex. In compound lesions, the dental tissues are organized into structures similar to teeth, whereas a complex odontoma comprises dental tissues in a haphazard arrangement.[18] Odontomas are the most common solid odontogenic lesion in children,[6,19] though less common in adults.[7] The majority occur in patients aged <20 years.[19] Usually, these lesions are incidental findings, but they may also be present because of delayed eruption of the permanent teeth, a common reason for referral to an orthodontist.[18,19] On radiological examination, they appear as well-defined radiopacities, sometimes in close association with the crown of an erupting tooth (Fig 1). Complex odontomas have a haphazard pattern of calcification on radiographs, with compound odontomas forming abnormal but tooth-like structures.[19] Both may rarely cause root resorption.[19] Histologically, both complex and compound odontomas have similar features. Both usually have a fibrous capsule surrounding various amounts of partially mineralized enamel, dentine, cementum, pulp, and odontogenic epithelium.[18] After local excision, recurrence is rare.[18]

Odontogenic Keratocyst

Odontogenic keratocysts are developmental cysts with a broad age range of presentation,[5,20-22] although they are the third most common cyst of the jaws in children.[6] They are most frequently identified in the second and third decades.[22] Many patients present asymptomatically, and the cyst is discovered during

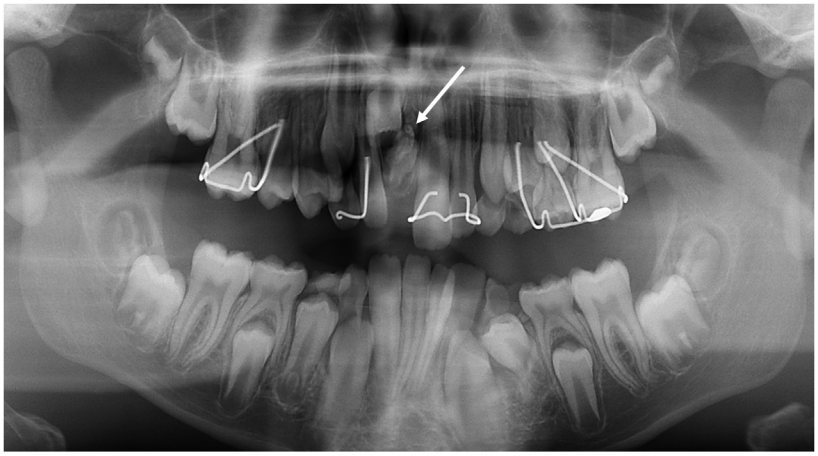

Fig 1. An orthopantomogram of a patient with an odontoma (*arrow*) and removable appliance. The odontoma is identified as a well-defined radiopacity in the maxilla and is causing failure of eruption of the permanent maxillary right central incisor.

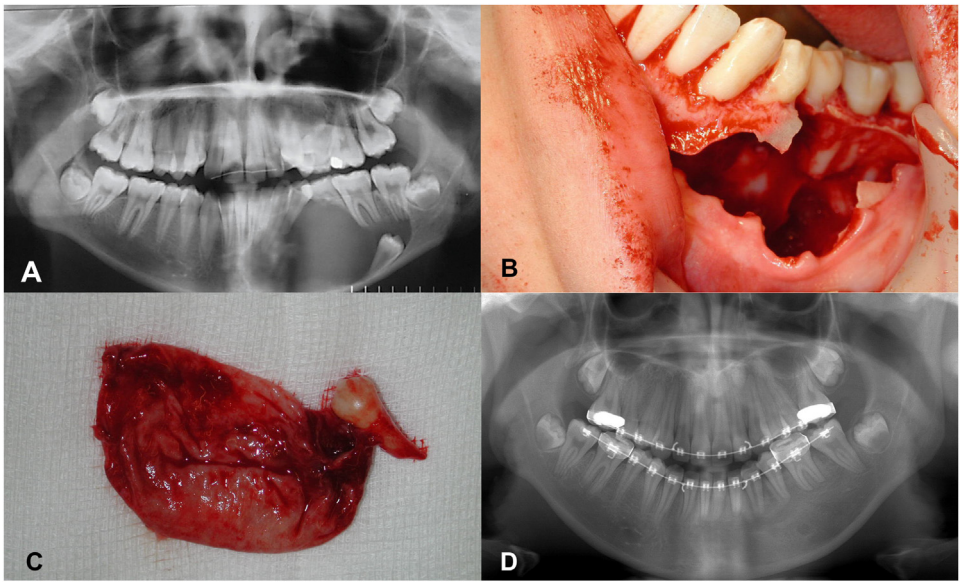

Fig 2. An example of an odontogenic keratocyst: **A,** An orthopantomogram showing a unilocular radiolucency occupying the mandibular left body and parasymphysis with the expansion of the jaw, a displaced adult premolar can also be seen; **B,** An intraoral photograph of the mandibular left cyst cavity after enucleation; **C,** A photograph of the enucleated cyst with adult premolar tooth; **D,** An orthopantomogram showing bony infill of the cyst cavity and fixed orthodontic appliances.

radiographic examination. However, patients may present with jaw swelling, pain, or sinus formation.[20-22] These cysts are more common in the mandible than the maxilla and tend to be located more posteriorly.[20-22] They appear radiologically as well-defined, corticated radiolucencies, which may be unilocular (Fig 2, *A*) or multilocular.[12,20] They are often described as having scalloped margins and may cause root displacement[12] or resorption.[13,20] Often, the differential diagnosis of these cysts is an ameloblastoma, making biopsy for histologic assessment a valuable tool before committing to enucleation of these lesions. The histology of these lesions comprises an uninflamed fibrous cyst wall lined by thin parakeratinized stratified

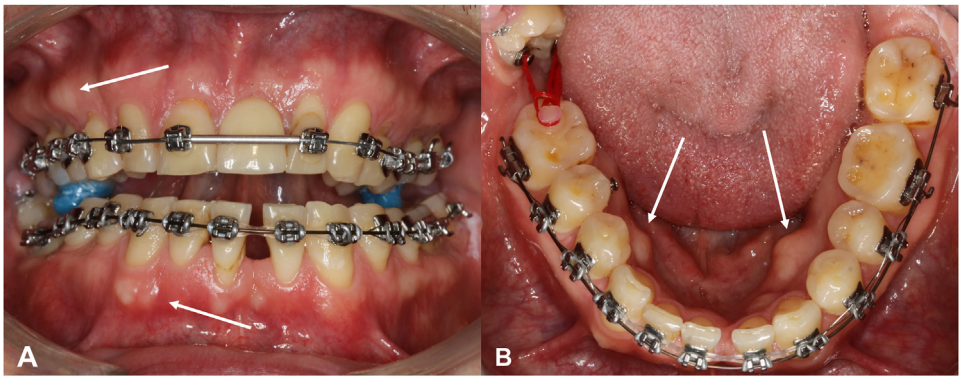

Fig 3. An example of bony exostoses: **A,** An intraoral photograph showing buccal exostoses (*arrows*) on the mandibular and maxillary alveolus; **B,** An intraoral photograph showing tori (*arrows*) on the lingual surface of the mandible.

squamous epithelium with palisading of the basal cells.[12] Although, as with any odontogenic cyst, if the lesion becomes inflamed, characteristic histologic features may be lost.[12] Treatment of these cysts is by enucleation (Figs 2, *B* and *C*), marsupialization, or, in rare circumstances, resection with the treatment often dictated by the size of the cyst, age of the patient and its association with adjacent structures.[12,20-22] There is ongoing debate about the most appropriate management of these lesions. The recurrence rate is up to 30%, with higher rates after enucleation compared with marsupialization or resection.[23]

Exostoses

Bony exostoses of the jaws are very common, though the reported prevalence is highly variable.[24] They are most commonly observed in the 35-65-year age group, but they also present in children[24] and are the most frequently observed bone pathology in this group.[6] They appear clinically as protuberances of the hard tissue of the jaws and palate and are classified as torus mandibularis (Fig 3, *B*), torus palatinus, or buccal exostoses (Fig 3, *A*) depending on the location.[8,24] They are rarely sent for histologic examination but will appear as normal cortical or cancellous bone when they are.[8,24] They are only removed when they are causing issues, such as with the fitting of a removable appliance or denture. Bony exostoses may ulcerate when traumatized, exposing the underlying bone. Often, these ulcers have a protracted course and may be slow to resolve. Care should be taken not to traumatize exostoses when taking intraoral radiographs or impressions. Occasional patients with spontaneous necrosis of bony exostoses have been reported.[25]

Giant cell granulomas

Both peripheral and central giant cell granulomas are reactive lesions with the same histologic features, the distinguishing feature being the involvement of bone. Central giant cell granulomas are uncommon but tend to present in children and young adults as opposed to older adults.[26] The peripheral form is more common overall and has an older mean age of presentation.[6,7,27] The central giant cell granulomas usually present as a painless swelling of the jaws, possibly with a blue to purple soft-tissue extension, and may cause displacement of teeth.[26] Alternatively, peripheral types occur outside of the bone and present as soft red, blue, or purple polypoid lesions, often on the gingivae with a predilection for the mandibular gingivae.[27] The radiological features of central giant cell granulomas are variable, but they are usually radiolucencies, which may be either unilocular or multilocular.[26] Displacement of teeth and root resorption is common.[26] The histologic features of these lesions are identical, comprising osteoclast-like multinucleated giant cells in a background of spindled to polygonal cells in a highly vascular stroma.[17] Treatment is by excision with curettage of the bone involved. Recurrence occurs in up to 49% of central cases[26] and approximately 10% of peripheral lesions.[27] Giant cell granulomas need to be distinguished from other lesions with giant cells that may present in the jaws. For example, blood tests for parathyroid hormone can help rule out brown tumors of hyperparathyroidism.

Inflammatory collateral cysts

Inflammatory collateral cysts are uncommon inflammatory odontogenic cysts accounting for approximately

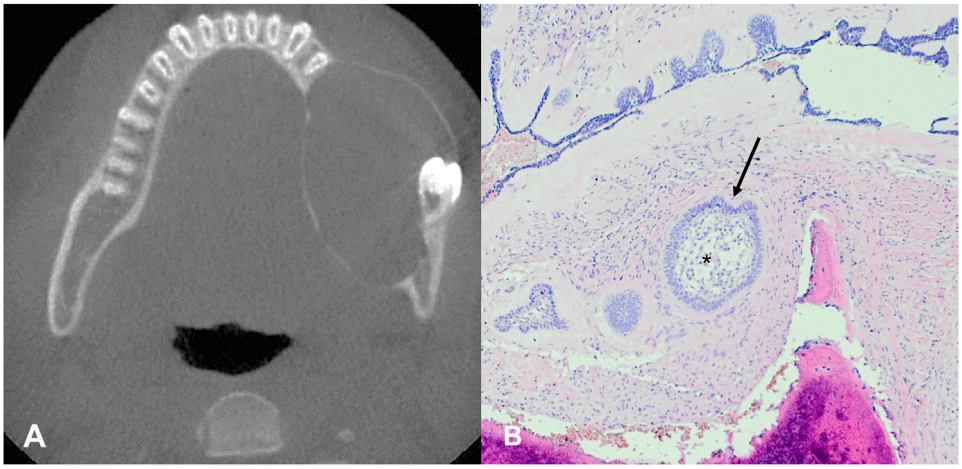

Fig 4. An example of ameloblastoma: **A,** An axial slice of a mandible CT scan showing a well-defined expansile radiolucent lesion in the left body of the mandible with an associated displaced adult molar tooth; **B,** A photomicrograph showing ameloblastoma in a follicular pattern (original magnification ×4). The *arrow* points to the palisaded ameloblast-like cells, and the *asterisk* shows the stellate reticulum-like material in the center of the island.

5% of all odontogenic cysts in adults[5,28] and 3% in children.[5] They have been given various names over time but are generally separated into paradental cysts or buccal bifurcation cysts, depending on where the cyst is located.[5,28,29] Paradental cysts are associated with the distobuccal aspect of the third molars, whereas buccal bifurcation cysts are present on the buccal aspect of the first or second molars.[17] They usually occur in younger patients with a mean age of presentation of 26 years for paradental cysts[5] and 17 years for buccal bifurcation cysts.[17] Paradental cysts may present with symptoms of pericoronitis, but buccal bifurcation cysts are often asymptomatic.[17,28] Though the radiographic appearance is variable, if identifiable on a radiograph, they appear as a well-defined and sometimes corticated radiolucency adjacent to the crown of a tooth.[28,29] The histologic appearance of an inflammatory collateral cyst is essentially the same as a radicular cyst, which is described above, and therefore clinic-pathologic correlation is required. Treatment for paradental cysts associated with third molars is often enucleation with extraction of the associated tooth, whereas enucleation with preservation of the tooth is likely when the cyst is associated with other teeth.[28]

Nasopalatine cyst

Nonodontogenic cysts can also occur in the jaws, such as the nasopalatine duct cyst. These cysts are more frequent in adults but also present in children.[6,7,30] Although many are asymptomatic, some patients present with swelling, drainage of fluid, or pain.[30] They are localized to the midline of the anterior maxilla, in which the remnants of the nasopalatine duct lie. Radiologically, they are symmetrical, well-defined radiolucencies in the anterior palate and may cause displacement of the teeth.[17] They have a mean diameter of 17 mm but can be as large as 60 mm[30] and the lamina dura of adjacent teeth is retained.[17] It is useful to confirm the vitality of the teeth adjacent to the cyst; vitality will be retained in a nasopalatine duct cyst. On microscopic examination, these cysts will have a fibrous wall and a lining consisting of a mixture of stratified squamous and respiratory epithelium.[17,30] Enucleation is curative, and recurrence is rare.

LESS COMMON ENTITIES

The following lesions of the jaw are less common than those discussed so far but often have more significant implications for the patient. They require more extensive treatment, often come with a risk of recurrence, or have a greater impact on a patient's function and appearance. We will discuss the 3 most common odontogenic tumors in children and young adults,[6] as well as the fibro-osseous lesions that occur in young adults and children.

Ameloblastoma

Ameloblastoma is the most common odontogenic tumor in adults and the second most common in children,[6,7] with approximately 15% of ameloblastomas seen in patients aged <20 years.[31] There are 2 forms:

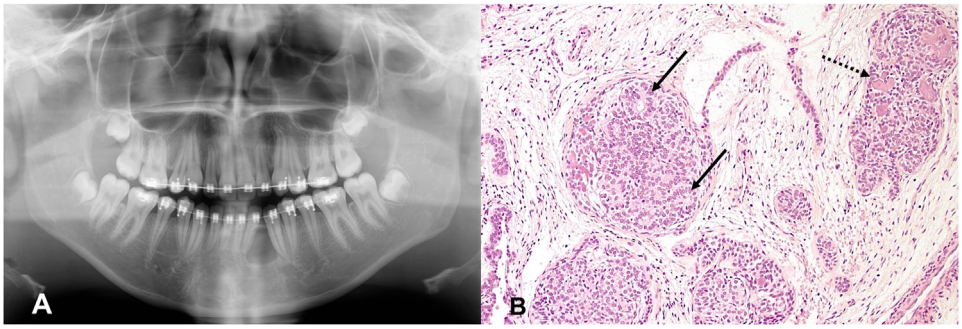

Fig 5. An example of an AOT: **A,** An orthopantomogram showing a well-defined radiolucency in the left parasymphysis between the mandibular left 2 and mandibular left 3 teeth; **B,** A photomicrograph showing an AOT (original magnification ×10), comprising islands of odontogenic epithelium forming duct-like structures (*solid*) and calcifications (*dashed*).

conventional ameloblastoma, which is a solid tumor, and unicystic ameloblastoma, which forms a single cyst.[17] Unicystic ameloblastomas tend to present in younger patients, with 50% arising in the second decade.[17] This is especially the case when the cyst is associated with an unerupted tooth. Alternatively, conventional ameloblastomas have a peak incidence in the fourth and fifth decades.[17] Conventional ameloblastomas are often locally aggressive tumors. Ameloblastomas are most often present in the posterior mandible, though they may occur anywhere in the jaws.[18,31] The most common symptom is painless swelling of the jaw, with tooth mobility and pain being less common.[32] The conventional type of ameloblastoma appears as a well-defined and corticated multilocular or unilocular radiolucency,[17,18] whereas unicystic ameloblastoma is unilocular.[17] They may also cause expansion of the jaws and root resorption.[13,17,18] The histologic appearance of conventional ameloblastoma comprises islands of central stellate reticulum-like cells surrounded by a peripheral layer of ameloblast-like cells, and there are many histologic variants (Fig 4).[17,18] The unicystic form comprises a fibrous cyst wall, a lining of palisading basal cells, and a stellate reticulum-like appearance to the upper epithelial layers.[17] Treatment of conventional ameloblastoma is by excision or resection, depending on the extent of the tumor.[31-33] For larger tumors, reconstruction of the surgical defect is required. Recurrence is common for these tumors, especially when more conservative management is employed.[18,31-33] Unicystic ameloblastomas are less aggressive and can usually be enucleated.

Adenomatoid odontogenic tumor

An adenomatoid odontogenic tumor (AOT) is the most common odontogenic tumor in children and young adults,[6] with 80% presenting before 30 years old[17] and half before 20 years old.[18] Although these lesions may manifest with other presentations, including as an extraosseous peripheral variant, 70% of patients have cystic lesions associated with an unerupted canine tooth.[34] An adenomatoid odontogenic tumor is more common in female patients, and two-thirds occur in the maxilla, particularly the anterior maxilla.[17,18,34] Most lesions are asymptomatic[34] and may be identified after delayed eruption of a tooth or as an incidental finding. The radiographic appearance is of a well-defined and often corticated unilocular radiolucency (Fig 5, *A*), usually associated with the crown of an unerupted tooth.[17,18] Calcifications may be seen within the radiolucency. Root resorption occurs in 17% of patients.[34] These lesions are formed from sheets of odontogenic epithelium, which appear to form ducts alongside variable amounts of dentine-like material, surrounded by a fibrous capsule (Fig 5, *B*).[17,18] Treatment is by enucleation, and recurrence is rare.[34]

Ameloblastic fibroma

Although ameloblastic fibroma is an uncommon odontogenic tumor, the majority is present in children and young adults,[35] with 80% diagnosed before 22 years old.[36] They usually present with the expansion of the jaw, though delayed eruption of teeth may be the first feature, and 12% are incidental findings.[36] They are more common in the posterior mandible than in other sites.[17,18,35,36] These lesions have a mean size of approximately 4 cm[35,36] but can be as large as 16 cm.[35] Radiologically, they are well-defined radiolucencies and may be multilocular or unilocular (Fig 6, *A*).[18,35,36] They may also display displacement of teeth and root resorption.[17] The microscopic appearance of these lesions comprises cords of bilayered odontogenic

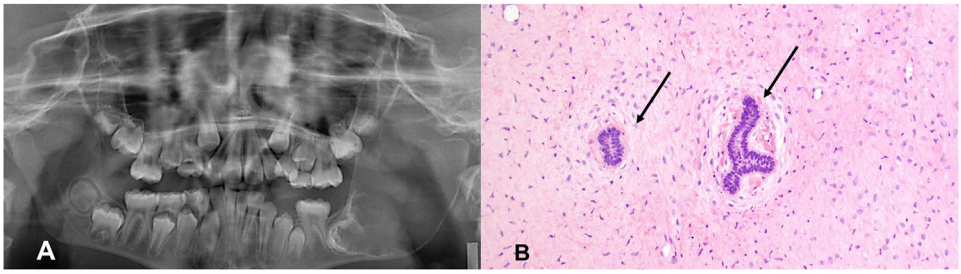

Fig 6. An example of an ameloblastic fibroma: **A,** An orthopantomogram showing a well-defined radiolucency occupying the left condyle, ramus, and posterior body of the mandible; **B,** A photomicrograph of an ameloblastic fibroma (original magnification ×10), comprising odontogenic mesenchyme with islands of odontogenic epithelium displaying peripheral palisading (*arrows*).

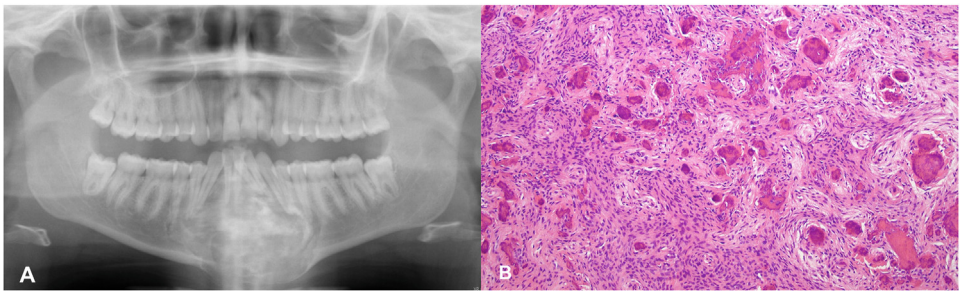

Fig 7. An example of an ossifying fibroma: **A,** An orthopantomogram showing a well-defined radiopaque lesion in the anterior mandible; **B,** A photomicrograph of an ossifying fibroma (original magnification ×10) comprising fascicles of spindle cells and variably sized calcifications, some containing osteocytes

epithelium within a myxoid cellular stoma resembling dental papilla (Fig 6, *B*).[17,18] Tumors are usually treated by enucleation but more aggressive or recurrent tumors may require resection.[17,18,35,36] Reported recurrence rate varies, and recurrence is more common in conservatively treated tumors.[17,35,36] Malignant transformation of ameloblastic fibroma is exceedingly rare.[36]

Fibrous dysplasia

Fibrous dysplasia is a developmental bone abnormality that, in 80% of patients, affects a single bone, most often the craniofacial bones.[17,37] When multiple bones are affected, it may be as part of McCune-Albright syndrome, in which patients also have café au lait pigmentation and endocrine disturbances such as precocious puberty.[37] Fibrous dysplasia is more common in young adults, though the beginning of the disease process can be detected in children.[6,38] Most patients present with unilateral involvement of the jaws, but bilateral lesions may also occur.[37,38] In addition, maxillary lesions are more common.[37,38] Generally, bone expansion is the only complaint[37,38] with pain or tooth mobility less common symptoms.[38] The radiographic appearance varies with the development of the lesion, initially presenting as radiolucency.[38] However, as they mature, they become more radiopaque with a ground-glass appearance and ill-defined margins.[37,38] Histologic examination of these lesions shows immature, haphazard strands of variably mineralized bone in a dense fibrous stroma.[37,38] Fibrous dysplasia grows with the patient, and so treatment is usually delayed until skeletal maturity.[38] Often, conservative surgical debulking to improve function and appearance is used.

Cemento-ossifying fibroma

There are 3 forms of cemento-ossifying fibroma: the classical type (CCOF), the juvenile trabecular type (JTOF), and the psammomatoid type (POF).[17,37] All 3 forms can present in children, although the JTOF and POF tend to occur more frequently in children and young adults.[37] Both the CCOF and JTOF occur in the jaws, with CCOF being more common in the mandible and JTOF showing equal distribution between the jaws.[17,37,39] However, POF usually presents in the orbital bones or the

paranasal sinuses,[17,37] so it will not be discussed further here. The primary presenting symptom is painless jaw swelling.[17,39,40] which is usually slow for CCOF but may be more rapid for JTOF.[17] All are benign neoplasms and appear as well-defined and often corticated lesions on radiographs with mixed radiolucency and radiopacity (Fig 7, *A*).[17,37,39,40] Displacement of teeth and root resorption may also occur.[17,37] Microscopic examination of CCOF shows encapsulated cellular fibrous connective tissue containing woven bone either in separate trabeculae or spheres with occasional less well-formed calcifications (Fig 7, *B*).[17,37] Although having a similar fibrous connective tissue, the calcifications within JTOF are more well formed with strands and anastomosing trabeculae of osteoid and woven bone lined with osteoblasts.[17,37,39] Treatment for CCOF is usually by enucleation with curettage, and recurrence is rare.[17] Treatment for JTOF is by enucleation or resection, but recurrence occurs in up to 21% of patients, with more frequent recurrence after enucleation.[17]

RARE BUT IMPORTANT ENTITIES

Despite the rarity of the following diseases, they are still some of the most common malignancies of the jaws and other bones of the craniofacial skeleton in children.[6,41] An understanding of the symptoms and radiological appearances of these entities will ensure appropriate and rapid referral is made. In addition, though medicine-related osteonecrosis of the jaws (MRONJ) is uncommon in the usual orthodontic patient, as adult orthodontics is becoming more popular, it may be encountered.

Langerhans cell histiocytosis

Langerhans cell histiocytosis is a clonal proliferation of myeloid dendritic cells; it is not malignant but may be life-threatening.[17,42,43] Although this condition can present in adults, it is much more prevalent in children with a median age of diagnosis at 3.5 years.[43] Overall, it is rare, affecting 5 in every 1 million children.[17,43] This disease may be a single system, with either 1 or multiple lesions affecting 1 organ, or a multisystem with $\geq$2 organs involved.[17,43] As such, a patient may present with a wide variety of symptoms in multisystem disease or more limited symptoms when the head and neck is the only affected site. Generally, for head and neck Langerhans cell histiocytosis, the most common symptom is swelling, followed by pain and systemic symptoms.[42] Any of the craniofacial bones, including the jaws, can be affected, as can the skin, gingiva, or lymph nodes of the head and neck.[17,42] The radiographic appearance is of an ill-defined, unilocular radiolucency, which may be single or multiple,[17,42] with the mandible more commonly affected than the maxilla.[42] Teeth often appear to be "floating" with the radiolucency. Histologically, the lesion comprises a destructive infiltrate of Langerhans cells, which have oval nuclei with groves, folds, or indentations, giving the cells a coffee bean appearance.[17] Eosinophils, as well as a mix of chronic inflammatory cells, are also seen.[17] Treatment for single-system disease is more conservative as patients have good outcomes with a near 100% survival rate.[43] Some lesions may spontaneously resolve, whereas others may be treated with enucleation or chemotherapy.[42,43] However, multisystem disease may be life-threatening, so chemotherapy is often required.[43]

Osteosarcoma

Osteosarcoma of the jaws presents slightly later than extragnathic osteosarcoma but still is most frequent in young adults with a mean age in the mid-30s.[44-46] The most common clinical manifestations are swelling, which may have associated pain and ulceration.[17,45] The mandible is more commonly affected than the maxilla.[44,45] The radiographic appearance of osteosarcomas varies, with most presenting as mixed radiolucencies and radiopacities.[17] Some subtle features which should be viewed with a high degree of suspicion for osteogenic malignancy include supracrestal bone deposition or asymmetrical widening of the periodontal ligament spaces. The more aggressive lesions will show the destruction of adjacent structures alongside periosteal reactions and soft-tissue extension.[17] The histologic appearance is variable with many subtypes; however, the most common finding is of highly atypical cells that produce an immature bone-like material called osteoid.[17,45] The majority of patients are treated with surgery alone, though some receive adjuvant chemotherapy or radiotherapy.[44,45] The 10-year survival rate is approximately 60% for these tumors, which is better than their extragnathic counterparts.[44]

Ewing sarcoma

Generally, Ewing sarcoma affects children and young adults,[46-48] with 50% presenting before 18 years old.[17] When affecting adults, it is seen in younger adults.[17,46] Up to 9% of Ewing sarcoma are in the head and neck, with approximately 50% affecting the craniofacial bones and others affecting the soft tissues.[17] The mandible is more commonly affected than the maxilla.[47,48] Soft-tissue Ewing sarcoma is discussed in the first paper of this series.[4] The clinical features of Ewing sarcoma in the jaws include swelling, pain, tooth mobility, paresthesia, and possibly fever.[46-48] Radiologically, these

Table II. A summary of management strategies of soft-tissue pathology as well as pathology of the jaws

Effect on orthodontic treatment	*Management*	*Examples*
It is likely to be unaffected	1. Reassurance, ± removal of cause, ± referral 2. Reassurance, referral, monitoring ± excision or medication 3. Referral, simple excision, ± removal of cause	1. Frictional keratosis, geographic tongue 2. Haemangioma, exostoses, orofacial granulomatosis, recurrent aphthous stomatitis, herpes simplex virus infection, candidiasis 3. Mucocele, fibrous hyperplasia, pyogenic granuloma, squamous papilloma, lipoma, periapical granuloma, radicular cyst, dentigerous cyst, inflammatory collateral cyst, nasopalatine cyst, odontoma
May need to be paused or revisit orthodontic treatment	1. Referral, excision 2. Referral: treatment is dependent on the degree of disease or underlying cause or relationship to the alveolar bone	1. Odontogenic keratocyst, giant cell granuloma, AOT, ameloblastoma, ameloblastic fibroma, cemento-ossifying fibroma, benign salivary gland tumors (eg, pleomorphic adenoma) 2. Langerhans cell histiocytosis, gingival hyperplasia, fibrous dysplasia
Highly likely to be affected and require cessation of orthodontic treatment	1. Referral, excision, ± adjunctive therapy	1. Rhabdomyosarcoma, Ewing sarcoma, osteosarcoma, squamous cell carcinoma, malignant salivary gland tumors (eg, mucoepidermoid carcinoma), MRONJ

lesions appear as poorly defined radiolucencies with the destruction of adjacent structures, including bone cortices and teeth.[46-48] These tumors appear as sheets and groups of small round cells with little cytoplasm and, unlike other malignant tumors, tend not to show pleomorphism.[17] Detection of *EWSR1* gene rearrangements can aid diagnosis.[17] Treatment is with a combination of surgery, radiotherapy, and chemotherapy.[49] The 5-year survival rate for local disease is 73%, whereas only 35% for metastatic disease.[46]

Medication-related osteoradionecrosis of the jaw

MRONJ is nonhealing necrosis of the jaws, usually in response to some form of trauma, after treatment with a medication that alters bone remodeling, such as bisphosphonates.[50] It is uncommon in patients undergoing orthodontic treatment, though patients with orthodontics triggering MRONJ are reported.[50,51] MRONJ is diagnosed when the bone of the jaws is exposed for at least 8 weeks with a lack of healing, as well as a history of antiresorptive drug therapy and no history of radiotherapy.[52] It is important to identify at-risk patients by taking a thorough clinical and drug history. If MRONJ is suspected, referral to an oral and maxillofacial surgeon is necessary for the complex management of these patients. Management should aim to be conservative, although some cases can be extensive or refractory to treatment, leading to resection of the affected part of the jaw.[52]

ORTHODONTIC MANAGEMENT

This section covers the management of both soft-tissue and bony pathology. The reader is referred to the first paper in this issue for details on soft-tissue pathology.[4] The evidence base for the management of pathology in orthodontic patients is scant and mainly based on individual case studies. A knowledge of these entities will ensure appropriate management or referral to the appropriate clinician for ongoing care. For reactive pathologies, simple adjustment of the orthodontic appliance to reduce trauma and aid oral hygiene will suffice. In some circumstances, orthodontic treatment may need to be paused (acute herpes infection) or revisited to allow for treatment and healing to occur (removal of an odontogenic keratocyst). There may occasionally be a need to amend a treatment plan because of the pathology. It is important to remember that atypical presentations can occur, and management is done on a case-by-case basis. A summary of management strategies is shown in Table II, with more specific considerations discussed below.

Biopsy

Though it is the decision of the clinician receiving the referral to biopsy any soft-tissue or bony pathology identified by the orthodontist, it is important to understand under what circumstances a biopsy is needed. Generally, an incisional biopsy is needed for pathologies that do not have a typical clinical presentation or in which several differential diagnoses are considered. Nonetheless, if a

lesion is likely reactive and excision is not part of the management, for example, in the case of recurrent aphthous stomatitis, a biopsy is often of limited value. However, for reactive lesions in which excision is indicated as part of the treatment, such as a fibroepithelial polyp (fibroma) or pyogenic granuloma, an excisional biopsy is useful. An excisional biopsy may also be used for lesions that appear to be benign clinically, such as many odontogenic cysts. However, if there is any doubt about the nature of an entity or there is any suspicion of a malignant neoplasm, a biopsy is mandatory.

Root resorption

Cysts, odontogenic tumors, giant cell granulomas, and malignant tumors can all cause root resorption. It is generally accepted that most patients who undergo fixed orthodontic treatment experience a degree of orthodontically induced root resorption. Weltman et al[53] report 90% of patients are affected. Linge and Linge[54] report an average loss of 1.5mm of root length per anterior tooth. This is usually clinically insignificant when roots are of normal length. However, if there are short roots because of any pathology at the start of treatment, this should be managed with careful planning of treatment objectives, mechanics, monitoring, and retention.

Root resorption will also be a major risk factor for those patients who have had cancer therapy, especially those who have had radiation therapy at an early age. Arrested root development can appear as short V-shaped roots or arrested root development with premature apical closure.[55]

Management of bony cysts

With respect to the staging of orthodontic treatment in relation to the enucleation of bony cysts, there have been case reports that have recommended waiting for evidence of clinical and radiographic bony healing before starting any active orthodontic treatment.[56,57] Kawai et al[58] suggest that after the removal of a benign jaw cyst, complete bone healing was seen at 4 months or longer after surgery. In the absence of robust evidence, it would be advised to assess for bony infill both clinically (assessment of mobility of teeth) and radiographically.

The decision to enucleate vs marsupialize a cyst undoubtedly needs to be made on a case-by-case basis. A multidisciplinary team approach with an orthodontist and surgeon, in which there are dentigerous cysts, would be recommended. A systematic review by Nahajowski[15] reported that approximately 62% of premolars associated with dentigerous cysts spontaneously erupted after cyst marsupialization. A young age (mean age 10 years) and root development not exceeding half were factors likely to favor spontaneous eruption. When this does not happen naturally, the tooth is amenable to orthodontic alignment, and there is bony infill; an unerupted tooth can be exposed and bonded to align with a variety of mechanics.

Cancer treatment

There are many considerations for patients, especially those who are growing and undergoing oncological treatment, to manage the presenting pathology. The treatment modalities can include chemotherapy, radiotherapy, surgery, or a combination. These can have an adverse impact on a patient's facial growth and dental development. The orthodontic management of pediatric cancer survivors is a vast subject, the details of which are beyond the scope of this paper. The degree of impact on patients depends on the patient's age, the location and extent of the primary disease, and the type and intensity of treatment.[59] Childhood cancer survivors are more likely to report microdontia, hypodontia, root abnormalities, enamel deformities, loss of teeth, gingivitis, and xerostomia.[60] Direct radiation of the tumor is a treatment modality for solid tumors such as rhabdomyosarcoma and Ewing's sarcoma. The radiation reduces vascularity and has a cytotoxic effect on epiphyseal chondrocytes.

As the efficacy of cancer treatment increases, so too does the number of cancer survivors, and thus, there are likely to be more of these patients accessing orthodontic treatment. In 2015, a questionnaire by Niell et al[61] found that few practitioners have treated >10 pediatric cancer patients. They also reported that although most orthodontists obtain the patient's previous cancer history, education about the treatment of pediatric survivors is limited and that more information on dental complications is needed.[61]

There has been a recent case-controlled study that reported that previous cytotoxic drug treatment significantly decreases the stability of orthodontic treatment when compared with a matched healthy control group.[62] Other considerations include any resulting trismus, the risk of osteoradionecrosis, and the need to assess patients for recurrence with magnetic resonance imaging (MRI) or computed tomography (CT).

MRIs, CTs, and cone-beam computed tomography

For MRIs in the cranial region, plastic, ceramic, or titanium brackets cause minimal distortion.[63] However, stainless steel causes significant distortion, rendering the image of the cranial region undiagnostic,[63] and it would be a worthwhile consideration to avoid these brackets if there is likely to be a need for future MRIs.

Stainless steel archwires used with nonmetal or titanium brackets should thus be removed before any MRIs are needed to assess the head and neck. If there is likely to be a need to use repeated CT scans, then it might be wise to avoid the use of fixed metal orthodontic appliances as this would cause significant artifacts on the image, rendering it undiagnostic.

Resections

Patients who have large resections should be managed by a multidisciplinary team. This team may include oral and maxillofacial surgeons, surgeons with interest in dentofacial deformity and who have expertise in bone grafting techniques and bone distraction techniques, restorative dentists (with interest in prosthodontics and implantology), orthodontists, pediatric dentists or the general dental practitioner, speech and language therapists, and psychologists.

CONCLUSIONS

Through careful examination of radiographs requested for orthodontic treatment planning, many early and asymptomatic lesions may be detected. Further, many of the lesions described present with displaced teeth or delayed eruption, making review by an orthodontist likely. As such, a working knowledge of the common and important diseases of the jaw bones will ensure accurate and early referral for the most appropriate management.

ACKNOWLEDGMENTS

The authors would like to thank Professor Jonathan Sandler for his contribution to clinical photographs.

REFERENCES

1. Kuhlberg AJ, Norton LA. Pathologic findings in orthodontic radiographic images. Am J Orthod Dentofacial Orthop 2003;123:182-4.
2. Cedro MK, Moles DR, Hodges SJ. Adult orthodontics—who's doing what? J Orthod 2010;37:107-17.
3. Keim RG, Gottlieb EL, Nelson AH, Vogels DS 3rd. 2013 JCO Orthodontic Practice Study. Part 1: trends. J Clin Orthod 2013;47:661-80.
4. Hankinson P, Brierley C, Brierley D. A review of oral pathology in orthodontics. Part 1: soft-tissue pathology. Am J Orthod Dentofacial Orthop 2024;165:7-17.
5. Jones AV, Craig GT, Franklin CD. Range and demographics of odontogenic cysts diagnosed in a UK population over a 30-year period. J Oral Pathol Med 2006;35:500-7.
6. Jones AV, Franklin CD. An analysis of oral and maxillofacial pathology found in children over a 30-year period. Int J Paediatr Dent 2006;16:19-30.
7. Jones AV, Franklin CD. An analysis of oral and maxillofacial pathology found in adults over a 30-year period. J Oral Pathol Med 2006;35:392-401.
8. Odell E. Cawson's essentials of oral pathology and oral medicine. London, England: Elsevier Health Sciences; 2015.
9. Mortensen H, Winther JE, Birn H. Periapical granulomas and cysts. An investigation of 1,600 cases. Scand J Dent Res 1970;78:241-50.
10. Martin LHC, Speight PM. Odontogenic cysts: an update. Diagn Histopathol 2017;23:260-5.
11. Delbem ACB, Cunha RF, Vieira AE, Pugliesi DM. Conservative treatment of a radicular cyst in a 5-year-old child: a case report. Int J Paediatr Dent 2003;13:447-50.
12. Martin L, Speight PM. Odontogenic cysts. Diagn Histopathol 2015;21:359-69.
13. Teo KW, Shi AH, Teh LY, Lee AMH. External root resorption in common odontogenic cysts and ameloblastomas of the jaw: A retrospective radiographic study in an Asian population. Oral Surg 2021;14:335-41.
14. Motamedi MHK, Talesh KT. Management of extensive dentigerous cysts. Br Dent J 2005;198:203-6.
15. Nahajowski M, Hnitecka S, Antoszewska-Smith J, Rumin K, Dubowik M, Sarul M. Factors influencing an eruption of teeth associated with a dentigerous cyst: a systematic review and meta-analysis. BMC Oral Health 2021;21:180.
16. Koca H, Esin A, Aycan K. Outcome of dentigerous cysts treated with marsupialization. J Clin Pediatr Dent 2010;34:165-8.
17. WHO Classification of Tumours Editorial Board. Head and neck tumours [Internet; beta version ahead of print]. Lyon, French Republic: International Agency for Research on Cancer; 2022.
18. Brierley DJ, Hunter KD. Odontogenic tumours. Diagn Histopathol 2015;21:370-9.
19. Philipsen HP, Reichart PA, Praetorius F. Mixed odontogenic tumours and odontomas. Considerations on interrelationship. Review of the literature and presentation of 134 new cases of odontomas. Oral Oncol 1997;33:86-99.
20. Chirapathomsakul D, Sastravaha P, Jansisyanont P. A review of odontogenic keratocysts and the behavior of recurrences. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006;101:5-9: discussion 10.
21. Morgan TA, Burton CC, Qian F. A retrospective review of treatment of the odontogenic keratocyst. J Oral Maxillofac Surg 2005;63:635-9.
22. Myoung H, Hong SP, Hong SD, Lee JI, Lim CY, Choung PH, et al. Odontogenic keratocyst: review of 256 cases for recurrence and clinicopathologic parameters. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2001;91:328-33.
23. Johnson NR, Batstone MD, Savage NW. Management and recurrence of keratocystic odontogenic tumor: a systematic review. Oral Surg Oral Med Oral Pathol Oral Radiol 2013;116:e271-6.
24. Antoniades DZ, Belazi M, Papanayiotou P. Concurrence of torus palatinus with palatal and buccal exostoses: case report and review of the literature. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1998;85:552-7.
25. Sonnier KE, Horning GM. Spontaneous bony exposure: a report of 4 cases of idiopathic exposure and sequestration of alveolar bone. J Periodontol 1997;68:758-62.
26. de Lange J, van den Akker HP, van den Berg H. Central giant cell granuloma of the jaw: a review of the literature with emphasis on therapy options. Oral Surg Oral Med Oral Pathol Oral Rad Endodontol 2007;104:603-15.
27. Katsikeris N, Kakarantza-Angelopoulou E, Angelopoulos AP. Peripheral giant cell granuloma. Clinicopathologic study of 224 new cases and review of 956 reported cases. Int J Oral Maxillofac Surg 1988;17:94-9.
28. Philipsen HP, Reichart PA, Ogawa I, Suei Y, Takata T. The inflammatory paradental cyst: a critical review of 342 cases from a

literature survey, including 17 new cases from the author's files. J Oral Pathol Med 2004;33:147-55.
29. Chrcanovic BR, Reis BMMV, Freire-Maia B. Paradental (mandibular inflammatory buccal) cyst. Head Neck Pathol 2011; 5:159-64.
30. Swanson KS, Kaugars GE, Gunsolley JC. Nasopalatine duct cyst: an analysis of 334 cases. J Oral Maxillofac Surg 1991;49:268-71.
31. Ord RA, Blanchaert RH, Nikitakis NG, Sauk JJ. Ameloblastoma in children. J Oral Maxillofac Surg 2002;60:762-70.
32. Zhang J, Gu Z, Jiang L, Zhao J, Tian M, Zhou J, et al. Ameloblastoma in children and adolescents. Br J Oral Maxillofac Surg 2010; 48:549-54.
33. Huang IY, Lai ST, Chen CH, Chen CM, Wu CW, Shen YH. Surgical management of ameloblastoma in children. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2007;104:478-85.
34. Chrcanovic BR, Gomez RS. Adenomatoid odontogenic tumor: an updated analysis of the cases reported in the literature. J Oral Pathol Med 2019;48:10-6.
35. Chen Y, Wang JM, Li TJ. Ameloblastic fibroma: a review of published studies with special reference to its nature and biological behavior. Oral Oncol 2007;43:960-9.
36. Buchner A, Vered M. Ameloblastic fibroma: a stage in the development of a hamartomatous odontoma or a true neoplasm? Critical analysis of 162 previously reported cases plus 10 new cases. Oral Surg Oral Med Oral Pathol Oral Radiol 2013;116:598-606.
37. Speight PM, Carlos R. Maxillofacial fibro-osseous lesions. Curr Diagn Pathol 2006;12:1-10.
38. Davidova LA, Bhattacharyya I, Islam MN, Cohen DM, Fitzpatrick SG. An analysis of clinical and histopathologic features of fibrous dysplasia of the jaws: A series of 40 cases and review of literature. Head Neck Pathol 2020;14:353-61.
39. Slootweg PJ. Juvenile trabecular ossifying fibroma: an update. Virchows Arch 2012;461:699-703.
40. Su L, Weathers DR, Waldron CA. Distinguishing features of focal cemento-osseous dysplasia and cemento-ossifying fibromas. II. A Clinical and radiologic spectrum of 316 cases. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1997;84:540-9.
41. Albright JT, Topham AK, Reilly JS. Pediatric head and neck malignancies: US incidence and trends over 2 decades. Arch Otolaryngol Head Neck Surg 2002;128:655-9.
42. Xu J, Gilbert JR, Sutton KS, Goudy SL, Abramowicz S. Head and neck Langerhans cell histiocytosis in children. J Oral Maxillofac Surg 2022;80:545-52.
43. Krooks J, Minkov M, Weatherall AG. Langerhans cell histiocytosis in children: history, classification, pathobiology, clinical manifestations, and prognosis. J Am Acad Dermatol 2018;78:1035-44.
44. Baumhoer D, Brunner P, Eppenberger-Castori S, Smida J, Nathrath M, Jundt G. Osteosarcomas of the jaws differ from their peripheral counterparts and require a distinct treatment approach. Experiences from the DOESAK registry. Oral Oncol 2014;50:147-53.
45. Bennett JH, Thomas G, Evans AW, Speight PM. Osteosarcoma of the jaws: a 30-year retrospective review. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2000;90:323-32.
46. Stewart BD, Reith JD, Knapik JA, Chi AC. Bone- and cartilage-forming tumors and Ewing sarcoma: an update with a gnathic emphasis. Head Neck Pathol 2014;8:454-62.
47. Margaix-Muñoz M, Bagán J, Poveda-Roda R. Ewing sarcoma of the oral cavity. A review. J Clin Exp Dent 2017; 9:e294-301.
48. Wood RE, Nortje CJ, Hesseling P, Grotepass F. Ewing's tumor of the jaw. Oral Surg Oral Med Oral Pathol 1990;69:120-7.
49. Olson MD, Van Abel KM, Wehrs RN, Garcia JJ, Moore EJ. Ewing sarcoma of the head and neck: the Mayo Clinic experience. Head Neck 2018;40:1999-2006.
50. Woolley J, Akintola O, Yates J, Calasans-Maia MD, de Albuquerque Calasans-Maia J, Kocherhina I, et al. The risk of osteonecrosis of the jaw and adverse outcomes in patients using antiresorptive drugs undergoing orthodontic treatment: a systematic review. Heliyon 2021;7:e05914.
51. Kalfarentzos E, Chliaoutakis A, Ntagiantis G, Vardas E, Christopoulos P. Orthodontic treatment as triggering factor of medication related osteonecrosis of the jaw in a breast cancer patient. Report of a rare case. J Clin Exp Dent 2023;15:e351-6.
52. Ristow O, Otto S, Troeltzsch M, Hohlweg-Majert B, Pautke C. Treatment perspectives for medication-related osteonecrosis of the jaw (MRONJ). J Craniomaxillofac Surg 2015;43:290-3.
53. Weltman B, Vig KW, Fields HW, Shanker S, Kaizar EE. Root resorption associated with orthodontic tooth movement: a systematic review. Am J Orthod Dentofacial Orthop 2010;137:462-76: discussion 412A.
54. Linge BO, Linge L. Apical root resorption in upper anterior teeth. Eur J Orthod 1983;5:173-83.
55. Elhaddaoui R, Bahije L, Chbicheb S, Zaoui F. Cervico-facial irradiation and orthodontic treatment. Int Orthod 2015;13:139-48.
56. Hameed O, Gwilliam J, Whaites E. Odontogenic keratocyst: an incidental finding during an orthodontic examination. J Orthod 2020;47:245-50.
57. Atwal A, Cottom H, Doyle P, Sandler J. Surgical/orthodontic management of a large mandibular odontogenic keratocyst (OKC). Dent Update 2019;46:473-9.
58. Kawai T, Murakami S, Hiranuma H, Sakuda M. Healing after removal of benign cysts and tumors of the jaws. A radiologic appraisal. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1995;79:517-25.
59. Dahllöf G, Huggare J. Orthodontic considerations in the pediatric cancer patient: a review. Semin Orthod 2004;10:266-76.
60. Kaste SC, Goodman P, Leisenring W, Stovall M, Hayashi RJ, Yeazel M, et al. Impact of radiation and chemotherapy on risk of dental abnormalities: a report from the Childhood Cancer Survivor Study. Cancer 2009;115:5817-27.
61. Neill CC, Migliorati C, Trojan T, Kaste S, Karydis A, Rowland C, et al. Experience and expertise regarding orthodontic management of childhood and adolescent cancer survivors. Am J Orthod Dentofacial Orthop 2015;148:765-70.
62. Mitus-Kenig M, Derwich M, Czochrowska E, Pawlowska E. Cancer survivors present significantly lower long-term stability of orthodontic treatment: a prospective case-control study. Eur J Orthod 2021;43:631-8.
63. Elison JM, Leggitt VL, Thomson M, Oyoyo U, Wycliffe ND. Influence of common orthodontic appliances on the diagnostic quality of cranial magnetic resonance images. Am J Orthod Dentofacial Orthop 2008;134:563-72.