ODONTOGENIC TUMORS: WHERE ARE WE IN 2017?
Odontojen Tümörler: 2017 Yılında Neredeyiz?

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Received: 05/07/2017
Accepted: 04/08/2017

ABSTRACT

Odontogenic tumors are a heterogeneous group of lesions of diverse clinical behavior and histopathologic types, ranging from hamartomatous lesions to malignancy. Because odontogenic tumors arise from the tissues which make our teeth, they are unique to the jaws, and by extension almost unique to dentistry. Odontogenic tumors, as in normal odontogenesis, are capable of inductive interactions between odontogenic ectomesenchyme and epithelium, and the classification of odontogenic tumors is essentially based on this interaction. The last update of these tumors was published in early 2017. According to this classification, benign odontogenic tumors are classified as follows: epithelial, mesenchymal (ectomesenchymal), or mixed depending on which component of the tooth germ gives rise to the neoplasm. Malignant odontogenic tumors are quite rare and named similarly according to whether the epithelial or mesenchymal or both components is malignant. The goal of this review is to discuss the updated changes to odontogenic tumors and to review the more common types with clinical and radiological illustrations.

Keywords: Odontogenic tumors; odontogenesis; update; ameloblastoma; odontoma

ÖZ

Odontojen tümörler, klinik davranışlarına ve histopatolojik özelliklerine göre hamartomdan maligniteye kadar değişen heterojen bir grup lezyondur. Bu tümörler, dişleri oluşturulan dokulardan köken al锔 için çenelere özgüdür ve genellikle diş hekimliğine bağlıdır. Odontojen tümörler normal odontogenez sürecinde olduğu gibi odontojen ektomezenkimal ve epitelyal arasındaki karşılıklı indüksiyon mekanizmasıyla ortaya çıkar ve bu tümörlerin sınıflamasında bu indüksiyon mekanizması baãz anlar. Odontojen tümörlerle ilgili en son güncelleme 2017 yılının başında yapılmıştır. Bu sınıflamaya göre; iyi huylu tümörler köken aldığı diş germi yapısına baãlı olarak epithelyal, mezenkimal (ektomezenkimal) veya mikst olarak sınıflanmıştır. kötü huylu tümörler ise oldukça enderdir ve iyi huylu tümör sınıflamasına benzer şekilde epithelyal, mezenkimal veya her iki komponentinde malign olmasına göre adlandırılır. Bu derlemenin amacı odontojen tümörleri son güncellemeler eşliğinde taramak ve en sak görülen tipleri klinik ve radyolojik resimleri ile gözden geçirmektir.

Anahtar kelimeler: Odontojen tümörler; odontogenezis; güncellemeler; ameloblastom; odontom

Keywords: Odontogenic tumors; odontogenesis; update; ameloblastoma; odontoma

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How to cite: Wright JM, Soluk Tekkesin M. Odontogenic tumors. Where are we in 2017?. J Istanb Univ Fac Dent 2017;51(3 Suppl 1):S10-S30.
**Introduction**

Odontogenic tumors (OT) are a heterogeneous group of lesions of diverse clinical behavior and histopathologic types, ranging from hamartomatous lesions to malignancy. OT are derived from ectomesenchymal and/or epithelial tissues that constitute the tooth-forming apparatus. Like normal odontogenesis, the odontogenic tumors represent inductive interactions between odontogenic ectomesenchyme and epithelium (1, 2). Therefore OT are found within the jaw bones (central types) or in the mucosal tissue overlying tooth-bearing areas (peripheral types). OT are basically divided into two primary categories; malignant and benign but the etiology is unknown. The majority of benign odontogenic tumors seem to arise de novo, whereas the malignant odontogenic tumors may arise de novo but more often arise from their benign precursor. The classification of odontogenic tumors is essentially based on interactions between odontogenic ectomesenchyme and epithelium. This dynamic classification is constantly renewed with the addition of new entities, and the removal of some older entities. The last update of these tumors was published in early 2017 (3). Table 1 and 2 summarize the changes of odontogenic tumors from the first WHO classification to date (3-5). In this review, we discuss odontogenic tumors relative to the latest updates and focus on the more common tumors with clinical and radiological illustrations.

| 1971 WHO classification | 1992 WHO classification | 2005 WHO classification | 2017 WHO classification |
|--------------------------|-------------------------|-------------------------|-------------------------|
| Ameloblastoma             | Epithelial origin       | Epithelial origin       | Epithelial origin       |
| Calcifying epithelial odontogenic tumor | Ameloblastoma | Ameloblastoma, solid / multicystic type | Ameloblastoma |
| Ameloblastic fibroma      | Squamous odontogenic tumor | Ameloblastoma, extraosseous / peripheral type | Ameloblastoma, unicystic type |
| Adenomatoid odontogenic tumor (adeno-ameloblastoma) | Calcifying epithelial odontogenic tumor (Pindborg tumor) | Ameloblastoma, desmoplastic type | Ameloblastoma, extraosseous / peripheral type |
| Calcifying odontogenic cyst | Clear cell odontogenic tumor | Ameloblastoma, unicystic type | Metastasizing (malignant) ameloblastoma |
| Dentinoma                |                        | Squamous odontogenic tumor | Squamous odontogenic tumor |
| Ameloblastic fibro-odontoma | Calcifying epithelial odontogenic tumor | Calcifying epithelial odontogenic tumor | |
| Odonto-ameloblastoma      | Adenomatoid odontogenic tumor | Adenomatoid odontogenic tumor | |
| Complex odontoma          | Keratocystic odontogenic tumor | | |
| Compound odontoma         | Mixed origin           | Mixed origin           | Mixed origin           |
| Fibroma (odontogenic fibroma) | Ameloblastic fibroma | Ameloblastic fibroma | Ameloblastic fibroma |
| Myxoma (myxofibroma)      | Ameloblastic fibro-dentinoma (dentinoma) and ameloblastic fibro-odontoma | Ameloblastic fibrodentinoma | Primordial odontogenic tumor |
| Cementomas                | Odonto-ameloblastoma   | Ameloblastic fibro-odontoma | Odontoma, Complex type |
| a. Benign cementoblastoma (true cementoma) | Adenomatoid odontogenic tumor | Odontoma, Complex type | Odontoma, Compound type |
| b. Cementifying fibroma   | Calcifying odontogenic cyst | Odontoma, Compound type | Dentinogenic ghost cell tumor |
| c. Periapical cemental yspasia (periapical fibrous dysplasia) | Complex odontoma | Odonto-ameloblastoma | |
| d. Gigantiform cementoma (familial multiple cementomas) | Compound odontoma | Calcifying cystic odontogenic tumor | |
| Melanotic neuro-ectodermal tumor of infancy | | | |
| Mesenchymal origin        | Dentinogenic ghost cell tumor | | |
| Odontogenic fibroma       | Odontogenic fibroma | Odontogenic fibroma | |
| Myxoma (odontogenic myxoma, myxofibroma) | Odontogenic myxoma / myxofibroma | Odontogenic myxoma / myxofibroma | |
| Benign cementoblastoma    | Cementoblastoma | Cementoblastoma | Cemento-ossifying fibroma |
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| 1971 WHO classification | 1992 WHO classification | 2005 WHO classification | 2017 WHO classification |
|-------------------------|-------------------------|-------------------------|-------------------------|
| Odontogenic carcinomas  | Odontogenic carcinomas  | Odontogenic carcinomas  | Odontogenic carcinomas  |
| Malignant ameloblastoma | Malignant ameloblastoma | Metastasizing (malignant) ameloblastoma | Ameloblastic carcinoma |
| Primary intra-osseous carcinoma | Primary intra-osseous carcinoma | Ameloblastic carcinoma – primary type | Primary intra-osseous carcinoma, NOS |
| Other carcinomas arising from odontogenic epithelium, including those arising from odontogenic cysts | Malignant variants of other odontogenic epithelial tumors | Ameloblastic carcinoma – secondary type, intraosseous | Sclerosing odontogenic carcinoma |
| Odontogenic sarcomas    | Odontogenic sarcomas    | Odontogenic sarcomas    | Odontogenic sarcomas    |
| Ameloblastic fibrosarcoma (ameloblastic sarcoma) | Ameloblastic fibrosarcoma (ameloblastic sarcoma) | Primary intraosseous squamous cell carcinoma – solid type | Odontogenic carcinosarcoma |
| Ameloblastic odontosarcoma | Ameloblastic odontosarcoma | Primary intraosseous squamous cell carcinoma derived from keratocystic odontogenic tumor | Odontogenic sarcomas |
| Odontogenic benign tumors, epithelial | Odontogenic sarcomas |

**Ameloblastoma**

Ameloblastoma is a benign but locally aggressive epithelial neoplasm that is one of the most common odontogenic tumors. Current genetic studies show mutations in genes that belong to MAPK pathway in many ameloblastomas. BRAFV600E is the most common mutation (6). WHO 2017 classification divided ameloblastoma into four categories; conventional, extraosseous / peripheral, unicystic, and metastasizing ameloblastoma.

**Clinical features**

Conventional ameloblastoma usually shows slow, painless expansion (Figure 1). The posterior area of
mandible is the most common location. They tend to grow in a buccolingual direction, resulting in significant expansion. The signs and symptoms are variable; including malocclusion, facial deformity, soft tissue invasion or loosening of teeth depends on the size of the lesion. The mean age is about 35 years, ranging from 4 to 92. Radiographically, a corticated multilocular radiolucency is common (Figure 2), however a unilocular appearance may be seen (7).

Figure 1. Ameloblastoma. Often presents with cortical expansion.

Conventional ameloblastomas have many different histopathologic subtypes, however none of them affect prognosis. Only the desmoplastic type has different clinical features, including a radiolucent-radiopaque appearance, and predilection for the anterior jaws, especially maxilla (8).

Unicystic ameloblastoma is a subtype of intraosseous ameloblastoma, consisting of a large single cyst. They tend to present a decade earlier than conventional ameloblastoma and radiographs often show a unilocular, well-demarcated radiolucency that surrounds the crown of the unerupted tooth, resembling dentigerous cysts (Figure 3). The ameloblastoma can grow into the lumen that is called the ‘intraluminal type’ or it can only be confined to the cyst lining epithelium, which is also called the ‘luminal type’. If ameloblastoma invaded the wall of the cyst, it was called ‘mural type’ in the 2005 3rd edition. This is one of the significant changes to the new classification because unicystic ameloblastomas have been traditionally treated conservatively, often by “cyst” enucleation, and recurrence has been uncommon. However, there is emerging evidence that unicystic ameloblastomas with mural invasion are known to act as conventional intraosseous ameloblastoma and should be treated as such (9).

Extraosseous (peripheral) ameloblastoma is a conventional ameloblastoma seen exclusively in the soft tissues of gingiva (Figure 4). Gingival extension of a intrabony ameloblastoma must be ruled out radiographically. Clinically, it is not distinguishable from other mucosal nodular lesions. The lesions mostly occur in the premolar region of the mandible, followed by the tuberosity region of maxilla.

Figure 2. Ameloblastoma. Typical multilocular radiographic features.
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Figure 3. Unicystic ameloblastoma. Often occurs in younger patients and like a dentigerous cyst radiographically.

Figure 4. Extraosseous ameloblastoma. Mucosal nodular lesion.

In the 2017 WHO classification, metastatic ameloblastoma was moved to the benign ameloblastoma subtypes from the malignant odontogenic tumors. The most important reason for this is both the primary and metastatic ameloblastomas are histopathologically identical to benign ameloblastoma. It occurs very rarely and none of the histologic findings observed in the primary tumor are specific for predicting metastasis. It can only be diagnosed after it has metastasized, most often to lung. Metastatic ameloblastomas are observed in the age range of 4-75 years with an average age of 30 years. The majority of cases are diagnosed 10 years after the first treatment (10, 11). This emphasizes the importance of ameloblastoma follow-up. The decision to move metastatic (malignant) ameloblastoma in the 2005 edition to the benign ameloblastomas in the 2017 edition was controversial and not unanimously agreed upon.

Histopathology

Histopathologically, ameloblastoma tends to have cystic changes which is often seen microscopically and even appreciated macroscopically in some cases. Many microscopic subtypes have been identified. However, it is known that they do not affect the biological behavior of the neoplasm. Follicular and plexiform types are the most common. There are also acanthomatous, granular cell, desmoplastic and basal cell types. The desmoplastic type was previously speculated to be more aggressive, but this was not conclusively proved with additional publications. The 2017 WHO classification, therefore, moved desmoplastic ameloblastoma to a histologic subtype without biological significance. Two types of cells are observed histopathologically in ameloblastoma. The first is columnar cells resembling normal ameloblasts that palisade around the epithelial islands, and the second are the more centrally located cells that resemble the stellate reticulum (12). Unicystic ameloblastoma is usually diagnosed after histopathologic examination because it appears like an odontogenic cyst both clinically and radiologically.

Treatment and prognosis

The treatment of conventional ameloblastomas is wide surgical excision with 1.5 cm margins (13). Conservative surgery results in a high recurrence rate. Unicystic ameloblastomas are less aggressive and are often treated with enucleation. In the WHO classification of 2017, it has been recommended that a mural type case should be treated as a conventional
ameloblastoma if it recurs (3). Extraosseous ameloblastoma has different biologic behavior and conservative removal with free margins is warranted. Long-term follow up is necessary. Recurrence may occur 10 years or longer after initial surgery.

**Squamous odontogenic tumor**

Squamous odontogenic tumor is a benign epithelial tumor that is very rare among odontogenic tumors. The tumor is usually intraosseous, but several peripheral cases have been reported in the literature.

![Figure 5. Squamous odontogenic tumor of the right mandible.](image)

**Histopathology**

Histopathologically, mature squamous epithelial islands of varying shape and size are observed within a mature fibrous connective tissue. The cells around the islands do not show palisading or reverse polarization that is characteristic of ameloblastomas. Microcystic change and typical individual cell keratinization may occur in the islands. Squamous odontogenic tumor-like islands can be observed in the wall of odontogenic cysts but it does not affect the prognosis.

**Clinical features**

It is seen equally in the mandible and maxilla in a wide range of ages from childhood to the eighties. Maxillary lesions are mostly located in the anterior region; whereas mandibular lesions are located in the posterior region. Radiographically, they present as a unilocular radiolucency (Figure 5), often characterized by triangular shape between the teeth in the lateral direction of a tooth (14, 15).

**Treatment and prognosis**

Curettage, enucleation, or local excision is usually adequate treatment. Recurrence has been reported rarely (14, 15).

**Adenomatoid odontogenic tumor**

Adenomatoid odontogenic tumor is a benign epithelial odontogenic tumor. These tumors constitute approximately 2-7% of all odontogenic tumors that are biopsied. Intraosseous and extraosseous types are described. Because of limited growth, the tumor is considered to be a hamartoma by many researchers.

**Clinical features**

The age range varies from 5 to 30, with a second decade peak. Female/male ratio is 2:1. The lesion is most commonly located in the anterior region of the maxilla associated with unerupted teeth. Radiologically, it is usually a well-demarcated unilocular radiolucency, but occasionally with small flecks of opacity internally. The tumor can be divided into two clinical types; follicular and extrafollicular. The most common type (73%) is the follicular type where there is a well-defined unilocular radiolucency surrounding an unerupted tooth crown; radiographically identical to a dentigerous cyst (Figure 6). The extrafollicular type (24%) is seen as a well-defined radiolucency which can be superimposed on the roots of a tooth that therefore, can often be misdiagnosed as an odontogenic cyst. The peripheral or extraosseous type is less common type (3%) (16-18).
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Figure 6. Adenomatoid odontogenic tumor. Classic radiographic presentation, unilocular radiolucency around the crown of an unerupted tooth in the anterior maxilla.

**Histopathology**

Generally, there is a thick, fibrotic capsule around the lesion. The tumor on cross-section may contain solid or cystic changes. The solid areas consist of multiple, variably sized nodules of spindled epithelial cells. Columnar epithelial cells form rosette /duct-like structures that are hollow in the middle. These structures are characteristic, but may be dominant or sometimes not observed at all. Glandular elements are absent. Adenomatoid odontogenic tumor-like areas can be observed in other odontogenic tumors, including odontoma and calcifying epithelial odontogenic tumor.

**Treatment and prognosis**

Simple enucleation is the most common treatment method. Although recurrent cases have been reported, this usually occurs due to incomplete excision (18). Its clinical behavior is more like hamartomas than neoplasms.

**Calcifying epithelial odontogenic tumor (Pindborg Tumor)**

Calcifying epithelial odontogenic tumor (CEOT) is a relatively rare benign epithelial odontogenic tumor. It is characterized by secreting a unique amyloid protein which is called ‘odontogenic ameloblastic associated protein’ (19) which often calcifies. There are peripheral and intraosseous types. Approximately 6% of cases are peripheral (20).
Figure 7. Calcifying epithelial odontogenic tumor. A mixed radiolucent-radiopaque lesion with an unerupted tooth at the right posterior of mandible

**Histopathology**

The tumor consists of polyhedral epithelial cells that exhibit distinct islands, cords and trabeculae. The stroma may be fibrotic. Sometimes cellularity is more obvious and may show distinct nuclear pleomorphism. However, this appearance is not related to malignancy. Variable amounts of an eosinophilic, hyalinized extracellular accumulation of protein matrix are usually seen.

This material is the amyloid protein called odontogenic ameloblast-associated protein (ODAM) which reacts with Congo red stain (19). This material calcifies, resulting in the round concentric calcifications termed ‘Liesegang rings’ which are typical for the tumor. In some cases these small calcifications combine to form large masses (20, 21). The histopathology of the peripheral type is similar to the intraosseous type.

**Treatment and prognosis**

The treatment is local surgical removal with tumor-free margins. The maxillary lesion tends to recur, with an overall recurrence rate of about 15%. Conservative excision is adequate for the peripheral variant (19-21).

**Odontogenic benign tumors, mixed**

**Ameloblastic fibroma**

Ameloblastic fibroma is a rare, mixed odontogenic tumor composed of dental papilla-like odontogenic ectomesenchyme and odontogenic epithelium. In addition to these features, ‘ameloblastic fibrodentinoma’ was used if there was dentin formation, and ‘ameloblastic fibro-odontoma’ terminology was used if both dentin and enamel were present in 2005 WHO classification (4). However, the 2017 WHO classification has emphasized that the appearance of such hard tissue formation is usually the first stage in maturation and more compatible with a developing odontoma (3).

**Clinical features**

Ameloblastic fibroma is usually present as a painless, and slowly growing mass. The tumor presents most frequently in the first two decades of life with a slight male predilection. They are discovered due to disturbances of tooth eruption or incidentally during routine radiographic examination. More than 80% of the cases occur in the posterior mandible. Radiographically, the tumor presents as a well-defined unilocular or multilocular radiolucency associated with a malpositioned tooth (Figure 8) (22, 23).
Histopathology

It is composed of both mesenchymal and epithelial components, both of which are considered neoplastic; hence “mixed” odontogenic tumor. The epithelial component consists of branching and anastomosing epithelial strands like dental lamina in a loose myxoid mesenchymal stroma, resembling dental papilla of the tooth bud. Collagen fibers are not observed.

Treatment and prognosis

Treatment choices are variable; most commonly conservative therapy for small and asymptomatic lesions or less commonly, aggressive surgery for extensive or local recurrent lesions. The recurrence rate is about 18%. Ameloblastic fibromas can rarely transform to ameloblastic fibrosarcoma when untreated or more commonly, following multiple local recurrences of a benign ameloblastic fibroma, with the subsequent recurrence consisting of a sarcoma. Long-term follow-up is necessary to detect recurrence and possible malignant transformation (23, 24).

Primordial odontogenic tumor

Primordial odontogenic tumor is a newly defined entity in the 2017 WHO classification. It was first described in 2014 (25). There are less than 10 cases published to date.

Clinical features

The tumor often affects patients in first two decades. Radiographically, a well-demarcated radiolucency associated with an unerupted third mandibular tooth is usually observed. It may cause displacement and resorption of adjacent teeth. The most commonly affected site is the molar region of the mandible.

Histopathology

Grossly, this very rare tumor is a multi-lobulated, solid mass without cystic change associated with an embedded tooth. Histopathologically, it is characterized by dental papillae-like, loose connective tissue with varying cellularity surrounded by a cuboidal/columnar epithelium resembling inner enamel epithelium of the enamel organ. The characteristic feature is the columnar or cuboidal epithelium covering the periphery of the tumor (26).

Treatment and prognosis

Enucleation is the treatment of choice. No recurrence has been reported to date.

Odontoma; compound and complex type

Odontomas are mixed epithelial and ectomesenchymal tumors composed of dental hard and soft tissues. They are generally regarded as a tumor-like malformations or hamartomas, rather than neoplasms. Odontomas are the most common odontogenic tumor. There are two types of odontoma; compound and complex. In complex odontoma, there is a single mass of haphazardly arranged soft and hard dental structures, whereas in compound odontomas, the hard and soft tissues are laid down in their appropriate anatomic relationships; forming small tooth-like structures (27).
Clinical features

Odontomas commonly occur in the first and second decades and usually are diagnosed during routine radiographic examination. They may be detected on investigation of a tooth failing to erupt or as abnormal swelling. Compound odontomas are mainly located in the anterior maxilla and appear as a collection of tooth-like structures surrounded by a radiolucent zone (Figure 9), whereas complex odontomas radiographically are found most often in the posterior mandible and consist of a homogeneous mass of calcified tissue surrounded by a thin soft tissue capsule (Figure 10) (27, 28). Odontomas occur frequently around unerupted teeth.

Figure 9. Compound odontoma. Small tooth-like structures with radiolucent halo representing the dental follicle in which odontomas develop.

Figure 10. Complex odontoma. The enamel, dentin and cementum are more haphazardly arranged. Also note the radiolucent periphery.

Histopathology

Enamel, dentin, and cementum-like tissue arranged in a haphazard pattern are observed in complex odontoma; in contrast the normal anatomic structure is encountered in compound odontoma. There is usually a fibrous wall in the periphery of odontomas which represents the dental follicle in which odontomas develop.

Treatment and prognosis:

Conservative surgery is an adequate treatment for odontomas. Recurrence is not observed when they are completely removed. Rarely dentigerous cysts occur in odontomas.

Dentinogenic ghost cell tumor

Dentinogenic ghost cell tumor (DGCT) is a very rare benign, but locally infiltrative mixed odontogenic tumor. It is also accepted as the solid, neoplastic form of calcifying odontogenic cyst. DGCT mostly occurs in intraosseous sites, less commonly in the soft tissue of the gingiva and alveolar mucosa.

Clinical features

The reported age of patients with the tumor ranges from 11 to 79 with a peak incidence between the 4th and 5th decades. The tumor is twice more common in males than females. The tumor occurs in the posterior maxilla and mandible, but the extraosseous variant shows a predilection for the anterior part of the jaws. Patients are usually asymptomatic. In some cases
resorption of cortical bone with extension into soft tissues can be observed. The extraosseous variant presents as a sessile, sometimes pedunculated, exophytic nodule of the soft tissue. Radiographically, most of the tumors show a unilocular, radiolucent to mixed radiolucent/radiopaque appearance depending on the amount of calcification (Figure 11). They may be multilocular (29-31).

![Image](image_url)

**Figure 11.** Dentinogenic ghost cell tumor. Mixed radiolucent/radiopaque pericoronal lesion of left posterior mandible.

**Histopathology**

Both intra- and extra-osseous types show similar histopathology. The basic histopathological feature is the presence of ameloblastoma-like islands. Minor cysts might form in the epithelial islands. A characteristic feature is the transformation of the epithelial cells into ghost cells. Some ghost cells undergo calcification. DGCTs produce dysplastic dentin or osteodentin-like material. Ghost cells may be trapped in this dysplastic dentin, which in some areas may be mineralized.

**Treatment and prognosis**

There is no optimal treatment choice due to the small number of cases reported. Because of the potential for recurrence with conservative surgery, wide local excision should be the treatment model for the intraosseous DGCT. More conservative excision is an appropriate treatment of the extraosseous type. Long follow-up is required for recurrences that may occur years later (29-31).

**Odontogenic benign tumors, mesenchymal**

**Odontogenic fibroma**

Odontogenic fibroma is a rare, benign mesenchymal odontogenic tumor. There are intraosseous and peripheral variants with the peripheral one more common. The 2005 classification recognized two variants of odontogenic fibroma; the simple or epithelium poor variant and the WHO or epithelium rich variant. The 2007 classification has removed the simple type because it is poorly defined and recognized at this time.

**Clinical features**

Central odontogenic fibroma has a wide patient age range and it is relatively common in females. While the tumors of the maxilla are located in the anterior region, mandibular tumors are located mostly in the molar region. Most of the cases appear as a unilocular radiolucent area with well-defined often sclerotic borders (Figure 12), but larger tumors may become multilocular. Peripheral odontogenic fibroma presents as a gingival mass, resembling fibrous hyperplasia. The peripheral type occurs twice as often in females than males and the incidence peak is between second to fourth decades of life (32, 33).

**Histopathology**

The histopathology of the peripheral type and the central type is similar. They are composed of variable amounts of small, inactive odontogenic epithelial islands/cords within cellular or collagenous connective tissue. The amount of epithelium is variable, as are calcifications.
Treatment and prognosis

Enucleation and curettage, conservative laser excision can be the treatment of central lesions and simple excision is sufficient for peripheral types. Recurrence is rare. It has been reported that recurrence occurs due to insufficient removal of the lesion (32, 33).

Odontogenic myxoma/myxofibroma

Odontogenic myxoma is the third most common odontogenic tumor after ameloblastoma and odontomas (34). The tumor is almost always located intraosseously, but peripheral types have been described (35).

Clinical features

The benign, slow growing but locally aggressive tumor is usually diagnosed in the second to fourth decades. They most commonly occur in the molar and ramus regions of the mandible. Maxillary lesions also tend to present in the posterior quadrant. Radiographically, small lesions may have a unilocular appearance. However, most lesions are multilocular radiolucencies with internal bony septa (Figure 13). These septa have been described as making a tennis racket–like or stepladder-like pattern, but this pattern is rarely seen. They are mostly fine, curved and coarse appearances (36, 37).

Figure 12. Central odontogenic fibroma. Radioluent lesion of the right maxilla.

Figure 13. Odontogenic myxoma. Characteristic radiolucency with fine internal opaque trabeculations of the right posterior mandible.
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Histopathology

Odontogenic myxoma consists of fine delicate stellate, fusiform and round cells in a bland myxoid stroma, somewhat resembling the dental papilla of the developing tooth germ. Bony invasion may be observed. Variable amounts of collagen fibers may be present. If the collagen is abundant in the stroma, it can also be called 'odontogenic myxofibroma' but this designation does not have clinical or prognostic significance.

Treatment and prognosis

The treatment choice is resection with free margins. However small lesions can be treated by conservative surgery with the expectation of a low risk of recurrence. Overall the recurrence is about 25% and long-term follow-up is required (38).

Cementoblastoma

Cementoblastoma is a benign odontogenic mesenchymal tumor that is associated with and attached to the roots of teeth. It is considered to be the only true neoplasm of cemental origin.

Clinical features

Cementoblastomas are slowly growing lesions and usually presents with painless expansion. Pain and displacement of surrounding teeth are rarely reported. The related teeth may be mobile and less frequently root resorption is seen. The tumor is often seen in the second and fourth decades of life with part more cellular. The active cementoblasts rim the trabeculae. These histopathological appearances are similar to osteoblastoma but the osteoblastoma seen in the jaws is not related to the root of a tooth.

Histopathology

Cementoblastoma consists of calcified cementum-like masses in a fibrovascular stroma. The middle part of the tumor is more mature and the peripheral

Treatment and prognosis

Conservative treatment is curative. Incomplete removal leads to recurrence (40).

Cemento-ossifying fibroma

Ossifying fibromas were divided into 3 subtypes in the 2017 WHO classification. The first is odontogenic and designated cemento-ossifying fibroma; others are psammomatoid and trabecular juvenile types. Cemento-ossifying fibroma, also known as ossifying fibroma or cementifying fibroma, is classified under the mesenchymal odontogenic tumor group, whereas the juvenile types which are not considered odontogenic are classified under fibro- and chondro-osseous lesions in the last classification.

Clinical features

Cemento-ossifying fibromas are slowly growing lesions and usually presents with painless expansion. Pain and displacement of surrounding teeth are rarely reported. The related teeth may be mobile and less frequently root resorption is seen. The tumor is often seen in the second and fourth decades of life with...
a mean age of 35 years with a prominent female predominance. The tumor is frequently located in premolar and molar areas of the mandible. Radiographically, there is a well-defined, unilocular radiolucency with varying amounts of opacification depending on the amount of hard tissue produced by the neoplasm (Figure 15) (41, 42).

Figure 15. Cemento-ossifying fibroma. Radiographic features in the right posterior mandible (a) with significant buccal expansion (b and c).

Histopathology

Cemento-ossifying fibromas may be encapsulated. The tumor consists of variable amounts of calcified tissue in a hypercellular fibrovascular stroma. The calcified material can resemble bone (trabecular with cellular inclusions) or cementum (often more globular and acellular). The neoplasm does not invade adjacent bone which allows them to be easily removed. Grossly, there is often a single mass or large fragments and this feature is important clinically in the differential diagnosis of cemento-osseous dysplasias from the cemento-ossifying fibromas.

Malignant odontogenic tumors

The malignant odontogenic tumors are rare. They all share similar clinical and radiographic features, and the distinction among this group of tumors is primarily differences in their histologic features. Things that should alert you to the possibility of a lesion being malignant include rapid growth, asymmetry, pain, paresthesia, anesthesia, and a poorly defined destructive osteolytic process. Accordingly, while this group of lesions will be discussed for completeness, only one will be illustrated (Figure 16).

Treatment and prognosis

Conservative surgical treatment usually does not result in recurrence. Massive lesions may require en bloc resection (41).
Figure 16. Odontogenic sarcoma. This could be any of the odontogenic malignancies. Note poorly marginated, destructive lucency. The root canals were performed because the patient was in pain.

Odontogenic carcinomas

Ameloblastic carcinoma

Ameloblastic carcinoma is a rare primary malignant epithelial odontogenic tumor showing histologic features of ameloblastoma. The tumor is the malignant counterpart of ameloblastoma and has cellular atypia and the ability to metastasize. BRAF V600E mutation has been found identical to those in other ameloblastic neoplasms (43).

Clinical features

Clinically there can be swelling, pain, rapid growth, trismus and dysphonia. Most cases arise in patients older than 45 years. The tumor is frequently located in the posterior region of the mandible. Radiographically, there is an irregularly marginated radiolucency often with cortical bone perforation and/or soft tissue invasion (43-45).

Histopathology

Ameloblastoma-like appearance with cytological atypia is seen in both primary and metastatic ameloblastic carcinomas. However, the classical features of ameloblastoma including reverse polarity and peripheral palisading are usually lost. Pleomorphism, altered nuclear-cytoplasm ratio, abnormal mitoses, vascular or nerve invasion are important features for the diagnosis. The presence of necrosis may be helpful. The mitotic rate is usually increased but the increase in mitotic activity alone is not valuable (44, 45).

Treatment and prognosis

The main treatment is radical surgical resection. Prognosis is quite poor. Lung metastasis develops much more commonly than locoregional lymph node metastasis (45).

Primary intraosseous carcinoma

In the 2005 classification, the primary intraosseous squamous cell carcinoma was divided into numerous entities based on their histogenesis. In the 2017 classification, one of the goals was simplicity and this group of lesions was incorporated as one under the umbrella of ‘primary intraosseous carcinoma’ (46). Primary intraosseous carcinoma is diagnosed only after other carcinoma types are excluded, particularly metastatic carcinomas from distant primary sites. Primary carcinomas are quite rare. They originate from the odontogenic epithelium, either from remnants left from odontogenesis, from the epithelial lining of an odontogenic cyst or other precursor epithelial lesions.

Clinical features

The clinical manifestations of the cases are not specific. Large lesions may cause cortical bone destruction and perforation. The tumor is observed in a wide age range with a mean age at diagnosis of 55-60 years. It frequently occurs in the corpus and posterior region of the mandible. Maxillary cases are mostly located in the anterior region. Radiographically, there is a radiolucent lesion with irregular cortical border (47, 48).

Histopathology

Histopathologically, almost all cases show small nests or islands of atypical squamous cells but without features of ameloblastoma. Significant keratinization is rarely seen. Usually the differentiation of the tumor is moderate. As mentioned, primary intraosseous carcinoma is a diagnosis of exclusion. The exclusion includes other malignant odontogenic carcinomas, metastatic carcinomas, intraosseous salivary gland carcinomas, and carcinomas of the maxillary region. Immunohistochemical stains are helpful in making these differences.
Treatment and prognosis

Radical resection with neck dissection is the primary treatment. Adjuvant radio- or chemotherapy can provide added benefit. Regional lymph node metastasis is not uncommon. However distant metastasis, usually to lung, is not frequent (49). The prognosis is poor. The cases arising from cysts may have a better prolonged course (50).

Sclerosing odontogenic carcinoma

Sclerosing odontogenic carcinoma, which was first described in 2008, has been added for the first time to the 2017 WHO classification. About ten cases have been reported to date (51, 52). Due to its new addition and the fact that few cases have been published, its features are not fully established.

Clinical features

The most frequent affected localization is the premolar and molar areas of the mandible with no sex predilection. Radiographically there is an ill-defined radiolucency with frequent cortical bone destruction (51, 53).

Histopathology

The hallmark of the tumor is single file cords and strands of polyhedral epithelial cells streaming within a stroma of dense sclerosis. Even though the cytological features are bland, the tumor is characterized by aggressive infiltrative growth into muscle and nerve. Given the rarity of the tumor, other odontogenic tumors and metastasis should be excluded before the diagnosis can be made.

Treatment and prognosis

Since only case reports have been reported in the literature, no specific treatment protocol has been established. It can be treated as a low-grade malignancy, therefore primary treatment is surgical resection. No metastatic cases and only one recurrent case after initial curettage have been reported to date (3).

Clear cell odontogenic carcinoma

Clear cell odontogenic carcinoma is rare, low-grade malignancy. The vast majority (88%) of the tumors has EWSR1 rearrangements detectable by fluorescent in situ hybridization (54).

Clinical features

The tumor has non-specific signs. It can cause root resorption and soft tissue invasion. However many cases are asymptomatic. The most frequently affected site is the mandible with a female predilection. Most cases occur in 4-7 decades, with a mean age of 53. Radiographically it appears as a destructive radiolucency with ill-defined margins (55, 56).

Histopathology

The tumor is characterized by predominantly sheets and islands of vacuolated and clear cells separated by a hyalinized to fibrous stroma. These cells show diastase-resistant periodic acid–Schiff (PAS) positivity and mucin-negativity that is important for the differential diagnosis of salivary gland neoplasms. The cytological features can be bland, with only mild atypia and few mitoses. Before making a diagnosis of clear cell odontogenic carcinoma, many clear cell-rich neoplasms, especially metastatic renal cell carcinoma, should be excluded (57).

Treatment and prognosis

The primary treatment is complete surgical resection. Adjuvant radiotherapy may also be considered (55).

Ghost cell odontogenic carcinoma

Ghost cell odontogenic carcinoma is an extremely rare, malignant odontogenic tumor. About 40% of the cases arise from benign, precursor ghost cell odontogenic lesions, the rest occur de novo (58).

Clinical features

The tumor has no specific signs and symptoms. All features are similar with other low grade malignancies. Slow growing, ulceration, root resorption or soft tissue invasion can be seen. Radiographically, the tumor is a destructive radiolucent lesion with ill-defined borders.
Histopathology

Ghost cell odontogenic carcinoma may arise from other benign ghost cell tumors; dentinogenic ghost cell tumor and calcifying odontogenic cysts. To make a diagnosis, it is important to observe ghost cells or precursor ghost cell lesions with pleomorphism, necrosis, and infiltrative growth pattern. Ghost cells can be varying numbers with large, pale-staining cytoplasm without nuclei. The malignant epithelial cells show sheets, strands, and islands in a fibrous stroma (58, 59).

Treatment and prognosis

Wide surgical resection is the primary treatment as with other oral carcinomas. The role of radiotherapy and aggressive multimodal therapy remain undefined (59).

Odontogenic sarcomas

Odontogenic sarcomas include a very rare group of malignant odontogenic tumors in which the epithelial component is cytologically benign, and the mesenchymal component is malignant. Ameloblastic fibrosarcoma is the most common type. If the tumor produces dentin, it can be called ‘ameloblastic fibroodontosarcoma’ and if enamel and dentin production is present it can be called ‘ameloblastic fibro-odontosarcoma’. Because there is no evidence that these designations have implications on outcome, they were all included in the uniform category of odontogenic sarcomas in the 2017 classification. Although the etiology is not clear, it is generally thought to originate from a precursor lesion, especially ameloblastic fibroma (3, 60).

Clinical features

The tumor shows a wide patient age distribution with a mean age of 30 years. The tumor is observed most frequently in the mandible as an expansible mass that can cause pain, paresthesia and dysesthesia. Almost half of the cases in the literature have been reported to be malignant transformation of ameloblastic fibroma. The radiograph shows irregularly marginated lesions (60, 61).

Histopathologic features

Histopathology of odontogenic sarcomas shows a mixed component. The epithelial component is benign and may be as evident as a classical ameloblastic fibroma or sometimes eradicated/compressed by the malignant mesenchymal component. The mesenchymal component has malignant features, including increased mitosis, variable degrees of cellularity and cytology atypia.

Treatment and prognosis

The recommended treatment is a wide surgical excision that provides uninvolved surgical margin. The efficacy of adjuvant radiotherapy and chemotherapy is controversial.

Odontogenic carcinosarcomas

Odontogenic carcinosarcomas are very rare mixed malignant tumors. There are only a few cases in the literature. In fact, it was a known entity that was excluded from the 2005 classification but was reinstated in the 2017 classification because of better documentation with immunohistochemistry (3, 4, 62).

Clinical features

Because of the rarity of this tumor, there are no distinct clinical features. The reported cases have occurred in the mandible and the age range is 9-63 years. Radiologic examination reveals a lytic lesion with ill-defined borders (62, 63).

Histopathology

Both epithelial and mesenchymal components of the tumor are cytologically malignant. Ameloblastic islands with malignant features are observed in the stroma composed of hypercellular, pleomorphic, fibroblastic cells. High proliferation index is seen in both carcinoma and sarcoma components (64). Care must be taken to not misdiagnose a spindle cell odontogenic carcinoma as odontogenic carcinosarcoma.

Treatment and prognosis

The main treatment is surgical resection. However, due to the very limited number of cases, the prognosis and treatment choices are controversial.

Source of funding
None declared.

Conflict of interest
None declared.
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