

## ODONTOGENIC TUMORS: THE SHORT VERSION

**T**UMORS IN THE JAWS THAT ARISE FROM ODONTOGENIC (tooth forming) tissues are referred to as odontogenic tumors. But what are “odontogenic tissues” and how do you get tumors from them in adults long after odontogenesis has ceased? If you remember the embryology and histology of tooth formation, you may skip the next three paragraphs and go directly to the tumors starting with “ameloblastoma”.

Recall that two types of embryonic tissues contribute to the formation of a tooth. Early in embryogenesis, future dental pulp cells (primitive ectomesenchyme) migrate from the neural crest to the jaws and settle out in areas where teeth are to be formed. They signal the overlying ectoderm (epithelium) to send down a cord of cells (the dental lamina) which will become the enamel organ. It is the inner layer of the enamel organ that will become ameloblasts that secrete enamel matrix. (Amelogenin is the main protein found in enamel matrix. The gene that encodes this protein is on the X chromosome.)

After the arrival of the enamel organ, the awaiting ectomesenchymal cells turn into dental pulp cells. The outer cells of the pulp that are adjacent to the ameloblasts differentiate into odontoblasts and make dentin matrix whereupon the ameloblasts make enamel matrix. After the crown forms, the inner and outer layers of the enamel organ squeeze out the two middle layers (stratum intermedium and stellate reticulum) and grow downward as a cylinder shaped structure (Hertwig’s root sheath) that outlines the root. So remember, a tooth is formed from two types of embryonic tissues, ectoderm and ectomesenchyme. It is one of the many wonders of embryogenesis that these tissues are genetically programmed so that they form a single rooted tooth in the front, a double rooted tooth in the midjaw, and double and triple rooted teeth in the posterior jaws. How do they know?

The point in telling you this is to refresh your memory about terminology and to tell you that all of these tissues do not undergo apoptosis when the job is done. Remnants of odontogenic epithelium remain in the periodontal ligament and gingiva forever. In the gingiva, they are called epithelial rests of Serres and in the periodontal ligament they are known as the rests of Malassez. It is not known if remnants of ectomesenchyme remain because it is indistinguishable from surrounding mesodermal tissues. It is from the epithelial rests (Serres and Malassez) that arise odontogenic

tumors in adults. There is a third source, the reduced enamel epithelium that envelopes the crown of unerupted teeth. Now the tumors.

### **AMELOBLASTOMA**

Ameloblastoma is a tumor in which the tumor cells form caricatures of the enamel organ and some of them resemble ameloblasts. However, they are incapable of making enamel matrix. This tumor occurs chiefly in middle age people long after odontogenesis has ceased. Presumably a carcinogen converts a cell in one of the epithelial rests to become a tumor cell. As such, it starts to divide endlessly to form a tumor. Remember the axiom, tumor cells tend to resemble the tissues from which they arise. Since cells in rests of Serres and Malassez were at one time capable of becoming ameloblasts, it should not come as a surprise that tumor cells resemble ameloblasts.

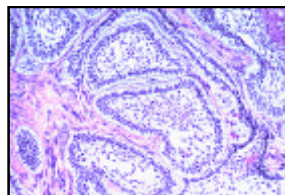
What are the main points about this tumor? It is unencapsulated and infiltrates surrounding bone marrow. Even though they are locally infiltrative, they do not metastasize. They may occur in any part of both jaws but most are in the middle and posterior regions of the mandible. Ameloblastomas are always purely radiolucent and may be unilocular but frequently become multilocular as they increase in size.

If not found and treated early, they will expand the jaw.



**FIG. 1** Ameloblastoma: a multilocular radiolucent lesion in the body and ramus of the mandible in a 29 year old female.

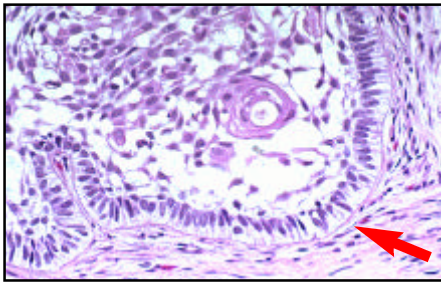
Histologically, the tumor cells appear as islands of odontogenic epithelium in a stroma of fibrous connective tissue.



**FIG. 2** Ameloblastoma, medium power microscopy. Islands of odontogenic epithelium in a stroma of fibrous connective tissue.

The cells in the center of the islands resemble stellate reticulum but may undergo squamous metaplasia

to become keratinizing squamous epithelium. The cells at the periphery of the epithelial islands are tall columnar cells that rest on a basement membrane separating them from the surrounding stroma.



**FIG. 3** Ameloblastoma, high power microscopy. The center and left are odontogenic epithelium. The fibrous connective tissue stroma is right and bottom. Notice the loose stellate reticulum-like appearance in the middle of the epithelial island and the tall columnar cells with reverse nuclear polarity at the outer edge of the epithelium (see arrow).

The nuclei of the tall columnar cells (ameloblasts) are typically found at the end of the cell most distant from the basement membrane, a feature referred to as “reverse nuclear polarity”.

The treatment of ameloblastoma is surgical excision. This may require removal of a large segment of the jaw. Simple curettage is usually met with recurrence.

Ameloblastomas that arise from rests of Malassez occur as intrabony tumors. Rarely, ameloblastoma arises from rests of Serres. Here they grow as extra-bony soft tissue tumors in the gingiva (Figure 4).



**FIG. 4** A peripheral ameloblastoma. This tumor arises from rests of Serres or alternately from basal epithelial cells in the gingiva in a manner analogous to cutaneous basal cell carcinoma.

Additionally, the reduced enamel epithelium around the crown of unerupted teeth may turn into ameloblastoma in which case it radiographically mimics a dentigerous cyst (Figure 5).

This type of tumor has been referred to as unicystic ameloblastoma or simply as cystic ameloblastoma and has a much better prognosis.

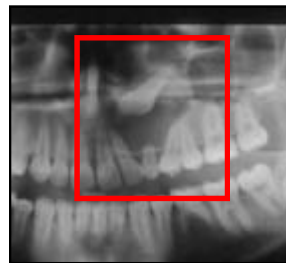


**FIG. 5** A cystic ameloblastoma associated with an unerupted and displaced molar tooth in a child. Note the hint at compartmentalization (multilocularity). It resembles an ordinary dentigerous cyst except that dentigerous cysts are ordinarily unilocular.

### ADENOMATOID ODONTOGENIC TUMOR (AOT)

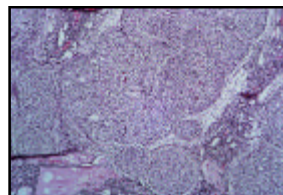
This is a tumor mostly of teenagers. It occurs in the middle and anterior portions of the jaws in contrast to ameloblastoma which is found mostly in the posterior segment. Two-thirds occur in the maxilla and it is more common in females. This tumor is encapsulated and is treated by curettage with a recurrence rate approaching zero.

The radiographic appearance is a unilocular radiolucency, often around the crown of an unerupted tooth in which case they resemble a dentigerous cyst (Figure 6).



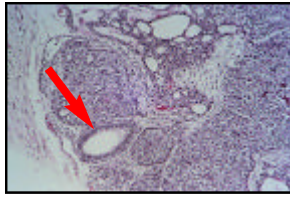
**FIG. 6** Adenomatoid odontogenic tumor (AOT) associated with an unerupted tooth #11. It resembles a dentigerous cyst. Some AOTs produce calcifications that may appear as “snowflake” densities.

Histologic examination reveals a thick capsule of fibrous connective tissue. The tumor fills the central cavity, there is little stroma. Tumor cells frequently form ball-like structures referred to as “rosettes” (Figure 7).



**FIG. 7** Adenomatoid odontogenic tumor, medium power. Note how the tumor cells form balls of cells that are called rosettes.

Another identifying feature is the presence of duct-like structures (Figure 8).



**FIG. 8** Adenomatoid odontogenic tumor. Note the duct-like structures (see arrow)

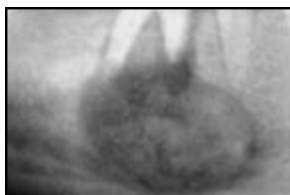
Small calcifications may be found in the tumor. If they are present in sufficient size and number, they may show on the radiograph as a “snow-flake” pattern. A homogeneous, eosinophilic and amorphous material may occasionally be found in AOT. Its identity is disputed. Some consider it a peculiar form of enamel matrix, others claim that it is a dentin-like material. This is of no clinical importance but does raise questions if this is a pure epithelial tumor (enamel matrix) or has an ectomesenchymal component (dentin matrix).

### ***CALCIFYING EPITHELIAL ODONTOGENIC TUMOR (CEOT, Pindborg tumor)***

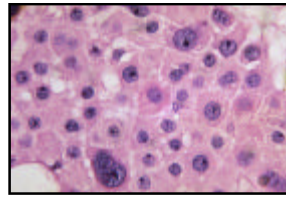
This tumor is so rare that it deserves little discussion. In 1958, Dr. J.J. Pindborg of Denmark described four cases of an unusual odontogenic tumor that still bears his name. This is the most “unodontogenic” tumor of the group, the tumor cells do not resemble odontogenic tissue. Tumor cells are squamous-like, they even have desmosomal attachments. There often is variation in nuclear size, shape and staining intensity—features that are often associated with malignancy (Figure 10). This tumor forms an amorphous material that is said to be amyloid or amyloid-like (Figure 11). Whatever it is, it calcifies in a concentrically lamellated “tree-ring” pattern known as Liesegang calcifications. This explains the name of calcifying epithelial odontogenic tumor.

CEOT lacks a capsule but apparently does not infiltrate as deeply into surrounding tissues as does ameloblastoma. Excision with a small margin of surrounding bone is usually curative.

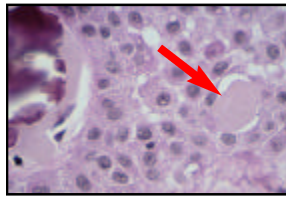
Radiographically, this tumor may appear as a radiolucent tumor but if sufficient calcifications are present, it becomes dense (Figure 9).



**FIG. 9** Calcifying epithelial odontogenic tumor in the body of the mandible. It appears as a radiolucent lesion with smoky dense areas.



**FIG. 10** CEOT, high power view. The tumor cells resemble squamous epithelium more than odontogenic epithelium. There is some variation in nuclear size and shape, but this is not a malignant tumor.

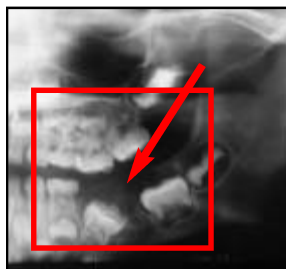


**FIG. 11** Calcifications (extreme left) in a CEOT account for the density noted on radiographs. These are thought to be calcified amyloid or amyloid-like material, some of which can be seen right of center as a pale eosinophilic globule (arrow).

NOTE: We have skipped malignant ameloblastoma, ameloblastic carcinoma, clear cell odontogenic carcinoma and odontoameloblastoma and squamous odontogenic tumors because they are too rare. They are covered in your text.

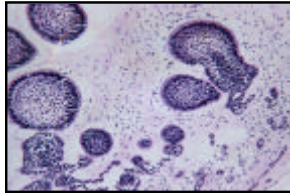
### ***AMELOBLASTIC FIBROMA***

This is a tumor of childhood, the typical patient is about 12 –14 years old, seldom is it seen beyond age 20. The posterior segment of the mandible is the most common location. Local swelling or failure of teeth to erupt on time or in proper alignment may call attention to the tumor. Ameloblastic fibromas are purely radiolucent.



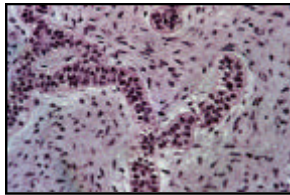
**FIG. 12** Ameloblastic fibroma in and around the crowns of lower molar teeth. It is subtle, the second deciduous molar tooth has been tilted downward by the tumor. Patient was a 5 year old boy.

Small lesions may be unilocular but larger lesions are ordinarily multilocular. Both odontogenic epithelium and odontogenic ectomesenchyme contribute to this tumor (an odontogenic mixed tumor not to be confused with the mixed tumor of salivary gland). The epithelium grows in small islands and cords (Figures 13 and 14).



**FIG. 13** Ameloblastic fibroma, medium power. Islands of odontogenic epithelium exhibit peripheral columnar cells. The stroma is cellular ectomesenchyme that resembles the dental papilla, the forerunner of the dental pulp.

In the larger islands, peripheral palisading of columnar cells with reverse nuclear polarity may be seen but seldom do the islands and cords open up large enough to form central stellate reticulum. The tissue surrounding the epithelium is cellular connective tissue that bears some resemblance to dental pulp. This is the ectomesenchymal component.



**FIG. 14** Ameloblastic fibroma, high power. Cords of epithelium lie in an ectomesenchyme stroma.

This tumor is clearly benign and is ordinarily treated by vigorous curettage. The recurrence rate is placed at about 15 %. Even though this tumor is comprised of both odontogenic epithelium and odontogenic ectomesenchyme, it does not secrete either enamel matrix or dentin. The reason for making this point will become apparent later.

### **ODONTOMA: COMPOUND AND COMPLEX TYPES**

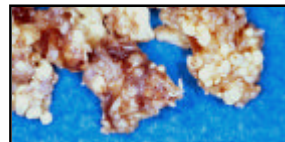
The tumors in which odontogenic differentiation is fully expressed are the odontomas. In these tumors, the epithelium and ectomesenchyme realize their potential and make enamel and dentin respectively. As a result, these tumors are mostly radiodense. In the compound odontoma, multiple small and malformed tooth-like structures are formed creating a “bag of marbles” radiographic appearance (Figure 15).



**FIG. 15** Compound odontoma, the “bag of marbles” appearance.



**FIG. 16** Compound odontoma in the body of the mandible of a 17 year old boy.



**FIG. 17** Compound odontoma of tumor in Figure 16, the small, closely spaced white bodies are individual malformed tooth-like structures.

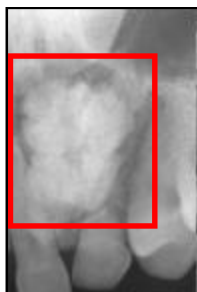


**FIG. 18** Compound odontoma, photomicrograph of decalcified specimen. Note the structure that resembles a tooth with a pulp (P), a surrounding mantle of dentin (D) capped by enamel (E), center and left of center.

In the complex odontoma, there is little or no tendency to form tooth-like structures. The dentin and enamel are entwined in a mass that bears no resemblance to teeth. The result is a solid, dense mass of hard tissue as seen in Figures 19, 20 and 21.



**FIG. 19** Complex odontoma, posterior maxilla of a child.



**FIG. 20** Complex odontoma in anterior maxilla. Deciduous tooth is retained.

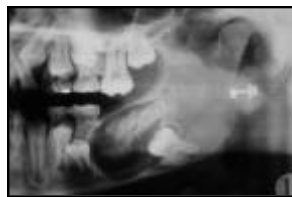


**FIG. 21** Complex odontoma, histopathology of decalcified specimen. The dentin (D) appears as thin strands of eosinophilic material and the enamel (E) is more purple.

Both types of odontoma are found in the early years, usually in the teens or early twenties. Compound odontoma is more common in the anterior jaw segment whereas the complex type is found more commonly in the posterior jaws. Many are associated with an unerupted tooth. Odontomas behave more like developmental abnormalities (hamartomas) than true neoplasms. Although they may reach a large size, they do eventually cease growing in contrast to true neoplasms which show continuous growth.

Treatment is elective surgery. They have a limited growth potential and cause no pain or cosmetic deformity.

Note: Now a brief, arcane discussion about the relationship of ameloblastic fibroma to odontomas. What would happen if you left an ameloblastic fibroma untreated? Would it eventually make dentin (the first hard tissue formed in odontogenesis) and become an ameloblastic fibro-dentinoma? And if still untreated, would it eventually make enamel (the other and always second hard tissue formed during odontogenesis) and become an ameloblastic fibro-odontoma? Examine Figure 22.



**FIG. 22** Ameloblastic fibro-odontoma, see text for comments about this tumor.

Microscopic examination of the radiolucent portion of this tumor revealed ameloblastic fibroma, there was no dentin or enamel. But within the radiodense areas,

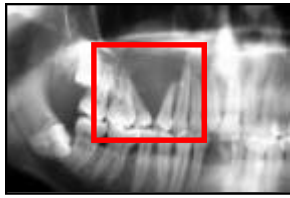
there was dentin and enamel. What's going on? The correct diagnosis would be ameloblastic fibro-odontoma. The question is: Is ameloblastic fibroma just the immature stage of odontoma? Or to turn that around, is an odontoma the end-stage of an ameloblastic fibroma? The compound and complex tumors are probably different tumors, not just different versions of the same tumor. The compound odontoma is probably a local form of hyperdontia, a hamartoma. It is not the end stage of something else. On the other hand, the complex odontoma is thought to be the end-stage of a tumor that began as an ameloblastic fibroma that progressed along the ameloblastic fibro-dentinoma — ameloblastic fibro-odontoma, mature complex odontoma pathway. The histologic diagnosis would depend on the stage during the tumor progression when it was biopsied. But there is a problem. Some people who have an ameloblastic fibroma have a recurrence years later and there is no evidence that it has progressed; there is no dentin or enamel formation. So the theory is that there are two varieties of ameloblastic fibroma, (1) a truly neoplastic variant that does not progress and (2) a hamartomatous variant (malformation) that left untreated will become a complex odontoma. In the early stage, it is not possible to tell them apart so they are all treated as if they are the neoplastic type.

ANOTHER NOTE: We skipped ameloblastic fibrosarcoma, granular cell ameloblastic fibroma, and odontogenic fibroma because this document is the short version.

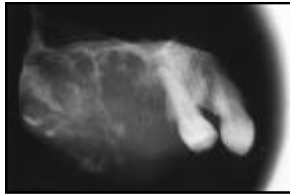
### ***MYXOMA (ODONTOGENIC MYXOMA)***

Tissue that is cell-poor and rich in mucopolysaccharide ground substance such as hyaluronic acid and chondroitin sulfate is said to be myxoid tissue. Tumors that have the same histologic quality are called myxoma (mix-oma). They are uncommon. Within the skeleton, they occur almost exclusively in the jaws. Extragnathic skeletal lesions are a rarity. Those that occur in the jaws are said to be of odontogenic origin but there is no hard evidence that it is so.

Myxoma is a tumor that occurs over a wide age range but most occur in the second and third decades. It is an unencapsulated, locally infiltrating tumor. If allowed to reach a large size, it takes a big operation to remove it. Like many odontogenic tumors, when small it is ordinarily unilocular but becomes multilocular as it enlarges. Since it does not produce a calcified matrix material, it is purely radiolucent. Figures 23 and 24 are examples of myxoma.

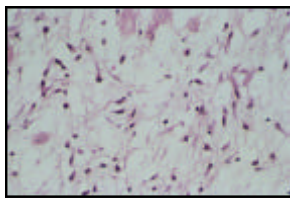


**FIG. 23** Myxoma appearing as a unilocular maxillary lesion.



**FIG. 24** Myxoma, radiograph of a resected specimen. Note the “wispy” trabeculations, a feature said to be characteristic of this tumor

Figure 24 is a radiograph of a myxoma of the maxilla that has been surgically removed. Notice that it is a destructive, lucent lesion but extending into the radiolucent area from the perimeter are wispy trabeculae of bone. This is said to be a characteristic feature of myxomas.

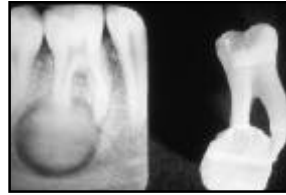


**FIG. 25** Myxoma, high power histopathology. Tumor cells lie randomly in a clear background of non-staining mucopolysaccharide ground substance.

Notice that the tumor cells are round to angular to stellate and some resemble tadpoles. These are “myxoblasts” which in reality probably are fibroblasts that are secreting a large amount of ground substance rather than collagen. The reason the background is clear is that hyaluronic acid and chondroitin sulfate do not stain with usual hematoxylin and eosin stain so it looks like the cells are floating in air.

### ***CEMENTOBLASTOMA (TRUE CEMENTOMA)***

As a group, odontogenic tumors are not common. Cementoblastoma is among the rarest of the rare. This tumor typically occurs around the roots of the lower posterior teeth. Like virtually all odontogenic tumors, it is benign but it expands the jaw, causes pain and requires surgical removal. Radiographically it appears as a ball of dense material attached to the end of the root (Figure 26).

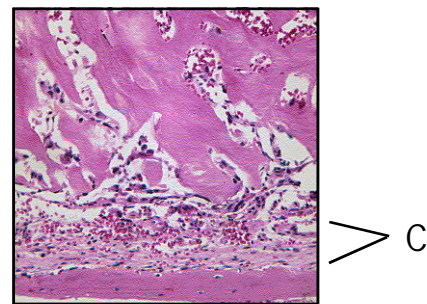


**FIG. 26** Cementoblastoma, typical radiographic appearance of a ball of cementum clinging to the root.



**FIG. 27** Cementoblastoma, gross specimen.

This dense material is presumed to be cementum and the tumor cell line that secretes it is cementoblasts, hence the name. So why the other name “true cementoma”? Recall that the lesion we know as cementoma is a self-limiting lesion ordinarily found in and around the apices of the lower incisor teeth. But the cementoblastoma is not self-limiting, it continues to grow until it is removed, hence it is a “true” tumor, a true cementoma. Maybe we should call the self-limiting cementoma by its other name, periapical cemental dysplasia. Histologically the mass of cementum is attached to the tooth root. As it expands, the cementoblasts at the periphery add new cementum.



**FIG. 28** Cementoblastoma, medium power histopathology of the decalcified specimen. The field is dominated by sheets of cementum with a rim of cementoblasts (c) with an outer rim of normal bone.

The layer of cementoblasts appear on the radiograph as a thin radiolucent line that abuts on surrounding bone. So the cementoblastoma appears as a ball of dense material with a thin halo of radiolucency (Figure 26).

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