Adenomatoid Odontogenic Tumor: A Case Report with Immunohistological Profile

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Abstract. *The adenomatoid odontogenic tumor (AOT) is an uncommon tumor of odontogenic origin, composed of odontogenic epithelium and characterized by slow but progressive growth. We report a rare case of AOT in an 18-year-old, who presented with a palpable bony-hard swelling in the anterior maxillary region. The tumor was radiographically well-defined, and exhibited unilocular radiolucency. Histologically, the appearance was of solid nodules of cuboid or columnar cells of odontogenic epithelium, forming typical nests or duct-like structures. Immunohistochemistry was positive for cytokeratins (CK) CK5/6, CK17, CK19 and negative for KI-67. The results were consistent with a diagnosis of AOT. Conclusion. A case of AOT is presented, emphasizing on the importance of recognizing neoplasms arising in odontogenic tissues. Recurrences seldom occur, and surgical cure is recommended*

The adenomatoid odontogenic tumor (AOT) is a benign hamartomatous non-invasive lesion, first-described by Steensland in 1905 (1). However, a variety of other terms have been used to describe this tumor, and Unal *et al*. (2) produced a list of all reported AOT nomenclatures; these include adenoameloblastoma, ameloblastic adenomatoid tumor, adamantinoma, epithelioma adamantium and teratomatous odontoma. Philipsen and Birn suggested the name "adenomatoid odontogenic tumor", which is now widely used (3). In the 2005 WHO classification, AOT is included under "odontogenic epithelium with mature, fibrous stroma without odontogenic ectomesenchyme" (4).

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Three clinical-pathological variants of AOT have been identified: intraosseous follicular, intraosseous extra-follicular, and peripheral. The follicular type is a central intraosseous lesion associated with an impacted tooth, while extrafollicular intraosseous AOT has no relation with a non-erupted tooth. The peripheral variant arises as a gingival fibroma or epulis attached to the labial, almost exclusively in the anterior maxillary gingiva. Intraosseous AOT may be found in association with non gingiva (5).

The age at which AOT occurs ranges from 3 to 82 years; the male-female ratio is 1:1,9 (6, 7). The lesion almost exclusively occurs intraosseously, with a 2.1:1 preference for the maxilla over the mandible (8). The rare peripheral type occurs almost exclusively in the anterior maxillary gingiva. Intraosseons AOT may be found in association with non-erupted permanent teeth (follicular type), in particular the four canines, which together account for 60% of cases; the maxillary canines alone account for 40%. The lesions are typically asymptomatic, but may cause cortical expansion and displacement of adjacent teeth.

Radiographically, AOT usually appears unilocular, although a few multi-locular cases have been reported. It must be differentiated from dentigerous cysts, which most frequently occur as a pericoronal radiolucency in the jaws. The dentigerous cyst encloses only the coronal portion of the impacted tooth, whereas AOT usually exhibits radiolucency surrounding both the coronal and the radicular aspects of the involved tooth (9). Irregular root resorption is seldom reported (10). Displacement of neighboring teeth due to tumor expansion is more common than root resorption. Minute, variable-shaped radiopacities are frequently found within the lesion; these are calcified deposits, and occur in 78% of AOTs. The extraosseous, peripheral, or gingival types of AOT are rarely detected radiographically, but there may be slight erosion of the underlying alveolar bone cortex (11). We present a case of AOT and highlight the immuno-histological profile.

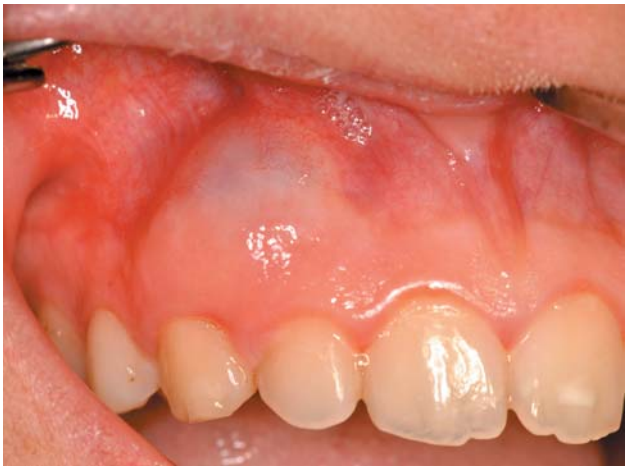

Figure 1. *Clinical aspect of the tumor.*

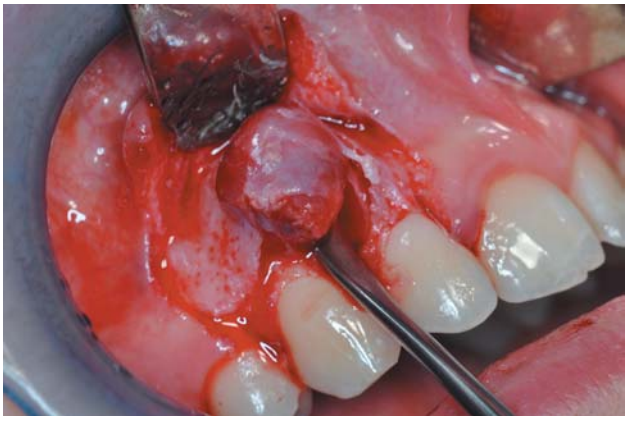

Figure 3. *Intraoperative view.*

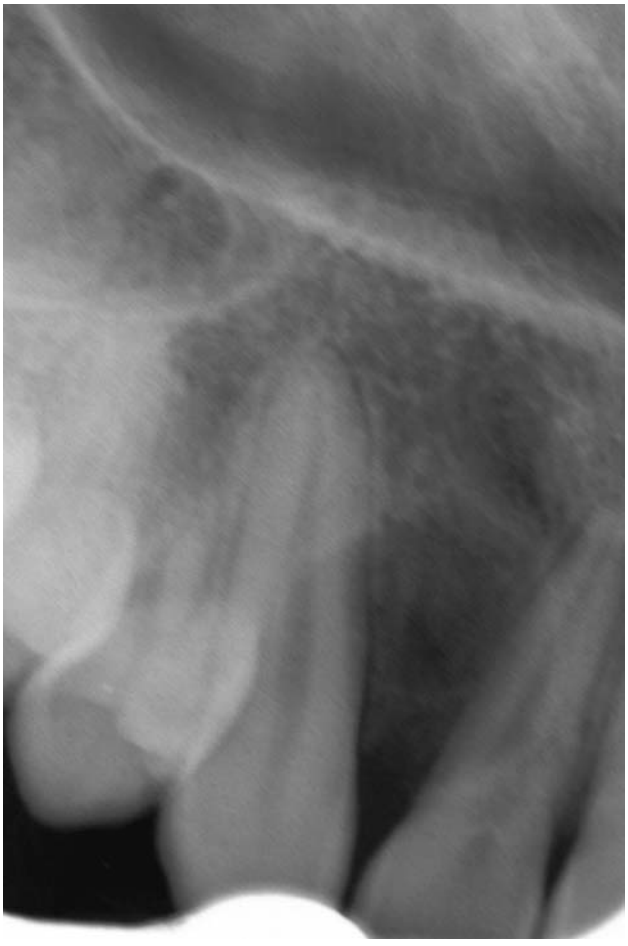

Figure 2. *Endoral radiograph showing the relationship between the adenomatoid odontogenic tumor and the root of the canine, with enlargement of the interdental space and mesially displaced root.*

Case Report

An 18-year-old woman was referred to our institute due to the 12 weeks presence of a non-painful neoformation in the right anterior maxilla, between the lateral incisor and canine, and which had increased in size. Intra-oral examination revealed a single diffuse swelling in the left anterior maxillary region, measuring about 1.4 cm × 1.0 cm (Figure 1). On palpation, the swelling was hard and non-tender.

Intraoral and panoramic radiography revealed a well-circumscribed unilocular radiolucency measuring about 1.4×1.0 cm, in correspondence with the lateral incisor and canine, with enlargement of the interdental space, and mesially displaced root (Figure 2).

Before removal, it was decided to perform a fine-needle aspiration of the lesion for cytological examination; this produced non-diagnostic material, due to the presence of abundant erythrocytes. A provisional diagnosis of a benign bony neoplasm of odontogenic or non-odontogenic origin was made. The patient underwent surgical curettage under local anesthesia.

The lesion was removed with a Deka erbium laser operating at 2,940 nm (Figure 3). Under local anesthesia, achieved with 2% carbocaine and 1:100,000 adrenalin, a full-thickness mucosal flap incision was performed along the marginal line from the maxillary right lateral incisior to the canine, with a 300-600 micron sapphire tip, (power setting) of 140 mJ, (frequency) of 20 Hz, with pulsed modality, water spray at 80-100 ml/min.

Using the same tip, but setting the instrument to 180 mJ power, frequency 15 Hz, pulsed modality, a breach was made in the bone, isolating and removing the neoformation, which presented a diameter of circa 1.5×1.2 cm.

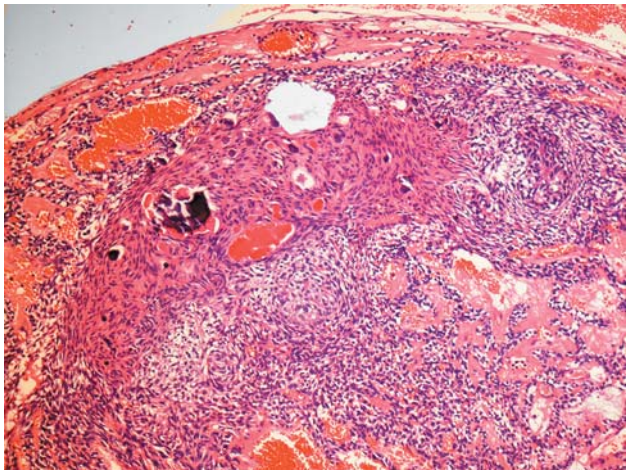

Figure 4. *Photomicrograph showing the odontogenic epithelium with duct-like structures. The spindle-shaped cells form sheaths and a whorled mass. Duct-like structures and areas of calcification areas are visible. (H&E, original magnification, ×20).*

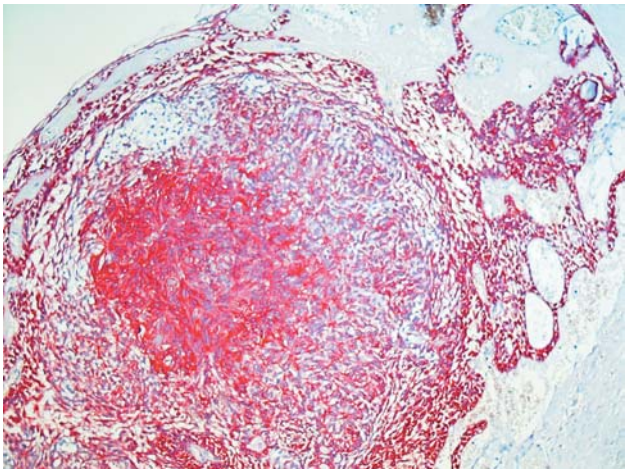

Figure 6. *Immunohistochemical stain for cytokeratin-17 showing positive immunoreaction (original magnification, ×20).*

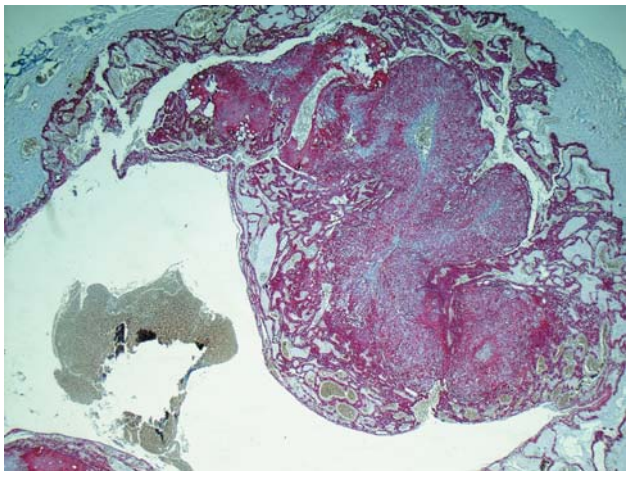

Figure 5. *Immunoreactivity for cytokeratin 5/6 is diffuse (original magnification, ×20).*

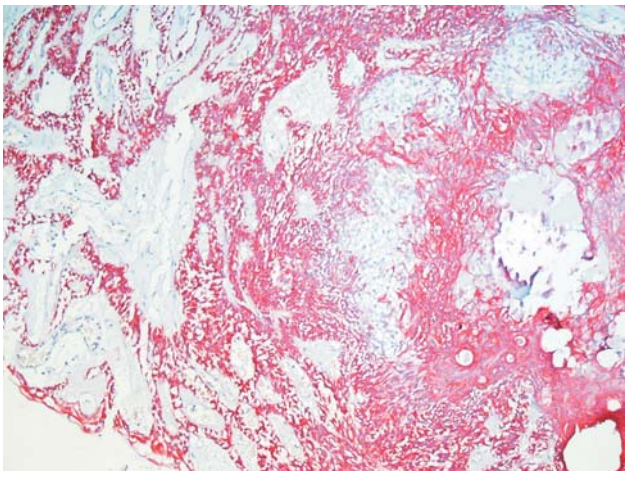

Figure 7. *Immunreactivity for cytokeratin-19 is strongly positive (original magnification, ×20).*

Sutures were placed, using silk 4/0 suture thread with V1 needle, and a 0.2% chlorhexidine gel was applied; the patient was instructed to apply this gel twice daily for two weeks.

The neoformation was sent for histopathological examination, and a diagnosis of "AOT" was rendered.

Histology. Gross examination of the enucleated specimen revealed uniform reddish-white soft tissue, measuring 1.5 cm × 1.2 cm . The tumor tissue was embedded in paraffin, and 4-μm thick sections were cut and stained with hematoxylin-eosin. Microscopical examination revealed a tumor of the odontogenic epithelium with duct-like structures. Spindle-shaped cells formed sheaths and a whorled mass. Areas of glandular or ductal patterns were intermixed with occasional spherical calcifications. Eosinophilic, amorphous, uncalcified material was observed within the lesion (Figure 4).

Immunohistochemistry. For immunohistochemistry, the avidin-biotin complex (ABC) method was applied. Sections were de-paraffinized with xylene for 15 min before rehydration through graded alcohol to water. Antigen retrieval was performed on the slides by placing them in a

Table I. *Immunohistochemical findings of the current case.*

Antibody	Supplier	Dilution	Clone	Antigen retrieval	Results
CK5/6	DAKO	1: 400	D5/16 B4	Citrate pH=6	+
CK17	DAKO	1: 100	MNF116	"	+
CK19	DAKO	1: 50	RCK108	"	+
Ki-67	DAKO	1: 200	MIB1	"	+2%

CK , Cytokeratin; Ki-67 (proliferative index); +, positive staining.

bath of 10 mM citric acid (pH 6) and boiling for 16 min using an autoclave.

A panel of monoclonal antibodies was used for the following markers (Table I): (CK5/6),(CK17), (CK19) and Ki-67. Slides with the primary antibodies were incubated overnight at room temperature in BSA. Negative controls were incubated with an irrelevant primary antibody. Positive controls were run using human specimens carrying the antigens investigated. Monoclonal antibody binding was visualized using the Envision+ System HRP (Dakocytomation with DAB DAKO) as substrate chromogen. Sections were counterstained with hematoxylin. Immunoreactivity was evaluated in terms of location and intensity. To quantify the staining properties of tumor cells, intensity of the staining reaction was graded as negative (–), weakly (+), moderately (++) or strongly (+++) positive.

Results

The findings of Immunohistochemistry are summarized in Table I. The tumor cells showed strong reactivity for CK 5/6, CK17 and CK 19 (Figures 5-7). The average MIB1 index for ki67 was low (around 2%).

Discussion

AOT is an uncommon, benign, well-circumscribed lesion derived from the odontogenic epithelium. Histologically, it constitutes whorled nests of epithelium, together with areas of glandular or ductal patterns intermixed with occasional spherical calcifications (12-14). Eosinophilic, amorphous, uncalcified material, known as "*tumor droplets*", may be present. In general, differential diagnosis is versus ameloblastoma, calcifying epithelial odontogenic tumor (CEOT), ameloblastic fibroma, and ameloblastic fibro-odontoma. CEOT exhibits larger and more numerous calcifying spherules within the eosinophilic cytoplasm of large cells, along with smaller cells with hyperchromatic nuclei; amyloid-like eosinophilic material is also present. Ameloblastoma has a characteristic lining, and an arrangement with stellate reticulum; furthermore, its usual location is in the mandible or posterior maxilla, unlike AOT, which is generally located in the anterior maxilla (12). In the present case, the histopathology of the lesions was very typical, and thus there was no problem of differential diagnosis.

Immunohistochemical and ultrastructural findings have shown that the eosinophilic deposits (amyloid-like material) most probably represent some form of enamel matrix (15). The immunohistochemical phenotype is characterized by a cytokeratin profile similar to that of the follicular cyst, or oral or gingival epithelium based on positive staining for CK5, CK17, and CK19 (16) and on a lack of staining for CK4, CK10, CK13, and CK18. Crivelini and co-workers detected CK14 in AOT, indicating that the lesion's origin is in reduced dental epithelium (17). In the case reported by Reinhard and co-workers, immunoreactivity was found for cytokeratins, with focal co-expression of vimentin and, surprisingly, *also* of smooth muscle actin, at the base of the broad duct-like zone. Coexpression of vimentin points to the neoplastic nature of the entity, and is in agreement with earlier reports on AOT immunohistochemistry (1-13). Mineralized and hyaline material does not exhibit immunohistochemical reactivity for cytokeratin, as would be expected. *In vitro*, the coexpression of cytokeratin and vimentin in the oral epithelium is well known (14). In the present case, the immunohistochemical profile (strongly positive for CK 5/6, CK17 and CK19) was consistent with other reports (15, 16), supporting a cystic or gingival epithelium profile.

The proliferation rate of AOT, in terms of Ki-67-positive tumor cells, is reported to be low in general (15, 18) and accounted for fewer than 1% of nuclei; the present results concerning Ki-67 are in line with those reports.

The histogenesis of AOT is still uncertain, although recent findings strongly indicate that it derives from a complex system of dental laminae or their remnants. It is often considered to be a hamartomatous lesion, rather than a true neoplasm (18), and debate is still lively as to whether AOT should be considered a hamartoma or a neoplasm (10).

All variants of AOT are well-encapsulated, and present an identical benign behavior. Conservative surgical enucleation or curettage is the treatment of choice, and only rarely does recurrence arise (10). For periodontal intra-bone defects caused by AOT, guided tissue regeneration with the membrane technique, after complete removal of the tumor, is recommended (19). The patient described in this case report is still healthy, without recurrence, 24 months after local excision, and is currently being followed-up.

Conclusion. The case of AOT presented emphasizes on the importance of recognizing neoplasms arising in odontogenic tissues. AOT has histopathological features making differential diagnosis sometimes difficult, and the clinical and radiographic features also often present similarities to

those of the odontogenic cyst; immunohistochemistry could be of assistance in this connection. Although recurrences are rare, follow-up is recommended.

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