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THE CALCIFYING EPITHELIAL ODONTOGENIC TUMOR

REVIEW OF LITERATURE AND REPORT OF AN EXTRA-OSSEOUS CASE*

by

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REVIEW OF LITERATURE

In 1955 and 1958, *Pindborg* described, based upon three cases, the calcifying epithelial odontogenic tumor as a distinct entity among the epithelial odontogenic tumors. Previously, four examples of the tumor were called "Adenoid adamantoblastoma" (*Thoma & Goldman* 1946), "Ameloblastoma of unusual type with calcification" (*Ivy*, 1948), "Malignant odontoma" (*Wunderer*, 1953) and "Cystic complete odontoma" (*Stoopack*, 1957). *Bernier* (1960) has classified the tumor as a variant of the simple ameloblastoma, and *Shafer, Levy & Hine* (1963) has described the tumor under the name "Pindborg tumor".

Since 1958, thirteen more cases of the calcifying epithelial odontogenic tumor have appeared in the literature including the present one and one in press. In addition the author has received histologic sections and clinical information on six more cases from the files of four pathologists. Table I summarizes some of the facts from the 26 cases known so far.

Except for *Gon's* patient, who was a Negro, all cases have been observed in Caucasians. Of the 26 cases 15 were men and 11 women. The average age for men was 42 years and for women 43 years. The oldest cases were in two women 68 years of age,

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Table I
Cases of calcifying epithelial odontogenic tumor

Investigator	Year	Sex	Age	Location	Embedded Tooth in Tumor Area
Thoma & Goldman	1946	M	32	Mandible, right	Canine
Ivy	1948	M	27	Mandible, left	Second premolar
Wunderer	1953	F	68	Maxilla, left	?
Stoopack	1957	M	26	Mandible, left	First molar
Pindborg	1958	M	42	Mandible, right	Second molar
		M	53	Mandible, left	Second premolar
		M	40	Mandible, left	First molar
Langer	1958	F	68	Mandible, left	?
Chaudhry et al.	1962	M	30	Mandible, right	Third molar
Shafer et al.	1963	M	47	Mandible, right	Third molar
Kramer	1963	F	56	Maxilla, left	+
		F	39	Maxilla, left	+
Ackerman	1964	M	58	Maxilla, left	?
Lucas	1964	M	28	Maxilla, left	?
Gon	1965	F	35	Maxilla, right	First molar
Vickers et al.	1965	M	52	Mandible, right	?
		M	43	Mandible, right	?
		F	38	Mandible, front	?
Pindborg (Present case)	1966	F	29	Attached gingiva of maxillary left lateral incisor	None
Pindborg et al.	1966	F	48	Maxilla, right	Third molar
Howell (La Jolla)		M	54	Mandible, right	?
		F	16	Attached gingiva of mandibular right central and lateral incisor	None
Howell & Davis (La Jolla)		F	33	Mandible, right	Second and third molar
Mellgren (Gothenburg)		M	62	Mandible, right	?
Miles (London)		M	28	Maxilla, left	?
Turner (Manchester)		F	45	Mandible, left	?

and the youngest was in a 16-year-old girl. The tumor has been found with approximately the same frequency in the four decades between 20 and 60 years. The tumor has affected the mandible in 17 cases (65 %) and the maxilla in 9 cases (35 %). There seems to be no predilection for either side of the jaws. The majority of the cases have been located in the premolar-molar region. Among the 15 cases where information is available as to the presence of embedded teeth, 13 had a non-erupted tooth (mostly molars) associated with the tumor.

Radiographic examination shows primarily a translucent area which may or may not be well demarcated from surrounding normal tissues. The central area of translucency will show islands of varying size of radiopacity which are associated with the embedded tooth if one is present. Some cases present a multilocular appearance composed of small compartments.

Histologically, the tumor consists of sheets of polyhedral epithelial cells in a connective tissue stroma. The epithelial cells tend to be closely packed, but are occasionally split up in islands or strands by a hyalinized stroma. The cell borders are distinct and the cytoplasm is slightly eosinophilic. The nuclei vary much in shape and size, but mitotic figures are rarely seen. The cytoplasm has a tendency to undergo degeneration and become homogeneous. The degenerated cytoplasm has an affinity for mineral salts and calcification occurs in the form of Liesegang's rings. The surrounding collagenous tissue may also become mineralized.

A histochemical study (Gon, 1965) has shown that the tumor cells are comparable to the cells making up the stratum intermedium of the enamel organ, suggesting an origin from that structure. This view was put forward by the author in 1958 and later supported by Chaudhry *et al.* (1962). Recent studies by Vickers *et al.* (1965) and Rantløv & Pindborg (1966) have demonstrated amyloid within the tumor cells and outside.

CASE REPORT

A 29-year-old woman was referred to the clinic because of a swelling of the left upper jaw. Five years ago the patient's dentist called her attention to a swelling in the region but nothing was done. There were no symptoms from the affected area. On examination, when the mouth was closed the left side of the upper



Fig. 1. An extra-osseous calcifying epithelial odontogenic tumor in a 29-year-old woman.

lip projected slightly. There was a tumor on the attached gingiva of the upper left lateral incisor (Fig. 1). The circular tumor, which measured about 1 cm in diameter, was well demarcated, firm and not movable over the underlying bone. The radiographic examination did not reveal anything abnormal in the region.

Under local anesthesia the tumor was removed; the alveolar process showed a slight shallow depression where the tumor had been. No connection between tumor and jaw could be demonstrated. The tumor was fixed in 10 % formalin, half of the tissue was decalcified. After embedding in paraffine serial sections were cut and stained with hematoxylin-eosin, van Gieson's connective tissue stain, alcian blue and PAS with and without diastase-treatment.

Histology. The tumor consists of polyhedral epithelial cells. A few areas are characterized by rather large, solid sheets of tumor cells (Fig. 2). However, most of the tumor containing area shows only scattered small islands of tumor tissue (Fig. 3). A number of the epithelial cells have undergone degenerative changes by

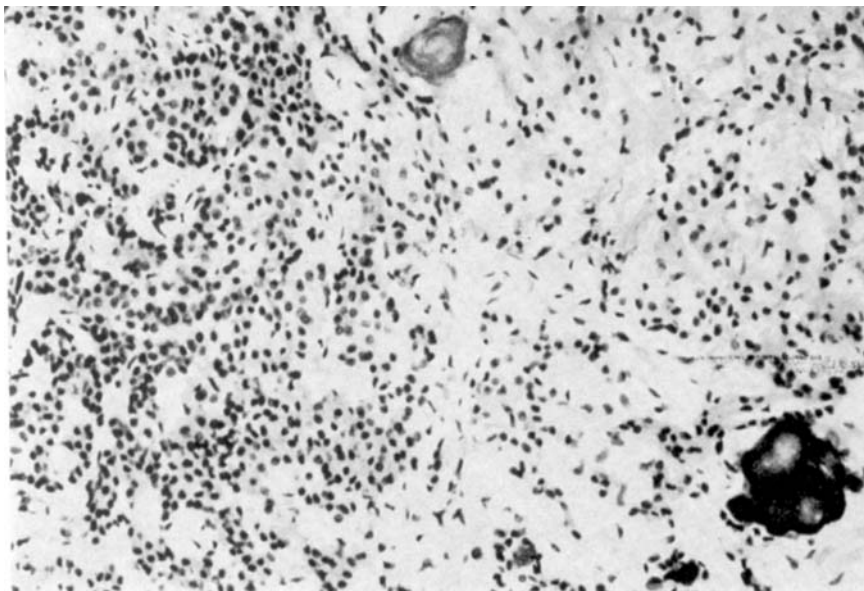


Fig. 2. Sheets of epithelial tumor cells with two areas of calcification. $\times 155$.

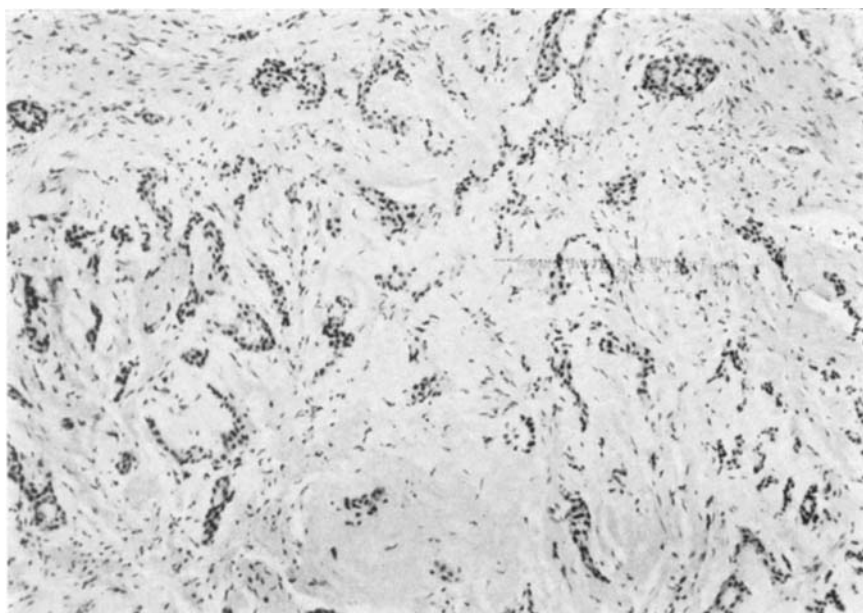
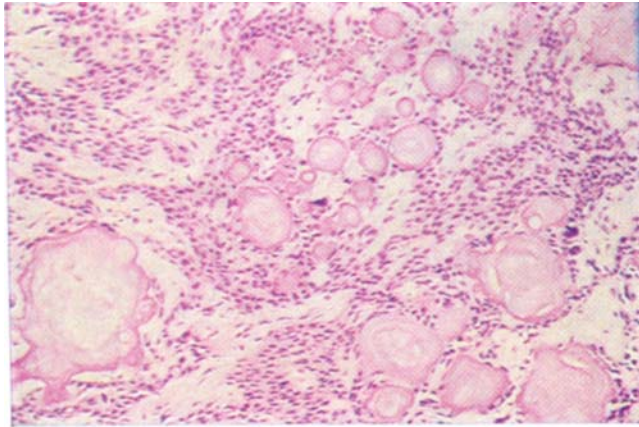


Fig. 3. Scattered islands of tumor tissue in slightly hyalinized stroma. $\times 90$.

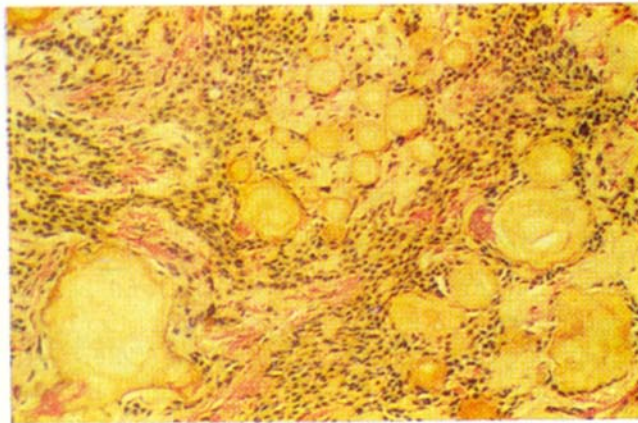
A. Hematoxylin-eosin stained section of demineralized tissue from calcifying epithelial odontogenic tumor. The section shows numerous areas of calcified tumor tissue. $\times 155$.

B. Van Gieson stained section of tumor from A. Note sparsity of collagen. $\times 155$.

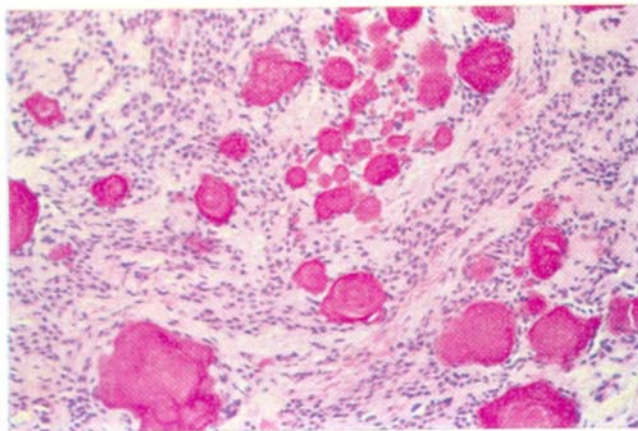
C. PAS stained section of tumor from A. Note strong PAS-positive reaction in calcified areas. $\times 155$.



A



B



C



Fig. 4. Small islands of tumor tissue exhibiting pyknosis of nuclei. $\times 600$.

which the cytoplasm has increased in size and become homogeneous with crescentic nuclei. In many areas the homogeneous substance has become the seat of calcification (Color plate A). The areas of calcification exhibit Liesegang's rings. Eventually, the calcified areas fuse together forming small conglomerates. The calcified cells show a strongly positive for PAS reaction after diastase-treatment (Color plate C). Most often, however, the homogenization and enlargement of cytoplasm lead to disruption of the cell membrane, whereby the homogeneous areas are lying free in the stroma. By means of the van Gieson stain, which stains the homogeneous areas yellow, these areas can easily be distinguished from the red-stained stroma containing collagen fibers (Color plate B). Apparently, the homogeneous substance remains almost unaffected as areas with tumor tissue contain only small amounts of collagen. Occasionally, the free homogeneous substance is surrounded by a tissue which is faintly metachromatic. After the tumor tissue has undergone some intracellular degeneration, small islands of epithelial cells exhibit pyknosis (Fig. 4).

Amyloid is also demonstrable in the tumor tissue, but this finding has been included in the study by *Ranløv & Pindborg* (1966). Eighteen months after the operation the patient did not show any signs of recurrence.

DISCUSSION

The tumor described above fulfills the following criteria for a calcifying epithelial odontogenic tumor: 1) presence of sheets of polyhedral cells, 2) development of an intracytoplasmic homogeneous substance, 3) occasional calcification of the homogeneous substance, and 4) rupture of the cell walls leaving calcified areas or pools of homogeneous substance in the stromal tissue. The present tumor, however, differs from most of the previously reported cases of calcifying odontogenic tumors by 1) being extra-osseous, 2) not being associated with an embedded tooth, and 3) not exhibiting great variations in the size and shape of nuclei of the tumor cells. Only one other extra-osseous case is known to the author and that is *Howell's* second case (see Table I), which also originated from the attached gingiva and was not associated with an embedded tooth.

The extra-osseous location raises the question about the origin of the tumor. The previously reported cases have lent support to the assumption that the tumor originates from a pre-existing dentigerous cyst and the tumor is the result of continued proliferation by the cells of the reduced enamel epithelium and in particular those of the original stratum intermedium. However, based on the case reported here, the present author can not exclude the possibility that the oral epithelium may be a site of origin. Unfortunately, the oral epithelium was not included in the surgical specimen from the present tumor. We know, however, from ameloblastomas and dentinomas that they may develop from the basal layer of the oral epithelium (*Manley, 1954, Pindborg, 1966*).

When comparing, histologically, the cases of the calcifying epithelial odontogenic tumor published so far it becomes evident that the tumor shows a great range of variation. In some cases the cellular picture is one of extreme pleomorphism, whereas others, for example, the present case, exhibit a rather uniform appearance of the tumor cells. Also the tendency of calcification

of the homogeneous substance varies a great deal. It is interesting to compare the strong PAS-positive reaction in the calcifying homogeneous substance with the same intensity of reaction in the calcifying epithelial metaplasia in ameloblastomas (*Pindborg & Weinmann*, 1958). In both types of odontogenic tumors the calcification seems to be preceded by a marked PAS-reaction. In his extensive histochemical study of the calcifying epithelial odontogenic tumor *Gon* (1965) explains the stromal changes by the production of a dermolytic enzyme causing destruction of collagen and reticulin, which is replaced in part by accumulations of the homogeneous substance produced by the tumor cells.

The present study supports the view expressed previously by *Pindborg* (1958) and confirmed by *Gon* (1965) and *Shear* (1965) that the calcifying epithelial odontogenic tumor ought to be considered a distinct entity among the epithelial odontogenic tumors. Apparently, the tumor is not so rare as was once supposed. Several cases might also appear from files where they have been recorded under other names.

SUMMARY

Twenty-six cases of the calcifying epithelial odontogenic tumor, derived from the literature and some unpublished cases, are reviewed with regard to sex, age distribution and location.

A case occurring in a 29-year-old woman is presented. The tumor was located, extra-osseously, in the attached gingiva of the upper left lateral incisor. The tumor, which histologically presented the typical features of a calcifying epithelial odontogenic tumor, appeared to have developed from the epithelium of the oral mucosa.

RÉSUMÉ

TUMEUR ÉPITHÉLIALE CALCIFIÉE ODONTOGÉNIQUE

REVUE DE LA LITTÉRATURE ET COMPTE-RENDU D'UN CAS EXTRA-OSSEUX

Vingt-six cas de tumeurs épithéliales calcifiées odontogénique, provenant de la littérature et quelques cas non publiés sont passés en revue en ce qui concerne le sexe, la répartition par âge et la localisation.

L'auteur présente un cas survenu chez une femme de 29 ans. La tumeur est extra-osseuse et localisée dans la gencive alvéolaire de l'incisive latérale supérieure gauche. La tumeur, qui présentait du point de vue histologique les traits typiques d'une tumeur épithéliale calcifiée odontogénique, semblait s'être développée au dépens de l'épithélium de la muqueuse buccale.

ZUSAMMENFASSUNG

DER KALZIFIZIERENDE, ODONTOGENE EPITHELIALE TUMOR ÜBERSICHT DER LITERATUR UND BERICHT EINES EXTRAOSSEALEN FALLES

Die Literatur und einige nicht veröffentlichte Fälle des kalzifizierenden, epithelialen, odontogenen Tumors (im ganzen 26 Fälle) wurden hinsichtlich des Geschlechts und der Verteilung nach Alter und Ort untersucht.

Der Fall einer 29-jährigen Frau wird näher beschrieben. Ihr Tumor wurde extraosseal, an der Gingiva propria von +2 gefunden und zeigte histologisch typische Züge eines kalzifizierenden, odontogenen Tumors, der sich vermutlich aus dem Epithel der oralen Mucosa entwickelt hat.

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