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A clinicopathological and immunohistochemical study of the calcifying epithelial odontogenic tumour (Pindborg tumour) in Malaysians

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Abstract

We reviewed the clinicopathological characteristics of 13 cases of calcifying epithelial odontogenic tumour (CEOT) (Pindborg tumour) diagnosed in the Division on Stomatology, Institute for Medical Research, Kuala Lumpur, over a 29-year period. There were eight female and five male patients. These consisted of eight (61.5 per cent) Malays, three (23.1 per cent) Chinese, one (7.7 per cent) Indian and one (7.7 per cent) Melanau. Their ages at presentation ranged from 19-61 years (mean age, 31.8 years). There were 12 central and one peripheral CEOT. Of these, 76.9 per cent of cases were located in the maxilla, the remaining in the mandible. The commonest clinical diagnosis was a dentigerous cyst (66.7 per cent). Enucleation was the main mode of treatment. Histologically, sheets and strands of polyhedral epithelial cells containing eosinophilic, homogeneous globules with Liesegang rings were observed. One case also showed extensive calcification and clear cell differentiation. Immunohistochemistry revealed a variable keratin staining of the CEOT epithelium, confirming its heterogeneity.

Key words: Jaw neoplasms; Odontogenic tumours

Introduction

The calcifying epithelial odontogenic tumour (CEOT) is a benign odontogenic epithelial neoplasm that occurs rarely in the jaws. The name CEOT was given by Pindborg (1955) who was the first to categorize it as a distinct clinicopathological entity. Consequently, this neoplasm was also widely known by its eponymous term, Pindborg tumour (Vap *et al.*, 1970; Wallace and MacDonald, 1974; Leipzig and Yau, 1982; Baunsgaard *et al.*, 1983; El-Labban, 1990; Takata *et al.*, 1993). In this article both terms will be used interchangeably.

The CEOT is an uncommon odontogenic neoplasm that comprises from 0.17 per cent to 1.8 per cent of all odontogenic tumours (Krolls and Pindborg, 1974; Franklin and Pindborg, 1976; Ai-Ru *et al.*, 1982). Most of these lesions arise centrally within the jaws especially in the premolar-molar region of the mandible (Franklin and Pindborg, 1976). A rare peripheral variant (five per cent) that occurs in the anterior maxillary or mandibular gingiva has also been described (Patterson *et al.*, 1969; Franklin and Pindborg, 1976; Takeda *et al.*, 1983). The CEOT generally affects patients around 40 years of age, exhibits no sex predilection and presents with few symptoms. Its radiographic characteristics include pericoronal radiolucencies in association with unerupted teeth and presence of scattered radiopacities within a radiolucent area (Oikarinen *et al.*, 1976; Andrade *et al.*, 1992; Lee *et al.*, 1992). Histologically it is composed of sheets of polyhedral epithelial cells associated with eosinophilic, homogeneous globules probably of an amyloid-like nature (Franklin and Hindle, 1976), which may become calcified and which may be liberated as the cells break down (Kramer *et al.*, 1992).

This study describes the clinicopathological features of 13 cases of CEOT diagnosed in the Division of Stomatology, Institute for Medical Research over a 29-year period. The immunohistochemical staining characteristics of these tumours, using markers for intermediate filament proteins, are also presented.

Materials and methods

Thirteen cases of CEOT of the jaws were retrieved from the biopsy records of the Division of Stomatology, Institute for Medical Research, Kuala Lumpur, for this study. These represented reported and consequent cases diagnosed in this division over a 29-year period (1967-95). The definition of a CEOT according to WHO (Kramer *et al.*, 1992) was applied in the selection of these cases. Clinical data with

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TABLE I
CLINICAL FINDINGS OF 13 CASES OF PINDBORG TUMOUR IN MALAYSIAN PATIENTS (1967–95)

Case	Age/Sex/Race	Site	Duration	Clinical presentation	Radiological presentation	Clinical diagnosis	Treatment
1.	19/F/Chinese	(R) maxilla (premolar-molar region)	1 year	Painless, bony-hard slow growing swelling. Bucco-palatal expansion	RL lesion with embedded (R) max. second premolar	AOT	Enucleation
2.	20/F/Chinese	(R) maxilla (incisal region)	UK	Firm, non-tender swelling	Buried (R) max. central and lateral incisors surrounded by abnormal bone	NA	Enucleation
3.	20/F/Malay	(L) maxilla (canine region)	1 month	Swelling. (L) max. canine clinically missing	RL lesion surrounding unerupted (L) max. canine	Dentigerous cyst	Enucleation
4.	20/F/Malay	(L) maxilla (canine-premolar region)	3 months	Buccal swelling Size: 2 cm	RL lesion surrounding unerupted (L) max canine and first premolar.	Dentigerous cyst	Enucleation
5.	21/M/Malay	(R) maxilla (canine region)	NA	Swelling. (R) max. canine clinically missing	RL lesion surrounding (R) max. canine	Dentigerous cyst	Enucleation
6.	24/M/Halay	(R) mandible (canine-premolar region)	1 year	Cystic swelling. (R) mand. first premolar clinically missing	ML lesion with unerupted (R) mand. first premolar	Dentigerous cyst	Enucleation
7.	28/F/Chinese	(R) mandible	NA	NA	NA	Dentigerous cyst	Enucleation
8.	31/F/Malay	(R) mandible (pre-molar-molar region)	2 months	Bony hard swelling on buccal aspect. Nontender	NA	Ossifying fibroma	Curettage
9.	31/M/Indian	(L) maxilla (pre-molar-molar region)	8 months	Painless, cystic swelling Gradual increase in size	NA	Dental cyst	Enucleation
10.	32/F/Melanau	(L) maxilla (premolar region)	2 week	Swelling	Unerupted tooth in RL lesion	Dentigerous cyst	Enucleation
11.	52/M/Malay	(R) maxilla (canine-premolar region)	1 year	Painless firm swelling on edentulous area	Erosion of underlying alveolar bone	NA	Excision
12.	55/M/Malay	(L) maxilla (third molar region)	NA	Ulcerated growth extending to hard and soft palate	(L) antrum involvement	NA	NA
13.	61/F/Malay	(R) maxilla (posterior alveolus)	>1 year	Large swelling with recurrent episodes of infection. Slowly increasing in size.	NA	Osseous neoplasm	Enucleation

F = Female (R) = Right NA = Not available max. = maxillary RL = Radiolucent AOT = Adenomatoid odontogenic tumour
M = male (L) = Left UK = Unknown mand. = mandibular ML = Multilocular

respect to age, gender, race, site, symptoms, radiological appearance, clinical diagnosis and treatment were obtained from case summaries accompanying these biopsy specimens. Radiographs, where available were also examined.

For light microscopic study, 4-5 μm thick sections of all cases stained with haematoxylin and eosin, and Congo red were examined.

For immunohistochemistry, 4–5 μm thick deparaffinised sections were utilized. Three intermediate filament proteins i.e. polyclonal keratin (TK; 41–65 kDa), monoclonal vimentin (57 kDA) and monoclonal desmin (53 kDa) were applied. The peroxidase-antiperoxiodase (PAP) technique was employed to detect keratin while the indirect method was performed for the identification of vimentin and desmin. Known positive controls were included for all antisera. Negative control staining was obtained by substituting the primary antibody with non-immune serum. All immunoreagents were obtained from Dakopatts, Copenhagen, Denmark.

Results

Clinical findings

Thirteen cases of CEOT were studied. Their clinical data are summarised in Table I. There were five male and eight female patients (male to female ratio was 1:1.6). These consisted of eight (61.5 per cent) Malays, three (23.1 per cent) Chinese, one (7.7 per cent) Indian and one (7.7 per cent) Melanau. Their ages at presentation ranged from 19 to 61 years (mean age, 31.8 years). There were 12 intraosseous and one extraosseous CEOT. Of these, 76.9 per cent occurred in the maxilla, the rest in the mandible. Radiographically, most cases presented as radiolucent lesions with variable amounts of scattered radiopacities (Figures 1 and 2). Six of the nine cases with known radiographic information were associated with unerupted teeth often mimicking a dentigerous cyst (Figure 2). A painless, slow-growing swelling was the commonest presenting symptom. Their duration of symptoms ranged from two weeks-

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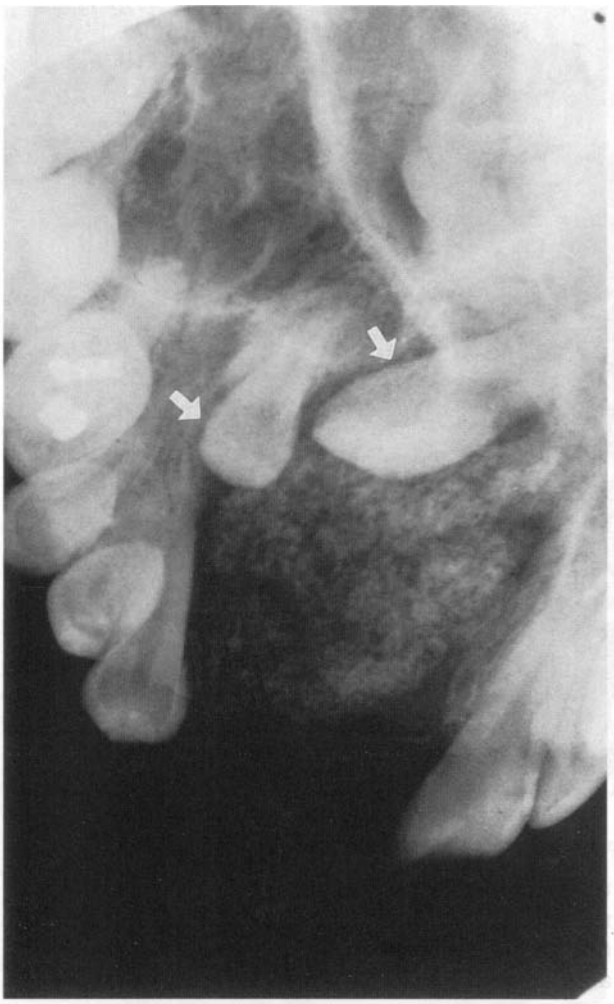

FIG. 1

Case No. 2 showing a maxillary lesion with a mixed radiolucent radiopaque appearance. Note unerupted right central and lateral incisors (arrows) in close relationship with the lesion.

one year (mean, 6.9 months). Enucleation was the main mode of treatment. One case presented with recurrence.

Macroscopic findings

The specimens in three cases consisted of soft tissue, another five were cyst linings which appeared to be attached to the amelocemental region of the associated tooth, and remaining five composed of an admixture of hard and soft tissues. In all, their sizes ranged from 1.0–4.0 cm at the greatest diameter.

Microscopic findings

In all cases, the lesional tissue consisted of varying proportions of polyhedral epithelial cells arranged in sheets and strands amongst a loose connective tissue stroma (Figures 3 and 4). These epithelial cells exhibited mild cellular and nuclear pleomorphism but mitoses were generally absent. Intercellular bridges were also occasionally evident. In addition, homogeneous eosinophilic spheroidal bodies of varying sizes were present within the tumour epithelium

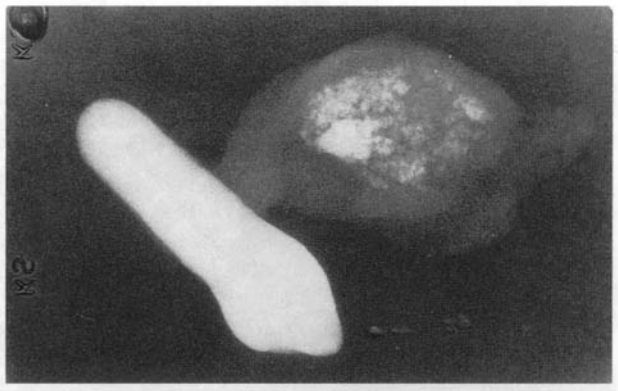

FIG. 2

Case No. 10. Radiograph of enucleated specimen showing a radiolucent lesion with scattered radiopacities. Note that the lesion is attached to the cervical region of the canine tooth.

and intervening stroma (Figure 3). These globules were Congo red positive and gave an apple-green birefringence under polarized light indicative of amyloid; concentric lamellar calcifications (Liesegang rings) within these bodies were also noted (Figure 4). In one case (No. 6) large amounts of mineralised tissue were associated with small clusters and nests of epithelial cells with a clear or vacuolated cytoplasm were observed (Figure 5): the former consisted of acellular cementum-like tissue with entrapped discrete or coalescing calcified lamellar bodies (Figure 5).

Immunohistochemical findings

In all cases, the tumour epithelium expressed variable keratin positivity with cells immediately surrounding the homogeneous globules showing the most intense staining (Figure 6). No reactivity for vimentin and desmin within the tumour epithelium was observed.

Discussion

This study shows that the Pindborg tumour is an uncommon jaw lesion among Malaysians. It accounts for about 0.6 per cent of all odontogenic neoplasms (as listed in the WHO monograph on *Histological Typing of Odontogenic Tumours*) (Kramer *et al.*, 1992) diagnosed in the Division of Stomatology over a 29-year period. The reported frequency of occur-

TABLE II

COMPARISON OF DEMOGRAPHICS OF CEOT IN PUBLISHED AND PRESENT SERIES

	Krolls and Pindborg (USA, 1974)	Ai-Ru *et al.* (China, 1982)	Present series (Malaysia, 1995)
Total number of cases	23	9	13
Frequency of occurrence	0.17%	1.8%	0.6%
Age range (year)	8–72	20–64	19–61
Mean age (year)	32.5	34.2	31.8
Male: Female ratio	1.3:1	1:3.5	1:1.6
Maxilla	5	8	10
Mandible	18	1	3
Intraosseous CEOT	22	7	12
Extraosseous CEOT	1	2	1

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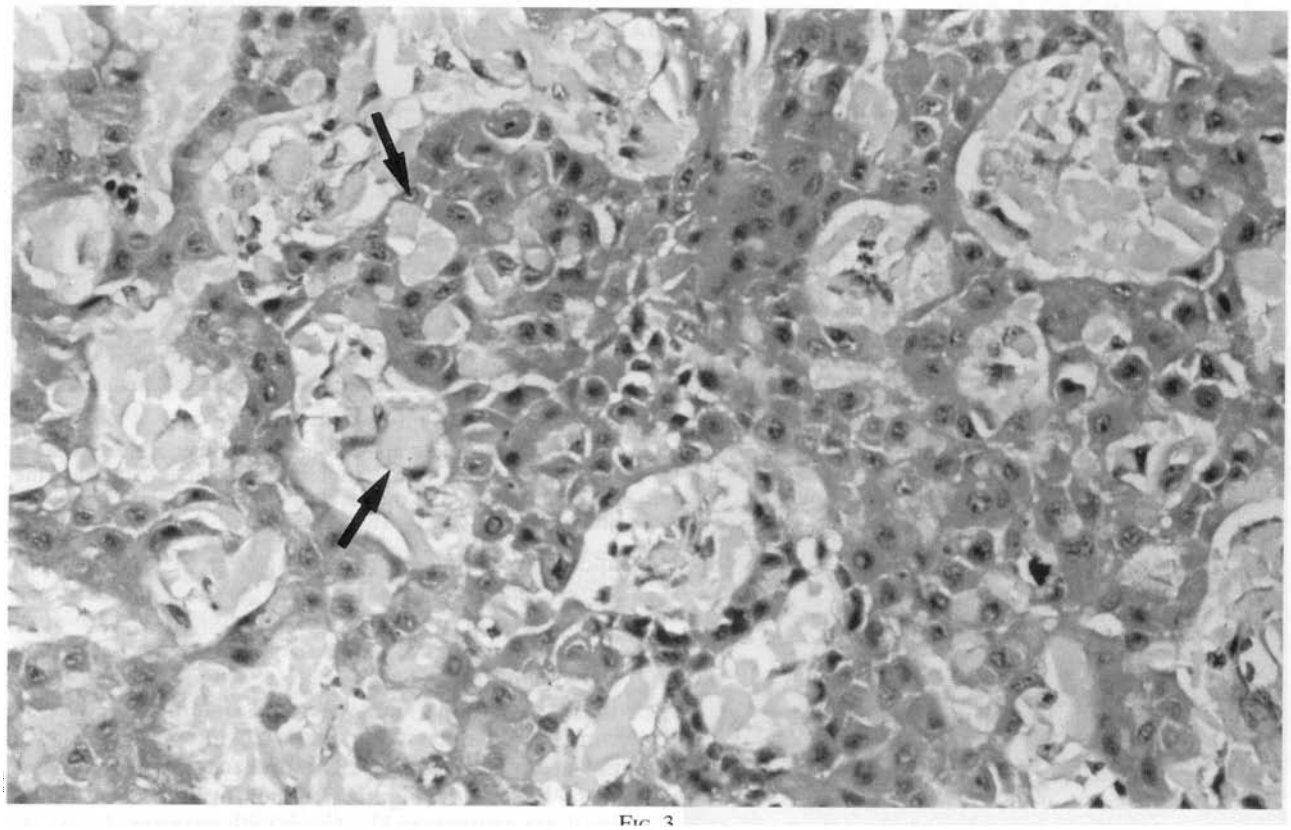

FIG. 3

Pindborg tumour. Note sheets of epithelial cells and entrapped homogeneous globules (arrows). (H&E; ×200).

rence of this neoplasm ranges from 0.17 per cent to 1.8 per cent (Krolls and Pindborg, 1974; Franklin and Pindborg, 1976; Ai-Ru *et al.*, 1982). A comparative analysis of the demographic characteristics of this tumour in Caucasians, Chinese and Malaysians revealed certain similarities and discrepancies (Table II). Age range and mean age were comparable in all three series. However the pattern of sex

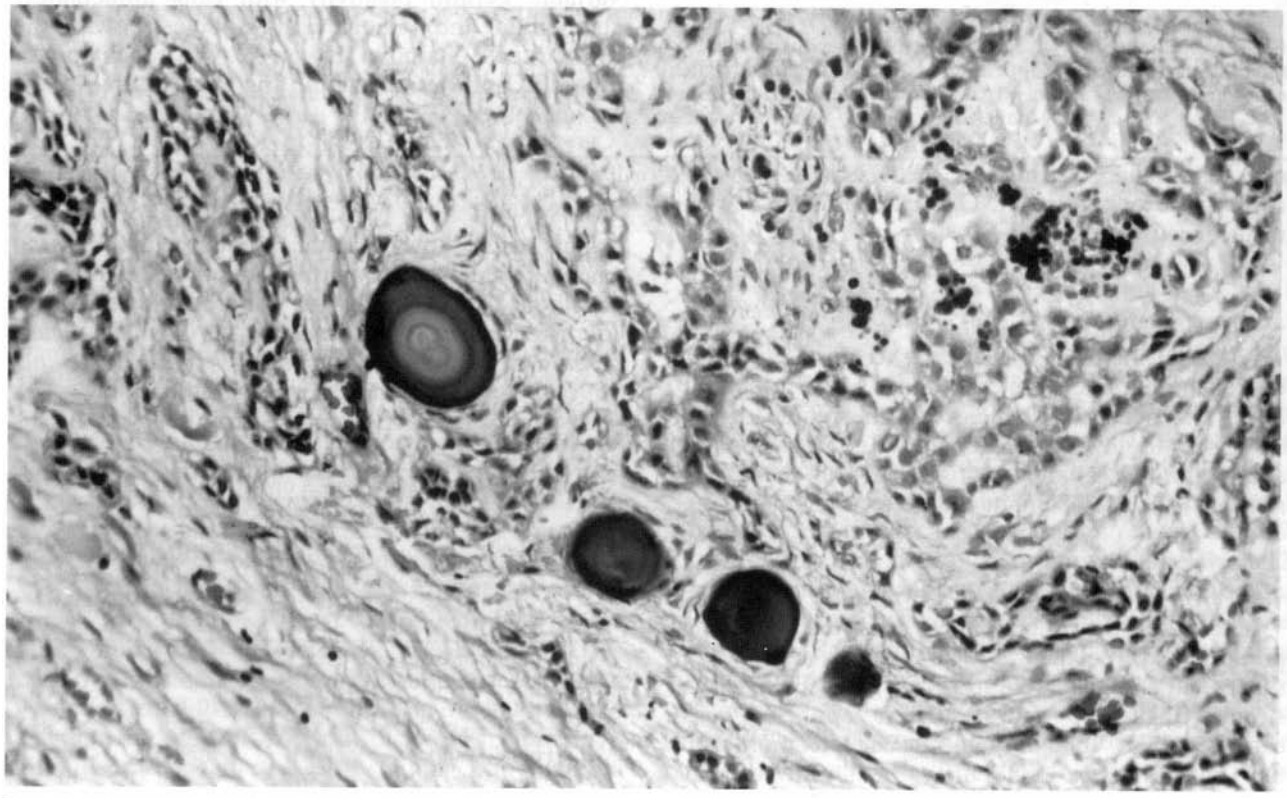

FIG. 4

Photomicrograph showing strands of tumour epithelium and scattered calcified, laminated spheroidal bodies. (H&E; ×100).

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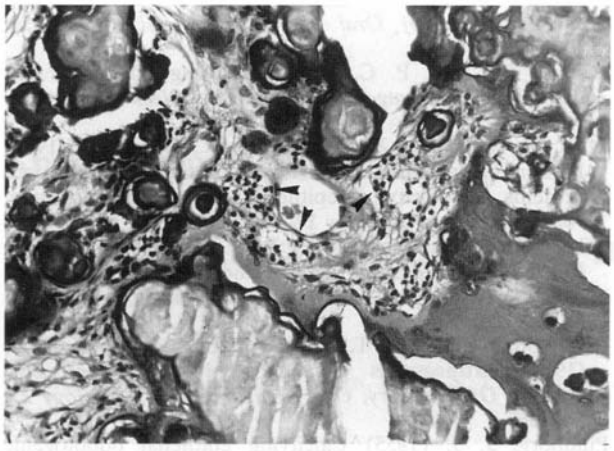

FIG. 5

Case No. 6 showing coalescing globules, sheets of acellular cementum-like tissue and nests of clear cell epithelium (arrows). (H&E; ×100).

distribution in our series seems to correlate more with Ai-Ru *et al.'s* study (1982). Furthermore, CEOT in Asians tended to occur more in the maxilla as opposed to a predilection for the mandible in instances of CEOT occurring in Caucasians. Extra-osseous lesions were generally rare with only one case (No. 11) reported in the present series.

Other than the central and peripheral variants of this neoplasm, the CEOT may also occur in the so-called combined epithelial odontogenic tumour (AOT-CEOT) (Damm *et al.*, 1983; Siar and Ng, 1987, 1991). The latter comprises primarily areas of adenomatoid odontogenic tumour (AOT) with smaller foci of CEOT. All three tumours i.e. AOT, AOT-CEOT and CEOT have been studied in Malaysians (Siar *et al.*, 1987; Siar and Ng, 1991; present study). Despite some overlapping clinical and histological characteristics, the AOT and AOT-CEOT are benign hamartomatous entities in contrast to the CEOT which is viewed as a locally-invasive neoplasm.

The histological characteristics of the CEOT are well-delineated (Kramer *et al.*, 1992). Over the years cellular variants namely clear cell, pigmented, Langerhans-cell containing, bone and cementum forming, and noncalcifying subtypes have been identified (Richardson *et al.*, 1974; Greer and Richardson, 1976; Asano *et al.*, 1990; El-Labban, 1990; Slootweg, 1991; Takata *et al.*, 1993). One case in our series also presented with clear cells and extensive acellular cementum-like calcification. The clinical significance of these cellular variations remains unclear.

In our limited immunohistochemical study, the observed variable keratin staining intensity of the CEOT epithelium confirmed previous findings that the latter is composed of a heterogeneous population of cells (Mori *et al.*, 1988). However, coexpression of vimentin and keratin within the tumour epithelium as previously reported (Mori *et al.*, 1988) was not observed here.

The Pindborg tumour is considered a less aggressive tumour than the ameloblastoma and responds well to conservative surgery. The reported recurrence rate ranges from 10 per cent to 14 per cent

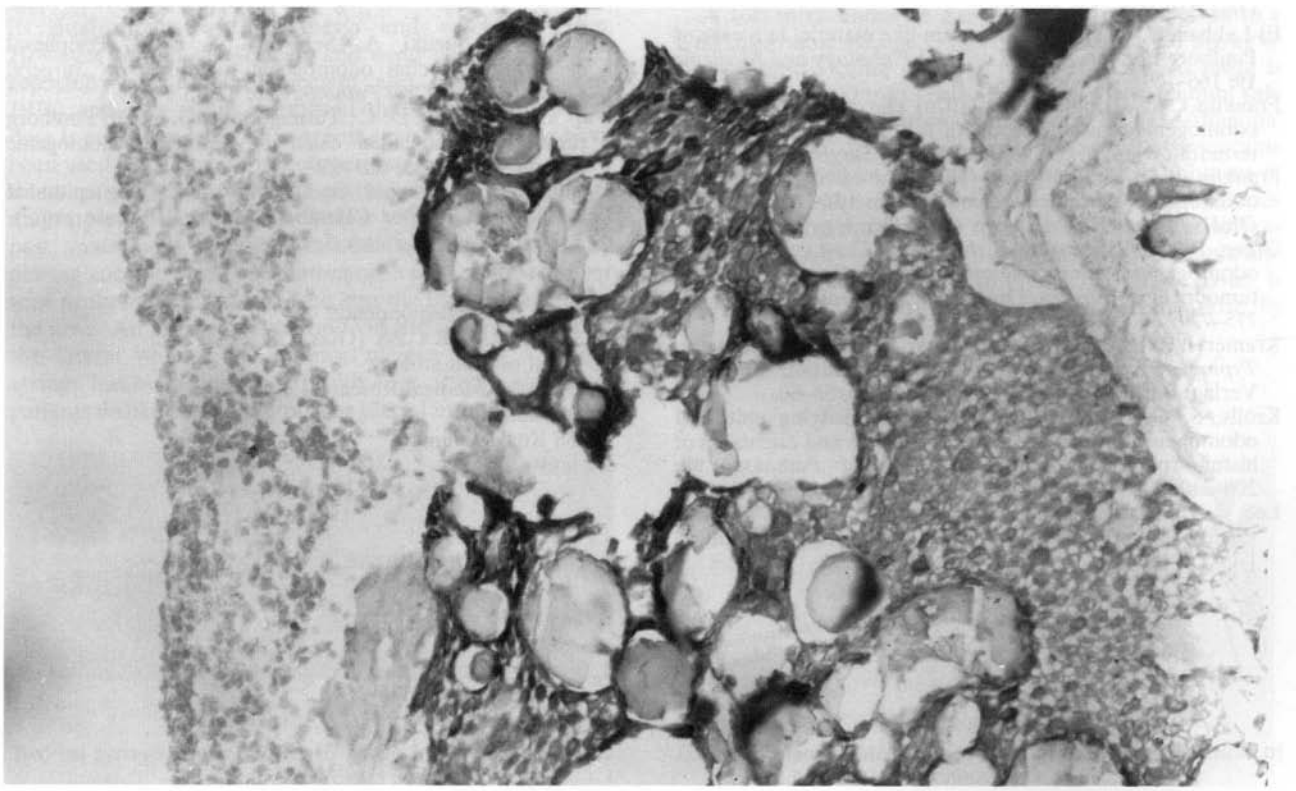

FIG. 6

Tumour epithelium expressing variable keratin positivity with those cells immediately surrounding the homogeneous globules showing the most intense staining. (PAP; ×100).

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(Krolls and Pindborg, 1974; Franklin and Pindborg, 1976). In our series, most of the cases were treated conservatively by enucleation. However, the outcome of their treatment and recurrence rate could not be evaluated due to the lack of follow-up information.

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