J Oral Pathol Med (2005) 34: 558–64

www.blackwellmunksgaard.com/jopm

Cytokeratin expression patterns for distinction of odontogenic keratocysts from dentigerous and radicular cysts

Christian Stoll[1], Carolin Stollenwerk[1], Dieter Riediger[1], Christian Mittermayer[2], Joachim Alfer[2]

[1]*Department of Oral and Maxillofacial Surgery, Aachen University of Technology, Aachen;* [2]*Institute of Pathology, Düren Hospital, Düren, Germany*

BACKGROUND: The clinical outcome of treatment of odontogenic cysts differs depending on separate entities. Particular clinical relevance must be attached to the distinction between odontogenic keratocysts, which have an evident tendency to recur, and other odontogenic cysts. The aim of this study was to evaluate cytokeratin (CK) expression patterns as an additional tool for characterization of different cysts as the histomorphologic appearance often is not decisive.

METHODS: Thirty cases of dentigerous and radicular cysts respectively as well as 15 cases of odontogenic keratocysts were considered. Expression of CK 5/6, 7, 10, 13, 17, 19 and 20 was determined in addition to Ki-67 immunohistochemically.

RESULTS: Expression of CK 17 was discernible in 93.3% of the odontogenic keratocysts, but only in 35.0% of dentigerous and radicular cysts under study ($P < 0.001$). CK 19 could be detected in 48.3% of dentigerous and radicular cysts, whereas odontogenic keratocysts were completely negative ($P < 0.002$).

CONCLUSION: Immunohistochemical detection of CK 17 and 19 seems to be a valuable additional parameter distinguishing between odontogenic keratocysts and other odontogenic – especially dentigerous – cysts which clinically are likely the most significant differential diagnoses in this context.

J Oral Pathol Med (2005) **34**: 558–64

Keywords: cytokeratin; dentigerous cyst; immunohistochemistry; keratocyst; odontogenic; radicular cyst

Introduction

Radicular cysts arise from the epithelial residues (rest of Malassez) in the periodontal ligament as a consequence of inflammation which usually follows the death of a dental pulp (1) and represent a part of more than a half of all odontogenic cysts (2). If a radicular cyst is retained in the jaws after removal of the associated tooth, the most characteristic sign, namely the adjacent root of a devital tooth, is missing. Differential diagnosis in relation to other cystic lesions may be difficult, particularly because the morphology of the epithelium varies depending on the degree of inflammation.

The dentigerous cyst is the most second-frequent cystic lesion of the jaws which usually encloses the crown of an unerupted tooth and is attached to its neck (2). It develops by pericoronal or intraepithelial accumulation of fluid spawned by the reduced enamel epithelium and is most often found in relation to the mandibular third molar (1). Histologically, the cystic wall is composed of a thin layer of connective tissue lined by two or three epithelial cell layers. The odontogenic keratocyst arises mainly posterior to the mandibular third molar and is characterized by a thin fibrous capsule and a lining of keratinized stratified squamous epithelium usually about five to eight cells in thickness. A keratocyst may envelop an adjacent unerupted tooth and sometimes a tooth may erupt into the cavity of a keratocyst. Such cases may be erroneously diagnosed as dentigerous cysts with keratinized lining. In contrast to radicular or dentigerous cysts, odontogenic keratocysts have a marked tendency to recur because of epithelial islands within the adjacent connective tissue or even separate daughter cysts (1, 3, 4).

There have been many attempts to confirm differential diagnosis by methods exceeding clinical examination, radiography, and histomorphology (3, 4) including determination of cytokeratin (CK) expression (5–18), but the variability of the results from different laboratories suggests the need for further refinement and standardization of the methodology (19). CKs are α-type fibrous polypeptides with molecular masses ranging from 40 to 68 kDa and are generally held to belong to the most fundamental markers of epithelial differentiation. In various human epithelia 20 distinct CK polypeptides have been revealed which can be divided into an acidic and a neutral-basic type subfamily (20). In the present immunohistochemical study, a panel of seven monoclonal antibodies was used to characterize

Correspondence: Priv.-Doz. Dr Dr C. Stoll, Department of Oral and Maxillofacial Surgery, University of Aachen, Pauwelsstraße 30, D-52074 Aachen, Germany. Tel.: +49 241 80 88267, Fax: +49 241 80 33 88267. E-mail: cstoll@ukaachen.de
Accepted for publication June 8, 2005

specific patterns of CK expression and localization. In addition, the proliferating activity was measured by Ki-67 detection.

Materials and methods

Thirty cases of dentigerous and radicular cysts respectively as well as 15 cases of odontogenic keratocysts were included. The individual diagnoses were carefully reconsidered by consensual interdisciplinary examination of clinical characteristics, radiographic features, and histomorphologic signs after routine staining with hematoxylin and eosin in each case. At operation, the youngest patient was 11 years and the oldest was 78 years of age, with a mean value of 38.2 years. Forty-seven patients were male and 28 female. Dentigerous cysts came from the mandible in 21 cases and from the maxilla in nine cases, mainly associated with the third molars. Radicular cysts were localized to the lower jaw in 13 and to the upper jaw in 17 cases. Half of these cases were found in the molar region, while the others were distributed over premolars, canines and incisors. Ten of the 15 odontogenic keratocysts included in this study were restricted to the mandibular angle. None of the patients was affected by a basal cell nevus syndrome (21).

Expression of CK 5/6, 7, 10, 13, 17, 19, 20 and Ki-67 was determined immunohistochemically using a standard biotin–streptavidin method. In brief, all of the cystic specimens had been routinely fixed in a solution of 4% formaldehyde in phosphate-buffered saline (PBS) at pH 7.6 and embedded in paraffin. Histologic sections were cut at 4 μm and mounted on poly-L-lysine-coated slides. Following dewaxing and rehydration, antigen retrieval was performed by heating in a microwave oven for 2×8 min at 600 W in a 10 mM aqueous citrate buffer at pH 6.0 under continuous equilibration of evaporated water. Primary monoclonal antibodies were obtained from DakoCytomation (Glostrup, Denmark) with the exception of anti-CK 19 antibody which was purchased from Sigma (St Louis, MO, USA). Clones, references, and dilutions are given in Table 1. In addition, negative controls, where the primary antibody was omitted, as well as controls with negative control mouse IgG1 (X 0931, clone DAK-GO1, dilution 1:100), IgG2a (X 0943, clone DAK-GO5, dilution 1:20), and IgG2b (X 0944, clone DAK-GO9, dilution 1:20, all from DakoCytomation) were used in order to demonstrate that the antibodies do not bind unspecifically to the tissue sections. For detection of CK 10, 13, 17, and Ki-67 the primary antibodies were diluted in PBS at pH 7.6 and the slides incubated for 1 h at 37°C. Incubation of the secondary biotinylated rabbit-antimouse antibody (DakoCytomation) at 37°C and the biotin–streptavidin complex conjugated with alkaline phosphatase (DakoCytomation) at room temperature followed for 30 min respectively. New Fuchsine was used as chromogen and Mayers haemalum for counterstaining. Finally, the slides were covered with Kaisers' glycerin gelatin and mounted with coverslips. For detection of CK 5/6, 7, 19, and 20 a TechMate™ 500, Automated Immunostainer with a ChemMate™, Peroxidase/DAB, Rabbit/Mouse Detection Kit (Dako) was used exactly following the instructions of the supplier (22).

Evaluation of the slides was performed by light microscopy at a 100- and 250-fold magnification. Assessing the expression of CKs determined in this study, those cases were classified as positive which showed positive cytoplasmic staining in more than 10% of the epithelial cells, whereas the others were defined as negative. In addition, the epithelial layers predominantly containing the positive cells were noted. For estimation of the proliferation activity, Ki-67-positive cell nuclei were counted in 10 randomly chosen visual fields of the cystic epithelium at a 400-fold magnification in each case. Statistical analysis was calculated with STATISTICA 6.1 data analysis software system (StatSoft, Tulsa, OK, USA) using Yates corrected chi-square test. A probability level of < 0.05 was regarded as statistically significant.

Results

CK 5/6 could be detected immunohistochemically in nearly all of the specimens included in this study independently of the relation to separate entities (Fig. 1). Only one of 30 dentigerous cysts and one of 15 odontogenic keratocysts were negative, whereas all of the others including the whole of the radicular cysts were positive without limitation of the staining to one or more particular cell layers.

CK 7 was discernible in only 12 of 30 radicular cysts and positive staining was restricted to the suprabasal and in three of 12 cases even to the superficial cell layers (Fig. 2a). In contrast, dentigerous cysts showed a positive staining in 23 of 30 cases (Fig. 2b). This represents a statistically significant difference between

Table 1 Clones, references, and dilutions of the primary antibodies used for immunohistochemistry

Primary antibody	*Clone*	*Isotype*	*Reference*	*Dilution*
Monoclonal mouse antihuman cytokeratin 5/6	D5/16 B4	IgG1, κ	(24)	1:200
Monoclonal mouse antihuman cytokeratin 7	OV-TL 12/30	IgG1, κ	(26)	1:800
Monoclonal mouse antihuman cytokeratin 10	DE-K10	IgG1, κ	(28)	1:100
Monoclonal mouse antihuman cytokeratin 10/13	DE-K13	IgG2a, κ	(30)	1:100
Monoclonal mouse anticytokeratin 17	E3	IgG2b, κ	(32)	1:20
Monoclonal anticytokeratin peptide 19	A53-B/A2	IgG2a, κ	(34)	1:20
Monoclonal mouse antihuman cytokeratin 20	K_s 20.8	IgG2a, κ	(36)	1:200
Monoclonal mouse antihuman Ki-67 antigen	MIB-1	IgG1, κ	(37)	1:60

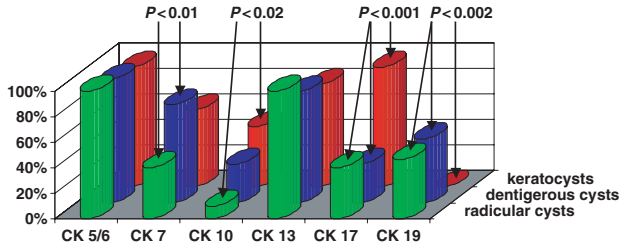

Figure 1 Percentage share of positive results in immunhistochemical staining against cytokeratins (CK) 5/6, 7, 10, 13, 17, and 19 detected in different entities of odontogenic cysts. Significant differences are indicated by probability levels.

radicular and dentigerous cysts at a probability level of < 0.01 (Fig. 1). However, staining pattern was similar to that of the radicular cysts with limitation of the positive cells to the suprabasal (20 of 23 cases) and superficial (three of 23 cases) layers. Odontogenic keratocysts were positive in nine of 15 cases and, once more, the basal layer was left blank in each case.

Only three of 30 radicular and nine of 30 dentigerous cysts showed a superficial expression of CK 10, while the others were completely negative (Fig. 3a). Odontogenic keratocysts were positive in seven of 15 cases and positive staining was visible in all of the suprabasal cell layers (Fig. 3b). Thus, a significant CK 10 was more frequently observed in keratocysts than in radicular cysts ($P < 0.02$; Fig. 1).

The distribution of the CK 13 expression was comparable to that of CK 5/6 with positive staining in nearly all of the cell layers in 30 of 30 radicular cysts, 26 of 30 dentigerous cysts and 12 of 15 odontogenic keratocysts (Fig. 1). A superficial staining was discernible in only five of 75 lesions at all.

Strong expression of CK 17 was evident in 14 of 15 odontogenic keratocysts with extension over the entire cystic epithelium (Fig. 4c). In contrast, a positive staining was discernible in only 12 of 30 radicular and nine of 30 dentigerous cysts. Moreover, in these cases staining appeared to be notably weaker and was restricted to isolated cell layers (Fig. 4a,b). However,

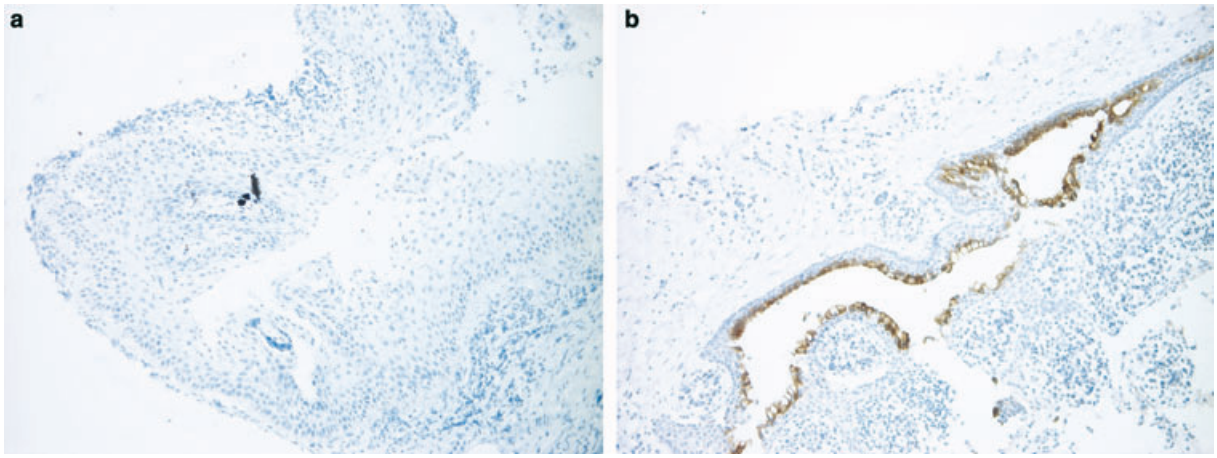

Figure 2 Lack of cytokeratin 7 expression in a radicular cyst (a) and positive superficial staining in a dentigerous cyst (b; original magnification ×100; chromogen: DAB).

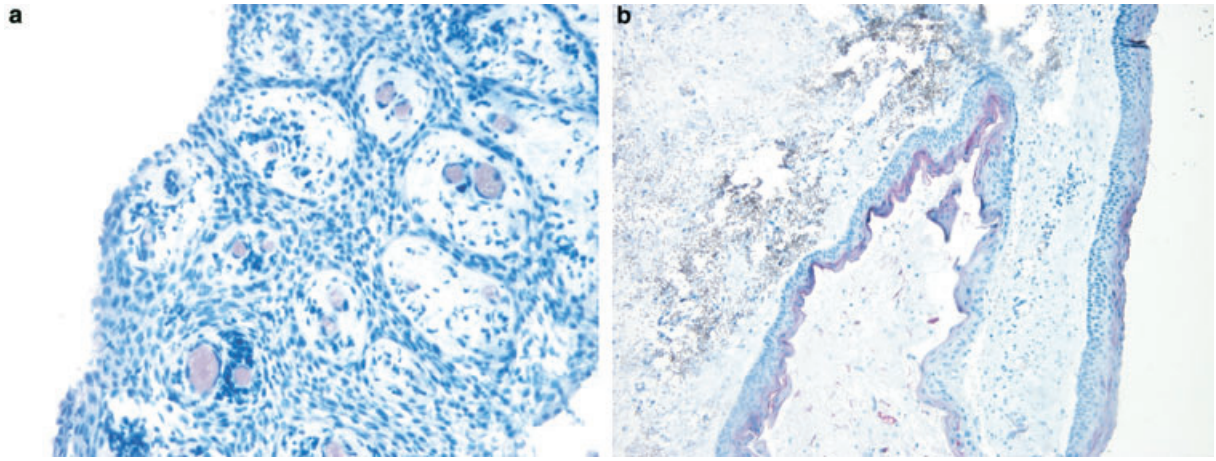

Figure 3 Negative immunohistochemical staining against cytokeratin 10 in the epithelium of a radicular cyst (a) and a positive result in the suprabasal layers of an odontogenic keratocyst (b; original magnification ×250 in 'a', ×100 in 'b'; chromogen: New Fuchsine).

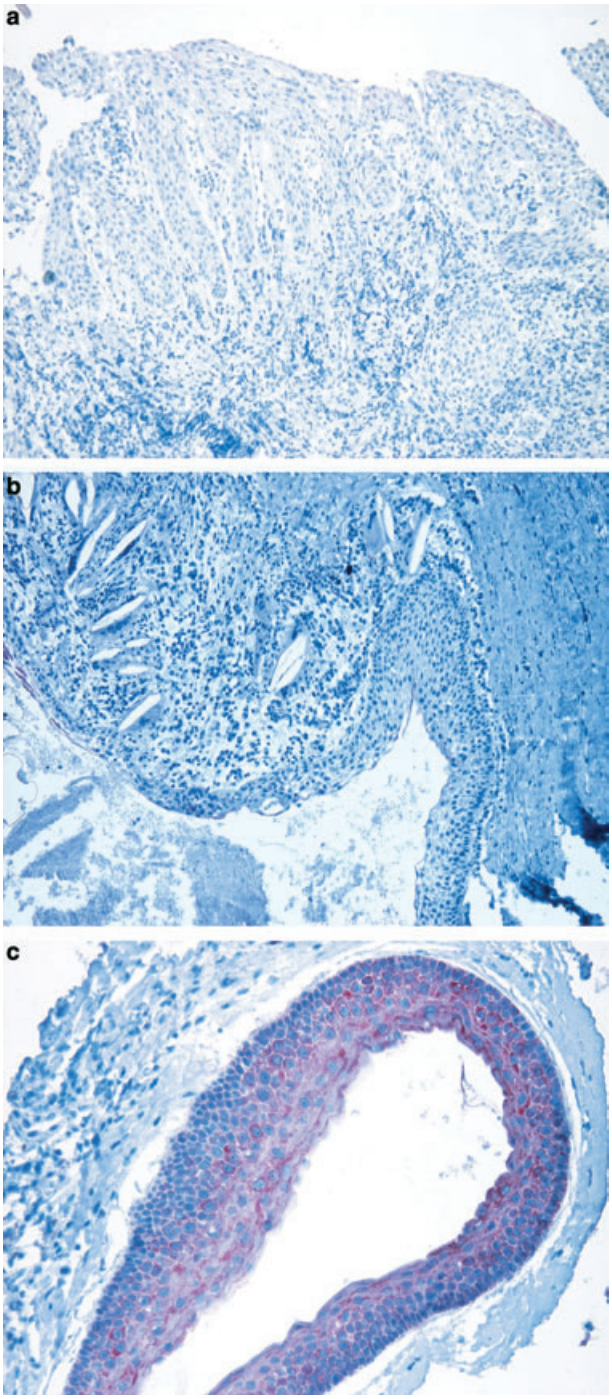

Figure 4 Weak expression of cytokeratin 17 in a radicular cyst (a) and dentigerous cyst (b). Stronger staining in an odontogenic keratocyst (c; original magnification ×100 in 'a' and 'b', ×250 in 'c'; chromogen: New Fuchsine).

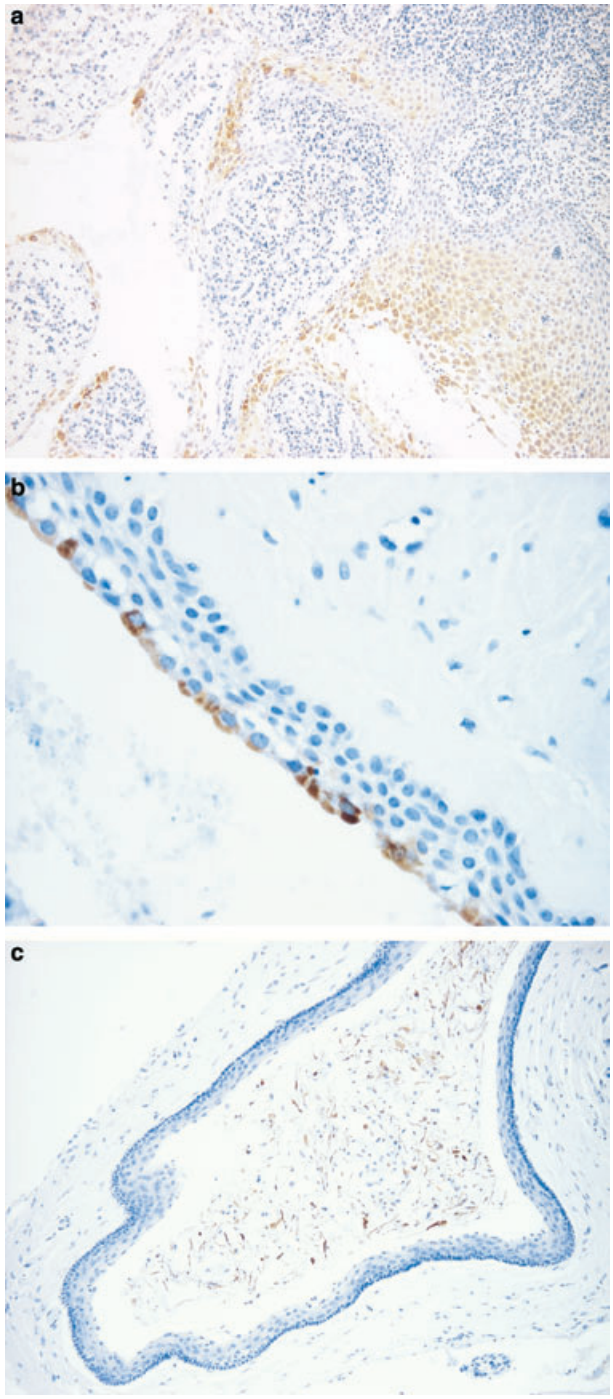

Figure 5 Positive suprabasal immunohistochemical staining against cytokeratin 19 in a radicular cyst (a) and dentigerous cyst (b). A negative result in an odontogenic keratocyst (c; original magnification ×100 in 'a' and 'c', ×250 in 'b'; chromogen: DAB).

even taking no account of this latter issue, there was a significant difference between odontogenic keratocysts on the one and radicular as well as dentigerous cysts on the other hand, at a probability level of < 0.001 (Fig. 1).

Radicular cysts showed a positive staining for CK 19 mainly in the suprabasal cell layers in 14 of 30 cases (Fig. 5a) and dentigerous cysts were positive in half of the cases (15 of 30) with limited superficial expression in eight of 15 cases (Fig. 5b), whereas odontogenic keratocyst were completely negative (Fig. 5c). Thus, odontogenic keratocysts significantly differed from radicular as well as dentigerous cysts in CK 19 expression ($P < 0.002$; Fig. 1).

Summarizing CK 17 and 19 expressions, 14 of 15 odontogenic keratocysts (93.3%) were positive for CK 17 and negative for CK 19 (Table 2). In contrast, this

Table 2 Detection of cytokeratin (CK) 17 and 19 in different cystic odontogenic lesions

Lesion	*CK 17–*	*CK 17+*
Radicular cysts		
CK 19–	8	**8**
CK 19+	10	4
Dentigerous cysts		
CK 19–	13	**2**
CK 19+	8	7
Odontogenic keratocysts		
CK 19–	1	**14**
CK 19+	0	0

immunohistochemical-staining pattern was found in only eight of 30 radicular cysts (26.7%) and two of 30 dentigerous cysts (6.7%). Positive CK 20 expression could not be demonstrated in the epithelium of any cystic lesion analyzed in this study.

Ki-67 was found in only 24 of 30 dentigerous cysts with 14.7 positive cell nuclei on average within 10 visual fields at a 400-fold magnification. Immunohistochemical detection of Ki-67 was more often positive in 25 of 30 radicular cysts with a mean value of 21.3 cell nuclei. Positive staining was mainly limited to the basal cell layers with a few solitary suprabasal cells concerning both entities. In contrast, detection of Ki-67 was positive in all of the odontogenic keratocysts under study with a mean value of 52.1 cell nuclei and most of the Ki-67-positive cells were found in the parabasal layers.

Discussion

Although dentigerous cysts and odontogenic keratocysts both arise from odontogenic epithelium and may have a similar radiographic and histologic appearance, their behavior in terms of recurrence is sufficiently different to warrant a distinct treatment and follow up. Differences in expression of CKs may allow a given epithelium to be characterized by a specific pattern of its CK components.

The CK 5 and 6 are both high-molecular weight, basic types of CKs which are produced by normal mammary epithelial cells, whereas tumor cells mainly produce CK 8, 18, and 19 (23). CK 5 is generally co-expressed with CK 14 by the basal cells of stratified squamous epithelia, whereas the different CK 6 isoforms were found in the suprabasal layers of proliferating complex epithelia in association with CK 16. Simple epithelia and non-epithelial cells, generally, are not labeled by the antibody used in this study (24). Nearly all odontogenic cysts under study turned out to be positive independently of their entities, which is in agreement with previous studies (8, 11, 18).

The CK 7 belongs to the neutral-basic type subfamily and its distribution is confined to simple non-keratinizing glandular and transitional epithelia (25). The antibody OV-TL 12/30 consistently labels a large number of simple, complex, and transitional epithelia in addition to ovarian mesothelium, luminal, and basal cells of the prostate, and myoepithelial cells (26). Other non-epithelial tissues, such as connective tissue, blood vessels, and lymphoid tissue, are negative with this antibody. Previous results concerning odontogenic cysts with different antibodies are contradictory. In one study all layers of odontogenic keratocysts as well as dentigerous and radicular cysts have been shown to be positive with an antibody reacting with CK 7, 17, and 19 (5), whereas in another paper with an antibody specific for CK 7, apart from isolated positive cells in a few lesions, only one of 25 radicular cysts was positive (7). More recent studies have revealed results comparable with ours, namely a part of 37% positive radicular cysts, 59% positive dentigerous cysts, and 29% positive odontogenic keratocysts (12) or 70% positive dentigerous cysts and 21% positive odontogenic keratocysts (18). However, in this study the antibody OV-TL 12/30 was able to discriminate between radicular and dentigerous cysts at a probability level of < 0.01.

The CK 10 is an intermediate-sized, acidic type CK and expressed in all suprabasal cells of the terminally differentiated epidermis simultaneously with CK 1, but is absent in basal cells. Together, CK 1 and 10 represent some of the first markers of epidermal differentiation (27). CK 10 has been implicated as marker for more differentiated cells in squamous cell carcinomas. The antibody DE-K10 labels all suprabasal layers of the epidermis, thymic Hassal's bodies and a variable amount of cells in some non-cornyfing stratified epithelia including vagina, ectocervix, and tongue (28). All simple and glandular epithelia and transitional epithelium of urinary bladder and urethra are not labeled by the antibody. As a marker of keratinized epithelium it was primarily found in about half of the odontogenic keratocysts under study. In dentigerous cysts with a share of 30% and particularly radicular cysts with 10% it was found less frequently. This difference between odontogenic keratocysts and radicular cysts was statistically significant at a probability level of < 0.02. While in one preceding study CK 10 could only be detected in some dentigerous cysts with an antibody labeling CK 1, 9, 10, and 11 (5), a superficial positive result was also found specifically in odontogenic keratocysts in many other investigations (6–8, 11, 13, 17, 18). Interestingly, this expression is not stable as some odontogenic keratocysts seem to dedifferentiate and lose the CK 10 expression after decompression (29).

The antibody, used for detection of CK 13 in this study, in principle reacts with both CK intermediate filament proteins 10 and 13. Nevertheless, on formalin-fixed, paraffin-embedded tissue sections the antibody recognizes only CK 13 (30), an acidic type CK that is present in suprabasal layers of non-cornifying stratified epithelia (31). No staining of CK 10-positive epithelia is seen in formalin-fixed, paraffin-embedded material. Like in other studies, CK 13 could be detected in the suprabasal cell layers of nearly all examined odontogenic cysts (5–8, 11, 14, 17, 18).

The CK 17 is a member of the acidic type subfamily, and its distribution is confined to basal and myoepithelial cells of a group of complex epithelia and

transitional epithelium as well as to the outer root sheet of hair folliculi. The antibody E3 labels the basal row of pseudostratified epithelium in the larynx, trachea, and bronchi, and the basal cell layer of the transitional epithelium in the urinary bladder (32). Additionally, it labels the myoepithelial cells in several tissues, including the salivary, sweat, and prostate glands, and the intralobular and, particularly, the extralobular zone in the breast. Suprabasal cells in bronchi and bronchioles are also reported positive with the antibody. In addition, the outer root sheet of hair folliculi stains positively with the antibody, as do endocervical columnar cells. Normal squamous stratified epithelia of epidermis, exocervix, and larynx, as well as all simple epithelia, are negative. The positive labeling of nearly all odontogenic keratocysts and only about one-thirds of the dentigerous cysts is in agreement with one preceding study (14). The only previous study examining CK 17 in radicular cysts utilized an antibody specific for CK 7, 17, and 19 resulting in a strong staining of all layers of all odontogenic cysts under study (5). Using the E3 antibody, it was possible to differentiate between odontogenic keratocysts on the one and radicular as well as dentigerous cysts on the other hand, with a probability level of < 0.001.

The CK 19 is the smallest known acidic type CK and differentially expressed in various human tissues without association with a basic CK (33). CK 19 can be detected in simple epithelia and basal cells of non-cornifying stratified squamous epithelia. The antibody used in this study reacts with the rod domain of human CK peptide 19 and may be used in formalin-fixed or Carnoy-fixed, paraffin-embedded tissue as well as on frozen sections of human tissue. It is a useful tool in discriminating carcinomas from tumors of different origin and for carcinoma subtyping using immunoblotting or immunocytochemical techniques. The antibody has also been shown to be a marker of pre-malignant lesions of the oral epithelium (34). Whereas in most previous studies all layers of all odontogenic cysts under study tended to be positive (5–8, 11, 18), in a more recent study the results were similar to ours with a completely absent staining in odontogenic keratocysts and a share of 68% positive radicular and 71% positive dentigerous cysts (12). These results open up new possibilities to distinguish odontogenic keratocysts from radicular and dentigerous cysts at a probability level of < 0.002.

The CK 20 is an integral, less acidic intermediate filament component and a major cytoskeletal keratin of the intestinal epithelium (35). CK 20 positivity has been reported in the vast majority of adenocarcinomas of the colon, mucinous ovarian tumors, transitional cell, and Merkel cell carcinomas, and frequently also in adenocarcinomas of the stomach, bile system, and pancreas. The antibody K_s 20.8 labels normal urothelium and the mature epithelium lining the villi of duodenal mucosa. CK 20 immunoreactivity has not been detected in a number of non-epithelial tissues tested, such as smooth muscle, blood vessel walls, lymph nodes, and tumor stroma (36). In agreement with a previous study all specimens of odontogenic cysts were completely negative (12).

In conclusion, apart from an enhanced proliferating activity determined by the MIB-1 antibody, odontogenic keratocysts seem to differ from radicular and dentigerous cysts in the expression pattern of individual CKs. The increased level of CK 10 expression is perhaps not stable particularly after decompression of the cysts (29). However, the results of the present study suggest the immunohistochemical determination of CK 17 and 19 to be a valuable additional parameter making a decision between odontogenic keratocysts and other odontogenic cysts which clinically is likely the most significant differential diagnosis in this context.

References

1. Kramer IR, Pindborg JJ, Shear M. *Histological typing of odontogenic tumours*, 2nd edn. Berlin, Germany: Springer, 1992; 34–42.
2. Shear M. *Cysts of the oral regions*, 3rd edn. Oxford, UK: Wright, 1992.
3. Shear M. The aggressive nature of the odontogenic keratocyst: is it a benign cystic neoplasm? Part 1. Clinical and early experimental evidence of aggressive behaviour. *Oral Oncol* 2002; **38**: 219–26.
4. Shear M. The aggressive nature of the odontogenic keratocyst: is it a benign cystic neoplasm? Part 2. Proliferation and genetic studies. *Oral Oncol* 2002; **38**: 323–31.
5. Hormia M, Ylipaavalniemi P, Nagle RB, Virtanen I. Expression of cytokeratins in odontogenic jaw cysts: monoclonal antibodies reveal distinct variation between different cyst types. *J Oral Pathol* 1987; **16**: 338–46.
6. Morgan PR, Shirlaw PJ, Johnson NW, Leigh IM, Lane EB. Potential applications of anti-keratin antibodies in oral diagnosis. *J Oral Pathol* 1987; **16**: 212–22.
7. Matthews JB, Mason GI, Browne RM. Epithelial cell markers and proliferating cells in odontogenic jaw cysts. *J Pathol* 1988; **156**: 283–90.
8. Gao Z, Mackenzie IC, Williams DM, Cruchley AT, Leigh I, Lane EB. Patterns of keratin-expression in rests of Malassez and periapical lesions. *J Oral Pathol* 1988; **17**: 178–85.
9. Gao Z, Mackenzie IC, Cruchley AT, Williams DM, Leigh I, Lane EB. Cytokeratin expression of the odontogenic epithelia in dental follicles and developmental cysts. *J Oral Pathol Med* 1989; **18**: 63–7.
10. MacDonald AW, Fletcher A. Expression of cytokeratin in the epithelium of dentigerous cysts and odontogenic keratocysts: an aid to diagnosis. *J Clin Pathol* 1989; **42**: 736–9.
11. Smith AJ, Matthews JB. Odontogenic epithelium and its residues. In: Browne RM, ed. *Investigative pathology of the odontogenic cyst*. Boca Raton, USA: CRC Press, 1991; 58–85.
12. Wagner Y, Filippi A, Kirschner H, Dreyer T. The expression of cytokeratin and p53 in odontogenic cysts. *Mund Kiefer Gesichtschir* 1999; **3**: 263–9.
13. August M, Faquin WC, Troulis M, Kaban LB. Differentiation of odontogenic keratocysts from nonkeratinizing cysts by use of fine-needle aspiration biopsy and cytokeratin-10 staining. *J Oral Maxillofac Surg* 2000; **58**: 935–40.
14. Meara JG, Pilch BZ, Shah SS, Cunningham MJ. Cytokeratin expression in the odontogenic keratocyst. *J Oral Maxillofac Surg* 2000; **58**: 862–5.
15. Lu DP, Tatemoto Y, Kimura T, Osaki T. Expression of cytokeratins (CKs) 8, 13 and 18 and their mRNA in

epithelial linings of radicular cysts: implication for the same CK profiles as nasal columnar epithelium in squamous epithelial lining. *Oral Dis* 2002; **8**: 30–6.
16. Lu DP, Tatemoto Y, Yokoyama T, Kimura T, Osaki T. Cytokeratin expression patterns in jaw cyst linings with metaplastic epithelium. *J Oral Pathol Med* 2002; **31**: 87–94.
17. da Silva MJ, de Sousa SO, Correa L, Carvalhosa AA, de Araujo VC. Immunohistochemical study of the orthokeratinized odontogenic cyst: a comparison with the odontogenic keratocyst. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2002; **94**: 732–7.
18. Pires FR, Chen SY, da Cruz Perez DE, de Almeida OP, Kowalski LP. Cytokeratin expression in central mucoepidermoid carcinoma and glandular odontogenic cyst. *Oral Oncol* 2004; **40**: 545–51.
19. Shear M. The aggressive nature of the odontogenic keratocyst: is it a benign cystic neoplasm? Part 3. Immunocytochemistry of cytokeratin and other epithelial cell markers. *Oral Oncol* 2002; **38**: 407–15.
20. Moll R, Franke WW, Schiller DL, Geiger B, Krepler R. The catalog of human cytokeratins: patterns of expression in normal epithelia, tumors and cultured cells. *Cell* 1982; **31**: 11–24.
21. Gorlin RJ, Goltz RW. Multiple nevoid basal-cell epithelioma, jaw cysts and bifid rib. A syndrome. *N Engl J Med* 1960; **262**: 908–12.
22. Sabattini E, Bisgaard K, Ascani S, et al. The EnVision++ system: a new immunohistochemical method for diagnostics and research. Critical comparison with the APAAP, ChemMate, CSA, LABC, and SABC techniques. *J Clin Pathol* 1998; **51**: 506–11.
23. Trask DK, Band V, Zajchowski DA, Yaswen P, Suh T, Sager R. Keratins as markers that distinguish normal and tumor-derived mammary epithelial cells. *Proc Natl Acad Sci U S A* 1990; **87**: 2319–23.
24. Clover J, Oates J, Edwards C. Anti-cytokeratin 5/6: a positive marker for epithelioid mesothelioma. *Histopathology* 1997; **31**: 140–3.
25. Glass C, Kim KH, Fuchs E. Sequence and expression of a human type II mesothelial keratin. *J Cell Biol* 1985; **101**: 2366–73.
26. van Niekerk CC, Jap PHK, Ramaekers FC, van de Molengraft F, Poels LG. Immunohistochemical demonstration of keratin 7 in routinely fixed paraffin-embedded human tissues. *J Pathol* 1991; **165**: 145–52.
27. Lessin SR, Huebner K, Isobe M, Croce CM, Steinert PM. Chromosomal mapping of human keratin genes: evidence of non-linkage. *J Invest Dermatol* 1988; **91**: 572–8.
28. Ivanyi D, Asink A, Groeneveld E, Hageman PC, Mooi WJ, Heintz APM. New monoclonal antibodies recognizing epidermal differentiation-associated keratins in formalin-fixed, paraffin-embedded tissue. Keratin 10 expression in carcinoma of the vulva. *J Pathol* 1989; **159**: 7–12.
29. August M, Faquin WC, Troulis MJ, Kaban LB. Dedifferentiation of odontogenic keratocyst epithelium after cyst decompression. *J Oral Maxillofac Surg* 2003; **61**: 678–83.
30. Ivanyi D, Minke JM, Hageman C, Groeneveld E, van Doornewaard G. Patterns of expression of feline cytokeratins in normal healthy epithelia and mammary carcinoma cells. *Am J Vet Res* 1992; **53**: 304–14.
31. Romano V, Raimondi E, Bosco P, et al. Chromosomal mapping of human cytokeratin 13 gene (KRT13). *Genomics* 1992; **14**: 495–7.
32. Troyanovsky SM, Guelstein VI, Tchipysheva TA, Krutovskikh VA, Bannikov GA. Patterns of expression of keratin 17 in human epithelia: dependency on cell position. *J Cell Sci* 1989; **93**: 419–26.
33. Bader BL, Magin TM, Hatzfield M, Franke WW. Amino acid sequence and gene organization of cytokeratin no. 19, an exceptional tail-less intermediate filament protein. *EMBO J* 1986; **5**: 1865–75.
34. Lindberg K, Rheinwald JG. Suprabasal 40 kd keratin (K19) expression as an immunohistologic marker of premalignancy in oral epithelium. *Am J Pathol* 1989; **134**: 89–98.
35. Moll R, Schiller DL, Franke WW. Identification of protein IT of the intestinal cytoskeleton as a novel type I cytokeratin with unusual properties and expression patterns. *J Cell Biol* 1990; **111**: 567–80.
36. Moll R, Löwe A, Laufer J, Franke WW. Cytokeratin 20 in human carcinomas. A new histodiagnostic marker detected by monoclonal antibodies. *Am J Pathol* 1992; **140**: 427–47.
37. Key G, Becker MH, Baron B, et al. New Ki-67-equivalent murine monoclonal antibodies (MIB 1–3) generated against bacterially expressed parts of the Ki-67 cDNA containing three 62 base pair repetitive elements encoding for the Ki-67 epitope. *Lab Invest* 1993; **68**: 629–36.