



Pattern of recurrence of nonsyndromic keratocystic odontogenic tumors

Trond I. Berge, Dr.Odont,^a Saedeh B. Helland, MSD,^b Andreas Sælen, MSD,^c Maria Øren, MSD,^c Anne Christine Johannessen, Dr.Odont, Cand.Med,^d Liv Skartveit, Dr.Odont,^e and Bjarte Grung, MSD^f

Objective. To describe and analyze recurrent pattern of KOTs according to time.

Study Design. This retrospective chart study evaluated histologically confirmed nonsyndromic keratocystic odontogenic tumors (KOT) treated at our institutions between 1975 and 2012.

Results. Mean age at time of diagnosis was 48 years, and male/female ratio was 1.8:1. The typical nonsyndromic KOT lesion was most often found in the posterior mandible, had radiographically smooth borders, and was associated with symptoms and clinical findings, perforated bone, with a thin capsule. Anterior jaw KOT were found more frequently in patients 50 years or older, and maxillary KOTs were more frequently infected. Treatment was enucleation (n = 70) or marsupialization with subsequent enucleation (n = 22). Observation time ranged from 0.5 months to 25 years (mean 53 months). Crude recurrence rate was 29%. Risk of recurrence increased until 7 years after treatment and then remained stable. Patients with impaired general health had a significantly increased risk of recurrence. Tumors in the posterior mandible that had bone perforation and a thin capsule and contained keratin showed increased recurrence rates. Although recurrence rates were similar for both treatment groups, the groups differed in size and tumor site; thus, the results of this study need to be confirmed in a prospective study.

Conclusions. Time-dependent recurrence pattern of KOTs is described and analyzed. The following follow-up protocol is suggested for patients with impaired health or large lesions: clinical and radiographic examinations at 2, 4, and 7 years, followed by intervals of 3 to 4 years; for other patients: clinical and radiographic examination at 4, 6, and 8 years, followed by intervals of 3 to 4 years. (Oral Surg Oral Med Oral Pathol Oral Radiol 2016;122:10-16)

Keratocystic odontogenic tumors (KOTs) are benign neoplasms of odontogenic origin. In 2005, a World Health Organization (WHO) working group¹ recommended that the older term *odontogenic keratocyst*, introduced by Philipsen in 1956,² be replaced by the term KOT to better reflect its neoplastic nature.³

Between 2.5%⁴ and 21.8%⁵ of suspected odontogenic cysts prove to be KOTs. The lesion presents clinically as a cyst with connective tissue capsule, epithelial layer, and a lumen containing liquid or keratin, although occasional solid tumors have been reported.⁶ Several

studies have shown a male predilection⁷⁻⁹ and a bimodal age distribution with peaks in the third and sixth decades.^{10,11} KOTs may also appear in the posterior mandible,^{11,12} show unilocular or multilocular radiolucency,¹³ and have a thin, friable capsule surrounding keratin masses or liquid. The tumor rarely displaces teeth or expands cortical bone but tends to hollow out regions of the jaw.¹⁴ Perforation of the lingual cortex is not uncommon, and the lesions may be exposed to secondary infection through perforation of the overlying mucosa.

The tumor is considered a locally aggressive lesion because it tends to become relatively large and exhibits a high rate of recurrence, with previous reports ranging from 15.3%¹⁵ to 58.3%.⁹ A majority of recurrences have been reported to occur within the first 5 years after treatment.^{16,17} Late recurrences have been reported up to 40 years after initial treatment.¹⁸ Myoung et al.⁹ found an increased recurrence rate in patients between 41 and 50 years of age.¹⁰

^aProfessor, Department of Clinical Dentistry, Faculty of Medicine and Dentistry, University of Bergen, Norway; Senior consultant, Department of Maxillofacial Surgery, Haukeland University Hospital, Bergen, Norway.

^bResident in Oral and Maxillofacial Surgery, Department of Clinical Dentistry, Faculty of Medicine and Dentistry, University of Bergen, Norway; Department of Maxillofacial Surgery, Haukeland University Hospital, Bergen, Norway.

^cDepartment of Clinical Dentistry, Faculty of Medicine and Dentistry, University of Bergen, Norway.

^dProfessor, Department of Clinical Medicine, Faculty of Medicine and Dentistry, University of Bergen, Bergen, Norway; Senior consultant in Oral Pathology, Haukeland University Hospital, Bergen, Norway.

^eAssociate professor (Retired), Department of Clinical Dentistry, Faculty of Medicine and Dentistry, University of Bergen, Norway.

^fOral Surgeon, Department of Oral Surgery, Stavanger University Hospital, Stavanger, Norway.

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Statement of Clinical Relevance

The keratocystic odontogenic tumor is known for its increased rate of recurrence. This study shows the time pattern of recurrences and some possible predisposing factors, which can be used to design individually adapted follow-up regimens.

Histologically, the appearance of KOTs is characterized by a parakeratinized stratified squamous epithelium. The nucleus persists in the outer layers of the keratinized epithelial cells. The basal layer exhibits a palisade pattern, with polarized and intensely stained nuclei of uniform diameter. However, a separate histologic entity, which is orthokeratinized and lacks nuclei in the outer layer and shows less aggressive behavior and significantly lower recurrence rates, was previously not distinguished from KOTs. Earlier reports on KOTs therefore included varying numbers of this orthokeratinized variant, which may have biased the reports on recurrence rates.¹⁹

A variety of treatment modalities are used for the treatment of KOTs: resection; enucleation²⁰ with or without excision of overlying mucosa and/or treatment of the bony defect with Carnoy's solution²¹ or cryotherapy²² to the bony defect; and marsupialization or cystostomy followed by enucleation. Different treatments have been suggested for different-sized tumors,²³ but lack of randomized controlled trials makes evidence-based recommendations difficult.²⁴

The aim of the present retrospective study, based on the current histologic definition of this tumor, was to analyze the clinical and radiographic characteristics of KOTs and their relationship to rate and timing of recurrences.

MATERIALS AND METHODS

This retrospective study identified 109 patients diagnosed with KOTs and treated between 1975 and 2012 at the Stavanger University Hospital, Haukeland University Hospital, Bergen, Norway, and Oral Surgery clinic, Dental School, University of Bergen, Bergen, Norway. No ethical approval (REK NORWAY West) was required for this study because of its retrospective nature. Clinical records from all 109 patients were reviewed. The diagnosis of KOT was verified by one oral pathologist (ACJ), based on histologic criteria defined by the WHO working group.³ A total of 17 patients were excluded for the following reasons: unconfirmable diagnosis (15); Gorlin-Goltz syndrome (1); and diagnosis of peripheral KOT (1). Age, sex, health condition, use of medication, subjective symptoms, clinical findings, radiographic findings, size and location of tumor, surgical findings and procedure, follow-up time, and time until relapse were all recorded.

Both analog and digital radiographs were used to calculate the two-dimensional size of each lesion. To measure the tumor size radiographically, NIS-Elements Microscope Imaging Software (Nikon Instruments Europe, Amsterdam, the Netherlands) was utilized. Analog radiographs were first measured using a manual millimeter ruler and subsequently imported to the

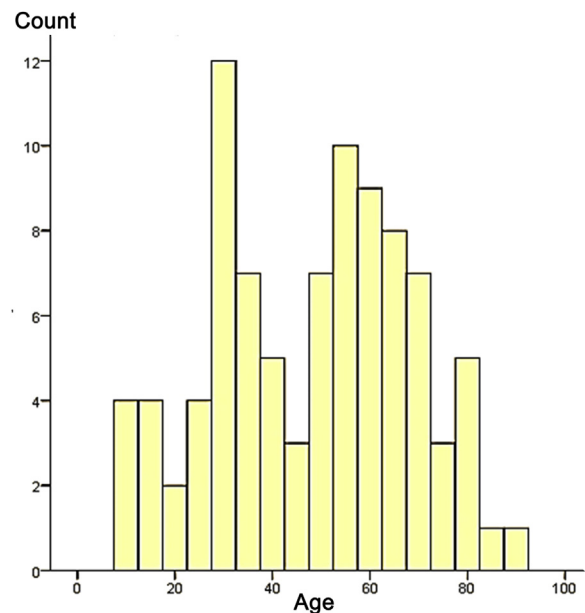


Fig. 1. Age distribution of 92 patients with keratocystic odontogenic tumors (KOTs).

software. The measurement function of the software was then calibrated according to this reference number. Digital radiographs were imported directly into the software. The manufacturer's software (Digora or Sidexis) for digital radiographic systems was used for calibration of digital intraoral radiographs. Each radiograph was measured vertically in these programs and was then calibrated in NIS-Elements Microscope Imaging Software (Nikon Instruments Europe, Amsterdam, the Netherlands). The limits of each lesion were marked manually. The software subsequently calculated the area of each lesion in square millimeters. All tumors were measured within ± 0.01 mm². The areas of portions of teeth or whole teeth within a lesion were not subtracted from the total.

Statistical analyses, except figures, were performed in IBM SPSS version 21.0 (SPSS Inc., Chicago, IL). The radiographic tumor sizes were categorized into small, medium, and large based on 33.3% percentiles. Differences in recurrence rates were analyzed using a χ^2 test and Cox regression analysis. The "R Project"²⁵ was used to produce 1 - Kaplan-Meier plots. The statistical level of significance was set at 5%.

RESULTS

The age distribution of the 92 patients with histologically confirmed KOTs is shown in Figure 1. Mean follow-up time was 66 months (5 years and 6 months), ranging from 0.5 month to 25 years. A total of 27 (29%) recurrences were seen. Mean time to recurrence was 53 months (range 9–280 months).

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