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Original article

# Study of Ki67 and CD10 expression as predictive factors of recurrence of ameloblastoma

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ABSTRACT

*Introduction:* Ameloblastoma is a rare, benign, purely epithelial odontogenic tumour, characterized by a high potential for local invasion and recurrence.
*Objective:* To study the epidemiological and histological characteristics of ameloblastoma. To study Ki67 and CD10 immunostaining in ameloblastoma and to investigate a possible correlation between these two markers and recurrence of this tumour.
*Methods:* An immunohistochemical study using Ki67 and CD10 monoclonal antibodies was performed on 37 paraffin blocks obtained from the Charles-Nicolle hospital pathology department in Tunis over a 9-year period (2004–2012). Statistical analysis was performed with Statistical Package for Social Sciences (SPSS) software version 15.1.
*Results:* This series of 37 cases comprised 21 males and 16 females (sex ratio: 1.3) with a mean age of 39 years (range: 7 to 70 years), corresponding to 36 cases of intraosseous ameloblastoma and one case of gingival ameloblastoma. Thirty-two cases were polycystic and 5 cases were unicystic. Eighteen cases of local recurrence were observed. No correlation was demonstrated between recurrence and the various clinical and histological parameters and treatment modalities. However, a significant correlation was demonstrated between recurrence and Ki67 and CD10 expression ($P = 0.000$ and 0.002, respectively).
*Conclusion:* The Ki67 proliferation index and stromal CD10 expression can be considered to be predictive factors of ameloblastoma recurrence.



## 1. Introduction

Ameloblastoma is the most common odontogenic tumour, representing about 1% of all tumours of the oral cavity [1]. This tumour arises from epithelial cell rests of Malassez after regression of the enamel organ. It affects the mandible and the maxilla in 80% and 20% of cases, respectively [2].

According to the latest WHO classification, ameloblastoma is subdivided into intraosseous (central) ameloblastoma and tissue (peripheral) ameloblastoma with various architectural variants [3].

It is a locally invasive tumour with a high tendency to recurrence [4] and even metastasis in rare cases [5]. This invasive nature of ameloblastoma has consequences for treatment, ranging from simple tumour resection to wide or even radical resection.

Recent studies have suggested that Ki67 and CD10 expression in tumour tissue may be associated with a more invasive profile and a higher risk of recurrence of certain tumours, including ameloblastoma [6,7].

The objectives of this study were to:

- identify the epidemiological and histological characteristics of ameloblastoma;
- study the immunohistochemical expression of Ki67 and CD10 in ameloblastoma, and investigate a possible correlation between these two markers and the recurrence rate of this tumour.

## 2. Material and methods

This retrospective study was based on a series of 37 cases of ameloblastoma collected in the Charles-Nicolle hospital pathology department in Tunis over a 9-year period (2004–2012).

The objectives of this study were to identify the epidemiological and histological characteristics of ameloblastoma, study the immunohistochemical expression of Ki67 and CD10 in this tumour, and investigate a possible correlation between these two markers and the ameloblastoma recurrence rate.

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Epidemiological and clinical data and outcome were collected by retrospective review of the patients' medical charts in the department of maxillofacial surgery of the same hospital. Histological slides were reviewed and tumours were classified according to the WHO 2005 classification [3].

Slides comprising the largest amount of tumour tissue and not containing any bone fragments were selected in each case and the corresponding blocks were retrieved.

The three-layer immunoperoxidase staining protocol was used, comprising a LEICA kit (NovoLink) with revelation by DAB (diaminobenzidine) chromogen.

Ki67 immunolabelling has an exclusively nuclear distribution with brownish staining and tumour cells presenting total nuclear, focal nuclear or nucleolar labelling are considered to be positive.

Ki67 immunolabelling was considered to be:

- low: 0 to 7% of tumour cells are labelled;
- moderate: 8 to 15% of tumour cells are labelled;
- intense: > 15% of tumour cells are labelled.

CD10 immunolabelling was evaluated by the score proposed by Ogawa et al. [8]: cytoplasmic immunolabelling was initially evaluated according to the following score:

- 0: no labelling;
- 1: weak cytoplasmic labelling;
- 2: moderate cytoplasmic labelling;
- 3: intense cytoplasmic labelling.

CD10 immunolabelling was then evaluated according to a semi-quantitative score:

- 0: < 10% of cells are labelled;
- 1: 10 to 25% of cells are labelled;
- 2: 25 to 50% of cells are labelled;
- 3: > 50% of cells are labelled.

After combining the immunolabelling intensity scores and the percentage of immunolabelled cells, immunolabelling was considered to be:

- negative: score 0–1;
- +: score 2;
- ++: score 3;
- +++: score 4–5.

Statistical analysis was performed with Statistical Package for Social Sciences (SPSS) software version 15.1. A descriptive and analytical study of the series was performed.

## 3. Results

This series comprised 21 males (56.8%) and 16 females (43.2%) with a sex ratio of 1.3 and a mean age of 39 years (range: 7 to 70 years). The tumour involved the mandible in 34 cases (94%) and the maxilla in 3 cases (6%). The long axis of the tumours ranged between 1 and 15 cm with a mean of 4 cm. This series comprised 36 cases of intraosseous ameloblastoma (97%) and one case of extraosseous gingival ameloblastoma (3%). Thirty-two cases were polycystic/solid (86%) and 5 cases were unicystic (14%), including 4 cases corresponding to a mural subtype and 1 case corresponding to a luminal subtype.

The corresponding architectural variant was specified for each of the various types of ameloblastoma.

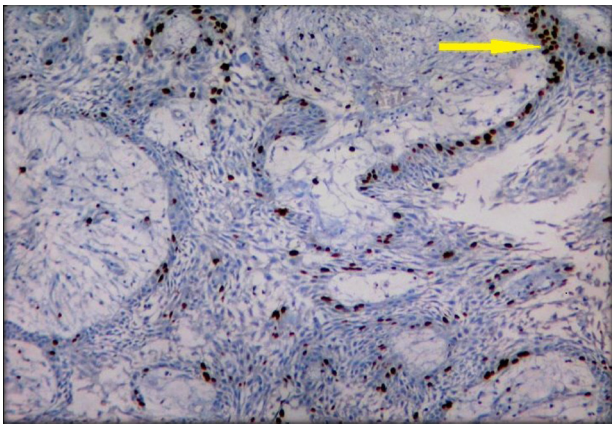

**Fig. 1.** Ki67-positive tumour cells with a Ki67 index of 14% (× 200). Arrow indicating labelled cells.

**Table 1**
Ki67 expression according to the histological characteristics of ameloblastomas.

| | Intensity of Ki67 labelling | | |
|---|---|---|---|
| | Weak (%) | Moderate (%) | Intense (%) |
| Site | | | |
| Mandibular | 11 (32) | 14 (42) | 9 (26) |
| Maxillary | 1 (33) | 1 (33) | 1 (33) |
| Size | | | |
| ≤ 4 cm | 6 (26) | 10 (44) | 7 (30) |
| > 4 cm | 5 (36) | 8 (57) | 1 (7) |
| Histological type | | | |
| Polycystic | 8 (25) | 17 (53) | 7 (22) |
| Unicystic | 3 (60) | 1 (20) | 1 (20) |
| Architectural variant | | | |
| Follicular | 7 (39) | 7 (39) | 4 (22) |
| Plexiform | 3 (30) | 4 (40) | 3 (30) |
| Other | 2 (22.1) | 4 (44.5) | 3 (33.4) |

## 4. Ki67 expression

In our study, the Ki67 proliferation index varied between 2% and 22% with a mean of 10.5% (Fig. 1) (Table 1). Ki67 immunolabelling was weak in 12 cases (30%), moderate in 15 cases (49%), and intense in 10 cases (21%).

Comparison of Ki67 expression with tumour site, tumour size, architectural variants and histological types did not reveal any statistically significant differences. However, immunolabelling was moderate and intense in the follicular variant.

## 5. CD10 expression by stromal cells

Immunolabelling was negative in 9 cases (24%), weakly positive in 10 cases (27%), moderately positive in 15 cases (41%) and intensely positive in 3 cases (8%) (Fig. 2) (Table 2).

No statistically significant correlation was observed between stromal CD10 expression and tumour site, tumour size, histological type and the various architectural variants.

## 6. Treatment modalities

All patients were treated surgically. Thirty-two patients (86%) were treated conservatively and 5 other patients (14%) underwent first-line radical surgery.

## 7. Outcome and recurrence

Mean follow-up was 79 months (range: 2 to 300 months) (Table 3). Two patients were lost to follow-up after one month.