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ORIGINAL ARTICLE

Ameloblastoma: a retrospective single institute study of 34 subjects

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ABSTRACT

Objective: This study aims to clarify demographic and clinical aspects of patients with ameloblastoma treated at a single Finnish institute during 1985–2016. Associations between predictor variables (gender and age) and outcome variables (location, tumour type, growth patterns and average tumour size) were sought.

Materials and methods: A retrospective cohort study was designed and implemented including 34 patients diagnosed with primary ameloblastoma and treated at the Helsinki University Central Hospital. Patient records were investigated, and tissue samples re-evaluated. The chi-square test was used on all categorized variables and *t*-test for continuous ones. A *p* value equal to or under .05 was considered significant.

Results: Males were slightly more predominant among the Finnish patients with ameloblastoma. Maxillary tumours were seen exclusively in male patients ($p = .034$). Additionally, these patients were older than patients with mandibular tumours ($p = .007$). A mixture in histological growth patterns was more common than originally anticipated. The study revealed a wide range of clinical signs and subjective symptoms, of which pain or other sensations were experienced most often.

Conclusions: This study of 34 subjects shows that southern Finnish patients with ameloblastoma do not substantially differ from patients in similar study designs.

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Introduction

Ameloblastoma is a benign, slowly growing, but locally aggressive odontogenic tumours originating from dental lamina and affecting primarily the jawbones. The risk of recurrence of ameloblastoma is high, reaching from 50% up to 90%. It affects equally men and women of all age groups, peaking in the fourth and fifth decades of life [1,2]. Ameloblastomas are divided into solid/multicystic, unicystic and peripheral ameloblastomas, and based on their histological growth pattern into follicular, plexiform, acanthomatous, granular cell, basal cell and desmoplastic ameloblastomas [2]. Signs or symptoms are subtle at the early stage, sometimes even non-existent but emerge progressively as the tumour grows. The treatment methods vary widely from conventional (enucleation, curettage, or surgical excision with peripheral osteotomy or adjuvant therapy) to radical (bone resection with 1 cm to 1.5 cm margins) [3]. The optimal treatment procedures remain a subject of debate [3,4].

Geographic and racial varieties exist in age of onset, sex ratios, location, histology and clinical findings [5,6]. For example, North American patients with ameloblastoma have been shown to be afflicted with ameloblastoma significantly later in life than patients in Asia [5]. In China and Africa, ameloblastoma is the commonest odontogenic tumour, while in North America, odontomas are considered more common [7–10]. Ameloblastoma cohorts collected in hospital districts tend to remain small. Every study on this rare tumour contributes toward resolving demographic differences.

The primary aim of the present study was to clarify clinical and pathological features of ameloblastoma in a single institution retrospectively. The secondary aim was to investigate any associations between location, type, growth pattern and size to gender and age.

Materials and methods

Study design

We included all patients who had been diagnosed with primary ameloblastoma at the Department of Pathology, Helsinki University Central Hospital (HUCH) and treated at

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the Department of Oral and Maxillofacial Diseases, (HUCH) during the 31-year period between March 1985 and February 2016. HUCH serves a population of 1.5 million inhabitants, covering about 27% of the Finnish population.

The Q-pati database of Department of Pathology was searched to identify patients with diagnosed ameloblastoma. The histopathological samples were evaluated, and patients' medical records were reviewed to collect clinical data.

Re-evaluation of histological samples

Formalin-fixed, paraffin-embedded, normal haematoxylin and eosin stained (HE) tissue samples were collected. One oral pathologist (JK) re-evaluated the specimens regarding the type and growth pattern. Ameloblastoma type was classified as solid/multicystic, unicystic, or peripheral. Growth pattern was classified as follicular, plexiform, or mixed (i.e. variations of follicular, plexiform, acanthomatous, desmoplastic, and granular cell patterns). Tumour sizes (mm) were collected from radiographic statements and if these were not available, from recorded pathological diagnosis.

Clinical data

The following demographic and clinical parameters were recorded from the patient files: age, gender, preoperative clinical signs (i.e. observed by the clinician), subjective symptoms (i.e. experienced by the patient), and location of the tumour. Tumour location was classified as maxillary or mandibular. Locations were further classified as subgroup anterior (i.e. region of incisors/canines), premolar, molar/posterior, or gingival. The information of recurrence was collected from patient records

Study variables and data analysis

The main outcome variables were location, type, growth pattern, and size of ameloblastoma. The explanatory variables were gender and age of the patient. For this purpose, patients were classified into age groups: <50 years and ≥ 50 years. Associations for the continuous variables were determined with the *t*-test and for the categorized variables with the chi-square test. Fisher's exact test was used to calculate the significance of growth patterns in recurring tumours compared to non-recurring tumours.

Ethical considerations

The Ethics Committee of Surgery and HUCH's Internal Review Board approved the study protocol (Dnro 151/13/03/02/2015). The study protocol follows the guidelines and ethical principles of the Helsinki Declaration.

Supplier

Technical assistance and laboratory equipment and material was kindly provided by Professor Caj Haglund's group.

Results

A total of 56 patients with primary ameloblastoma were initially identified from the Q-pati registry. Of these patients, 22 had to be excluded due to missing samples and relevant patient information, leaving 34 patients (60.7%) for the present analysis. In three of these cases, we relied on the primary pathological diagnosis reports due to lost slides or paraffin blocks.

Patient characteristics

Patient characteristics are presented in Table 1 and Figure 1. The male:female ratio was 1.6:1. Mean age was 48.2 years: for males 55 years and females 37 years. The tumour was most often located on the mandible and particularly the molar/posterior region. The solid/multicystic tumour type was more frequent than other types, and a mixed growth pattern was more common than other growth patterns. Figure 2 demonstrates some of the variation seen in histology. Mean tumour size was 42.5 mm (range 10–90 mm). For two tumours, we found no reliable records of tumour size.

Association between gender and location ($p = .034$) was seen in this cohort as male patients had more maxillary tumours than female patients. We detected an association between age groups under and over 50 years and location ($p = .007$). Maxillary tumours occurred to older persons when compared to mandibular tumours (Table 2). Tumour size in male patients was on average 47.5 mm and in female patients 34.1 mm. Despite the 13.4 mm size difference, no significant association could be seen ($p = .083$) with gender.

Table 1. Descriptive statistics of 34 patients with ameloblastoma.

	All patients ($n = 34$)	% of 34
Gender		
Males	21	62
Females	13	38
Age (years)		
Range	13.8–83.3	
Mean	48.2	
Location		
Mandible	28	82.4
Maxilla	6	17.6
Location subgroups		
Mandible/molar/posterior	17	50.0
Mandible/premolar	7	20.6
Maxilla/molar/posterior	5	14.7
Mandible/anterior	3	8.8
Mandible/gingival	1	2.9
Maxilla/premolar	1	2.9
Type of ameloblastoma		
Solid/multicystic	27	79
Unicystic	6	18
Peripheral	1	3
Growth pattern of ameloblastoma		
Mixed	27	79
Plexiform	6	18
Follicular	1	3
Size of ameloblastoma (mm)[a]		
Range	10–90	
Mean	42.5	

[a]In two patients, tumor size could not be identified.

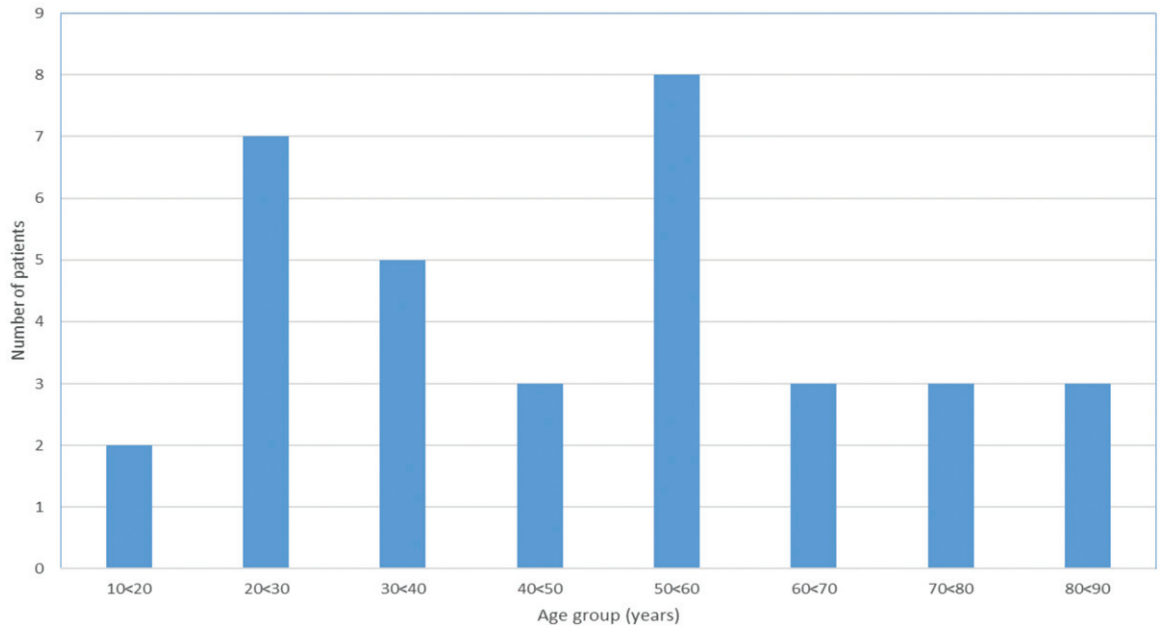

Figure 1. Age distribution in 34 patients with ameloblastoma.

Of 34 tumours, 11 recurred. Table 3 demonstrates growth patterns in different ameloblastoma types and non-recurring and recurring tumours. Recurrence in our material does not seem to depend on growth pattern. ($p = .5773$)

Symptoms and clinical signs

The subjective symptoms and clinical signs are presented in Table 4. The commonest subjective symptoms experienced by the patients were pain/vaguer sensations (19/34, 55.9%) and enlargement of the jaw (12/34, 35.3%). Only six patients had no subjective symptoms whatsoever. The commonest clinical finding was enlargement of the jaw (29/34, 85.3%). Only one (2.9%) patient had no clinical signs of the tumour; however, this patient experienced pain in the affected area.

Discussion

The aim of the present study was to clarify clinical and pathological features of ameloblastoma. The major finding seen in this cohort was the high average onset age in male patients, especially patients with maxillary tumours. Additionally, in our patients the signs and symptoms were rather diverse, and pain or sensation were more frequent than reported previously [6]. An insight to histological patterns revealed several variations of growth patterns that typically are simplified in research papers probably for clarity reasons. Our results regarding location, sex, and tumour size are in concordance with reports with similar study settings.

Our cohort consists of almost twice as many male as female patients. A somewhat similar phenomenon has been reported before by Reichart et al. and Dhanuthai et al. Our study data of 34 patients showed a higher average onset age than reported by Reichart et al. [6]. In line with our results, Dhanuthai et al. [5] reported North American patients to have a mean age of 48.54 ± 0.54 years. Patients in Asia on the other hand were younger. This may reflect the fact that Finnish patients are genetically closer to the North American patients. In our study cohort, the male patients tended to have larger tumours even though we did not find statistical correlation. The reason for this might be that male patients tend to delay seeking medical help, which sometimes postpones the diagnosis [11]. Since ameloblastoma is a relatively asymptomatic, slow growing tumour, it can be speculated that the tumour has existed long before diagnosis, perhaps in male patients with larger jaw structures even longer than in female patients, especially when age increases. As maxillary tumours seem to appear in older patients we could further contemplate that these tumours are detected later than the ones in mandible. This may be due to the fact that maxillary tumours have more space to grow without major symptoms. The male predominance in maxillary tumours may in addition cause the fact that these tumours were diagnosed later than tumours in female patients.

In our tumour material we had 6 (18%) unicystic tumours of which only one recurred (16%). Of solid/multicystic tumours 9/27 (33%) recurred. The single peripheral type ameloblastoma recurred as well. This may be because they did not realize at first that the lesion was an ameloblastoma. Of studied ameloblastomas 79% had mixed growth patterns and only 21% had a uniform growth pattern. It can be speculated that acanthomatous and desmoplastic growth patterns are responses to tissue reactivity due to the ongoing tumour process (Figure 2(c,d)). Our results confirm the known fact that growth patterns do not reflect recurrence [2]. However, it must be acknowledged that the variance of growth patterns makes comparing difficult.

Preoperative signs were present among nearly all patients. Expansion of the jaw was the commonest sign, similarly to Reichart et al. [6], and occurred in almost every patient. In our study, 14.7% (5/34) of patients had discharge from the tumour area. In some cases, the tumour was infected, and a

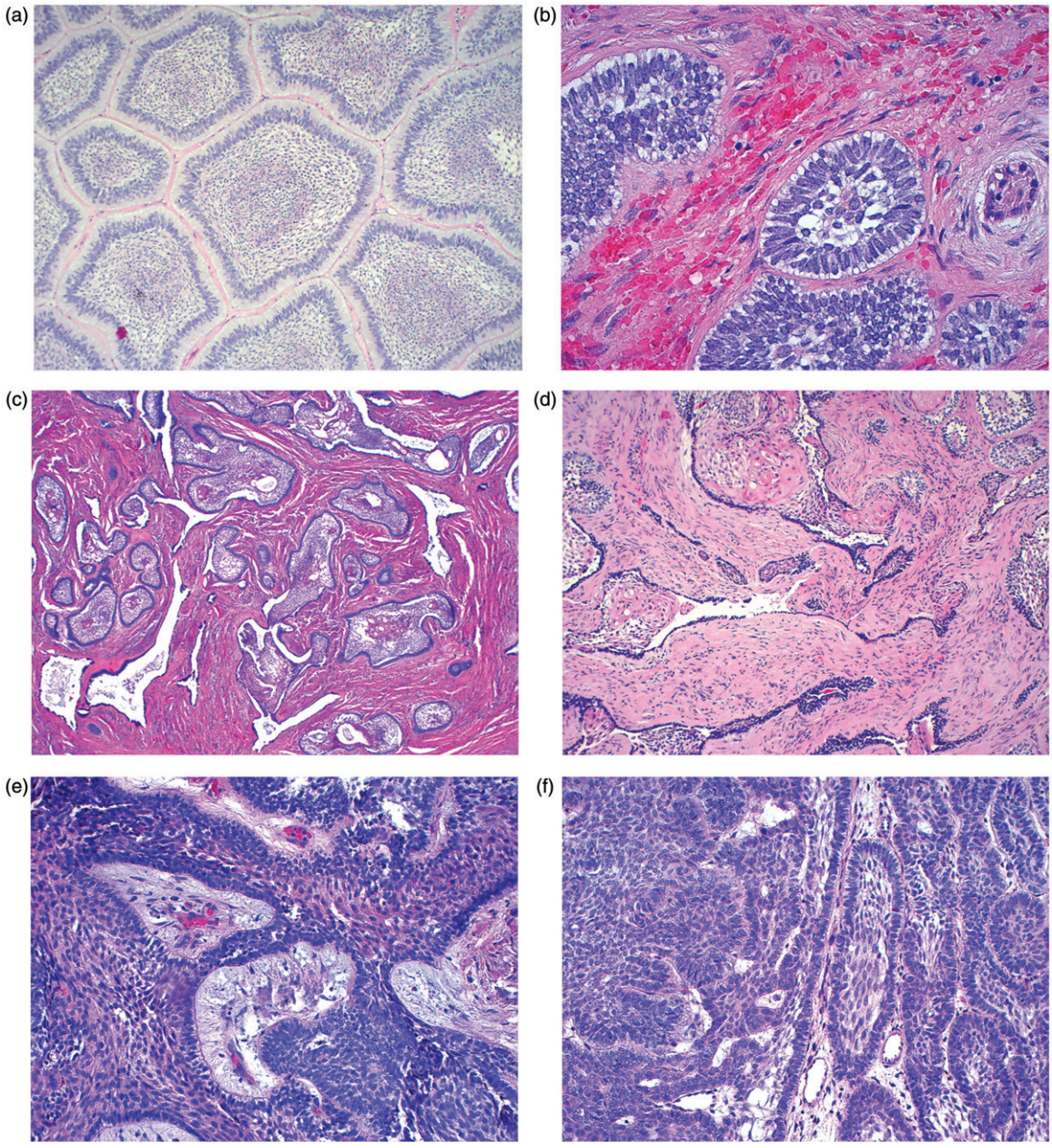

Figure 2. Ameloblastoma, histological variances of growth patterns in slides of HE stains. Follicular growth pattern, islands of tumor follicles with scant stroma [(a) magnification ×100]. Follicular ameloblastoma islands in an abundant stroma [(b) magnification ×400]. Follicular ameloblastoma with acanthomatous metaplasia [(c) magnification ×100)]. Follicular, desmoplastic, and acanthomatous growth patterns [(d) magnification ×100)]. Strands of plexiform tumor growth with stromal islands [(e) magnification ×200]. Follicular and plexiform pattern in a cell-rich tumor [(f) magnification ×200].

Table 2. Association between predictors and outcomes in 34 patients with ameloblastoma.

	Mandible ($n = 28$)	% of 28	Maxilla ($n = 6$)	% of 6	Solid ($n = 27$)	% of 27	Unicystic ($n = 6$)	% of 6	Mixed ($n = 27$)	% of 27	Plexiform ($n = 6$)	% of 6	Average size (mm)
Gender													
Males	15	54 %	6	100 %	18	67 %	3	50 %	16	59 %	5	83,3 %	47.5
Females	13	46 %	0	0 %	9	33 %	3	50 %	11	41 %	1	16,7 %	34.1
	$p = .034$ (jaw vs. gender)				$p = .248$		$p = .514$		$p = .555$		$p = .231$		$p = .083$
Age group													
<50 years	17	61 %	0	0 %	12	44 %	5	83 %	13	48 %	3	50,0 %	42.2
≥50 years	11	39 %	6	100 %	15	56 %	1	17 %	14	52 %	3	50,0 %	42.8
	$p = .007$ (jaw vs. age group)				$p = .203$		$p = .072$		$p = .672$		$p = 1.000$		$p = .948$

Size analyzed by *t*-test, all other by chi-test.

Table 3. Growth patterns compared to type and recurrence.

	Solid/multicystic	Unicystic	Peripheral	Non-recurring tumor	Recurring tumor	Total
Mixed	24	2	1	19	8	27 (79.4%)
Plexiform	3	3	0	3	3	6 (17.6%)
Follicular	0	1	0	1	0	1 (2.9%)
Total	27	6	1	23	11	34 (100%)

Table 4. Subjective symptoms and clinical signs of ameloblastoma in 34 patients.

	Number of patients	% of 34
Subjective symptoms[a]		
Pain or vaguer sensations	19	55.9
Enlargement of the jaw bone	12	35.3
No subjective symptoms	6	17.6
Paresthesia	3	8.8
Discharge	2	5.9
Epistaxis	2	5.9
Ulcer	2	5.9
Fistula	2	5.9
Congested nose	1	2.9
Tooth deviation	1	2.9
Unhealed extraction socket	1	2.9
Clinical signs[b]		
Enlargement of the jaw bone	29	85.3
Radiological signs without symptoms	6	17.6
Tooth mobility	5	14.7
Discharge	5	14.7
Soft tissue swelling	3	8.8
Fistula	3	8.8
Ulceration	2	5.9
Visible tumor mass	2	5.9
No clinical signs	1	2.9

[a]experienced by the patients;
[b]observed by the clinician.

pus-like discharge was noticed accompanied by swollen lymph nodes. Only six (17.6%) cases were incidental radiological findings.

Pain or focal sensations are rarely mentioned as a frequent symptom [12–14]. Milman et al. reported that only 16% of patients experienced pain [15]. In our study, pain or focal sensation symptoms were present in almost 55.9% of cases; however, this number also includes the feeling of pressure and vague sensations, which were not considered in the Milman et al. study. Filizzola et al. reported that one third of their 70 cases had experienced tumour-associated symptoms emphasizing pain and discharge [16]. Altogether there might be differences in the way clinicians report signs and symptoms. In our material, these aspects were recorded rather concordantly and offer an insight into various symptoms experienced by the patient and signs observed by the clinician.

Finnish patients with ameloblastoma do not seem to differ from other populations histologically. The proportion of mixed growth pattern seems significantly large compared with other studies. Usually the predominant growth pattern determines the histological classification, which partly explains the difference. In our study, all the cases with histological variation were classified mixed to point out the interesting diversity of possible growth patterns in an ameloblastoma tumour. Ameloblastomas with cystic and follicular growth patterns are suggested to invade the inferior alveolar nerve more often than a solid ameloblastoma with plexiform growth pattern [17]. The precise description of the growth pattern and radiological findings are therefore important to provide the best treatment option. The longer the tumour persists, the more frequently recurrences appear; and the more conservative treatment procedures the patient has undergone, the greater the risk of malignant transformation [3,18].

The study cohort was small, demonstrating that ameloblastoma is a rare tumour also in Finland. A substantial portion of cases had to be excluded because of a lack of material including paraffin blocks and clinical information. Some tissue samples were unfortunately old, torn, and fragmented and did not provide accurate information. Some tissues had been decalcified and thus had lost the clearest architecture. In most cases, there existed only a portion of the tumour; some samples were biopsies. The known limitation of this study is that the amount of cases possible to evaluate is low.

To our knowledge, other Norther European studies focusing on clinical data of ameloblastomas do not exist. A collective study of Scandinavian patients with ameloblastoma would give scientifically more reliable insight into Nordic patients with ameloblastoma. Furthermore, it would be interesting to study how many patients with ameloblastoma develop a metastasizing ameloblastoma or an ameloblastic carcinoma. For this, as well, a collective Scandinavian cohort would be beneficial.

Conclusions

Ameloblastoma is a rare tumour in Finland. This study gives insight into the profile of patients with ameloblastoma among a southern Finnish population. To conclude, Finnish patients with ameloblastoma differed mostly from previous studies in being predominantly male, older, and experiencing more subjective symptoms: mainly pain and weaker sensations.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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