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Retrospective Study of Ameloblastoma: The Possibility of Conservative Treatment

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ABSTRUCT

At our institutions, most cases of the solid or multicystic type were treated as conservatively as possible in order to avoid disadvantages of radical treatment. The aim of present study was to retrospectively analyze the ameloblastoma cases diagnosed at our two institutions, to classify them according to the criteria of the 2005 WHO classification, and to evaluate the possibility of using a conservative approach for the surgical treatment of ameloblastoma.

Maxillary cases, unicystic cases, peripheral cases and resection-treated cases were excluded from this study. In 23 tumors of mandibular solid or multicystic ameloblastoma, a patients' age, gender, location, clinical signs, duration, radiographic appearance, preoperative diagnosis, ameloblastoma subtypes, treatment, and recurrence were investigated.

The recurrence rate (48.7%) in this study was lower than the reported recurrence rate after conservative treatment for solid or multicystic ameloblastoma and was higher than the reported recurrence rate of ameloblastoma, inclusive of other types. However, all patients who were diagnosed with recurrences have maintained their quality of life and were satisfied for at least several years after the conservative treatment. In conclusion, we demonstrated one possibility that a conservative approach might be employed in the surgical treatment of ameloblastoma (even of the solid or multicystic type).

INTRODUCTION

Ameloblastomas are the second most common benign odontogenic tumors [9, 22]. They occur mainly in the mandible, especially affecting the molars, the mandibular angle and the ramus [3]. They interfere with both function and facial esthetics. Although ameloblastomas are considered to be benign, they are locally invasive with a high rate of recurrence [9, 20, 22, 24, 25].

The treatments used for ameloblastoma are varied, depending on the histological type and the location, as resection (marginal or segmental), enucleation, curettage,

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marsupialization or a combination of these techniques can all be effective [11, 18, 20, 22, 24, 25]. In spite of these many treatment methods identified in the literature, there is still controversy about the therapy based on the clinical presentation or histopathological characteristics of the tumors [11, 18, 20, 22, 24, 25]. The recurrence rates of ameloblastoma are reported to be as high as 15% to 25% after radical treatment [24, 25] and 55% to 90% after conservative treatment [8, 18, 20, 24]. Therefore, wide resection of the jaw in accordance with the treatment of malignant tumors is often recommended for ameloblastoma [8, 18, 20, 21]. On the other hand, recent advances in the understanding of the biological features of ameloblastoma have led to more successful conservative surgical treatments [11, 18, 23]. Regardless, when the surgical treatment is selected, it is necessary to consider various factors, such as the type of tumor, its anatomical location, the extent of disease, the histological and radiographic characteristics of the tumor, as well as the patient age and compliance.

There are three main types of ameloblastomas that must be recognized and differentiated, because they have different treatments and prognoses, and are divided according to the histopathological description into the solid or multicystic, unicystic and peripheral types [9, 22]. The solid or multicystic type is more aggressive and requires a more radical treatment than the other types, and has a relatively higher rate of recurrence [18, 20]. However, the resection of the mandible, including the condyle and wide anterior region results in serious cosmetic, functional and reconstructive problems in growing young patients [5, 19, 28].

At our institutions, most cases of the solid or multicystic type were treated as conservatively as possible in order to avoid these disadvantages, if the patients desired conservative treatment. The various risks of late recurrence and malignant changes, based on the evidence in the literature [17, 30], have been explained to the patients.

The aim of present study was to retrospectively analyze the ameloblastoma cases diagnosed at our two institutions, to classify them according to the criteria of the 2005 World Health Organization (WHO) classification [9], and to evaluate the possibility of using a conservative approach for the surgical treatment of ameloblastoma.

MATERIALS AND METHODS

Materials

This was a nonrandomized, retrospective (historic) cohort study of patients. Thus, this study was granted exemption of institutional review board approval by our institution. Records from 37 patients with maxilla or mandibular ameloblastoma who had been treated in the Department of Oral and Maxillofacial Surgery, Kakogawa East City Hospital, Kakogawa, the Department of Oral and Maxillofacial Surgery and the Department of Oral and Maxillofacial Surgery, Kobe University Graduate School of Medicine, between December 2001 and April 2012 were included in this study. The minimum follow-up was eight months. The patients' ages ranged from 7 to 84 years (mean, 38.8 years). Each patient's age, gender, tumor location, clinical signs and symptoms, duration of symptoms, radiographic appearance of the tumor, preoperative diagnosis, ameloblastoma subtype, treatment and recurrence were abstracted from the case summaries. In total, 34 tumors in this series were mandibular, accounting for 91.9% of cases, and three cases were maxillary, accounting for 8.1% of cases. The maxillary ameloblastoma cases were excluded from this study. Of the 34 patients with mandibular ameloblastoma, there were 17 cases (50.0%) of the solid type, 11 cases (32.4%) of the multicystic type, three cases (8.8%) of the unicystic type, one case (2.9%) of the desmoplastic type and two cases (5.9%) of the peripheral type. The patients with unicystic and peripheral type were excluded from this study because the behavior and recurrence rates

of these lesions differ from those of the solid or multicystic type. The desmoplastic type was included in the multicystic type with respect to clinicopathological characteristics.

Methods

For the analysis of mandibular ameloblastoma, the site of occurrence was categorized as anterior, body and posterior based on the region affected. For the mandible, the posterior region was defined to include the ramus, angle, coronoid process and condyle. Sections of all primary and recurrent tumors stained with hematoxylin and eosin were retrieved and reviewed to reclassify them according to criteria of the recent WHO classification of odontogenic tumors [9]. All of the recurrent tumors had no histological changes or malignant transformation.

The treatment methods were classified into three group: conservative treatment (*i.e.* enucleation, marsupialization followed by enucleation, or enucleation with bone curettage without a safety margin), resection with a bone margin (*i.e. en bloc* resection or marginal mandibulectomy with some safety margin and jaw continuity) and segmental resection or maxillectomy (*i.e.* hemimandibulectomy or partial maxillectomy with some safety margin and loss of jaw continuity). The difference between resection with a bone margin and segmental resection was defined as whether or not the mandibular bone had lost its continuity. Marginal or segmental resection was performed if the tumor had obviously perforated the bony cortices and infiltrated the soft tissue. Of the 34 patients with mandibular ameloblastoma, conservative treatment was administered in 28 cases (82.4%), resection with a bone margin was performed in three cases (8.8%) and segmental resection was performed in three cases (8.8%). Resection and segment resection cases were excluded from this study.

A total of 23 mandibular ameloblastoma cases (solid or multicystic type) were treated with conservative treatment.

The disease-free survival function curves of the patients with or without a recurrence were obtained using the Kaplan-Meier method.

RESULTS

The results are summarized in Table I. The patient follow-up period ranged from 8 to 130 months after primary surgery. Three of the 23 cases were followed up for less than five years. During this time, 10 recurrences developed. The types of surgical treatment and recurrence data for the ameloblastomas are shown in Table II. Recurrences were observed in 10 patients (recurrence rate: 48.7%), all of whom had received conservative treatment. Ten (100%) recurrent tumors consisting of solid type tumors (four cases: 40.0%) and multicystic type tumors (six cases: 60.0%) were also recorded. Regarding the histological patterns of the recurrent tumors, there were plexiform type tumors (three cases: 30.0%), follicular type tumors (six cases: 60.0%) and desmoplastic type tumors (one case: 10.0%).

Figure 1 show the disease-free survival function curves with conservative treatment. Figures 2 and 3 show the disease-free survival function curves with the clinicopathological and histological patterns of the primary ameloblastomas. Figure 4 show the disease-free survival function curves with the variants of primary conservative surgical treatment.

Table I. The summary of data on 23 ameloblastoma cases with conservative treatment

Factor	N (%)
Age and gender (n=23)	
Age (average, 28.5; range 7-59)	
Gender	
Male	12 (52.2)
Female	11 (47.8)
Location site on mandible	
Body	9 (39.1)
Posterior	14 (60.9)
Clinical signs and symptoms	
None (incidentally at dental radiographic examination)	12 (52.2)
Facial deformity	9 (39.1)
Odontogenic ploblems	2 (8.7)
Radiographic appearance	
Unilocular	12 (52.2)
Multilocular	11 (47.8)
Preoperative diagnosis	
Ameloblastoma	17 (73.9)
Dentigerous cyst	3 (13.0)
Others	3 (13.0)
Clinicopathological subtypes	
Solid	12 (52.2)
Multicystic	11 (47.8)
Histological subtypes	
Plexiform	11 (47.8)
Follicular	11 (47.8)
Desmoplastic	1 (4.4)
Conservative treatment	
Enucleation after marsupialization	6 (26.1)
Enucleation with bone curettage	7 (30.4)
Enucleation only	10 (43.5)

Table II. The characteristics of 10 cases of recurrent ameloblastoma

Case Numbar	Age(yr)	Gender	Site	Radiographic appearance	Clinicopathological subtypes	Histological subtypes	Primary treatment
1	13	Female	Body	Multilocular	Solid	Plexiform	Enucleation after marsupialization
2	18	Male	Posterior	Multilocular	Multicystic	Follicular	Enucleation with bone curettage
3	33	Female	Body	Multilocular	Solid	Follicular	Enucleation
4	7	Female	Body	Unilocular	Multicystic	Follicular	Enucleation after marsupialization
5	36	Female	Body	Multilocular	Multicystic	Follicular	Enucleation with bone curettage
6	36	Male	Posterior	Multilocular	Solid	Plexiform	Enucleation
7	59	Male	Body	Unilocular	Solid	Plexiform	Enucleation
8	19	Male	Posterior	Unilocular	Multicystic	Follicular	Enucleation after marsupialization
9	28	Male	Posterior	Unilocular	Multicystic	Desmoplastic	Enucleation
10	15	Female	Posterior	Unilocular	Multicystic	Follicular	Enucleation after marsupialization

Recurrence onset* and treatment					
First (months)	Treatment	Second (months)	Treatment	Third (months)	Treatment
48	Enucleation	38	Enucleation	-	---
44	Enucleation with bone curettage	-	---	-	---
15	Enucleation with bone curettage	20	Enucleation with bone curettage	-	---
22	Enucleation with bone curettage	-	---	-	---
24	Enucleation with bone curettage	29	Enucleation with bone curettage	22	Enucleation with bone curettage
5	Enucleation	10	Enucleation	-	---
5	Enucleation	-	-	-	---
42	Enucleation	-	-	-	---
11	Enucleation	7	Enucleation	-	---
5	Enucleation	-	-	-	---

* Onset refers to duration from primary treatment to subsequent recurrence (s)

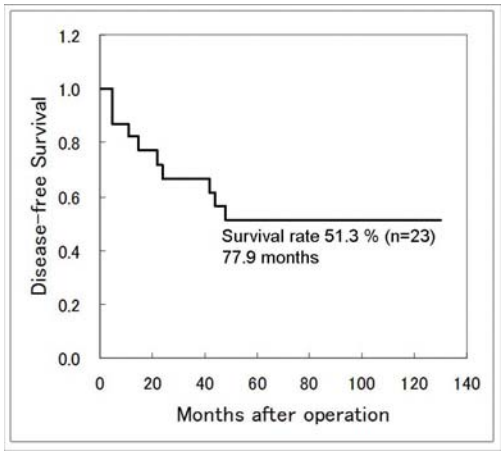

Figure 1. Disease-free survival function curves with conservative treatment

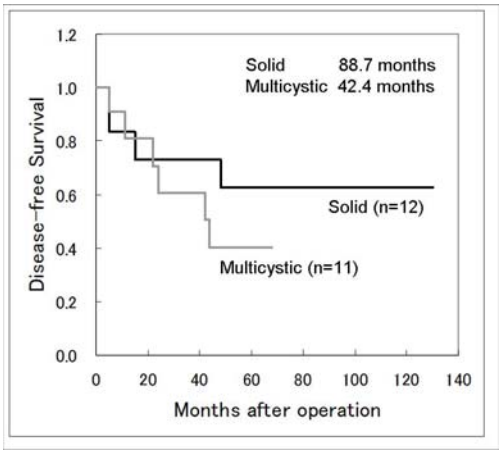

Figure 2. Disease-free survival function curves with the clinicopathological patterns

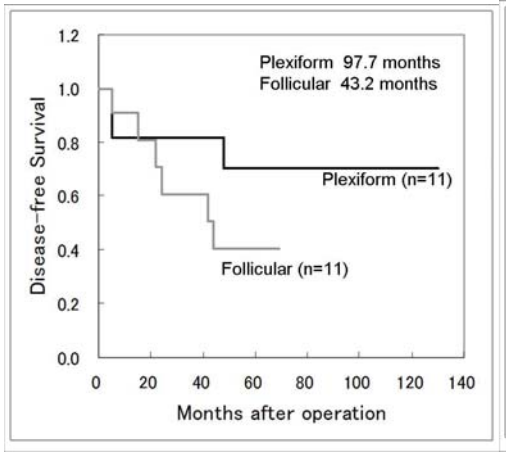

Figure 3. Disease-free survival function curves with the histological patterns

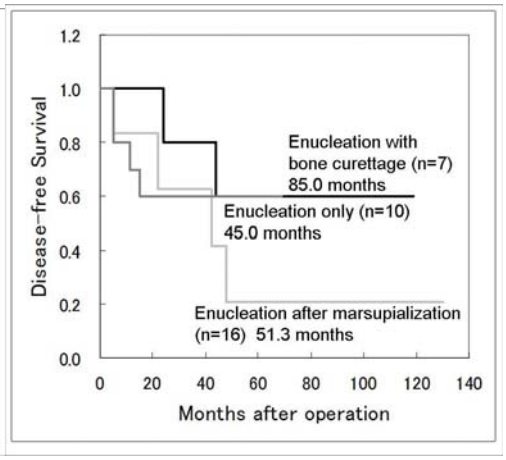

Figure 4. Disease-free survival function curves with the variants of primary conservative surgical treatment

DISCUSSION

Even if ameloblastoma is considered to be benign, it is locally invasive and recurs at a high rate [14, 20, 24, 25, 29]. The treatment of adult ameloblastomas differs according to the literature and remains a controversial issue [3, 8, 11, 17, 18, 2-24, 25]. For the treatment of ameloblastoma, we select the most suitable treatment from various procedures after giving consideration to the age of the patient, location of the tumor and the nature and extension of the disease in order to both correct the disease and to restore the normal form and function of the jaw and face. In this study, we demonstrated the possibility that a conservative approach can be successfully employed in the surgical treatment of ameloblastoma of the solid type (high risk of recurrence).

The present series of 23 cases of ameloblastoma of the solid or multicystic type showed a mean age of 28.5 years, which is in agreement with two previous meta-analyses [15, 22]. It is well known that ameloblastoma occurs more frequently in the mandible than in the maxilla, and that these tumors are located mainly in the body and posterior mandible [22]. In the present study, most ameloblastomas were also found in the mandible and were located in the body and posterior regions. Several studies have reported that the most common presenting complaint of ameloblastoma patients was painless swelling (facial deformity) [13, 15, 22]. However, in this study, 12 of the total cases (52.2%) were asymptomatic, similar to a previous report [1]. A unilocular radiolucency was the most commonly encountered radiographic presentation in the present study (52.2%). However, this result is not in agreement with the findings of other studies [13, 26, 29].

Ameloblastomas are unique tumors with a strong tendency to recur after treatment [11, 12, 19]. Recurrence in ameloblastoma is believed to be the result of several risk factors, notably tumor subtype, treatment method, and tumor behavior [11, 22]. Tumors with a follicular, granular, or acanthomatous growth pattern have a reportedly high likelihood of recurrence, whereas desmoplastic, plexiform, and unicystic subtyes have a relatively low recurrence potential [11, 22]. In this study, the recurrent tumors exhibited a follicular growth pattern (median time: 43.2 months) or more than a plexiform growth pattern (median time: 97.7 months), similar to the findings of these reports [11, 22].

The solid or multicystic type is locally more invasive than other types, and the preferred treatment is generally wide surgical resection [3, 18, 20, 21]. Wide surgical resection also removing the overlying soft tissue has been suggested if the tumor has perforated the bony cortices [18]. In contrast, the unicystic type has a cyst-like behavior, and a more conservative surgical approach is the treatment of choice [11, 15, 18, 23]. Historical articles on solid or multicystic ameloblastomas suggested a recurrence rate of 60-80% with local conservative treatment only [10, 16, 25]. In this study, cases of the solid or multicystic type were treated conservatively with enucleation or enucleation with bone curettage. In addition, 10 (43.5%) of the 23 cases of solid or multicystic ameloblastoma exhibited recurrence following conservative treatment. This result is lower than the reported recurrence rate after conservative treatment for solid or multicystic ameloblastomas [10, 16, 25]. However, the recurrence rate observed in this study was higher than the reported recurrence rate of ameloblastoma, inclusive of other types (unicystic and peripheral types, etc…), which ranges from 15.9% to 20.6% [13, 22]. In particular, three of the 23 cases were followed up for less than five years. The shortest follow-up in this group of patients was eight months. This is not long enough to determine a reliable recurrence rate. Therefore, we will investigate the long-term outcomes in future work.

In conservative treatment of this study, the recurrence rate of ameloblastomas was higher in enucleation only than in enucleation with bone curettage. A major factor is cancellous

bone infiltration by ameloblastomas. It is generally known that there is a significant association between the type of treatment and recurrence rate in ameloblastoma [4, 6, 14]. Therefore, wide surgical resection has been used to treat solid ameloblastomas to prevent possible recurrences [7, 8, 18]. We also considered that radical treatment must be performed in cases of ameloblastoma not approachable by enucleation. However, these surgeries are invariably associated with serious problems for the patient, such as masticatory dysfunction, mutilation, facial deformity and abnormal mandibular movements. To help prevent these problems associated with a radical treatment (complete resection of the lesion site), there has been a trend in the scientific community during the last decade to employ less invasive treatment methods for ameloblastomas, after carefully considering the individual clinical, radiographic and histopathological variables of each case [2]. The rate of recurrence is an important factor for selecting the type of treatment, but other factors are also important and must be considered, including potential morbidities and the patient's quality of life (QOL) [2]. Therefore, in light of the important fundamental concepts illustrated by this study, our philosophy has been to provide a treatment that is as minimally invasive as possible, choosing enucleation when it is possible, in order to conserve the mandibular bone and to decrease the morbidity associated with radical segmental resection. The patients who were treated at our institutions agreed with this opinion, and all understood the risks of recurrence. All patients who were diagnosed with recurrences have maintained their QOL and were satisfied for at least several years after conservative treatment. However, a second operation was required within a period of five years in 43.5% of the cases. Also, a large number of local recurrences is a risk factor for malignant transformation [30], and this should be kept in mind during the follow-up of such patients, although there was no malignant transformation or metastasis in this study. Recently, Simon et al. reported a means of performing reconstruction that is less invasive than the use of free microsurgical fibula flaps to repair defects after radical treatment [27]. They also reported that immediate reconstruction using reconstruction plates, autogenous particulate bone grafts and platelet-rich plasma produce a better QOL than that observed in patients treated without reconstruction. Such findings may change the opinion that radical treatment is invariably associated with serious problems with respect to the QOL of the patient.

Postoperative follow-up is important in the management of ameloblastoma because of the high rate of recurrence, which depends on factors such as the choice of treatment of the primary lesion, extent of the lesion, site of origin, proliferation of residual tumor not removed during surgery, and implantation of neoplastic tissue in other locations during surgery. The duration between the initial treatment and development of recurrent lesions ranged from five to 48 months, with a mean of 22.1 months. It has been reported that most recurrences of ameloblastoma are diagnosed within the first five years after the initial treatment [19, 22, 29], and our present study confirmed these findings. Indeed, all but one recurrence occurred within four years after the first operation. We suggest that patients should undergo a close follow-up, including an orthopantomograph, every six months for the first five years and every 12 months for the subsequent five years to diagnose recurrences at an early stage. We suggest that orthopantomography should then be performed every 2-3 years after the first 10 years of follow-up, because some papers have reported recurrences after a disease-free period of 25 years [5, 28]. Computed tomography is recommended for further investigations to clarify the features of the recurrence if recurrence is suspected on the basis of panoramic radiography.

At our institutions, most cases of the solid or multicystic type were treated as conservatively as possible in order to avoid the disadvantages of radical treatment. Therefore,

the recurrence rate (48.7%) in this study was lower than the reported recurrence rate after conservative treatment for solid or multicystic ameloblastoma and was higher than the reported recurrence rate of ameloblastoma, inclusive of other types (unicystic and peripheral types). However, all patients who were diagnosed with recurrences have maintained their QOL and were satisfied for at least several years after the conservative treatment. In conclusion, we demonstrated one possibility that a conservative approach might be employed in the surgical treatment of ameloblastoma (even of the solid or multicystic type).

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