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Any Optimal Treatment for the Keratocystic-Odontogenic Tumor Yet? A Questionnaire among Syrian Oral and Maxillofacial Surgeons

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Abstract*: The keratocystic-odontogenic tumor could be existed inside the jaw bone, with a characteristic lining of parakeratinized stratified squamous epithelium. It is considered to be a benign tumor with high recurrence rate, and could be a uni- or multi-cystic tumor; usually occurs in the third or fourth decade of one's life time. There are many methods for treating such tumor as marsupialization, curettage, osteotomy, or enucleation and marsupialization with safe border curettage. Unfortunately, there is no consensus on a uniform treatment plan, and there are a lot of arguments regarding the best way of treatment.*

The aim of this study was to determine, by means of a questionnaire, the best surgical treatment of keratocystic odontogenic tumor according to surgeons' subjective opinions.

Materials and methods: A questionnaire consisted of several questions was presented to 63 oral and maxillofacial surgeons in four hospitals in Damascus, and in the maxillofacial surgery department in Syrian Private University to determine the best treatment of keratocystic-odontogenic tumor. The questionnaire was answered during an interview with the surgeon. An internet search was made to obtain all literature research regarding this controversial subject.

Results: In the literature, there was no agreement on a specific treatment method for keratocystic odontogenic tumor. According to the questionnaire, the best choice through the survey was bone resection.

Conclusion: The treatment of keratocystic odontogenic tumor remains a controversial issue. The differences in treatment methods were related to every individual clinical case considering several factors. Every case should be treated individually.

1. Introduction

The keratocystic-odontogenic tumor is a tumor that exists inside the bone, with a characteristic lining of parakeratinized stratified squamous epithelium. It is considered to be a benign tumor with high recurrence rate, and could be of a uni- or multi-cystic form; usually occurs in the third or the fourth decade of one's life time, most commonly in men than in women. Within the body of the mandible, that tumor is mostly seen in the molars' region and in the vertical ramus (1), and is associated with nevoid basal cell carcinoma syndrome (2). In 1956, Barnes described the odontogenic keratocyst as a cyst with keratinized stratified squamous epithelium of odontogenic origin (3). In 2005, World Health Organization (WHO) changed the name to become keratocystic-odontogenic tumor (KOCT), and could be diagnosed by radiographic exam, while the definitive diagnosis could be obtained by pathological examination.

There are many methods for treatment; marsupialization, curettage, osteotomy, or enucleation and marsupialization with safe border curettage. Unfortunately, there is no consensus on a uniform treatment plan, and there are a lot of arguments regarding the best way of treatment, though several factors interfere with the treatment plan (4).

2. Literature Review

The keratocystic odontogenic tumor is considered to be a dangerous lesion of oral cavity potentially for its aggressive infiltrative behavior, quick growth, wide

expansion, injury of the near structures, and highly recurrence rate, which branches small cysts with a thin liner hard to remove which causes a recurrence and regrowth of the lesion (5) and associated with nevoid basal cell carcinoma syndrome (2). KOCT could be found in both the maxilla and the mandible, anterior and posterior region, in adults and young ones, most commonly in the mandible 60% to 80% in posterior regions of the mandible body and ramus; occurs much more in men than women (6, 7).

A study was conducted in 2005 by Ortakoğlu and it has been shown that the KOCT was associated with impacted third molars, and it might be a cyst of the impacted third molar of uni- or multi-cystic origin (8). It attacks the adjacent tissues and structure, which causes absorption in bones and adjacent teeth.

There are multiple treatment ways :

1. ostectomy
2. enucleation
3. resection with curettage
4. curettage
5. marsupialization
6. resection with supplementary treatment
7. carony solution after resection

According to Walid Ahmad (9), in order to choose the best treatment, the following factors should be taken into consideration: size, location, the relationship with adjacent structure, lesion nature, and the histological changes of the lesion. Researches have not reached a consensus on the appropriate treatment of Keratocystic Odontogenic tumor. In 2000, a study was conducted to determine the best way of surgical treatment where the mucous membrane of the soft tissue was removed, and supplementary treatments were applied, which consist of : carony solution and curettage, freezing and decompression. The results of this study suggested that resection with supplementary treatments is the most successful way, and gives a lower rate of recurrence (10). In 2006, Giuliani conducted a study and used this treatment plan: pressure application, curettage only, resection only, but recurrence appeared in all cases (11).

In 2012, Sivaraj Sivanmala et al. conducted a research regarding the best method, and it has been shown that the use of carony's solution after lesion resection was the best choice, because no recurrence case were reported after five years of observation (12). It was shown previously that the use of chemical solution enhances the elimination of the epithelial remains and small cysts, which reduces recurrence rate (13-15). According to Porgel (16), it was found that when using carony solution after resection, the recurrence rate was reduced by (2.5%) compared to using resection alone. And it seemed that this procedure was less aggressive, with a low recurrence rate. Also, applying carony solution to the cyst cavity for 3 minutes after resection gave good results in recurrence compared to using resection alone.

In 2006, Shear and Xinguang (17) found out that the perfect treatment would be resection and curettage, then applying supplementary treatment like liquid nitrogen, or carony solution, or trichloroacetic acid, because these solutions have the ability to kill the epithelial remains and small cysts. Morgan et al. found out that the usage of supplementary treatment with resection reduces recurrence rate by 18% (18). There are many surgeons who prefer more conservative way in keratocystic odontogenic tumor treatment, but still there is no ability to specify the good supplementary treatment accurately.

According to Bande et al. (19), the resection was the best method, which most treatments depend upon and the usage of cooling and chemical fixation made a significant difference in result. Auluck et al. (20) used many treatment methods, observations, and recording recurrence rate; it was found that recurrence rate in osteotomy was 0%, in resection with removing bones' edges and carony solution 0%, in resection with bone curettage only 18%, in enucleation only 26.9%, and in marsupialization 40%. The recurrence rate in resection with carony solution application 50%, and it was found that the recurrence rate in all cases reach 23.15%.

Several studies used other strategies in treatment. Marsupialization was applied to a large lesion before the surgery to affect the lesion characteristics and size, and it was found that the lesion was stopped from growing and began to decay and reduce, and then a simple curettage could be done. But this method was not effective when the lesion extended to the mandible ramus; there was also no recurrence when the lesion was a single chamber, while there was recurrence in many cases where the lesion was multi-chambers, so if this method should be used, the size of the lesion and whether it's a single or multi chambers should be taken into consideration (11, 16, 21-23). The usage of the decompression method which contains two stages; (1) decompression inside the cyst then (2) resection of the lesion, and then using a surgical pipe for drainage, showed that the keratocystic-odontogenic tumor became smaller and its lining transformed to become similar to the oral lining, and so it became much easier in resection (24). In 2007, Kolokythas et al. found out that the recurrence rate by using osteotomy was high (18%) (25). In contrary to this study, many other studies did not mention any recurrence by using this method (26).

In cases where the lesion was large and advanced, marsupialization and decompression were used, but recurrence rate in marsupialization was 40% and could not destroy the cyst remains (27).

Otherwise, enucleation with curettage was more difficult than marsupialization because of the thinner epithelial liner which may fracture. And the way it

contacted with the bones and soft tissues especially when it perforated the cortical bone where a recurrence rate of 17% was mentioned (28). According to Kolokythas et al. the treatment plan must depend upon lesion size, recurrence, radiological evidence of cortical bone perforation, and the anatomical location of the KOCT where it is difficult to do enucleation in case the lesion expanded to the mandibular ramus (25). The surgical treatment has negative sides because it needs continuation especially with large recurred lesions for the follow up plan reduce recurrence, while Bramley recommended surgery with resection and bone plantation (29).

Lrvine and Bowerman assured the necessity of bone graft usage in large surgeries of large lesions (14). Madras and Lapointe found out that the best treatment was ostectomy or resection with carony solution with or without ostectomy (30).

Some studies and their results are demonstrated in Table (1).

A study by Kinard et al. (2013) was conducted to figure out the relation between Gorlin syndrome and recurrence rate of KOCT (52), and it was found that when Gorlin Syndrome accompanied with the tumor the recurrence rate was over 4%, and so it needed more attention and effective treatment.

Stoelinga and Bronkhorst found out too that recurrence rate was over 4.5% where it needed to undergo a special treatment protocol (35).

Ramaglia et al. found that 65% to 75% from all recurred cases was associated with Gorlin syndrome and needed a special treatment (2).

In 2013, Kapoor's study showed that there was no evidence assured that recurrence cause associated with Gorlin syndrome (53).

According to our knowledge, there are yet no studies regarding the surgeons' attitude in Damascus, Syria towards the opinion about the best treatment option for KOCT.

3. Materials and Methods

A questionnaire was presented to 63 oral and maxillofacial surgeons in four different hospitals in Damascus/ Syria; namely Ibn al nafees hospital, Al moujtahed hospital, Tishreen military hospital, and 601-military hospital, as well as in Maxillofacial surgery department in the Syrian Private University to obtain their opinions about the best treatment option of keratocystic odontogenic tumor.

The questionnaire included inquiries about the following issues: the period of time spent in the field of oral and maxillofacial surgery, the favorite treatment method of KOCT, factors affecting treatment methods, the method belief to be the best as a treatment option in all cases.

The questionnaire was answered during interviews with the surgeons.

A research in the internet (PubMed and Google scholar) was made to obtain all research in literature related to this controversial issue.

4. Results

Sixty-three maxillofacial surgeons participated in the survey, 48 surgeons were males (76%), and 15 surgeons were females (23%) (Table 2). The duration of which the surgeons spent as maxillofacial surgeons was as follows:

5 to 10 years (18 surgeons) were 28%, 10 to 20 years (36 surgeons) were 75%, and over 20 years (9 surgeons) were 14% (Table 3).

The survey showed that 31 maxillofacial surgeons (49%) preferred ostectomy as successful treatment. However, curettage with carony solution application was preferred by 19 surgeons (30%), and enucleation was preferred by 18 surgeons (28%).

Marsupialization alone was preferred by 10 surgeons (15%), but marsupialization with curettage was preferred by 7 surgeons (11%), and bone curettage was preferred by 6 surgeons (9%).

Ostectomy with bone graft was less preferred by the surgeons (4%) (Table 4).

It was shown that many factors influenced the selection of the most effective method of treatment for surgeons and they were:

Age; it was the most influential factor among surgeons in choosing the treatment method, and they were (59 Specialist) about 93%, while the lesion size was the second factor in influencing the treatment method among surgeons (54 Specialist) about 85%.

Anatomical location; it played a role in choosing the treatment way (37 Specialist) about 58%. Gender; it was a factor which affected the choosing treatment method among (25 specialist) about 39%.

Financial status, radiographic changes, recurrence, and the patient's' health were also factors which influenced the treatment method (Table 5).

Ostectomy was the preferred treatment among 9 maxillofacial surgeons, about 14%, because it was the successful way and could be applied in all cases.

While bone curettage with carony solution was preferred among 6 surgeons, 9%, as a successful method in all cases.

Fifteen maxillofacial surgeons (23%) agreed that there was a successful treatment method that could be applied in all cases, while 48 maxillofacial surgeons (77%) disagreed.

Table (6) shows the treatment method which can be applied in all cases.

Age was shown to be a factor in determining the treatment way among maxillofacial surgeons, as the results showed that 51% of surgeons preferred marsupialization with peripheral bone curettage in patients under 18 years, while 63% of surgeons preferred osteotomy for patients over 18 years (Table 7).

Lesion size was also a factor in determining the treatment method, where our results showed that 63% of surgeons use marsupialization with bone resection when the lesion was large in size, and 81% of surgeons followed curettage if the lesion was small (Table 8).

The location of the lesion also played a role in determining the treatment way, where results showed that 53% surgeons follow curettage in maxilla and 61% follow osteotomy in mandible (Table 9).

5. Discussion

The main purpose of all maxillofacial surgeons was to eliminate the lesion in every possible way, and that is according to location, size, age, and patient's opinion. But one must keep in mind that there are positive and negative sides to all treatments' options.

Our study showed that among all of the applied treatment ways (i.e. ostectomy, curettage, carony solution, complete resection, marsupialization, marsupialization with curettage, peripheral bone curettage, osteotomy with bone graft), ostectomy was the best and most successful treatment method according to the participated surgeons (49% of the participants). However, the surgeons did not prefer osteotomy in patients under 18 years, because of the incomplete growth of the facial bones.

In case the lesion was large and expanded to important anatomical structures, they used another treatment method which was more conservative, which agreed with Sivaraj Sivanmalai (12).

Some patients do not agree with ostectomy procedure, so another treatment method should be taken into consideration, curettage with carony's solution would be second choice and 30% of surgeons preferred this method especially with cooperative patients, these results agreed with several studies (18, 23, 30, 35). However, according to these studies, recurrence rates reach 16% during 10 years recall.

While the complete resection was preferred by 28% surgeons, this result agreed with Irvine and Bowerman (14), and no recurrence rates were mentioned during a 5-year recall.

According to the literature, complete resection had been shown to be difficult because when removing the epithelial layer of the keratocystic odontogenic tumor with adjacent structures and a thinner liner, recurrence occurred and the rate was between 14% to 55% after one year to 21-year recall (31, 40, 45).

Marsupialization was also one of treatment methods at 15 % mentioned by participated surgeons. The results agreed with studies mentioned that marsupialization gave good results and no recurrence case was recorded during 5 years recall (30, 46).

While marsupialization with curettage was another treatment method and was preferred by 11% of participant surgeons, because marsupialization alone was not useful according to specialists and needed special treatment protocol and cooperative patient, and also the financial status of the patients took place, but results of a study made by Pogrel and Jordan proved that it was a good method, more safe, and tissues conservative, no recurrence cases were mentioned during 4 years recall (16). This method was more approved than curettage alone where only 9% of surgeons approved. However, the results of a study conducted by Partridge and Tower (48) showed a recurrence rate 9% after one year and two months recall, and in other studies the recurrence rate was 37.5% after more than 5 years recall (30). Ostectomy with bone graft was less chosen with only 4% of surgeons, although no recurrence case were mentioned.

6. Conclusion

The treatment of keratocystic odontogenic tumor remains controversial issue. After reviewing the literatures and questionnaire of several maxillofacial surgeons, we did not find a unified opinion about treatment, neither from the basic lines of choosing treatment nor from the causes. The differences in treatment methods were related to every individual clinical case considering the lesion. Every case should be treated individually.

There are many factors that could affect the treatment plan, including lesion size, location, age, patient's opinion, whether the lesion is primary or recurrent, or related to Gorlin syndrome or not.

The best method after the survey was ostectomy but some patients refused that procedure, so the surgeon had to choose another treatment method.

7. Recommendations

Surgeons must evaluate every case separately; taking into consideration the recurrence, and the damage of the adjacent tissues with several treatment methods.

If we use the appropriate treatment method for the appropriate patient, we can reach the desired results. Age, size, lesion location, and patient's opinion must be taken into consideration. All cases must go under observation for more than 5 years.

Surgeon's character must help in determining the treatment method, and there must be a correct study of the case. Ostectomy remains the most approved procedure in most maxillofacial surgeons opinion, and it is preferred to be the first choice for surgeons in treating keratocystic odontogenic tumor.

8. Table Captions

Table (1): Studies considering KOCT

RECURRENCE RATE %	CASE FOLLOW-UP IN YEARS	TREATMENT	Nr. OF LESIONS	STUDY
24	1 – 8	Enucleation	29	Kondell and Wiberg [31]
10	≥ 5	Resection with carony solution and curettage	70	Hsun-Tau C [32]
35	1 – 15	Enucleation	49	Meara et al. [33]
0	2 – 8	Ostectomy	31	Bataineh and Qudah [34]
11	1 – 25	Resection with carony solution	82	Stoelinga [35]
29	>5	Enucleation	63	El-Hajj and Anneroth [36]
38	>5	Resection with marsupialization	16	
0	>5	Resection with safe sides	1	
50	>5	Resection with marsupialization + safe sides	2	
0	>5	Ostectomy	3	
9	1 – 19	Marsupialization with resection	23	Marker et al. [37]
0	1.8-4.8	Marsupialization with later resection	10	Pogrel and Jordan [16]
14	2	Decompression then curettage	30	Maurette et al. [38]
55	1-24	Enucleation	11	Morgan et al. [18]
18	1-24	Bone curettage	11	
0	1-24	Bone curettage with carony solution	13	
50	1-24	Resection with carony solution	2	
0	1-24	Ostectomy	3	
18	17-19	Decompression then curettage	44	Brondum and Jensen [39]
25	>1.6	Marsupialization	12	Bowne [40]
23	>1.6	Enucleation	72	
18	5-17	Enucleation (one segment)	28	Forssell et al. [41]
56	5-17	Enucleation (multi segments)	41	

60	5-17	Marsupialization	5	
33	1-7	Enucleation	12	Jensen et al. [42]
38	1-5	Enucleation with marsupialization	13	
14	1-21	Enucleation	52	Voorsmit et al. [43]
3	1-10	Resection with carony solution	40	
18	1-10	Enucleation	22	Chuong et al. [44]
0	1-10	Ostectomy	1	
51	≥5	Enucleation	57	Vedtofte and Praetorius [45]
31	>5	Enucleation	13	Zachariades et al. [46]
0	>5	Ostectomy	1	
0	>5	Marsupialization	1	
0	>5	Decompression with resection	1	
30	>5	Enucleation	465	Madras et al. [30]
9	>5	Resection with carony solution	122	
18	>5	Resection with curettage	11	
8	>5	Resection with carony solution then curettage	83	
38	>5	Resection with marsupialization	29	
33	>5	marsupialization	18	
13	>5	Marsupialization then resection	108	
0	>5	Ostectomy	39	
62.5%	5 – 10	Resection with marsupialization	16	Pindborg and Hansen [47]
0%	2	marsupialization	2	Partridge and Towers [48]
36.7%	2	Resection then primary coverage	30	
9%	2	Curettage and removing the periosteum then coverage	11	Irvine and Bowerman [14]
0%	2	Resection with immediate bone graft	2	
16.7%	>5	Resection	7	
0%	>5	Enucleation	6	
0%	>5	Ostectomy	2	
25%	2	Marsupialization	4	Eyre and Zakrzewska [49]

11.5%	1	Resection with marsupialization using liquid Nitrogen	26	Schmidt and Pogre (50)
0%	1.5	Decompression	2	Jung, Lee and Park (51)
37.5%	>5	Bone curettage	16	Madras J and Lapointe H (30)
0%	>5	Marsupialization	3	
0%	>5	Ostectomy	2	

Table (2): Distribution of sample according to gender

	Number of surgeons	Percentage
Surgeons	63	100%
males	48	76%
females	15	23%

Table (3): Distribution of sample according to years spent in specialization

Years spent in specialization	Numbers	Percentage
5 to 10 years	18	28%
10 to 20 years	36	75%
Over 20 years	9	14 %

Table (4): Percentages of preferred treatment options for KOCT

Preferred treatment	Numbers of surgeons	Percentage
ostectomy	31	49%
Curettage with carony solution	19	30%
Enucleation	18	28%
Marsupialization	10	15%
Marsupialization with curettage	7	11%
Bone curettage	6	9%
Ostectomy with bone graft	3	4%

Table (5): Factors that may affect the treatment according to the surgeons

Effective factors in treatment	Numbers of surgeons	Percentage
Age	59	93%
Lesion size	54	85%
Lesion location	37	58%
Gender	25	39%
Financial status	18	28%
Radiographic changes	15	23%
Recurrence	14	22%
Patient's health	13	20%
Pervasion	13	20%
Soft tissues	3	4%

Table (6): Surgeons' opinions regarding the best treatment for KOCT

Is there a successful treatment way that can be applied in all cases?	Numbers of surgeons	Percentage
Ostectomy	9	14%
Bone curettage + carony solution	6	9%
Total	15	23%

Table (7): Preferred choice of treatment for KOCT in relationship to the age of the patient

Age	Preferred method	Percentage
Under 18 years	Marsupialization + peripheral bone curettage	51%
Over 18 years	ostectomy	63%

Table (8): Preferred choice of treatment for KOCT in relationship to the lesion size

Lesion size	Preferred method	Percentage
Large size	Marsupialization + bone resection	63%
Small size	Curettage	81%

Table (9): Preferred choice of treatment for KOCT in relationship to the lesion location

Lesion location	Preferred method	Percentage
Maxilla	Curettage	53%
mandible	ostectomy	66%

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