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Enucleation with or without Adjuvant Therapy versus Marsupialization with or without Secondary Enucleation in the Treatment of Keratocystic Odontogenic Tumors

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Author`s Contribution

[1,2]Substantial contributions to the conception or design of the work; or the acquisition, [4,6]Active participation in active methodology, [2,3]analysis, or interpretation of data for the work, [5,6]Drafting the work or revising it critically for important intellectual content

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ABSTRACT

Objective: In order to assess enucleation with or without adjuvant therapy and marsupialization with or without secondary enucleation on patient outcomes regarding recurrence rates, complications and healing times in the context of KOT.

Methodology: In this cohort study, a total of 150 participants diagnosed with Keratocystic Odontogenic Tumors. Patients were divided into four groups: enucleation with adjuvant therapy; enucleation without adjuvant therapy; marsupialization alone; and marsupialization then second surgery for enucleation. The outcomes of the study were recorded in terms of recurrence of the tumor and its complete regression Other outcomes like the recovery period of the patient, the occurrence of complications, and functional capacities were also noted for all the patients.

Results: The recurrence rate in the enucleation with adjuvant therapy group was 8%, mean time to recurrence: 20±3.5 months while for enucleation without adjuvant therapy was 18% with mean time to recurrence of 21±4.0 months. Higher complications rate was noted in enucleation with adjuvant therapy at 10% and 15% in enucleation without adjuvant therapy. Marsupialization alone resulted in a recurrence rate of 13% (mean time to recurrence: 22±3.8 months, the complication rate was 7%. Marsupialization followed by secondary enucleation showed the lowest recurrence rate at 4% (mean time to recurrence: 25±4.1 months and the complication rate of 8%.

Conclusion: Thus, adjuvant therapy and marsupialization with secondary enucleation proved to be less likely to result in the high recurrence rate that marsupialization alone causes and enucleation is less likely to result in high recurrence rate that leaving the mass in causes.

Keywords: Keratocystic Odontogenic Tumors, Enucleation, Adjuvant Therapy, Marsupialization, Recurrence Rates, Treatment Efficacy.

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Introduction

Keratocystic odontogenic tumors (KOTs) are benign odontogenic cystic lesion that originate from the dental lamina and they are considered to be locally aggressive. Historically they were placed in the group of odontogenic cysts but based on their biological potential they are now classified as tumors. These lesions are particularly defined by capsule that is primarily fibrous and the

interior lining covered by stratified squamous epithelium which has an increased tendency to reoccurs. KOTs are noted for the voluminous nature of the cell growth and these are likely to disrupt the adjacent anatomical structures.

KOTs, therefore, represent some of the most frequently described odontogenic cysts comprising 10% of the total cases of odontogenic cysts.[1] It is commonly established in the youthful group, and the incidence is more dominant in men as compared to women. It was reported that these tumours affects the posterior regions of mandible in most cases, however, they can anywhere within the jaw. The clinical relevance of KOTs is related to their potential of aggressive behavior within the loco-regional compartment and recurrence with devastating consequences on the patient's quality of life, if appropriate measures are not put in place.[2] It is important that the child is diagnosed as early as possible and this is to avoid such problems as displacement in teeth, untoward growth of the jaws and frequently, interference with normal growth and function of the jaws. [3]

The effects of KOTs are not just significant but also far reaching especially to the aspect of oral health of individuals. This means that these tumors which develop in the mouth can lead to severe pain, swelling and discomfort that affects chewing and speaking abilities. In severe cases, they cause facial disproportionation/ disfigurement. Most patients with KOT have a great chance of recurrent disease, which implies that more than one surgery may be necessary to correct defector even with the use of flaps.[4] These include follow-up needs and possibly other procedures can also influence the quality of life, as patient has to undergo constant monitoring and possible treatments of relapses.[5]

Surgical therapy is a common form of management that is often administered for KOTs and one of the most common types of surgery is enucleation. The outcome of this procedure significantly relates to the efficiency of tumor excision and the minimal invasion of the adjacent structures.[6] Several adjuvants are used for enhancing surgeries of enucleation like Radiation therapy, Chemotherapy, Hormonal therapy, and Immunotherapy. Enucleation is eliminated since this adjuvant treatment is intended to complement enucleation's outcome by dealing with the residual elements of the tumor that might exist as well as lead to the lesion's recurrence.[7]

Another type of management strategy is marsupialization where the tumor is debulked, and then the cystic cavity is left open so that its size gradually decreases. In this technique cyst wall is opened in the area of the flap, and the edges of this window are sutured to the surrounding tissues to keep the opening patent for continuous drainage and epithelialization. Eventually this intimidate the size of the tumor and lessen the effect on the anatomical structures around the tumor site.[8] Sometime after marsupialization, a secondary enucleation is done to eliminate the rest of the tumor. This follow-up procedure is normally done once the size of the cystic cavity has been considered small enough to enable surgeries to remove any remaining tumor parts easily.

Controversy which management plan for KOTs is better still exists. Although enucleation with adjuvant therapy is accepted as one of the standard treatment options, the success rates can be quite different and recurrence is always a possibility. On the other hand, marsupialization then secondary enucleation is relatively safe and less risky at the initial stage but might prove to need a follow up surgery. The probabilities of these treatments can vary depending on issues like the size and location of the tumor, and the state of health of the patient.[9]

The rationale for comparing the results of enucleation with or without post-operative adjuvant treatment with marsupialization followed by secondary enucleation or not is to provide well-founded recommendations for the approach to KOTs. Thus, by evaluating the results of these therapeutic interventions, professional workers and scientists will be able comprehend the advantages and disadvantages of each of them. This comparison is supposed to help achieve improved patient care by pointing out the least unfavourable approaches to meeting the three key goals: prevention of KOTs recurrence, reduction of potential complications, and promotion of QoL in KOTs-affected patients.

Methodology

Keratocystic Odontogenic Tumors (KOTs) treatment interventions were evaluated with help of this retrospective cohort study. The research work was done on the data of five years from January of the year 2018 to the December of the year 2022 in department of Oral and Maxillofacial Surgery Rawal Institute of Health Sciences Islamabad.

The study recruited patients with clinical diagnosed KOTs who either had enucleation with/without adjuvant treatment or marsupialization with/without secondary enucleation. Histopathological examination confirmed the diagnosis of all selected patients, and they were

subsequently followed up for at least 2 years after treatment. Those patients who had insufficient information in the medical records, cases with malignancies, patients, who received any other treatment for KOTs were excluded from the study. Along with the demographic data including age, gender and size, location and mode of presentation for the tumour were taken and recorded.

The patients were divided into four treatment groups based on four protocols followed in their treatment. The first group was enucleation done with adjuvant therapy. Enucleation involved the globe removal through the removal of the KOT along with the firm fibrous capsule around it and one or more treatments to minimize the risk of the tumor recurrence, cryotherapy, or chemical burns. In cryotherapy, liquid nitrogen was used to treat the surgical site while in chemical cauterization agents like phenol were used to kill what remained of the epithelial cells.

The second group included enucleation done without additional treatment. In these cases, the tumor was removed through surgery without any additional interventions for the type of tumor being diagnosed in the patients. Marsupialization made up the third group in which the tumor was only partially removed and the cystic cavity left partly open to gradually heal. Marsupialization was done by making a window in the cyst's wall and stapling it to the adjacent tissue, offering a chance for constant drainage and re-epithelialization of the wound.

The fourth group was of patients who underwent marsupialization, and then secondary enucleation. Following initial marsupialization, the rest of the tumor was then shaved off during a second surgery because of a more aggressive removal and tackling of any remaining cystic components.

The outcomes of the treatment procedures were measured and assessed with regard to several parameters. Primary outcomes were recurrence rates, and the absence of the tumors. Treatment Failure was assessed as the re-emergence of KOTs in the same or nearby area as where they were initially treated. This was checked clinically with the help of physical and radiographic examinations. Recurrence was considered complete when no tumour or residual cystic lesion could be identified in follow-up investigations.

Other secondary end points included time to regain recovery, postoperative complications, and functional standing. The complication assessed in terms of infection, bleeding, or injury to the adjacent structures'. Functional outcomes are defined as the evaluation of the treatments effect on the oral functions that involve chewing, speaking, and general oral care.

The results of the study were analysed using statistical Package for Social Science (SPSS v. 25). The qualitative data like recurrence rate and complications were presented as frequency and percentages and analyzed with Chi-square test. with reference to the. The quantitative data like recovery time and functional outcomes were analyzed using one-way ANOVA test. P-value < 0.05 were considered statistically significant.

Results

The study sample included 150 patients diagnosed with Keratococystic Odontogenic Tumors (KOTs) with the mean age of 32±8.7 years. Regarding the gender distribution, the study involved 90 (60%) male participants and 60 (40%) female patients. The tumor sites were primarily in the posterior region of the mandible affecting (70%) majority of the patients while the remaining (30%) had the maxilla affected. Pain and swelling before treatment was noted in 68% of patients, and shifting of the adjacent tooth or resorption of the bone in 45% of the cases.

Among fifty patients operated by enucleation with advanced adjunct therapy, the rate of recurrence was 8% with four patients who had recurrence. The mean time to recurrence was 20±3.5 months. The complication rate of this group was 10% and the complications were wound infection 6%, transient numbness 3% and minor bleeding 1%. The healing period of these patients' injuries was 4.0±1.0 weeks on average (table I).

Table I: Distribution of Recurrence and Complication Rate.

Treatment Type	Number of Patients	Recurrence Rate (%)	Complication Rate (%)
Enucleation with Adjuvant Therapy	50	8%	10%
Enucleation without Adjuvant Therapy	45	18%	10%
Enucleation without Adjuvant Therapy	30	13%	7%
Marsupialization followed by Secondary Enucleation	25	4%	8%

There were 45 patients who underwent enucleation without any adjuvant therapy, and their corresponding recurrence rate was noted to be considerably higher with

a rate of 18% during follow-up period. The mean time to recurrence was observed 21±4.0 months in this group. Similarly, the rate of the complications 15%, in this group was also noted to be higher than other groups. The complications were distributed as wound infection (8%), increase in postoperative pain (5%), and transient numbness (2%). The average time (5.1±1.3 weeks) for recovery was recorded to be bit higher.

In the third group 30 patients who underwent marsupialization only, the recurrence was noted in 4 (13%) patients who developed the disease again at a mean of 22±3.8 months. The complication rate was observed to be a little lower than that of primary cases. The most common of which were delayed wound healing in 4 % and minor infection in 3% patients. The mean number of days to recovery was 6.0±1.2 weeks (table II).

Table II: Distribution of Mean time to recurrence and mean recovery time.

Treatment Type	Mean Time to Recurrence (months)	SD (months)	Mean Recovery Time (weeks)	SD (weeks)
Enucleation with Adjuvant Therapy	20	3.5	4.0	1.0
Enucleation without Adjuvant Therapy	21	4.0	5.1	1.3
Enucleation without Adjuvant Therapy	22	3.8	6.0	1.2
Marsupialization followed by Secondary Enucleation	23	4.1	6.5	1.3

The results of patients who were operated within the group of 25 patients who underwent marsupialization followed by secondary enucleation also reported low recurrence rate at 4%, with one patient who developed recurrence after mean follow up of 23±4.1 months. The complication rate for this group was 8 percent comprising minor bleeding 4%, and minor jaw stiffness 4 percent. The average days for recovery were also calculated slightly higher that was 6.5±1.3 weeks; These figures are higher than the primary procedure.

Thus, when comparing the recurrence rates, it can be observed that the presence of adjuvant therapy resulted in a significantly lower tumor regrowth rate compared to patients who underwent enucleation without adjuvant therapy (8% vs. 18%, p = 0.04). Likewise, marsupialization after which by secondary enucleation reduce the rating of recurrence compared to marsupialization alone, (4% vs. 13%, p= 0.00). These results further imply that adjuvant therapies and secondary enucleation are helpful in the reduction of the disease recurrence rates.

In regard to the complications, the following differences were observed: There was a somehow lower percentage of complication in the group enucleated with adjuvant therapy (10%) compared to the group enucleated without the aid of adjuvant therapy, which was 15% but this difference was not statistically significant having a p-value of 0.25. The cumulative rate of complications was similar between the two groups where marsupialization was done alone and where marsupialization was followed by secondary enucleation, which was 7% and 8% respectively, without any statistically significant difference (p = 0.68).

The comparison of different treatment modalities on the basis of recurrence rate was done with the help of Chi-square test which showed that enucleation with adjuvant therapy had relatively low rate of recurrence compared to enucleation without adjuvant therapy ($\chi^2 = 4.98$, p =0.04). No significant difference was observed between marsupialization, followed by secondary enucleation as compared to the simple marsupialization ($\chi^2 = 5.12$, p =0.35).

For the continuous variables like the recovery time of the patients, the t-test showed that patients having enucleation with adjuvant therapy had lesser recovery time in comparison to the patient who had enucleation without any adjuvant therapy (mean difference = 0.9 weeks, P= 0.02). Recovery time of marsupialization alone and secondary enucleation after marsupialization was almost similar, mean difference of 0.5 weeks, p = 0.35. (Table III)

Table III: Comparison of Recurrence rate among different treatment groups.

Comparison	Chi-Square Value	P-Value
Enucleation with vs. without Adjuvant Therapy	4.98	0.04
Marsupialization Only vs. Secondary Enucleation	5.12	0.35
Enucleation with Adjuvant Therapy vs. Without	4.98	0.04
Enucleation with Adjuvant Therapy vs. Without	5.12	0.03

Discussion

The main objective of this present research was to compare the KOTs treatment options: primary

enucleation with or without additional treatment, and marsupialization with or without secondary enucleation. This comparison revealed that enucleation with adjuvant therapy is likely to exhibit lesser recurrence rates as compared to similar operation. Similarly, there are indications that marsupialization followed by secondary enucleation would produce better results with reference to recurrence rates compared to the similar operation. The 8% recurrence rate for those who underwent enucleation complimented by adjuvant therapy was relatively lesser compared with enucleation alone 18% proving that in addition to treatments like cryotherapy, chemical cauterization helps to get a clear margin of the tumor and thus avoids regrowth. Similarly, marsupialisation followed by second line enucleation indicated a recurrence rate of 4% this being compared to 13% of patients who underwent marsupialization only, therefore it is recommended to use the two-stage procedure in patients with larger or more aggressive neoplastic lesions.[10-12]

The conclusions made in this study are consistent with the existing body of knowledge: it is common to encourage the application of adjuvant treatments in enucleation surgeries, as well as to discuss the advantages of secondary enucleation after marsupialization.[13,14] For example, there are publications that have shown cryotherapy and chemical cauterization therapies that help in decreasing the probabilities of a recurrence from remaining epithelial cells that cannot be eradicative.[15] in the initial surgery. In the same respect, secondary enucleation is advocated in the literature evidenced through its effectiveness in attaining cleaner margins of the tumor especially after the initial step of marsupialization which aids in containing the size and work of the lesion. The lower occurrence rates obtained in this research correspond with these reports, thus strengthening the appropriateness of employing such progressive therapy modalities.[16,17]

Clinical practice implications are rather large based on these findings. Such adjuvant treatments should be planned for a routine approach at the stage of enucleation in patients with KOT for the reason that an individual enucleation has a higher risk of a recurrence.[18] Thus, the use of such adjuvants as cryotherapy or chemical cauterization expanding the treatment algorithm will help to improve the chances of complete tumor ablation and a decrease in the need for additional operations. In the same way, for the bigger or complicated KOTs, marsupialization before the secondary enucleation seems to be the great approach because it can effectively reduce the rates of recurrences and may also enhance the long-term prognosis of the patients' statuses.[19]

These findings may help reconsider the existing practice guidelines for treating patients and consider the implementation of such approaches. For instance, oral and maxillofacial surgeons should examine the possibilities of postoperative adjuvants in enucleation surgeries and should assess the advantages of the step by step management if marsupialization is planned. Through the use of these evidence-based practices, clinicians shall be able to improve patients' outcomes, reduce the likelihood of relapse, and ultimately intensify the success rates of treatment.[20]

Future prospective, randomized studies should be conducted which will help to compare the effectiveness of these treatment modalities even in a better way. Such studies would offer a much higher category of evidence by eliminating other extraneous factors, which influence the choice of participants. Also, further studies should evaluate survival rates and the rates of recurrent diseases in the individuals exposed to the mentioned treatment techniques, along with late complications and patient quality of life. Studying molecular and histological features of recurrent KOTs can also give a clue about why some of the lesions are more inclined to regrowth and ways of changing treatment modalities to cope with the problem.[21]

Conclusion

The findings of this present study demonstrated that enucleation with adjuvant treatment is an efficient option for treatment plan of KOTs. The findings have revealed high improvement when enucleation has been supplemented with adjuvant therapies in comparison to enucleation alone Secondly, marsupialization followed by secondary enucleation improves the outcomes compared to simple marsupialization only. Surgically, enucleation with additional adjuvant therapies must be advised when dealing with KOT based on its relapse risk level. Furthermore, it is advisable to perform both stages, namely, the marsupialization and enucleation secondly because this leads to higher tumor control and reduced rates of the tumor relapses.

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