

CORRELATION OF RECURRENCE OF PLEOMORPHIC ADENOMA OF PAROTID GLAND WITH TUMOR SIZE AND RESECTION MARGIN: A RETROSPECTIVE STUDY

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**ABSTRACT**

Introduction: The recurrence of pleomorphic adenoma has been attributed to various surgery related and pathology related factors. Our objective was to correlate the recurrence of the pleomorphic adenoma of parotid gland with tumor size and resection margin.

Materials and Methods: This study was a retrospective review of patients at a single tertiary care center who underwent operations for pleomorphic adenoma of the parotid gland between 2011 and 2021. Demographic data, details of surgical interventions, histopathological reports and recurrence rates were studied. The recurrence of pleomorphic adenoma was correlated with the size of the tumor and resection margin. Chi-square and regression analysis were used for statistical analysis.

Result: A total of 157 patients were included in the study. The recurrence rate of the tumor of size up to 2 cm, 2-4cm and larger than 4cm were 0%, 1.1% and 14.3% respectively. Adequate surgical margin was achieved in 66.7%, 52.1% and 42.8% of patient with tumor up to 2cm, 2-4cm and larger than 4cm respectively. No recurrences were seen in patients with adequate surgical margin whereas 5.6% of the patients with exposed tumor had recurrence. Tumor with both inadequate resection margin and large size (4cm or larger) had recurrence rate of 33.33%.

Conclusion: This study demonstrated size of pleomorphic adenoma and resection margin after parotidectomy as significant factor for recurrence. The tumor more than 4cm in diameter with inadequate resection margin had high recurrence of 33.33% which is close to enucleation. Moreover, it is difficult to obtain adequate soft tissue margin in larger tumors.

Keywords: Parotid Tumors, Pleomorphic Adenoma, Recurrence, Resection Margin, Tumor Size

INTRODUCTION

Pleomorphic adenoma is the most common parotid gland neoplasm of salivary glands comprising 50-60% of all parotid tumor.¹ Surgery is the standard treatment for pleomorphic adenoma. In earlier studies, recurrence rate following enucleation were as high as 40%.² The enucleation favored direct incision of the exposed tumor, curettage of the contents and sharp dissection of the visible capsule with resultant unacceptable recurrence.³ Pleomorphic adenoma are well known for their microinvasion of the capsule and tumor buds with thin fibrous capsule.⁴ The standard surgical treatment for

pleomorphic adenoma is parotidectomy with facial nerve preservation. The reputed advantage of parotidectomy is that it ensured an adequate margin around the tumor. However, even with standard excisions up to 81% have some degree of capsular exposure.⁴ Extracapsular dissection is an alternative approach to the removal of pleomorphic adenoma involving meticulous dissection immediately outside the tumor capsule while still preserving facial nerve and is distinct from enucleation. It is precise, slow, careful operation done in bloodless field in the plane of the tumor capsule which is not usually

ruptured. The recurrence rate in the extracapsular dissection is comparable to standard parotidectomy (1.9% and 1.8%).³

The exact cause of pleomorphic adenoma recurrence has remained elusive. There may be various pathology related (capsule thickness, capsule integrity, pseudopodia, multicentricity) and surgery related (rupture of the tumor, spillage of the tumor contents, insufficient margin of resection, inadequate excision) factors that may contribute to recurrence.⁵ There are many studies which have shown that tumor free margin is important in preventing recurrence of the disease.^{5,6,7} But there also studies which suggested tumor free margin can rarely be achieved in pleomorphic adenoma of parotid because of its proximity to facial nerve and still the recurrence rate can be quite low.⁸ The size of the tumor as a factor for recurrence is debatable. Only few studies have attributed the tumor size with the recurrence of pleomorphic adenoma.^{6,7} However, several authors^{9,10} has debated the excision of pleomorphic adenoma of parotid should be based on size. In this study we correlated size of the pleomorphic adenoma and the resection margin with the recurrence and calculated the cumulative risk of having both large size and inadequate soft tissue margin for the recurrence of the disease.

MATERIALS AND METHODS

Between 2011 and 2021, 261 patients underwent parotidectomy for a parotid tumor at Sir Ganga Ram Hospital, Delhi, India. Of these tumors 196 were pleomorphic adenoma. The cases with no follow up and the cases with inconclusive histopathological reports were excluded from the study. Total 147 cases were included in the study. The mean follow up period was 6.3 years (2 to 15 year). Histopathology reports of all these cases were reviewed to determine the size of the tumor and adequacy of resection margin. The size of the tumor was categorized in 3 category : less than equal to 2cm, more than 2 cm and less than or equal to 4 cm and more than 4cm and recurrence was recorded in each group. Resection margin was categorized adequate if minimum of 1mm margin was seen all around. The correlation of tumor size and resection margin was done with tumor recurrence. Chi-square and regression analysis were used for statistical analysis. Ethical approval was taken for the study.

RESULT

A total of 157 patients were included, 76 male and 81 female patients. The average age at first operation was 38.3±14.8 years (8-75 years). The size of the tumor ranged

from 0.8cm to 7cm. Out of 42 patients with tumor of up to 2cm no recurrence was seen, whereas 1 recurrence was seen in patient with tumor of 4cm and 3 recurrence were seen in patients in whom tumor was larger than 4cm. The regression analysis of the size of the tumor with recurrence showed significant correlation with p value of 0.0002 and odd ration of 4.38 (95% confidence interval: 1.7, 11.3).The size of the tumor and recurrence is summarized in table 1.

Table 1: The size of the tumor and recurrence

Tumor size	Number	Recurrence (%)	p-value
≤ 2cm	42 (26.8%)	0 (0%)	<0.0002
> 2cm and ≤ 4 cm	94 (59.9%)	1 (1.1%)	
> 4cm	21(13.4%)	3 (14.3%)	

Out of 157 patient 86 (54.8%) had excision with adequate margin and 71 (45.2%) had excision with positive margin. Adequate margin was achieved in 66.7% of tumor up to 2cm, 52.1% in tumor larger than 2cm and up to 4cm and in 42.8% in tumor larger than 4cm (table 2). The correlation of size of the tumor with inability to get adequate margin was statistically significant with p value of 0.032 and odd ratio of 0.75.

Table 2: Correlation of tumor size with ability to achieve adequate margin

Tumor size	No.	Tumor exposed		Adequate margin achieved		p-value
		Number (%)	Recu.	Number (%)	Recu.	
≤ 2cm	42	14 (33.3%)	0	28/42 (66.7%)	0	0.032
>2cm & ≤4cm	94	45 (47.9%)	1	49/94 (52.1%)	0	
> 4cm	21	12(57.2%)	3	9/21 (42.8%)	0	

There were no recurrences in the cases with adequate margin. All four recurrence were seen in the tumor with exposed margin group which was statistically significant (p=0.030) and has been shown in table 3. Tumor larger than 4cm and exposed margin had recurrence rate of 33.33%.

Table 3: The resection margin and recurrence

Resection margin	Number	Recurrence	p-value
Tumor exposed	71 (45.2%)	4 (5.6%)	0.030
Adequate margin	86 (54.8%)	0 (0%)	
>4cm tumor with exposed margin	12 (7.6%)	4(33.33%)	

DISCUSSION

Pleomorphic adenomas are slowly growing tumor which can reach a large size if left untreated and is well known

for recurrence. Historically recurrence rate was up to 40%.² Recurrence of the pleomorphic adenoma has been mostly attributed to the surgical factor like rupture of tumor, insufficient margin of resection, capsular exposure and incomplete excision. With current standard treatment the recurrence rate of pleomorphic adenoma is around 1.8 to 1.9%.³ However, even with standard surgical procedure up to 81% of excised tumor have some degree of capsular exposure and in up to 61.5% the capsular exposure exceeded 50% of discernable surface.⁴ Witt et al revealed focal capsular exposure occurring in virtually all parotid surgery for pleomorphic adenoma.⁸ The reported incidence of recurrence is far less than high risk surgical factors. There are other tumor related factors like capsular integrity, capsular thickness, multi-centricity and tumor size. Zbařren¹¹ et al in their study found up to 73% of pleomorphic adenomas had 1 or more capsular characteristics such as incomplete capsule, capsule penetration, pseudopodia, and satellite nodules.

In the present study we correlated tumor size with the recurrence and found that 14.3% of the patient with tumor larger than 4cm had recurrence, whereas only 1.1% of patient with tumor up to 4cm had recurrence which was statistically significant with p-value <0.0002. This may be attributed to the fact that larger tumor may have thinner capsule and larger pseudopodia. Li et al¹² found that satellite nodules were more common in tumors larger than 4cm than in smaller tumors. The satellite nodules also extended greater distance from capsule in larger tumors (up to 8.88mm). In the study done by Riad et al,⁶ the average size of the non-recurrent tumor was 30mm compared to 43.1mm in the recurrent tumor and concluded that recurrence of pleomorphic adenomas was related to tumor size. Naeim, et al¹³ enunciated that tumor overall size is related to capsular thickness with small tumor possessing thicker capsule and larger tumor possessing thin capsule. However Webb et al⁴ were unable to confirm any relationship between tumor size and capsular thickness. Riad et al⁶ found that safety margin of resection was inversely correlated to the tumor size and in tumor larger than 4 cm no margin could be obtained during surgery whereas in tumor smaller than 3cm safety margin of more than 10mm could be obtained which could explain higher recurrence in larger tumors.

In the present study all recurrences were seen in the tumor with capsule exposure and no recurrence was seen in those with adequate margin which was statistically significant (p=0.03). Riad et al⁶ showed tumor recurrence was inversely related to the thickness of safety margin in which the mean thickness of the safety margin in patient who had no recurrence was 5.99mm compared

to 1.29mm in the recurrent tumor group. Dulguerov et al⁵ in his meta-analysis concluded that recurrence of pleomorphic adenoma was related to the positive margin and capsular exposure. Vuřak et al¹⁴ in their study found that 87.5% of patient who underwent enucleation had recurrence while 32% of those who underwent excision with sharp dissection had recurrence. There were no recurrences in superficial parotidectomy and total parotidectomy stressing the adequacy of margin necessary to prevent recurrence.

The extent of safety margin required for parotidectomy is debatable. In the study done by Ghosh et al,⁷ recurrence of the tumors widely present at the margin was 17.6% where as those with 1mm margin all around was 1.8% and had finding that even slightest of normal cuff of tissue was sufficient to ensure low recurrence rate. However many study has suggested extent of margin should be based on size of the tumor. Li et al suggested more conservative approach of modified partial superficial parotidectomy for tumor less than 4cm and conventional superficial parotidectomy for tumor larger than 4cm in an aim to obtain margin of 10mm. Quan et al¹⁰ concluded 1cm-surgical margins are safe for the tumors less than 4 cm, and the tumors more than 4 cm should be treated with superficial parotidectomy. In our study, no recurrences were seen in tumors with normal tissue margin of 1mm even for 4cm or larger tumors. This finding was in accordance with Ghosh et al.⁷ Our study also demonstrated no recurrences in tumor less than 4cm even if there was capsule exposure and inadequate safety margin. Similarly in the study done by Witt et al⁸, factors which are thought to influence the recurrence of pleomorphic adenoma like tumor size, patient age, gender, tumor location and duration of follow up were controlled with matched pairs and evaluated recurrence outcome on capsular exposure and found no recurrence with 8-9 years follow up period in patients with smaller than 4cm tumor who underwent superficial parotidectomy, extracapsular dissection or total parotidectomy. However in the same study virtually all patients had focal capsular exposure. Despite capsular exposure Witt et al suggested pleomorphic adenoma of less than 4cm size treated by less complete parotidectomy are not at higher risk of recurrence.⁸

In the present study both tumor size and resection margin were significant factor for recurrence. The tumor with both large size (4cm or larger) and exposed margin or inadequate resection margin had high recurrence rate of 33% which was close to enucleation. We didn't find study recording cumulative risk associated with both large size and exposed margin. Thus, in large tumor because

of the thin capsule, higher breach in capsule and larger pseudopods, the microscopic eradication of tumor may be difficult to achieve resulting in higher recurrence thus may necessitate larger resection margin in such tumors. It is possible that capsular exposure along with the invasion of the exposed capsule by tumor which occurs more frequently in larger tumors may contribute to the recurrence.

CONCLUSION

This study demonstrated size of the pleomorphic adenoma and resection margin after parotidectomy as significant factor for recurrence. The larger tumor of more than 4cm in diameter with inadequate resection margin had high recurrence of 33.33% which is close to enucleation. Moreover, it is difficult to obtain adequate soft tissue margin in larger tumors. So, great care should be taken to prevent capsule breaching and maintain adequate soft tissue margin while excising large tumor. Currently there is no fixed protocol for surgical management of pleomorphic adenoma based on its size. Greater margin would be appropriate for tumor larger than 4cm whereas more conservative approach can be undertaken in smaller sized tumors. However, due to retrospective nature of this study, further prospective randomized studies may be helpful in deciding the optimal treatment of pleomorphic adenoma of parotid glands.

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