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Recurrent Parotid Pleomorphic Adenomas: Our Clinical Experience

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Original Investigation

Abstract

Objective: The aim of our study was to present our findings in a series of patients who were treated for recurrent parotid pleomorphic adenoma with their clinical, surgical, and follow-up information and to discuss them in light of the recent literature.

Methods: Eleven patients who had revision surgery for recurrent pleomorphic adenoma at our institution were retrospectively analyzed for the clinical and radiological features of their lesions, surgery type, facial nerve management, and follow-up period.

Results: Seven patients were females and four were males with an average age of 45 years. All patients underwent previous surgeries at other institutions. Revision surgery was performed with superficial parotidectomy in six patients and total conservative parotidectomy with preservation of the facial nerve in five patients. Two patients had lesions involving the facial nerve branches necessitating sacrifice of involved branches. One patient was given adjuvant radiotherapy because of adjacent lymphatic vessel involvement with tumor cells. During the mean follow-up period of 9.1 years, there were no recurrences in any of the patients.

Conclusion: Management of patients with recurrent parotid pleomorphic adenomas must be carefully planned according to the size, location, and multicentricity of the tumor and involvement of the facial nerve. Surgery should aim at reaching tumor-free surgical margins. Sacrifice of the facial nerve should be considered only in cases with direct involvement. In the postoperative period, patients must be followed up regularly for early diagnosis of recurrences.

Keywords: Parotid neoplasms, pleomorphic adenoma, recurrence, surgery

Introduction

Among all benign parotid tumors, pleomorphic adenoma is the most common tumor with a ratio of 60%–70%. It is seen more frequently in the fourth and fifth decades of life, particularly in women (1). Pleomorphic adenoma-a benign tumor-occurs when epithelial and myoepithelial cells are organized in different morphological systems (2). It generally appears as a mass that is painless, slow-growing, and does not affect the facial nerve functions in the parotid (3). Its treatment is complete surgical excision of the mass (4).

Tumor seeding that occurs during surgery, inadequate excision, and damage in tumor pseudocapsules are accepted reasons that cause recurrent disease (3, 5). The first hypothesis regarding recurrent pleomorphic adenomas was first asserted by Patey and Thackray (6) in the 1950s and is associated with finger-like extensions, i.e., pseudopods, which are microscopically found protruding from the tumor pseudocapsule. It is believed that surgeries applied close to the pseudocapsule structure of the tumor increase the risk of recurrence by causing insufficient resection of the microscopic extensions, i.e., pseudopods, protruding from the tumor pseudocapsule (7). Another reason is tumor seeding, which is common in the surgical field, after opening the pseudocapsule structure of the tumor during surgery. In the majority of patients with recurrent pleomorphic adenomas, increased recurrence rates of up to 5% have been detected in the follow-up of patients who have multifocal tumors around the incision scar and when it is known that the tumor has been opened during surgery (8, 9). It was reported that 20 to 45% of the recurrence rates were encountered in patients who underwent simple enucleation (2, 7). The re-

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currence rates were found to decrease up to 1 to 4% in patients who underwent superficial parotidectomy and up to 0 to 0.4% in patients who underwent total parotidectomy (5).

The preferred strategy for the therapy of recurrent pleomorphic adenoma is not fully understood. Various treatment modalities have been reported, ranging from totally untreated patients to radical parotidectomies, in which the facial nerve branches are sacrificed, and adjuvant radiotherapy applied (4, 7, 10-12). In our study, our approach to recurrent pleomorphic adenomas was discussed with review of the literature by discussing the clinical and surgical characteristics and follow-up results of 11 patients who had recurrence at an average of 11.9 years after the first surgery.

Methods

Between January 1990 and January 2016, 156 cases whose records could be accessed after parotid surgery in our clinic and whose histologic findings were obtained as pleomorphic adenoma were investigated. Out of these, 11 patients who were operated due to recurrent pleomorphic adenoma were retrospectively evaluated in terms of follow-up results in addition to gender, age, duration of follow-up, and clinical, radiological, and operative characteristics. Microsoft Excel 2013 (Microsoft Excel, Microsoft Corp., Washington, USA) was used in recording and processing the patient data. Due to the retrospective design of the study, the patient's consent was not received. This study was approved by the Board of Ethics of Non-Interventional Researches of Dokuz Eylül University with the decision dated and numbered as 2015/27-02.

Results

Seven of the patients undergoing revision surgery due to recurrent pleomorphic adenoma were female (64%) and 4 were male (36%); the mean age was 45 (28-64) years. The first surgery of all the patients who underwent revision surgery was performed out of our clinic. The average time between the initial surgeries of the patients and their visits to our clinic due to recurrences was 11.9 years (ranging from 2 to 21 years). From their epicrisis, pathology report, and history, it was found that 9 (82%) patients underwent enucleation and 2 (18%) patients underwent superficial parotidectomy. Ten out of these 11 patients were operated because of initial recurrences. One patient (patient no. 3) underwent surgery for the fifth recurrence. Recurrent tumors of three patients had deep lobe extension, and there was a dumbbell-like tumor extending to the parapharyngeal space in one of the patients (Figure 1).

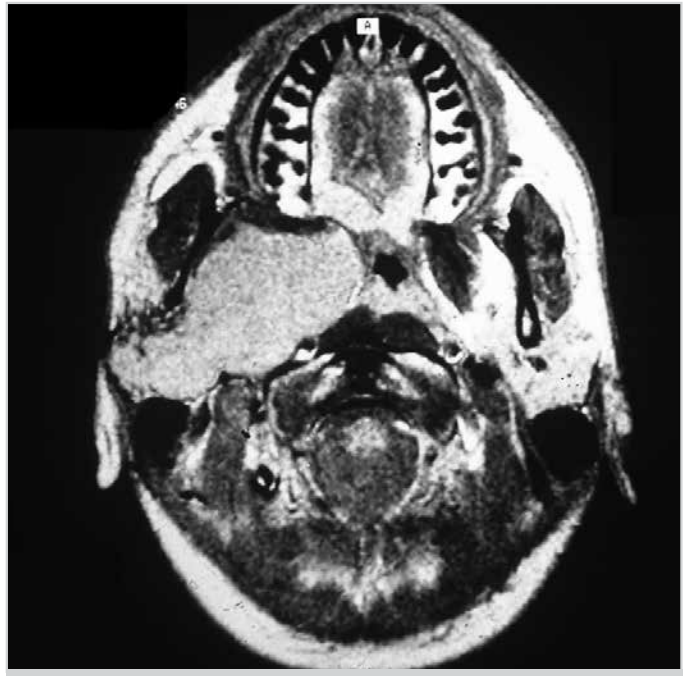

Figure 1. A dumbbell-like tumor causing the involvement of parotid deep lobe and parapharyngeal space (patient no: 1)

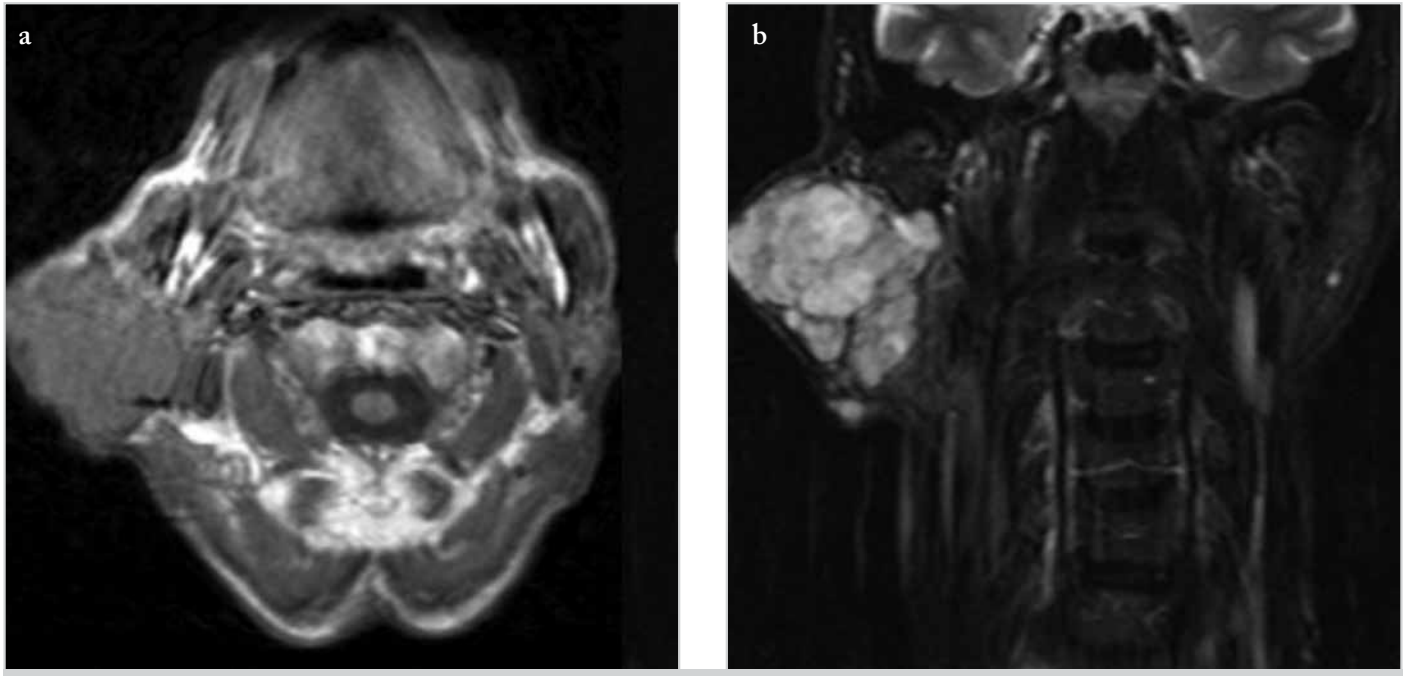

Figure 2. a, b. MRI imaging of the mass showing the right parotid deep lobe extension in patient no. 5. (a) The isointense appearance of the mass is observed in the T1-weighted section. (b) The hyperintense and multifocal appearance of the mass is remarkable in the T2-weighted section

Table 1. Demographic, clinical, and follow-up characteristics of the 11 patients operated due to recurrent pleomorphic adenoma

	Gender	Age	Number of recurrence	Type of first surgery	Elapsed time after the initial surgery	Location of recurrence	Type of revision surgery	Postoperative complication
Patient 1	M	28	1	Enucleation	5 Years	Deep lobe and parapharyngeal space extension	Total parotidectomy	Early paralysis of the facial nerve branches, late recovery, but synkinesis
Patient 2	F	41	1	Enucleation	8 Years	Superficial lobe	Superficial parotidectomy	Paresis in Facial nerve marginal branch -temporary
Patient 3	F	42	5	Enucleation	15 Years	Superficial lobe	Superficial parotidectomy + Masseter muscle excision	Periorbital fasciculations
Patient 4	F	46	1	Enucleation	19 Years	Superficial lobe	Superficial parotidectomy	None
Patient 5	M	64	1	Enucleation	10 Years	Deep lob extension	Total parotidectomy + RT	None (Received RT due to postoperative lymph vessel spread)
Patient 6	M	47	1	Enucleation	20 Years	Superficial lobe	Superficial parotidectomy	None
Patient 7	F	54	1	Enucleation	15 Years	Deep lob extension	Total parotidectomy	Two buccal branches associated with tumor were sacrificed - Frey syndrome
Patient 8	F	37	1	Enucleation	8 Years	Deep lob extension	Total parotidectomy	Frontal branch was sacrificed- There is some movement on the right mouth corner; motionless right eyebrow and eyelid
Patient 9	F	53	1	Superficial Parotidectomy	2 Years	Superficial lobe	Superficial Parotidectomy	None
Patient 10	M	45	1	Enucleation	21 Years	Superficial lobe	Total parotidectomy	None
Patient 11	K	39	1	Superficial Parotidectomy	8 Years	Superficial lobe	Superficial Parotidectomy	None

E: male; F: female; RT: radiotherapy

Figure 3. Preoperative view of patient no. 5. It is observed that the tumor has a multifocal structure

Due to recurrent pleomorphic adenomas, superficial parotidectomy (55%) was performed in 6 patients; further, by preserving the facial nerve, total conservative parotidectomy (45%) was performed in 5 patients. Skin incision scars that resulted from former surgeries of all the patients were included in the specimens. Magnification through an operation microscope or loop was employed during surgery. Facial nerve neuromonitoring (NIM-Response 2.0; Medtronic, Minnesota, USA) was used in 8 patients (patient nos. 4–11) who were operated after the year 2000.

The clinical, operative, and follow-up characteristics of 11 patients with recurrent parotid pleomorphic adenoma are listed in Table 1. Tumor-related facial nerve branches were sacrificed in 2 out of the 5 cases (in 2 out of 11 patients; 18%) (patient nos. 7 and 8): here, 2 facial nerve functions were preoperatively observed to be normal, conservative parotidectomy was performed as revision surgery by preserving the facial nerve, and loss in the related facial nerve motor functions was observed in the postoperative period. One of our patients in whom superficial paroti-

Figure 4. Postoperative surgical specimen of patient no. 5. It is observed that the tumor has a multifocal structure and the previous incision scar is included in the specimen

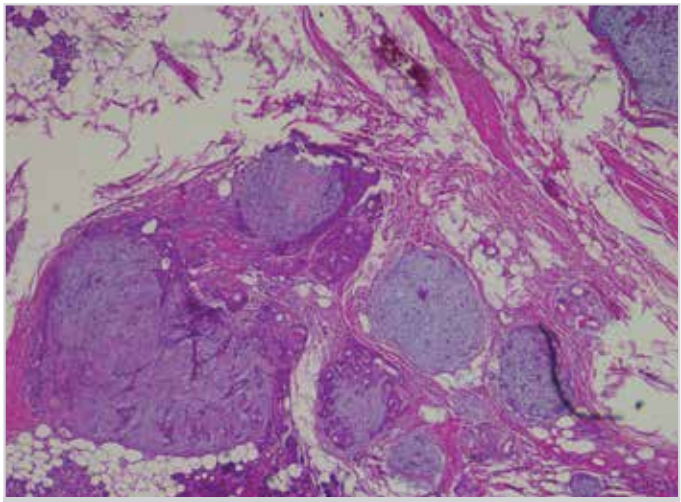

Figure 5. Pleomorphic adenoma areas in the form of well-circumscribed islands in the adipose tissue (patient no: 9) (H & E; original magnification ×10)

dectomy was performed as revision surgery received additional radiotherapy because the tumor was found to be multifocal in the histopathological examination and the tumor cells were observed in the lymph vessels (patient no. 5) (Figure 2-4). Due to the fact that the tumor tissues were observed on the masseter muscle surface, the masseter muscle was also partly included in the specimen of a patient (patient no. 3). None of these patients experienced any new recurrence during the follow-up of 9.1 years on average (1–26 years).

Discussion

Parotidectomy is the accepted standard treatment for parotid pleomorphic adenomas, in which the facial nerve is dissected and preserved, and the tumor is removed along with the surrounding intact tissue (2, 8). In the study of Riad et al. (5), it has been shown that damage to the tumor pseudocapsule and tumor seeding are independent risk factors for recurrence. In addition, tumor size, lack of safe surgical margins, and tumor associated with facial nerves are considered to play a role in the cause of recurrence. However, it has been found that these are the risk factors that lead to recurrence generally due to the damage in the pseudocapsule and tumor seeding (5). It has been found that the recurrence rates are 9 times higher in patients who underwent enucleation than superficial parotidectomy (8). In a recent study, the time between the recurrent disease after the initial surgery and the presentation was observed to be 7-10 years, and this duration was significantly shorter in patients who underwent enucleation as the first surgery (9).

Age and gender were not considered as prognostic factors in terms of the cause of recurrent disease in the series of 114 cases of Renehan et al. (12) and in the series of 31 cases of Carew et al. (13). However; in some studies, the female gender has been identified as a risk factor for recurrent disease (7, 10). There was a female majority in our series of 11 cases with a ratio of 64%. However, because of the limited number of patients, the relationship between the age and gender and the recurrence was not investigated in our study.

In the diagnosis of recurrent parotid pleomorphic adenoma, magnetic resonance imaging (MRI) is a preferred radiological examination method in order to better visualize the multifocal structure of the lesion and to detect the deep lobe and parapharyngeal space extension. It also helps to identify any residual parotid tissue (9). The tumor often has low intensity in the T1-weighted series and high intensity in the T2-weighted series. It can demonstrate moderate contrast enhancement in a contrast-enhanced series (9). However, MRI may not be able to detect all the foci. Although some nodules are identified by the surgeon with the aid of magnification during the surgery, they are often specified in the final specimen by the pathologist (3). Ultrasonography (USG) is mostly used for the follow-up after parotid surgeries. Zinis et al. (2) reported that they detected recurrent tumors in 12.1% patients through routine USG follow-up in their series. In our series, 5 patients were evaluated with USG before the operation and MRI was used in the diagnosis of 10 patients. The multifocal appearance of lesions in all the cases was noted in the MRI sections, which played a role in determining the surgical plan (Figures 1 and 2). In addition, during surgeries for all our cases, loop or operation microscope was used: it was observed that the magnification of the tumor helped the surgeon in recognizing the multiple foci of the tumor and in the exploration of the facial nerve.

According to the tumor location, superficial or total parotidectomy could be performed in pleomorphic adenomas recurring after an improperly performed surgical procedure (9). There is no indication of absolute total parotidectomy in a patient in whom enucleation or limited superficial parotidectomy was applied and in whom superficial tumor recurrence was detected in the previous surgery; however, the scarring of the previous surgical incision should be included in the specimen (9). Many authors, primarily Stennert et al. (3), opined that total parotidectomy would be appropriate for the resection of the multiple foci that could be missed

in patients with recurrent disease after superficial parotidectomy (3, 10). However, in a more recent study conducted by the same group of researchers, it was reported that a 52% recurrence was encountered despite performing total parotidectomy (2, 7). The enucleation applied in 9 out of 11 cases presented in our study was thought to be the most important factor in recurrence etiology.

If the tumor is in contact with the facial nerve, even with superficial or total parotidectomy to be performed, the presence of intact surrounding tissue may not be guaranteed. It has been reported that the risk of leaving a microscopic disease or causing microscopic tumor seeding may be high while the facial nerve is dissected (2, 8) (Figure 5). In this case, extended or radical parotidectomy, including the affected facial nerve branches, should be considered. The rate of inclusion of the facial nerve branches in resection was found between 14 to 30% in patients operated due to recurrent pleomorphic adenomas (2, 9). In our series, because the tumor was associated with the facial nerve in 2 patients in whom the facial nerve functions were observed as natural in the preoperative period, the involved facial nerve branches were required to be sacrificed in order not to leave out the microscopic disease. The rate of inclusion of the facial nerve branches in the resection, which was determined as 18% in our series, was evaluated in accordance with the literature.

The rates of temporary and permanent facial nerve paralysis in the postoperative period in the parotid surgery were reported as 9.1 to 64% and 0 to 3.9%, respectively (9). When evaluated in terms of the surgeries performed for recurrent parotid pleomorphic adenomas, this ratio was found to be significantly increased, temporarily to 90-100% and permanently to 11.3-40% (9). This rate increases with the number of revision surgeries performed, and the high complication rate has been attributed to the inability to distinguish the scar tissue from the facial nerve (9, 12, 14). In some studies, it has been observed that intraoperative facial nerve monitoring shortens the operation time, reduces the risk of permanent facial nerve paralysis, and shortens the postoperative recovery time of facial nerve motor functions (15, 16). Liu et al. (16) specified the rate of permanent facial nerve paralysis as 10.7% in patients who underwent total parotidectomy due to recurrent pleomorphic adenomas under intraoperative nerve monitoring and as 23.3% in patients for whom monitoring was not performed. However, it was determined that nerve monitoring did not shorten the surgical time and was not effective on the degree of facial paralysis in patients who underwent superficial parotidectomy due to recurrent disease (16). Intraoperative continuous facial nerve neuromonitoring was applied in 8 patients in our series. In the postoperative period, temporary decrease in facial nerve motor functions was observed in 2 patients (18%), and one of them showed improvement with synkinesis. The rate of temporary facial nerve involvement in our series was evaluated to be consistent with the literature.

Local control rates were found between 36 to 98% after the first revision surgery due to recurrent parotid pleomorphic adenomas (2, 7, 10, 17, 18). Wittekindt et al. (7) detected a recurrence rate of 42% over a 5-year follow-up and 75% over a 15-year follow-up. It was reported in another study that the recurrence rates increased along with the prolongation of the follow-up duration, i.e., 14% over a 5-year follow-up period, 31% over a 10-year follow-up period, and 57% over a 20-year follow-up period (2). No recurrence was observed in our 11 patients during the average follow-up period of 9.1 years.

When the literature is reviewed, the risk of malignant transformation, recurrence, multifocal development, and biologically more aggressive characterization of the tumor increases after revision surgery in recurrent parotid pleomorphic adenomas (9). In the result of the postoperative histopathologic evaluations of all the 11 patients who were presented in our study and in whom revision surgeries were performed in our clinic due to recurrent disease, it was reported that the tumor was in the multifocal structure and a close follow-up in terms of recurrence would be appropriate. There was no additional recurrence or malign transformation in our case series.

One of our patients who underwent superficial parotidectomy as revision surgery was directed to radiotherapy because the tumor was multifocal in the post-operative histopathological examination and the tumor cells were seen in the lymph vessels. In a review of Witt et al. (9), it was reported that adjuvant radiotherapy increased the rate of local control in patients with multifocal tumor and more than one recurrent disease, and it would be suitable in selected patients who have the risk of facial nerve damage in the case of recurrence.

Conclusion

In the treatment of cases with recurrent parotid pleomorphic adenomas after inadequate surgery, an appropriate surgery should be carefully planned in experienced hands by considering the tumor size, location, multifocal structure, and its relation with facial nerves. Surgery should aim to provide a safe surgical margin. The facial nerve should be considered to be sacrificed only in patients in whom a direct involvement is detected. Regular follow-up of these patients in the postoperative period is important for the early detection of possible additional recurrences.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Dokuz Eylül University Noninvasive Research Ethics Board (2015/27-2).

Informed Consent: Informed consent was not received due to the retrospective nature of the study.

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