OPEN ACCESS

Clinical utility of frozen section examination of lymph nodes in the level 2 neck during surgical treatment of parotid gland lesions

Parotis bezi lezyonlarının cerrahi tedavisi sırasında seviye 2 boyundaki lenf düğümlerinin donuk kesit incelemesinin klinik faydası

Ali Bayram[1] , Nuri Ünsal[1] , Aycan Şahin Genç[1] , Mehmet Yaşar[1] , Fatma Şenel[2]

[1]Department of Otolaryngology, Kayseri City Training and Research Hospital, Kayseri, Türkiye
[2]Department of Pathology, Kayseri City Training and Research Hospital, Kayseri, Türkiye

ABSTRACT

Objectives: This study aims to report the frozen section examination (FSE) results of level 2 lymph nodes (LNs) during parotidectomies for parotid masses preoperatively diagnosed as a benign lesion and to evaluate the possible role of FSE in the diagnosis and treatment plan of these patients.

Patients and Methods: The prospective study was conducted on patients who underwent parotidectomy with a preliminary diagnosis of a benign parotid lesion between May 2018 and June 2023. Among 120 patients who underwent parotidectomy, 30 patients (24.79%; 23 males, 7 females; mean age: 53.3±12.3 years; range, 22 to 79 years) who had FSE examination of level 2 LNs during parotidectomy were identified. The age, sex, fine-needle aspiration biopsy (FNAB), FSE, and final histopathology reports were evaluated from the patient records. All parotidectomies were performed by the same surgeon using the modified Blair incision, and level 2 LNs were harvested to ascertain the histopathological content through FSE during the surgery.

Results: Twenty-five (83.3%) of the 30 patients had a preoperative FNAB, and it was compatible with the final histopathology in 20 (66.67%) patients. The most common parotid lesions were Warthin's tumor (60%) and pleomorphic adenoma (36.67%), respectively. The FSE of all LNs was reported as reactive, and FSE did not alter the treatment plan in any patient.

Conclusion: An LN metastasis detected with FSE may be utilized as an adjunctive diagnostic tool during parotidectomy to prevent the preoperative misdiagnosis of a high-grade malignancy as a benign parotid gland lesion. Although the present study did not demonstrate such a contribution to a false-negative preoperative diagnosis of primary malignancy, the absence of a metastatic LN disease may be an auxiliary finding to confirm the diagnosis of a benign gland disease.

Keywords: Frozen section, lymphadenopathy, neck, parotid neoplasms.

ÖZ

Amaç: Bu çalışmada, ameliyat öncesi benign lezyon tanısı konulan parotis kitleleri nedeniyle yapılan parotidektomiler sırasında seviye 2 lenf nodlarının (LN) donuk kesit inceleme (DKİ) sonuçlarının raporlanmasını ve DKİ'nin bu hastaların tanı ve tedavi planındaki olası rolünün değerlendirmesi amaçlandı.

Hastalar ve Yöntemler: Bu prospektif çalışma, Mayıs 2018 - Haziran 2023 tarihleri arasında benign parotis lezyonu ön tanısıyla parotidektomi yapılan hastalar üzerinde gerçekleştirildi. Parotidektomi yapılan 120 hasta arasından, parotidektomi sırasında seviye 2 LN'lerde DKİ incelemesi yapılan 30 hasta (%24.79; 23 erkek, 7 kadın; ort. yaş: 53.3±12.3 yıl; dağılım, 22-79 yıl) belirlendi. Hasta kayıtlarından yaş, cinsiyet, ince iğne aspirasyon biyopsisi (İİAB), DKİ ve nihai histopatoloji raporları değerlendirildi. Tüm parotidektomiler aynı cerrah tarafından modifiye Blair insizyonu kullanılarak gerçekleştirildi ve ameliyat sırasında DKİ ile histopatolojik içeriği tespit etmek için seviye 2 LN'ler çıkarıldı.

Bulgular: Otuz hastanın 25'inde (%83.3) ameliyat öncesi İİAB yapıldı ve 20'sinde (%66.67) nihai histopatoloji ile uyumluydu. En yaygın parotis lezyonları sırasıyla Warthin tümörü (%60) ve pleomorfik adenom (%36.67) idi. Tüm LN'lerin DKİ'si reaktif olarak rapor edildi ve DKİ hiçbir hastada tedavi planını değiştirmedi.

Sonuç: Donuk kesit inceleme ile tespit edilen bir LN metastazı, parotidektomi sırasında yüksek dereceli bir malignitenin ameliyat öncesinde benign bir parotis bezi lezyonu olarak yanlış teşhis edilmesini önlemek amacıyla yardımcı bir tanı aracı olarak kullanılabilir. Bu çalışmada, primer malignitenin ameliyat öncesi yanlış negatif tanısına katkı gösterilmemiş olsa da, metastatik bir LN hastalığının bulunmaması, benign bez hastalığı tanısını doğrulamak için yardımcı bir bulgu olabilir.

Anahtar sözcükler: Donuk kesit, lenfadenopati, boyun, parotis neoplazmları.

Salivary gland tumors account for approximately 6 to 8% of all head and neck neoplasms. Approximately 80 of these tumors are benign and most commonly arise from the parotid gland.[1] The diagnosis and treatment of salivary gland tumors present several challenges due to the complex clinicopathological features and different biological behaviors of the lesions.[2]

Although its use has been declining since the widespread use of fine-needle aspiration biopsy (FNAB), frozen section examination (FSE) is still widely used in the diagnosis and management of parotid gland tumors.[3] Although FSE can be utilized to diagnose the primary tumor and to exclude the presence of a high-grade malignancy requiring neck dissection during parotid gland surgery, it is mostly used for surgical margin control and nerve or nodal disease involvement due to the difficulties in determining the diagnosis of parotid tumors with FSE.[4]

The negative effect of lymph node (LN) metastases (LNMs) on survival in parotid gland malignancies is well-known.[5] In the literature, the rate of occult metastasis of these malignancies to the neck has been reported up to 48% depending on the histopathology.[6] Level 2 is the neck region, where LNM is most frequently observed in patients with parotid gland malignancies.[5-8] Nevertheless, in patients who underwent parotidectomy with a preliminary diagnosis of benign parotid lesion, lymphadenopathies (LAPs) may still be encountered during surgery, particularly in level 2. In these patients, FSE can provide additional data regarding the histopathologic content of these LNs and a possible metastatic disease originating from a misdiagnosed primary malignant lesion. The present study aimed to report the FSE results of level 2 LNs during parotidectomies for parotid masses preoperatively diagnosed as a benign lesion and to evaluate the possible role of frozen sections in the diagnosis and treatment plan of these patients.

PATIENTS AND METHODS

The prospective study was conducted on patients who underwent parotidectomy with a preliminary diagnosis of benign parotid lesion at the Department of Otolaryngology and Head and Neck Surgery of Kayseri City Training and Research Hospital between May 2018 and June 2023. Preoperatively, the lesions were determined to be benign by FNAB, along with the combined evaluation of clinical and radiological findings. Patients who had an FSE of level 2 LNs during parotidectomy were determined, and the age,

sex, FNAB, FSE, and final pathology results were evaluated from the patient records. Patients with a preoperative diagnosis of a malignant tumor and those with incomplete hospital records were excluded from the study. One hundred twenty-one patients underwent parotidectomy with a preliminary diagnosis of benign parotid lesion during the study period. Of these patients, 30 (24.79%; 23 males, 7 females; mean age: 53.3±12.3 years; range, 22 to 79 years) with LAPs in level 2 underwent FSE (Table 1). Written informed consent was obtained from the participants. Ethical approval was obtained from Kayseri City Training and Research Hospital Clinical Research Ethics Committee (Date: 20.06.2023, No: 853). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Histopathologic examinations were performed by two pathologists experienced in head and neck lesions. All parotidectomies (partial, superficial, deep, and total) were performed by the same surgeon using the modified Blair incision. In our clinic, FSE was not routinely performed to reveal the primary tumor diagnosis in parotid gland lesions during the parotidectomy procedure. However, neck level 2 was routinely examined through inspection and palpation due to its proximity to the surgical field. If any LAPs were detected, at least one LAP was harvested (preferably the largest one if there were multiple LAPs) and sent for FSE for evaluation of its histopathological content.

Statistical analysis

Statistical analysis was performed using IBM SPSS version 21.0 software (IBM Corp., Armonk, NY, USA). Data were presented as mean ± standard deviation (SD). The chi-square test was used for categorical variables. A p-value <0.05 was considered statistically significant.

RESULTS

Twenty-five patients had a preoperative FNAB, which was compatible with the final histopathological examination in 66.67% (n=20). Five patients did not undergo preoperative FNAB; the determination that their lesions were benign was made based on the combined evaluation of clinical and radiological findings. Of these 30 patients, the most frequent parotid tumors were Warthin's tumor (n=18; 60%) and pleomorphic adenoma (n=11; 36.67%). One patient was diagnosed with Warthin's tumor by FNAB, but the final diagnosis was chronic sialadenitis. The FSE of all LAPs was reported as reactive, and FSE did not alter the treatment plan in any patient. The final

				Table 1	
			Demographic and histopathologic characteristics of patients who underwent	
			FSE of LAPs in neck level 2	
No	Age/Sex	FNAB	FS of LN	Primary diagnosis
1	59/M	WT	Reactive	WT
2	36/M	PA	Reactive	PA
3	22/M	PA	Reactive	PA
4	56/M	-	Reactive	WT
5	33/F	PA	Reactive	PA
6	55/M	WT	Reactive	WT
7	62/M	WT	Reactive	WT
8	54/F	Suspicious	Reactive	WT
9	56/M	WT	Reactive	CS
10	51/M	WT	Reactive	WT
11	44/M	PA	Reactive	PA
12	57/M	WT	Reactive	WT
13	59/F	PA	Reactive	PA
14	50/M	PA	Reactive	PA
15	65/M	-	Reactive	WT
16	79/M	-	Reactive	WT
17	67/F	-	Reactive	WT
18	52/M	WT	Reactive	WT
19	43/F	PA	Reactive	PA
20	56/F	WT	Reactive	WT
21	57/F	ND	Reactive	PA
22	55/M	WT	Reactive	WT
23	57/M	PA	Reactive	PA
24	33/M	PA	Reactive	PA
25	69/M	WT	Reactive	WT
26	58/M	ND	Reactive	WT
27	36/M	-	Reactive	PA
28	59/M	WT	Reactive	WT
29	69/M	WT	Reactive	WT
30	50/M	PA	Reactive	WT

FSE: Frozen section examination; lesion, LAPs: Lymphadenopathies; FNAB: Fine-needle aspiration biopsy; FS: Frozen section; LN: Lymph node; WT: Warthin tumor; PA: Pleomorphic adenoma; CS: Chronic sialadenitis; ND: Non-diagnostic.

histopathological reports of all harvested LAPs were compatible with FSE in all patients.

DISCUSSION

In the literature, the contribution of FSE to the diagnosis of parotid tumors during parotidectomy is controversial. In some studies, the technique was reported to have a similar diagnostic accuracy to that of FNAB, while others have claimed that its utilization may not be beneficial after a benign FNAB report.[3,9,10] Frozen section examination harbors multiple limitations for the diagnosis of salivary gland neoplasms as a primary diagnostic method due to the complex morphology of these tumors and the significant overlapping of cytopathological

characteristics of benign and malignant tumors.[11] Furthermore, a single section is usually taken along the longest central axis of the lesion to avoid tissue artifacts; hence, adequate sampling that fully represents tumor characteristics may not be obtained during the procedure.[12] Another factor that creates difficulty in the diagnosis of the primary tumor with FSE is the occurrence of tissue artifacts due to the rapid freezing of the tissue that consequently causes the loss of some histopathological diagnostic features of the primary tumor. Immunohistochemical studies, which are important for the diagnosis of specific tumor types, such as extranodal marginal zone lymphoma developing from Warthin tumor, cannot be performed effectively during FSE. In conclusion, considering the difficulties such as limited sample size, tissue artifacts, and inability to perform immunohistochemical studies, rapid microscopic evaluation may provide limited diagnostic utility compared to formalin-fixed paraffin-embedded tissue evaluation methods, particularly in the diagnosis and grading of malignant salivary gland tumors.[12] In our clinic, FSE is primarily employed for surgical margin control and the assessment of LNM and nerve invasions in the management of parotid lesions, rather than primary tumor diagnosis.

In parotid malignancies, metastatic LAPs most commonly occur in the neck level 2.[5-8] High-grade malignancy, extraparotid extension, a tumor size of 4 cm or more, and facial nerve involvement increase the risk of neck disease that necessitates more advanced treatment, including therapeutic neck dissection or radiotherapy.[13,14] In parotid neoplasms, final histopathological examinations may reveal a malignant tumor, even in patients initially diagnosed with a benign parotid lesion through clinical, radiological, and histopathological evaluations before surgery. Considering the difficulties in the diagnosis of parotid tumors by FSE, FSE of the LAPs detected intraoperatively in neck level 2 for possible metastatic involvement may be instructive for the clinicians in the diagnosis of a high-grade parotid tumor and may aid in establishing an accurate intraoperative surgical plan, including total parotidectomy and therapeutic neck dissection. Parotidectomies performed using the modified Blair incision facilitate the surgeon in LN examination of this region. During the parotidectomies performed in our clinic, we observed that a significant number of patients who underwent parotidectomy with a preoperative diagnosis of a benign parotid lesion had LAPs in level 2 (24.79%), which can be easily harvested during surgery. Although the FSE of all LAPs was reported as reactive, and FSE did not alter the treatment plan in any patients in the present

study, FSE of level 2 LAPs may have a potential role in the detection of patients with a false-negative preoperative diagnosis of primary malignancy. By contrast, demonstration of the absence of a metastatic LAP by FSE may be utilized as an adjunctive diagnostic method, supporting the diagnosis of a benign primary lesion during surgery.

The present study had several limitations. Due to the retrospective nature of the study, a heterogeneous group of patients with lesions of various sizes and histopathologic types located in different anatomical regions of the parotid gland were included in the study. Therefore, data regarding which patients had a higher prevalence of level 2 LAPs were limited. Similarly, FSE could not be performed by a pathologist blinded to the patients' clinical and histopathologic records. Since a disease-free LN may have been sent for FSE during surgery, clinicians should keep in mind that the region may still involve an occult or clinical LN metastatic disease. Careful preoperative ultrasonography and FNAB can also reveal the content of these LNs with high accuracy. However, a modified Blair incision allows the surgeon to examine the area by inspection and palpation due to the proximity of neck level 2 to the parotidectomy site. In cases where LAPs are detected in the region during surgery, we believe that FSE may be a useful and practical method for clinicians to determine the histopathological content of these LNs.

In conclusion, LAPs located in neck level 2 may be easily harvested and examined through FSE during parotidectomy. An LNM detected with FSE may be utilized as an adjunctive diagnostic tool during parotidectomy to prevent the preoperative misdiagnosis of a high-grade malignancy as a benign parotid gland lesion and, therefore, may provide a significant contribution to establishing a proper surgical treatment plan during surgery. Although the present study did not demonstrate such a contribution to a false-negative preoperative diagnosis of primary malignancy, the absence of a metastatic LN disease may be an auxiliary finding to confirm the diagnosis of a benign gland disease. Multi-institutional studies with large patient cohorts may provide further data regarding the potential role of FSE of LAPs located in this region during parotidectomy.

REFERENCES

1. Spiro RH. Salivary neoplasms: Overview of a 35-year experience with 2,807 patients. Head Neck Surg 1986;8:177-84. doi: 10.1002/hed.2890080309.

2. Grasl S, Kadletz L, Janik S, Riedl A, Erlacher B, Formanek M, et al. Fine-needle aspiration cytology and intraoperative frozen section in parotid gland tumour surgery: A retrospective multicenter analysis of 417 cases. Clin Otolaryngol 2019;44:461-5. doi: 10.1111/coa.13314.

3. Wong DS. Frozen section during parotid surgery revisited: Efficacy of its applications and changing trend of indications. Head Neck 2002;24:191-7. doi: 10.1002/hed.10072.

4. Suzuki M, Nakaegawa Y, Kobayashi T, Kawase T, Matsuzuka T, Murono S. The role of frozen section biopsy for parotid gland tumour with benign fine-needle aspiration cytology. J Laryngol Otol 2019;133:227-9. doi: 10.1017/S002221511900029X.

5. Suzuki M, Nakaegawa Y, Kobayashi T, Kawase T, Matsuzuka T, Murono S. The role of frozen section biopsy for parotid gland tumour with benign fine-needle aspiration cytology. J Laryngol Otol 2019;133:227-9. doi: 10.1017/S002221511900029X.

6. Voora RS, Panuganti B, Califano J, Coffey C, Guo T. Patterns of Lymph Node metastasis in parotid cancer and implications for extent of neck dissection. Otolaryngol Head Neck Surg 2023;168:1067-78. doi: 10.1002/ohn.167.

7. Dell'Aversana Orabona G, Salzano G, Abbate V, Bonavolontà P, Committeri U, Seidita F, et al. Malignant tumours of the parotid gland: Management of the neck

8. Jinnin T, Kawata R, Higashino M, Nishikawa S, Terada T, Haginomori SI. Patterns of lymph node metastasis and the management of neck dissection for parotid carcinomas: A single-institute experience. Int J Clin Oncol 2019;24:624-31. doi: 10.1007/s10147-019-01411-3.

9. Seethala RR, LiVolsi VA, Baloch ZW. Relative accuracy of fine-needle aspiration and frozen section in the diagnosis of lesions of the parotid gland. Head Neck 2005;27:217-23. doi: 10.1002/hed.20142.

10. Patel KR, Scognamiglio T, Kutler DI, Kuhel WI, Gromis J, Phillips CD, et al. Retrospective assessment of the utility of imaging, fine-needle aspiration biopsy, and intraoperative frozen section in the management of parotid neoplasms: The Weill Cornell Medical College Experience. ORL J Otorhinolaryngol Relat Spec 2015;77:171-9. doi: 10.1159/000381678.

11. Mantsopoulos K, Bessas Z, Sievert M, Müller SK, Koch M, Agaimy A, et al. Frozen section of parotid gland tumours: The head and neck pathologist as a key member of the surgical team. J Clin Med 2022;11:1249. doi: 10.3390/jcm11051249.

12. Choy KCC, Bundele MM, Fu EW, Li H, Gan JYJ, Rao NCL, et al. Risk stratification of parotid neoplasms based on intraoperative frozen section and preoperative fine needle aspiration cytology. Eur Arch Otorhinolaryngol 2022;279:2117-31. doi: 10.1007/s00405-021-07015-w.

13. Chisholm EJ, Elmiyeh B, Dwivedi RC, Fisher C, Thway K, Kerawala C, et al. Anatomic distribution of cervical lymph node spread in parotid carcinoma. Head Neck 2011;33:513-5. doi: 10.1002/hed.21479.

14. Armstrong JG, Harrison LB, Thaler HT, Friedlander-Klar H, Fass DE, Zelefsky MJ, et al. The indications for elective treatment of the neck in cancer of the major salivary glands. Cancer 1992;69:615-9. doi: 10.1002/1097-0142(19920201)69:3<615::aid-cncr2820690303>3.0.co;2-9.

(including the clinically negative neck) and a literature review. Br J Oral Maxillofac Surg 2021;59:665-71. doi: 10.1016/j.bjoms.2020.08.026.