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Research Article

Diagnostic accuracy of fine-needle aspiration cytology for extrathyroidal head-and-neck lesions performed by a cytopathologist with the assistance of radiologist: A single-center study

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ABSTRACT

Objective: In recent years, several publications have described the use of ultrasound-guided fine-needle aspiration (FNA) by cytopathologists to achieve better diagnostic accuracy. Some cytopathologists enroll in courses to learn and apply ultrasound (US) guidance themselves. However, no standard procedure has been established that cytopathologists can follow to perform US for FNA. Alternatively, FNA can be a useful tool when cytopathologists collaborate with radiologists. Here, we aimed to evaluate the diagnostic accuracy of FNA for non-thyroidal head-and-neck masses retrieved by a cytopathologist with US guidance provided by a radiologist.

Material and Methods: The FNA results for non-thyroidal head-and-neck masses at a private clinic using the Scandinavian FNA model with radiologist–cytopathologist collaboration were compared with the histopathology results.

Results: In all, 1890 patients who underwent FNA were identified, among whom 1435 (76%) also had histopathological results. Non-cystic lesions were obtained from lymph nodes (LNs), salivary glands, and soft tissue, while the other lesions were cystic in nature. For FNA, the accuracy was 99.4%, the sensitivity was 99.6%, the specificity was 99.3%, the positive predictive value was 99.3%, and the negative predictive value was 99.6%. No FNA results were non-diagnostic. Surgical follow-up revealed that only eight of the 1435 assessments (0.5%), all performed for LN lesions, yielded false-negative or false-positive results.

Conclusion: The present study is based on single-center observations. The use of FNA, when performed by a specialized cytopathologist and with US assistance from a radiologist, produces accurate results and sufficient material for analysis, especially for LNs in extrathyroidal head-and-neck lesions. This study also reveals that the technique is a low-cost and effective process. The way in which FNA is presented here indicates that this procedure would be useful and ideal for any health service.

Keywords: Cytopathologist–radiologist collaboration, Diagnostic accuracy, Fine-needle aspiration cytology, Head-and-neck masses, Scandinavian model fine-needle aspiration clinic

INTRODUCTION

Fine-needle aspiration (FNA) is a medical procedure whose effectiveness has only recently been recognized due to difficulties in promoting this approach to other clinicians.[1,2] These difficulties are related to the objective of the procedure, which is to distinguish whole tissue from the cellular components obtained from a small-tipped needle. As a result, its diagnostic accuracy

has long been questioned. The publications, innovations, and courses that originated at Karolinska Hospital in Sweden contributed to the increased international attention given to the Scandinavian FNA method in the late 1970s and early 1980s. The prominent academics involved in these new developments included Torsten Löwhagen, Josef Zajicek, Pier Esposti, and Sixten Franzén.[3]

FNA has finally received widespread recognition in the medical community over the past few decades. The procedure is increasingly recognized by clinicians as a crucial part of their evaluation of patients who have palpable or radiologically identified mass lesions in different organs. When executed appropriately and when the samples are assessed by qualified cytopathologists, FNA is a reliable, fast, cost-effective, and valuable diagnostic method. This minimally invasive method avoids undesirable side effects, including patient discomfort, which, combined with its high accuracy, has dispelled the doubts in the medical community about this procedure.The pioneers mentioned above played a pivotal role in promoting FNA within the medical community and in helping FNA gain acceptance within the field of diagnostic medicine.[4,5]

According to numerous studies, despite several disadvantages, FNA is an effective and accurate method for the first-line diagnosis of head-and-neck masses, as it allows clinicians to further understand their the patients' needs.[6-11] FNA has excellent overall diagnostic accuracy for different types of lesions, including 95% accuracy for all head-and-neck masses, 95% for benign lesions, and 87–93% for malignant lesions.[12-15]

Execution of the method according to the relevant procedures, an adequate material yield, and the cytopathologist's experience are critical factors that influence the diagnostic accuracy of FNA for lesions in the head-and-neck, as well as other sites.[16,17] Ideally, FNA is performed after sufficient representative material is retrieved, the aspirate is appropriately prepared, and the sample is transported to the laboratory so that the cytopathologist can evaluate it under the appropriate circumstances. As stated by Kojcan, the "FNA technique is simple but not banal. It requires a certain manual dexterity in the same way as surgical procedures do." Such dexterity is thus necessary before diagnostic samples can be obtained.[15]

Radiologists have historically been specialists in the use of ultrasound-guided FNA (USG-FNA) in hospital settings.[11-16] However, studies have also indicated that ear, nose, and throat physicians (ENTs) use ultrasonography or palpation to perform FNA on head-and-neck lesions.[17-19]

Furthermore, increasing numbers of publications have described the use of USG-FNA by cytopathologists to achieve better diagnostic accuracy and lower percentages of non-diagnostic aspirates.[20-33] However, no standard procedure has been established that cytopathologists can follow when they use ultrasound (US) for FNA. Some cytopathologists, particularly those in the United States, seek assistance from sonographers, whereas others enroll in courses to learn and apply US guidance themselves. However, these approaches are not broadly followed worldwide.[22-25,28-29]

Based on our experience and the results from other similar studies, we believe that FNA can be a helpful tool when cytopathologists collaborate with radiologists to obtain samples.[27,30-32] Consulting the patient, ensuring an exchange of views between the cytopathologist and the radiologist, and visualizing the lesion on US enables the cytopathologist to orient the lesion to be diagnosed, which facilitates the cytodiagnosis. This practice reduces inadequate material acquisition and prevents pitfalls.

We examined the data from 1890 patients who underwent FNA for extrathyroidal head-and-neck lesions at a private practice where the FNA technique was performed by both a cytopathologist and a radiologist. These data were obtained over 25 years, and among the patients, 1435 (76%) had known histopathology data. In addition, we evaluated the utility and diagnostic accuracy of the FNA procedure performed according to our model.

MATERIAL AND METHODS

Data were extracted from the medical records of the corresponding author's private cytopathology practice on his own initiative, and during this process, patient privacy was respected. Patients were provided information verbally about the procedure. Written consent was also obtained from each patient. Our study posed no additional risks and did not adversely affect the welfare of the subjects involved. The principles outlined in the Declaration of Helsinki were followed.[34] Clearance was obtained from the Kocaeli University Medical School Institutional Ethics Commission. All patients with extrathyroidal head-and-neck lesions who were referred to our clinic by various physicians for FNA from November 1999 to December 2023 were included in the study. All FNA procedures were performed and evaluated by the corresponding author according to the USG-FNA model described below. Histopathological examinations were performed by the regional university teaching hospital and pathology departments at other hospitals, primarily by the first author (BYB) and other pathologists. The cytopathologist (NP) was not involved in any of the histological diagnoses.

Description of the model used in our private practice setting

For 25 years, the corresponding author (NP) has been using USG-FNA in his private cytopathology practice in tandem

with and under the supervision of a radiologist. When he worked as a cytopathology subspecialty fellow at the Cytology Unit, Department of Pathology (Head: Prof Jahn Nesland) at Radium University Hospital of Oslo University, Norway, from March 1992 to March 1993, he learned this procedure from Sixten Franzén and other experts in the unit. Accompanied by a radiologist performing US guidance, Dr. Sixten Franzén, a trailblazer in the field of the Scandinavian FNA model, employed FNA on his own using the rapid onsite cytological assessment (ROSE) technique at the Cytology Outpatient Clinic of the Radium University Hospital of Oslo [Figure 1].[31]

In this procedure, the cytopathologist ascertains the patient's medical history before performing FNA and assesses the information obtained from the patient's current and prior imaging exams. This consequently allows the cytopathologist to gain a basic understanding of the patient. The US examination is performed by a radiologist in our private office who also diagnoses the lesion and interprets its nature. The cytopathologist (NP) performs FNA for extrathyroidal head-and-neck lesions using 22G (black hub), 23G (blue hub), and 25G (orange hub) needles attached to a 5-cc syringe; a 10-cc syringe with an attached pistol grip syringe holder can be substituted in cases of certain hard masses.

Our radiologist does not prefer gel as a medium for performing US; instead, after the gel is applied, the radiologist covers the US transducer with a thin surgical glove. Betadine is then applied between the transducer and the skin; subsequently, the US signal is visualized on the screen, and FNA is performed through guidance from the signal.[32]

Using a freehand technique, one or two aspirations are acquired. We can maneuver more freely to acquire samples from head-and-neck masses in the remaining narrow area with a 5-cc syringe even when the US transducer is being applied. The cytopathologist produces the slides and cell blocks and then saves the aspirate for any further investigations and the onsite cytological assessment. In addition to using the Diff-Quik® stain (Code XYZ123, ABC Corporation, USA) on one or two slides, the Papanicolaou stain is used for direct smears (Code PAP456, DEF Ltd, UK).

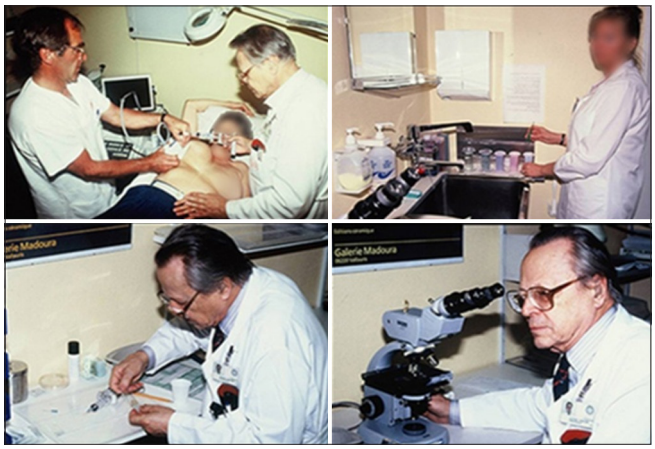

Figure 1: Picture showing Dr. Sixten Franzén during a fine-needle aspiration (FNA) procedure with ultrasound guidance from a radiologist at the FNA clinic at the Norwegian Radium Hospital in 1993 (photo and layout by Dr. NP) (courtesy of the Department of Pathology, Oslo University Hospital).

Histopathological data

The first author (BYB) screened every patient in the patient registry from November 1, 1999 (when the private practice was established), to December 31, 2023, and noted the details of the extrathyroidal head–neck masses. He then reviewed each name and individually compared the names to the data in the coauthor's private practice computer system. Next, the first author compared the cytology results with the biopsy findings retrieved from the computer system of the regional university hospital where she was employed. Histopathological examinations were performed by the regional university teaching hospital and the pathology departments of other hospitals, mainly by the first author (BYB) and other pathologists. The coauthor was not involved in the evaluation of the histopathology results, and since the two authors were not in contact, bias in the authors' findings was avoided.

Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences software (version 26.0). The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated according to the standard formulas described by Florkowski.[33] Confidence intervals were calculated at the 95% level. The following formulas were used: "sensitivity = TP/(TP + FN), specificity = TN/(TN + FP), PPV = TP/(TP + FP), and NPV = TN/(TN + FN)". Confidence intervals were calculated using the Wilson method.[33]

The first author performed the statistical analysis, in which he calculated the specificity, sensitivity, and accuracy of the cytological diagnoses with respect to the histological diagnosis. For patients who received a histological diagnosis, the sensitivity, specificity, PPV, NPV, and accuracy of the cytological review were assessed. In accordance with the methods of Florkowski,[33] the lesions were classified into the following categories: (i) true positive (TP), when the cytological and histological diagnoses were both positive for malignancy; (ii) true negative (TN), when the cytological and histological diagnoses were both negative for malignancy; (iii) false positive (FP), when the cytological diagnosis was positive for malignancy while the histological

diagnosis was negative for malignancy; and (iv) false negative (FN), when the cytological diagnosis suggested that the lesion was benign but the histological diagnosis was positive for malignancy.

RESULTS

Baseline clinical data

From November 1, 1999, to December 31, 2023, 1890 patients who underwent extrathyroidal head-and-neck FNA were identified. Histopathology results were obtained for 1435 of these patients (76%).

Among the entire cohort, 850 were male (45%), 1040 were female (55%), and 83.8% were younger than 65 years of age. Non-cystic lesions were found in the following anatomical sites: lymph nodes (LNs), 1,416 (74.9%); salivary glands, 327 (17.3%); and soft tissues, 87 (4.6%). The remaining 60 lesions (3.2%) were cystic in nature.

The diagnoses obtained from FNA and histopathology were grouped into five diagnostic categories according to the nature of the lesions: (i) non-diagnostic (inadequate), (ii) non-neoplastic, (iii) negative for malignancy, (iv) suspected malignancy, and (v) positive for malignancy, as described in similar studies by Rammeh *et al*., Petrone *et al*., and Kliassov *et al*.[7,8,26]

Since the head-and-neck region contains various anatomical sites, a separate cytological classification is currently recommended for each site. Since using a separate classification for each anatomical site may increase the complexity in the scope of our study, we preferred to employ a general classification used in similar studies based on the cytological-histopathological nature of the lesions to preserve diagnostic integrity among various head-neck sites. Table 1 lists the FNA results according to age, sex, location, mean lesion diameter, and diagnostic category.

Table 1: Breakdown of FNA results (age, sex, localization, and diagnostic category) into various parameters.

Parameter	All patients (*n*=1890)
Age, *n* (%)	
<65 y	1584 (83.8)
≥65 y	306 (16.2)
Gender, *n* (%)	
Male	850 (45.0)
Female	1040 (55.0)
Localization of FNAC specimens, *n* (%)	
Lymph node	1416 (74.9)
Salivary gland	327 (17.3)
Cyst	60 (3.2)
Soft tissue and skin	87 (4.6)
Lesion/tumor diameter (mm) ± standard deviation	22.1±10.3
Distribution of diagnostic category, *n* (%)	
Non-diagnostic	0 (0.0)
Non-tumoral	1068 (56.5)
Negative for malignancy	233 (12.3)
Suspicious for malignancy	61 (3.2)
Diagnostic of malignancy	528 (28.0)

FNA: Fine-needle aspiration, FNAC: Fine-needle aspiration cytology

Anatomical lesion data

The breakdown of the FNA surgical follow-up results by anatomical region and the percentages of available histological results based on cytological diagnosis were as follows: head-and-neck LNs, 1,416/1,024 (72.3%); salivary glands, 327/286 (87.4%); cystic lesions of the neck, 60/60 (100%); and soft-tissue, subcutaneous lesions, 327/65 (19.8%).

Table 2 provides a detailed list of the cytological and histological distributions of the lesions by anatomical site.

Cytohistological correlations and FN/FP results

Among the 1890 patients who underwent FNA, 1435 (76%) also had a histological diagnosis. Among these patients, 8 (0.55%) had FP or FN FNA results, all of which were obtained from LN lesions. Specifically, FN results were observed in 5 (0.4%) of the 1024 LNs with confirmed biopsy results, whereas 3 (0.3%) cases yielded FP results. No FP or FN cases were identified in non-lymphoid sites among patients with available surgical follow-up data. The relevant details are provided in Table 3.

In addition, Table 4 presents the diagnostic performance metrics of our study, including an accuracy of 99.4%, a sensitivity of 99.6%, a specificity of 99.3%, a PPV of 99.3%, and an NPV of 99.6%.

In our study, we observed FP and FN results, primarily in LN cases, due to specific technical and biological factors. Three "false-positive nodes" were reactive lymphoid hyperplasia. However, cytological sampling was performed in areas densely populated with germinal center cells, which led to misinterpretation as suspicious for malignancy. In addition, in three cases of granulomatous lymphadenitis, significant cytolysis during the FNA process contributed to their erroneous classification as metastatic nasopharyngeal carcinoma or lymphoma. With respect to "false-negative lymph nodes," one case of metastatic carcinoma and one case of lymphoma were misdiagnosed as reactive lymphoid hyperplasia due to FNA sampling from non-representative, histologically normal areas of the LNs. Several measures

Table 2: Cytological and histopathological results according to the anatomical location of the lesions

	Cytopathological diagnosis (*n*=1890)	Histopathological diagnosis (*n*=1435)
Lymph node, (%)		
Non-diagnostic	0 (0.0)	0 (0.0)
Non-tumoral	900 (47.6)	567 (39.5)
Negative for malignancy	-	-
Suspicious for malignancy	32 (1.7)	-
Diagnostic of malignancy	484 (25.6)	457 (31.8)
Total	1416 (74.9)	1024 (71.4)
Salivary gland, (%)		
Non-diagnostic	0 (0.0)	-
Non-tumoral	79 (4.2)	45 (3.1)
Negative for malignancy	192 (10.2)	193 (13.4)
Suspicious for malignancy	12 (0.6)	-
Diagnostic of malignancy	44 (2.3)	48 (3.3)*
Total	327 (17.3)	286 (19.9)
Soft tissue and skin, (%)		
Non-diagnostic	0 (0.0)	0 (0.0)
Non-tumoral	29 (1.5)	17 (1.2)
Negative for malignancy	0 (0.0)	0 (0.0)
Suspicious for malignancy	17 (0.9)	-
Diagnostic of malignancy	41 (2.2)	48 (3.3) *
Total	87 (4.6)	65 (4.5)
Cyst, (%)		
Non-diagnostic	0 (0.0)	0 (0.0)
Non-tumoral	60 (3.2)	60 (4.2)
Total	60 (3.2)	60 (4.2)

*Histopathological "diagnostic of malignancy" numbers also include those that are "suspicious for malignancy" according to FNA

have been implemented to minimize these diagnostic errors. These are outlined as follows: (i) An experienced radiologist provided US guidance during FNA, ensuring precise needle placement for obtaining adequate and representative samples; (ii) an interventional cytopathologist who completed a cytopathology fellowship trained in the USG-FNA procedure performed the aspiration and had over 25 years of experience in FNA, which significantly reduced sampling errors; and (iii) for patients with initial suspicious findings, additional diagnostic techniques, such as repeated aspirations and cell blocks for immunocytochemistry, were employed when necessary.

Our findings highlight the critical roles of the sampling technique and site selection in cytological accuracy. Although non-lymphoid anatomical sites were not analyzed in detail for FP or FN results in our study, expanding this analysis to include other sites could provide a broader understanding of diagnostic pitfalls.

From a clinical perspective, errors in LN evaluations can have significant consequences, including delayed or inappropriate treatment. The misinterpretation of granulomatous lymphadenitis as metastatic carcinoma or lymphoma may lead to unnecessary systemic therapies, whereas the misdiagnosis of metastatic carcinoma or lymphoma as reactive hyperplasia could delay critical oncological interventions. To address these challenges, we recommend the integration of adjunctive diagnostic tools such as immunocytochemistry or molecular techniques alongside fine-needle aspiration cytology (FNAC) to increase diagnostic accuracy. Furthermore, meticulous attention to representative sampling, particularly in complex cases such as lymphadenopathy, remains essential to minimize errors and improve patient outcomes.

Data from the literature

We generated a table with our data and those from several articles comparable to our research that were obtained in a literature review [Table 5]. The table included a selection of recent trials focused on non-thyroidal head-and-neck masses, but studies that focused solely on the salivary gland were excluded from the study. We compared our data with the findings of other publications.

A group of illustrative cytological images of various head-and-neck lesions are also presented in Figures 2-5.

DISCUSSION

Study data

Among our patients, lesions were most common in the LNs of the head-and-neck (1,416 of 1890 patients who underwent FNA, 71%). Among the 1435 lesions with confirmed histological diagnoses, the FNA results for 8 (0.5%) were FN or FP, and all were from LNs. No FN or FP results were obtained at other sites.

These 8 FN+FP results corresponded to 0.78% of the 1024 patients with a histologically confirmed diagnosis. Five of these were FNs (0.4%), while three were FPs (0.3%). Among the two patients with FP results, one was diagnosed

Table 3: FP and FN results of fine-needle aspiration cytology (*n*=8).

Localization	Cytological diagnosis	Histological diagnosis	FN/FP results
LN	Reactive lymphoid hyperplasia	Metastatic carcinoma non-Hodgkin lymphoma	FN (*n*=2)
	Suspicious for malignancy	Reactive lymphoid hyperplasia	FN (*n*=3)
LN	Non-Hodgkin lymphoma	Granulomatous lymphadenitis	FP (*n*=2)
	Metastatic nasopharyngeal carcinoma	Granulomatous lymphadenitis	FP (*n*=1)

LN: Lymph node, FN: False-negative, FP: False-positive

Table 4: Diagnostic sensitivity, specificity, accuracy, and positive and negative predictive values of fine-needle aspiration cytology (*n*=1435).

Parameter	All patients (%)	Lymph node (%)	Salivary gland (%)	Cyst (%)	Soft tissue and skin (%)
Accuracy	99.4	99.2	100	100	100
Sensitivity	99.6	99.3	100	-	100
Specificity	99.3	99.1	100	100	100
Positive predictive value	99.3	98.9	100	-	100
Negative predictive value	99.6	99.5	100	100	100

Table 5: Head-and-neck cytology series in the literature.

	Year	Patients	Accuracy (%)	Sensitivity (%)	Specificity (%)	Inadequacy (%)
Tandon *et al.*[10]	2008	2702	95.1	89.5	98.5	29.6
Kraft *et al.*[35]	2008	75	93.0	97.0	70.0	32.0
Robitschek *et al.*[19]	2010	81	96.5	N/A	N/A	16.1
Wu *et al.*[21]	2011	100	97.0	100	86.0	1.0
Göret *et al.*[11]	2015	866	96.7	94.6	97.9	16.0
Rammeh *et al.*[7]	2018	265	93.5	92.0	94.9	N/A
Petrone *et al.*[8]	2020	301	94.0	92.7	94.0	2.6
Kliassov *et al.*[26]*	2022	143	N/A	89.0	93.0	7.0
Present study	2024	1435	99.4	99.6	99.3	0.0

*This article covers aspirates from all areas of the body, including the head-neck area

with non-Hodgkin lymphoma through FNA, while the other was diagnosed with nasopharyngeal carcinoma metastasis due to a diagnosis of nasopharyngeal fullness at the clinic. "Granulomatous lymphadenitis" was reported in the LN biopsy results of both patients. Given that the FN and FP rates are <1%, our findings confirm that FNA is a reliable diagnostic technique for the evaluation of head-and-neck LN lesions.

Table 4 indicates that FNA had an accuracy of 99%, a sensitivity of 99%, a specificity of 99%, a PPV of 98.9%, and an NPV of 99.5% in the diagnosis of LN lesions. In the literature, the accuracy of FNA in the diagnosis of LN lesions ranges from 82% to 94.4%.[35-37]

In our study, the accuracy for the identification of head-and-neck LN lesions was 99.2%, which exceeds the values reported in the literature. This high accuracy highlights the potential of FNA as a first-line diagnostic method for patients with neck lymphadenopathy. FNA can serve as a triage tool for lymphadenopathy, particularly in busy outpatient settings, as it allows clinicians to rapidly determine the type of lymphadenopathy in a cost-effective manner. Further diagnostic approaches may then be tailored on the basis of the FNA findings.[38-41]

It has been reported that hematologists, oncologists, and some internists approach LN FNA cautiously in patients with head-and-neck lymphadenopathy who are admitted to hematology or oncology outpatient departments.[39] However, scheduling an excisional biopsy in a busy hospital setting is often challenging, and attending physicians may avoid such biopsies for preliminary assessment.[40-42]

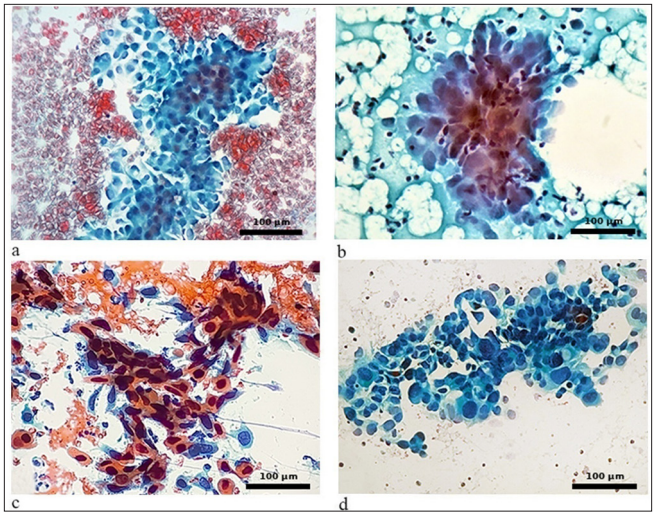

Figure 2: Head-and-neck lymph node metastatic lesions; cytological images (all verified by histology): (a) Thyroid papillary carcinoma, (b) nasopharyngeal carcinoma, (c) squamous cell carcinoma (tongue), and (d) adenocarcinoma (lung). All the samples were stained with Papanicolaou stain and are shown at ×400.Scale bar = 100 µm.

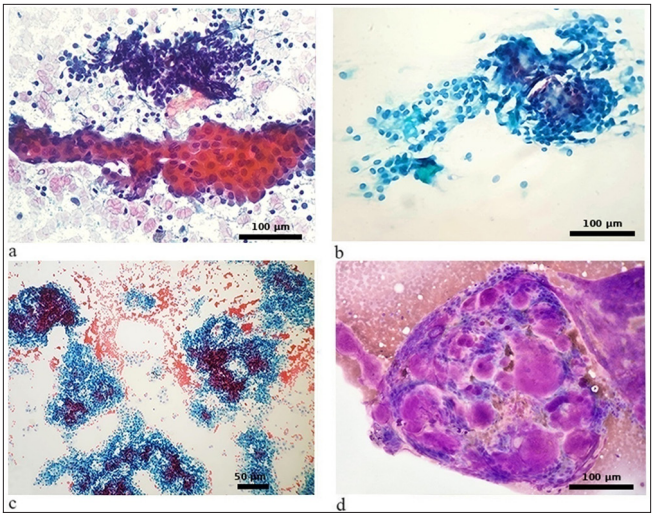

Figure 4: Salivary gland lesions; cytological images (all were verified with histology): (a) Warthin's tumor, (b) pleomorphic adenoma, (c) malignant: high-grade mucoepidermoid carcinoma, and (d) malignant: adenoid cystic carcinoma. (a-c) were stained with Papanicolaou; (d) was stained with Diff-Quik® Stain, ×400. (a, b, d) Scale bar = 100 µm. (c) Scale bar = 50 µm.

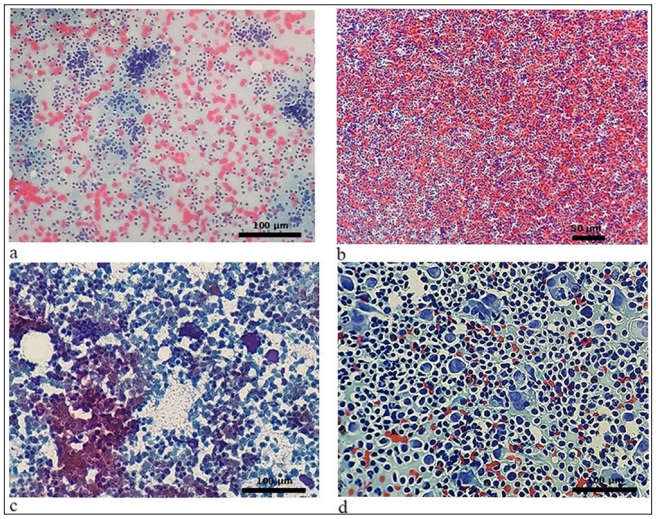

Figure 3: Head-and-neck lymphoid disorders in the lymph nodes; cytological images (all verified by histology): (a) Reactive hyperplasia, (b) small cell lymphoma (follicular), (c) diffuse large B-cell lymphoma, and (d) classic Hodgkin's lymphoma (mixed type). All the samples were stained with Papanicolaou and are shown at ×400. (a, c, d) Scale bar = 100 µm. (b) Scale bar = 50µm.

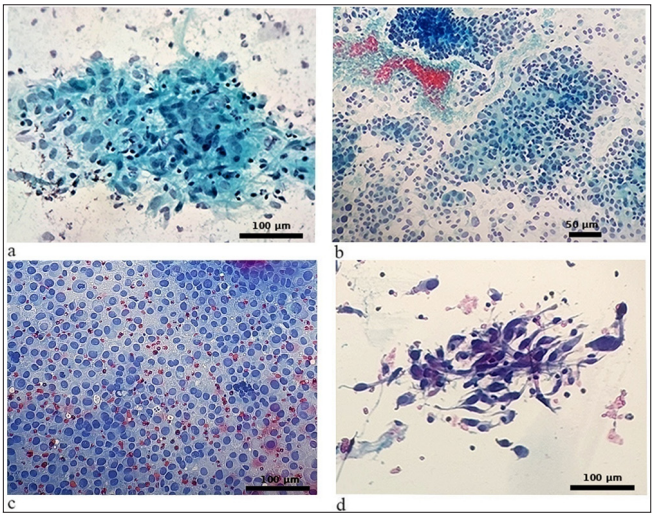

Figure 5: Head-and-neck soft-tissue lesions; cytology images (all were histologically verified): (a) Granuloma (sarcoidosis), (b) neuroendocrine tumor (medullary thyroid carcinoma, high serum calcitonin level), (c) plasma cell tumor (extramedullary plasmacytoma), and (d) spindle cell malignant midline tumor, neck (high-grade soft-tissue sarcoma). All the samples were stained with Papanicolaou and are shown at ×400. (a, c, d) Scale bar = 100 µm. (b) Scale bar = 50 µm.

Some authors have argued that collaboration between an experienced cytopathologist and a radiologist in performing FNA can result in high diagnostic accuracy for infections, granulomatous lymphadenitis, metastatic malignancies, high-grade lymphomas, and some subtypes of Hodgkin lymphomas.

However, the role of FNA in the initial diagnosis and subclassification of primary lymphoid malignancies is still debated, and LN FNA cytology is not widely accepted for obtaining a conclusive diagnosis of lymphoma.[41]

The use of LN FNA is associated with several limitations. Historically, the most challenging aspect of LN FNA cytology has been the differentiation of reactive lymphoid proliferations from malignant proliferations, particularly for low-grade

lymphomas. FNA can be used to easily diagnose high-grade lymphomas and offers benefits by providing the doctor with a possible preliminary diagnosis of lymphadenopathy.[38,40,42] Tissue biopsy for immunohistochemical profiling and further research techniques (flow cytometry and molecular analysis) for the formulation of treatment protocols are typically performed after the cytological diagnosis of lymphoma through FNA.[39,42]

Consistent with other studies, we believe that FNA is a useful and affordable method for the initial cellular assessment of LN lesions if a skilled cytopathologist and radiologist collaborate in a hospital setting. Although the primary diagnosis of lymphoma through needle aspiration cytology is typically not definite, it can provide insight into the nature of the disease and can recommend a course of further diagnostic testing.[36-40,42]

Cytologists who are particularly interested in this topic have recommended FNA as a helpful technique. However, for head-and-neck masses, ENT specialists are typically the first to see patients and refer them for FNA. FNA should, therefore, be considered as a first-line assessment by ENT specialists. In terms of the prevalence of the method, it is important to consider publications that pose the question "How much do we know about FNA?" and whose findings indicate that, when performed appropriately, positive outcomes from the procedure can be achieved, particularly for patients who seek treatment from hospital ENT departments.[43,44]

FNA is acknowledged as an easily applicable, rapid, and reliable method for the preliminary assessment of salivary gland lesions. Due to these factors, FNA is a popular choice for the initial diagnosis of salivary gland masses.[43] Despite the heterogeneity in the literature, FNA cytology (FNA) has a high specificity that ranges between 86% and 100% and a sensitivity that ranges between 64% and 90% in the diagnosis of salivary gland lesions.[44]

Some publications claim that core-needle biopsy (CNB) should be used in place of FNA to assess salivary gland lesions. However, CNB carries a greater risk of complications than does FNA, including the possibility of hemorrhage, pain, facial nerve damage, or tumor seeding. Neither FNA nor excisional biopsy can be substituted with CNB. Thus, USG-guided FNAC is the preferred method for the assessment of salivary gland lesions. When surgery is not appropriate, and FNA does not produce results despite a few repetitions, CNB may be attempted.[35] FNA is the first option when salivary gland lesions are diagnosed in our medical setting, but CNB is discouraged.

Uniformity and standardization have been recently introduced to the cytology reporting system due to the extensive use of the Milan classification when salivary gland lesions are diagnosed through FNA, which has resulted in an increase in the specificity and sensitivity of the procedure for benign and malignant lesions. This subsequently led cytopathologists and clinicians to gain a better understanding of the terminology used in salivary gland lesion diagnoses.[45] However, since our first case was in 1999, the Milan classification was excluded from the scope of this study. Classical general terminology was applied as previously described in section 3.1 (clinical data). Our data regarding the FNA of the salivary glands were different from the findings of previous studies published in the literature. The accuracy, sensitivity, and specificity, as well as the PPV and NPV in our study, all reached 100%.

The diagnostic accuracy may differ on the basis of factors associated with the knowledge and experience of the cytopathologist and/or aspirator, who obtains the representative yield from the lesion, prepares the material for cytological assessment, processes it according to cytological evaluation, sends it to the laboratory, and examines it.

We identified histopathological malignancy in 11 of 17 patients with a diagnosis of "suspected malignancy" for their soft tissue and subcutaneous neck nodules; the remaining six patients did not undergo biopsy. Thirty-seven of the 41 patients with a suspected malignant lesion were correctly classified (90.2%), whereas no biopsies were performed for the other four patients. Therefore, 48 patients had a histopathological diagnosis of malignancy for soft-tissue/subcutaneous nodules. Most of the 29 patients whose soft tissue and subcutaneous nodules were assessed as "non-tumoral" after FNA were cytologically diagnosed with abscesses (18/29).

Six of the 17 patients whose lesions were classified as cytologically "suspicious" did not undergo a biopsy. Schwannoma was the most frequent histological diagnosis for patients who underwent biopsy (7/11).

Most of the 41 benign tumors were cytologically diagnosed as lipomas (16/41), of which 14 had an identical histopathological diagnosis [Table 2].

Most of the cystic lesions were branchial cysts (45/60). Others were reported as thyroglossal cysts, and after complete resection, their histopathological diagnoses were consistent with the cytological diagnoses.

FNA provides valuable information for the preliminary diagnosis of subcutaneous soft-tissue masses as well as for the identification of the nature of cystic lesions in the neck area. In cases where it is sometimes difficult to determine the precise diagnosis for head-and-neck soft-tissue lesions, FNA can also serve as a helpful tool for differentiating between benign, borderline, and malignant lesions.[46]

FNA model implemented with the cooperation of cytopathologists and radiologists

"Making decisions about the whole lesion on the basis of a few drops of liquid material retrieved with the help of a needle

and syringe" is the fundamental tenet of FNA; however, 50 years passed before the medical community accepted this tenet. Although this currently accepted procedure appears straightforward, as with other medical interventional procedures, training, and experience are needed to perform FNA properly.

Like the tango, FNA is a "two-person" process and requires the assistance of two professionals: the examiner and the individual obtaining the sample.

Cytopathologists are well aware of the three crucial steps in the FNA procedure: (i) successful aspiration that yields a sufficient and representative amount of cellular material; (ii) proper handling of the aspirate in accordance with the cytological examination requirements, such as the generation of high-quality smears devoid of artifacts, fixation of the slides in accordance with staining protocols, and preservation of the material for future analysis (such as through cell blocks); and (iii) optimal cytological evaluation of the aspirated material.

Unfortunately, cytopathologists have little influence on the first two crucial stages of the FNA procedure, which constitute the cornerstone of a reliable cytological diagnosis. If the first two stages are not performed correctly, the FNA will most likely yield a result of "non-diagnostic" or "contains insufficient material," which will be disappointing to the patient and will betray the confidence of doctors who request FNA. As previously indicated, the number of publications in which the cytopathologist performs US on their own has increased, which has resulted in a decrease in the number of non-diagnostic results and a corresponding increase in diagnostic accuracy.

Provided that the relevant requirements are satisfied, it can be easy to establish this model in a private practice setting, but it would be more challenging in a hospital setting. The attitude of hospital management toward the establishment of an "outpatient FNA clinic" constitutes the most crucial element. The amount and distribution of additional income received by the physician and the radiologist who perform USG-FNA may generate issues for systems that gain additional revenue from performing the procedure in hospitals.

For these reasons, we believe that the model in which the cytopathologist and the radiologist collaborate to perform FNA produces beneficial outcomes. The conclusions drawn in our study appear to be consistent with this view.

Clinicians generally consider FNA as the first-line diagnostic technique for assessing various head-and-neck lesions. This is an inexpensive method that can be executed quickly and is well accepted by patients, with a low rate of morbidity and good diagnostic accuracy. Nonetheless, research has demonstrated that FNA yields effective and precise diagnostic outcomes when the individual evaluating the test is also the one who retrieves the aspirate material. Our study describes the findings from our 25 years of experience. Research has demonstrated that the use of FNA, when performed by a cytopathologist with the assistance of radiologist-guided US, produces accurate results (diagnostic accuracy and high specificity, sensitivity, PPV, and NPV) and yields sufficient material for the assessment of extrathyroidal head-and-neck lesions. Compared with the other series included in our investigation, our findings are more accurate.

Aside from the hospital administration, we believe that the cytopathologist's knowledge of and experience with the FNA procedure, as well as his or her willingness and dedication, are the most crucial elements in the establishment of the FNA model outlined in our study.

Future research recommendations

Future studies should consider multicenter validation of this collaborative FNA model and its application in the diagnosis of malignancies at other anatomical sites. However, several challenges should be addressed to ensure successful implementation across multiple institutions. These include:

- Standardization of procedures: Variability in FNA techniques, equipment, and operator expertise across centers may impact diagnostic accuracy. Establishing a unified protocol for performing and interpreting FNA is essential to minimize inconsistencies.
- Training and expertise variability: The skill levels of the cytopathologists and radiologists who perform the procedure can differ significantly. The implementation of structured training programs and proficiency assessments can help maintain consistency and reliability.
- Intercenter collaboration and data sharing: Ethical approval, data-sharing agreements, and coordination among multiple institutions may pose logistical challenges. The development of a centralized database and standardized reporting criteria could facilitate collaboration and data harmonization.
- Technical limitations: Access to high-quality US devices and ROSE may vary across centers, potentially affecting diagnostic outcomes. Efforts should be made to improve the availability of these resources at all participating institutions.

In addition, hospital management should recognize the importance of supporting and facilitating the cooperation necessary for the successful implementation of this model. Three key components for its effective integration include:

i) FNA performed in an outpatient clinic setting, which allows for efficient workflow and patient management;
ii) A cytopathologist experienced in USG-FNA who can ensure optimal sample collection and interpretation;
iii) A radiologist committed to collaboration who can

actively engage in the procedure alongside the cytopathologist to increase diagnostic accuracy.

However, the establishment of outpatient FNA clinics at public institutions may not be met with universal acceptance by hospital administrations. In healthcare systems where additional income is derived from in-hospital procedures, financial concerns regarding revenue distribution among physicians who perform US-guided FNA could pose barriers. If hospital management is willing to adopt this model, institutional support for cytopathologist-assisted FNA in an outpatient setting could greatly increase accessibility and efficiency.

Addressing these challenges will be crucial for the broader implementation of this collaborative model and will ultimately improve the accuracy and accessibility of FNA procedures across various healthcare settings.[23,25,28,29,31]

Limitations

- Single-center study: This research was conducted at only one center, which may limit the generalizability of the results to different populations.
- Long data collection process: Study data were collected between 1999 and 2023. Advances in diagnostic methods and technologies during this time may have affected the homogeneity of the results.
- Lack of molecular analysis: Molecular analyses were not included in this study. This has limited the ability to obtain more in-depth information about the molecular characteristics of the lesions.
- Limited number of patients: A limited number of patients, especially those with rare lesions, may affect the power of the statistical analyses.
- Retrospective design: This study has a retrospective design, which may increase the risk that some clinical or demographic information may be missing or insufficient.

SUMMARY

In recent years, several publications have described the use of USG-FNA by cytopathologists to achieve better diagnostic accuracy. Some cytopathologists elect to enroll in courses to learn and apply US guidance themselves. However, FNA can be a helpful tool when cytopathologists collaborate with radiologists. Although the present study reflects the experience of a single center, it illustrates that the application of FNA in this way produces accurate results and sufficient material for analysis, especially for LNs in extrathyroidal head-and-neck lesions. This study also reveals that the FNA technique is a low-cost and effective procedure.

AVAILABILITY OF DATA AND MATERIALS

The data that support the findings of this study are available from the corresponding author on reasonable request. The data are not publicly available due to privacy or ethical restrictions.

ABBREVIATIONS

DQ: Diff-Quik stain
FNA: Fine-needle aspiration cytology
PAP: Papanicolaou stain
ROSE: Rapid onsite cytological assessment (ROSE) technique
US: Ultrasound
USG-FNA: Ultrasound-guided fine-needle aspiration cytology

AUTHOR CONTRIBUTIONS

BYB: Data curation, formal analysis, histology work for surgically resected specimens whenever applicable, tabulation, literature searching, and writing–original draft; NP: Conceptualization, methodology development, all FNAs and cytology work, literature searching, supervision, writing–review, and editing. Both authors read and approved the final manuscript. Both authors have participated sufficiently in the work and agree to be held accountable for all aspects of the work. All authors meet ICMJE authorship requirements.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was reviewed and approved by the Institutional Ethics Committee for the School of Medicine at the University of Kocaeli (project number: 2025/95; approval ID: GOKAEK-2025/05/18, date: March 11, 2025). Informed consent was obtained from all of the patients before the fine-needle aspiration cytology procedure and surgical resection, whenever applicable. The study was conducted in accordance with the Declaration of Helsinki.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

EDITORIAL/PEER REVIEW

To ensure the integrity and highest quality of CytoJournal publications, the review process of this manuscript was conducted under a **double-blind model** (authors are blinded for reviewers and vice versa) through an automatic online system.

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