

Diagnostic Accuracy of Fine Needle Aspiration Cytology of Lymphadenopathies: Sensitive Tool

Poornima Raghunathan¹, Anisha Hari², Sridhar Honnappa³

¹Post graduate, Department of Pathology, M.S. Ramaiah Medical College, Bengaluru

²Post graduate, Department of Pathology, M.S. Ramaiah Medical College, Bengaluru

³Associate Professor, Department of Pathology, M.S. Ramaiah Medical College, Bengaluru

Received: 25-10-2023 / Revised: 23-11-2023 / Accepted: 26-12-2023

Corresponding Author: Dr. Poornima Raghunathan

Conflict of interest: Nil

Abstract:

Introduction: Fine needle aspiration cytology (FNAC) is a simple, cost effective and sensitive diagnostic modality for initial assessment of lymphadenopathies with varying aetiology. The advantages of FNAC are, it is safe, rapid and inexpensive with minimal trauma done at an outpatient setup or at bedside.

Aim: To assess the accuracy of FNAC of lymphadenopathies with emphasis on the discordant cases between cytological and histopathological diagnoses.

Materials and methods: A two-year retrospective study was done from January 2017 to December 2018; a total of 300 cases underwent FNAC of lymphadenopathies. 140 cases were included in the study with both cytology and histopathology correlation along with relevant clinical history and investigations were gathered.

Results: Out of 140 cases, the cytological diagnoses were found to be benign in 56 cases (40%) and malignant in 84 cases (60%). The cervical lymph node was the commonest site (59.5%). The most common metastatic malignancy was squamous cell carcinoma (59.5%) from the oral cavity tumours (54%). The most common benign lesion was chronic granulomatous lymphadenitis (47.6%). The sensitivity, specificity, positive predictive and negative predictive value of FNAC was 94.6%, 98.1%, 98.8% and 91.2%. Histopathological correlation showed diagnostic discordance in 10 cases (7.14%).

Conclusion: FNAC is a safe, simple and inexpensive effective diagnostic tool for evaluation of lymphadenopathies and can be used as a modality for first line of investigation. However, histopathological evaluation of the lymph node is required to confirm primary lymphoid malignant cases. It is the gold standard and cannot be replaced.

Keywords: FNAC, lymphadenopathies, metastatic malignancies, cytology.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Lymph nodes were the first organs to be biopsied by fine needle aspiration in 1930 by Martin and Ellis. In 1967, Zajicek and Franzen at Karolinska Hospital, Sweden defined precise diagnostic criteria for diagnosis of lymph node lesion. [1] Lymphadenopathy is one of the commonest clinical presentations of patients, attending the outdoor clinics in most hospitals. The aetiology varies from an inflammatory process to a malignant condition. [2]

Fine needle aspiration cytology (FNAC) of lymph node has become an integral part of the initial diagnosis and management of patients with lymphadenopathy due to early availability of results, simplicity, and, minimal trauma with less complication. [3] De May has summarized the advantages of FNAC with the acronym SAFE means Simple, Accurate, Fast and Economical. [4]

Malignancies in lymph nodes in our country are predominantly metastatic in nature with an incidence varying from 65.7% to 80.4% and lymphomas range from 2% to 15.3% among lymph nodes aspirated from all sites. The diagnosis of metastatic tumour to the lymph node on cytological smear is crucial and highly reliable. This would be the sole indication for searching the primary tumour, especially in cases of unknown primary malignancy. [5,6]

Aim: The aim of this study was to assess the diagnostic accuracy and reliability of FNAC of lymph nodes, in comparison to the results of histopathology in an attempt to highlight with an emphasis on discordant cases between the cytology and the histopathology.

Materials and Methods

A two-year retrospective study was conducted from January 2017 to December 2018 with a total of 300 cases which underwent FNAC of lymphadenopathies. FNAC was performed with the help of a 22-gauge disposable needle attached to 10 ml syringe. Smears were fixed in 95% ethyl alcohol and stained with Hematoxylin and Eosin as well as Papanicolaou stains. The histopathological assessment was advocated in the included cytologically benign cases either due to clinical persistent, multiple, or enlarging lymphadenopathy or due to suspicious radiological features. The histopathological examination was performed in the included malignant metastatic cases as the metastatic work up of such cases failed to identify the primary tumors or was received along with the radical resections specimens of the primary tumors. The cytopathological diagnoses then were compared with the histopathological results of the same excised nodes. In cases of discrepancy, histopathologic results were considered the gold standard. For all discordant cases, special attention was focused on the cytomorphological features.

Inclusion Criteria: 140 cases were included in the study with both cytology and histopathology correlation along with relevant patient demographic details, clinical history and radiological and laboratory investigations were gathered.

Exclusion Criteria:

1. FNAC cases with no concurrent histopathological specimen received for correlation were excluded.
2. Acellular aspirates were excluded from the study

Statistical Analysis: Diagnostic sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy, and discordance rate were calculated. All these values were compared with other studies.

Results

In this study, the male to female ratio was found to be in a ratio of 1.1:1 with age of presentation ranged from 8- 90 years in males and 6-76 years in females. Most common group of lymph nodes involved were cervical group of lymph nodes -133 cases (88.5%), supraclavicular lymph nodes – eight cases (5.7%), axillary group of lymph nodes- seven cases (5.0 %), and inguinal group of lymph nodes - two cases (0.8%).[Table 1]

The cytological diagnoses were found to be benign in 56 cases (40%) and malignant in 84 cases (60%) [Table 2]. Reactive lymphadenitis in 35 cases (62.5%), granulomatous lymphadenitis in 16 cases (28.5%) and acute necrotizing lymphadenitis in five cases (8.9%) were the benign cases reported.

Table 1: Common sites of lymph node involvement

Lymph nodes	No. of cases
1. Cervical group	133
2. Supraclavicular lymph nodes	8
3. Axillary group	7
4. Inguinal group	2
Total	140 cases

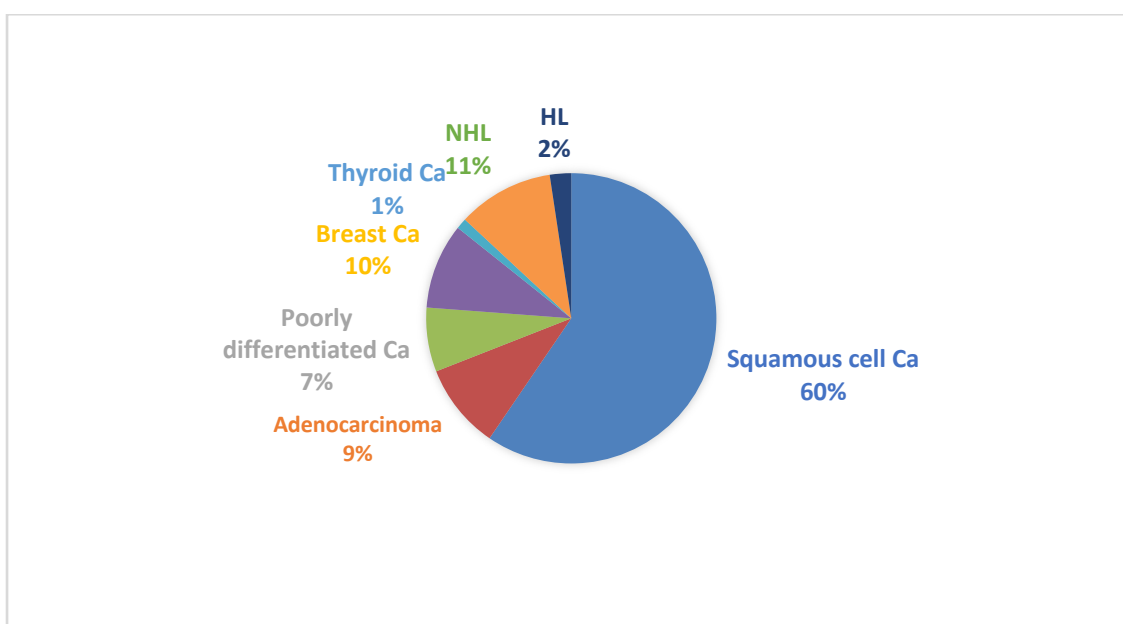


Figure 1: Distribution of malignant cytopathological diagnoses

Among the malignant cases, 73 FNA smears (86.9%) were diagnosed as metastatic tumours.

Among the primary lymphoid malignancies, 11 cases were diagnosed, out of which 09 cases (10.7%) were NHL and 02 cases (2.3%) were HL [Table 2]. Squamous cell carcinoma was the most common metastatic malignant tumour to the lymph nodes, seen in 50 cases (59.5%), followed by

metastatic adenocarcinoma in eight cases (9.5%) metastatic breast carcinoma in eight cases (9.5%), poorly differentiated carcinoma in six cases (7.1%) and metastatic papillary thyroid carcinoma in one case (1.1%) [Table 3].

The common site of the primary tumours of these metastatic lymphadenopathies is listed in the Table 3.

Table 2: Distribution of cytopathological diagnoses among the different group of lymph nodes

Cytopathological diagnoses	No. of cases	Total cases
1. Granulomatous lymphadenitis	35	56 Benign cases
2. Reactive lymphadenitis	16	
3. Acute suppurative lesion	05	
4. Secondary metastasis to LN	73	84 Malignant cases
1. Hodgkins's lymphoma	02	
6. Non-Hodgkin's lymphoma	09	

The cytopathological diagnoses then were correlated with the histopathological diagnoses of the same excised nodes. Among the 56 cytologically benign cases, 51 cases (91.1%) were proved histopathologically to be benign, true negative and 5 cases (8.9%) were diagnosed histopathologically as malignant, false negative. 84 cases (100%) cytologically diagnosed malignant cases, 83 cases proved to be histopathologically to

be malignant, true positive and one case misdiagnosed as malignant was histopathologically benign, false positive.

Accordingly, the overall diagnostic sensitivity, specificity, positive predictive value, and negative predictive value of FNAC of cervical lymph nodes for this study were 94.6 %, 98.1 %, 98.8 % and 91.1 %.

Table 3: Distribution of cytopathological diagnoses in metastatic malignant lymphadenopathies and sites of primary tumor

Metastatic lymphadenopathies	Site	No. of cases	Total
Squamous cell carcinoma	Buccal cavity	26	50
	Tongue	3	
	Larynx	10	
	Tonsils	1	
	Oesophagus	10	
Adenocarcinoma	Gastric	5	8
	Duodenum	3	
Breast carcinoma	-	-	8
Poorly differentiated carcinoma	-	-	6
Thyroid carcinoma	-	-	1

Correlation	No. of cases
Diagnostic concordance	130 cases (92.8%)
Diagnostic discordance	10 cases (7.2%)

Statistics	Percentages
Sensitivity	94.6 %
Specificity	98.1 %
Positive predictive value	98.8 %
Negative predictive value	91.1 %

Table 4: Correlation of the cytopathological and histopathological diagnoses of lymphadenopathies - concordant and discordant cases

Sl. No.	Cytopathological diagnoses	No. of cases	Histopathological diagnoses				
			Reactive LN	Granulomatous LN	Metastasis	HL	NHL
1.	Granulomatous lymphadenitis	35	-	35	-	-	-
2.	Reactive lymphadenitis	16	12	01	01	-	02

3.	Acute suppurative lesion	05	-	03	01	-	01
4.	Secondary metastasis	SCC	50	-	-	50	-
		Adenocarcinoma	08	-	-	08	-
		Others	15	-	-	15	-
5.	HL	02	-	-	-	02	
6.	NHL	09	01	-	-	-	08

Histopathological correlation showed diagnostic concordance in 130 cases (92.8%) and discordance in 10 cases (7.2%).

Discussion

The lesion arising in lymph nodes can be found in patients ranging from an early to advanced age. This was correlated with our findings where the youngest patient in the present study was six years old and the oldest one was 90 years old. Hafez et al [5] found that benign lesions were more common in the third decade, whereas malignant lesions were more common in the fifth decade that was almost comparable to our study. Similar findings were seen in the study by Saha et al. [8] Hence, if older patients present with cervical lymphadenopathy, we must suspect and rule out malignancy by doing a thorough clinical and pathological examination. India is the country with the highest burden of TB that mainly involves the lungs followed by cervical lymph nodes. The portal of entry of TB bacilli into cervical lymph nodes is usually tonsils or adenoids. This could be the reason for the high number of granulomatous lymphadenitis in the present study. Infections of upper respiratory tract or oral cavity can lead to cervical lymphadenitis that may be responsible for the more cases of nonspecific reactive lymphadenitis. [11] This study showed 56 benign cases (40%) and in 84 malignant cases (60%) in the cytological diagnoses. Reactive lymphadenitis in 35 cases (62.5%), granulomatous lymphadenitis in 16 cases (28.5%) and acute necrotizing lymphadenitis in five cases (8.9%) were the benign cases reported. This study showed

a high percentage of malignant cases compared to the benign cases, the reason attributed due to selection of cases that had undergone lymph node excision after FNAC either due to clinical, or radiological, or cytological suspicion of a malignancy. Similar findings were documented in the study by Hafez et al. [5] In the present study, all the cases with metastatic carcinoma to the nodes showed exact corroboration with histopathological examination. The diagnostic accuracy of these cases was 100%. The most common metastatic tumor was squamous cell carcinoma and the primary site was from the oral cavity with higher incidence noted in males compared to females, followed by metastatic adenocarcinoma as the second most common tumor. In our study, the overall diagnostic accuracy of FNA of lymphadenopathies has a high concordance between cytopathological and histopathological diagnoses. And findings in this study are on par and with close comparison in results published by various Indian and International studies. [Table 5] Histopathological correlation showed diagnostic concordance in 130 cases (92.8%) and discordance in 10 cases (seven .two %). One case was diagnosed as lymphoma on FNAC, but histopathology correlation revealed reactive lymphadenitis. A study by Mendon et al and Arul et al, found that if the aspirate from reactive lymph node is derived from the large germinal center, the proportion of the large cells such as centroblasts and dendritic cells as well as the number of mitosis might be impressive enough to suggest lymphoma. [11,16].

Table 5: Comparison of results of present study with previous studies

Study	No. of patients	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)
Pramod et al [9]	399	93.8	94.6	93.8	99.8	71.6
Gunjan et al [10]	156	90.9	67.2	82.2	82.6	82.2
Arul et al [11]	188	82.4	98.1	95.2	90.3	96.2
Hafez et al [5]	157	90.9	67.2	82.2	82.6	81.3
Abdul et al [12]	44	78.6	66.7	79.3	-	-
Barui et al [13]	87	88.8	100	-	100	98.36
Adhikari et al [14]	55	100	100	90.9	100	100
Present study	140	94.6	98.1	92.8	98.8	91.1

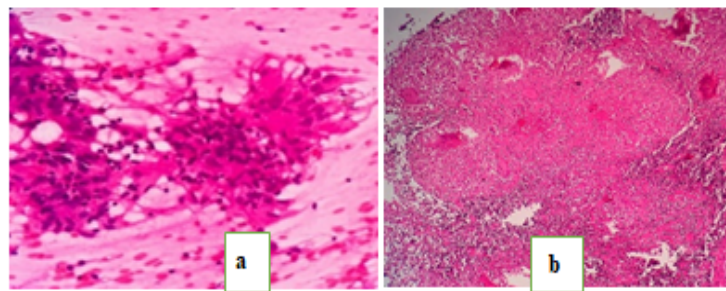


Figure 1: (a) Cytosmear showed granulomatous lymphadenitis suggestive of TB (H&E, ×400). (b) H&E section showed granulomatous lymphadenitis

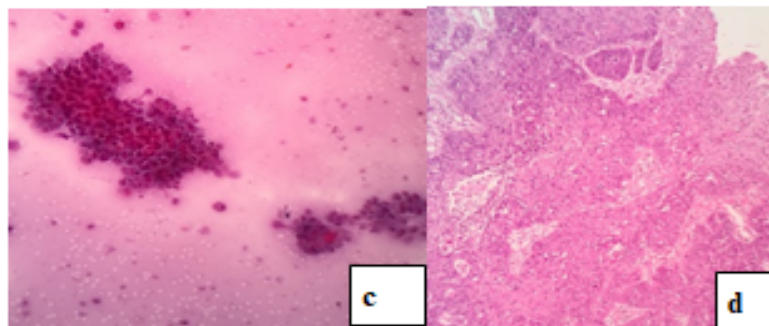


Figure 2: (c) Cytosmear showed lymph node - positive for malignancy, metastatic squamous cell carcinoma of TB (H&E, ×100) (d) H&E section showed metastatic squamous cell carcinoma to lymph node (H&E, x100)

In the present study, this could be the reason for the false positivity. In this study, Five. Six % of false negative rate was observed. Two cases of NHL were underdiagnosed as benign on FNAC, turned out to be NHL- low grade follicular lymphoma on histopathological examination.

Alwan et al, observed that the low-grade NHL including grade 1 and grade 2 follicular lymphoma with minimal cytological atypia remain very difficult to be evaluated cytologically and they are usually misdiagnosed as reactive lymphoid hyperplasia. [17]

Brandao et al, reported that the follicular lymphoma might present a particular difficulty in FNAC specimens to distinguish follicular lymphoma from reactive hyperplasia was largely due to the fact that the interfollicular areas in

follicular lymphoma might contain large number of small lymphocytes as well as histiocytes that aspirated with the neoplastic cells. [18]

Two cases were misdiagnosed as acute necrotizing lymphadenitis one turned out to be metastatic squamous cell carcinoma with tumour necrosis and the other high grade diffuse large cell lymphoma with extensive necrosis on histopathology. It can attribute to the reason being extensive tumour necrosis.

Another case was misdiagnosed as reactive lymphadenitis on FNAC, on histopathology was reported as small metastatic deposit of papillary thyroid carcinoma, this can be due to the representative sampling of the lymph node during FNAs that a microdeposit of tumor in the nodes can be missed. [19]

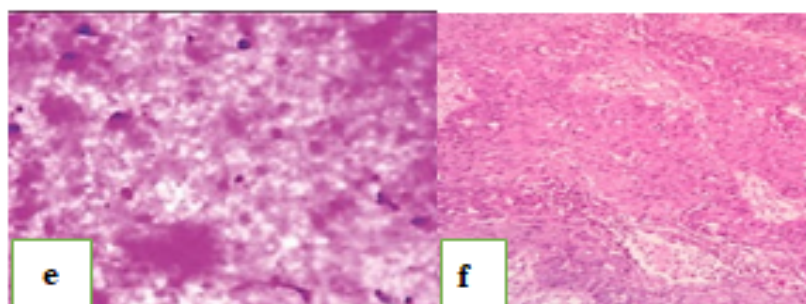


Figure 3: False negative case-(e) Cytosmear showed acute necrotizing lymphadenitis (H&E, ×400). (f) H&E section showed metastatic squamous cell carcinoma- with extensive necrosis (H&E, ×100)

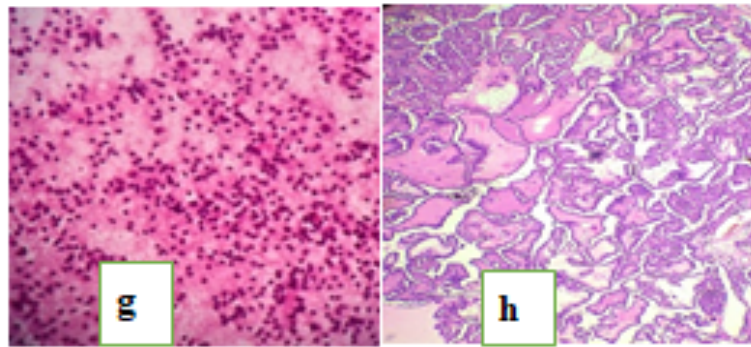


Figure 4: False negative case-(g) Cytosmear showed reactive lymphadenitis (H&E, ×100) (h) H& E section revealed small metastatic deposit of papillary thyroid carcinoma in the lymph node (H&E, x100)

The overall diagnostic sensitivity, specificity, positive predictive value, negative predictive value and the diagnostic accuracy of FNAC of cervical lymph nodes for this study were 94.6%, 98.1%, 98.8%, 91.1% and 92.8%.

Conclusion

FNAC is a safe, simple and inexpensive, effective and minimally invasive diagnostic tool for evaluation of lymphadenopathies with good concordance between cytological and histopathological diagnoses.

It can be used as a modality for first line of investigation of lymphadenopathies, for diagnostic workup for metastatic malignancies and also in aspirates where biopsies are not done routinely.

However, histopathological evaluation of the lymph node is required to confirm primary lymphoid malignancies. It is the gold standard and cannot be replaced.

References

- Martin HE, Ellis E. Biopsy needle puncture and aspiration *Ann Surg.* 1930;92:169-81.
- Zajichek J; Aspiration Biopsy; part-I cytology of lymph node *act.* 1974;4.
- Alam K, Khan A, Siddiqui F, Jain A, Haider N, Maheshwari V. Fine needle aspiration cytology (FNAC): A handy tool for metastatic lymphadenopathy. *Int J Pathol.* 2010; 10:2.
- Wu M, Burstein DE. Fine needle aspiration. *Cancer Invest.* 2004; 22:620-8.
- Hafeez HN, Tahoun N. Reliability of fine needle aspiration cytology (FNAC) as a diagnostic tool in cases of cervical lymphadenopathy. *Journal of the Egyptian National Cancer Institute.* 2011; 23:105-114.
- Wilkinson AR, Mahore SD, Maimoon SA. FNAC in the diagnosis of lymph node malignancies: A simple and sensitive tool. *Indian J Med Paediatr Oncol.* 2012; 33(1):21-24.
- Howlett DC, Harper B, Quante M, Berresford A, Morley M, Grant J. Diagnostic adequacy and accuracy of fine needle aspiration cytology in neck lump assessment: results from a regional cancer network over a one year period. *J Laryngol Otol.* 2007; 121(6):571-9.
- Saha MD, Dasgupta S, Sen S. Spectrum of Cytopathological Findings in Cases of Lymphadenopathy-A 3 Years Study. *J Dental and Med Sciences.* 2016; 3:59-63.
- Pathy PC, Subhransu KH, Dash S, Sagarika S, Sasmita P, Rout N. Analysis of FNAC in diagnosis of lymphadenopathy-a retrospective study from a regional cancer centre, Cuttack, Odisha. *Int J Res Med Sci.* 2017; 5:5287-5292.
- Upadhyay GP, Rameshchandra MT. Evaluation of fine needle aspiration cytology as the initial diagnostic test in cases of cervical lymphadenopathy. *Int J Res Med Sci.* 2016;4: 5103-5107.
- Arul P, Masilamani S, Akshatha C. Diagnostic efficacy of fine-needle aspiration cytology in the evaluation of cervical lymphadenopathy. *J Sci Soc.* 2016; 43:117-21.
- Abdulnabi HM. The predictive value of fine needle aspiration cytology in the assessment of cervical lymphadenopathy. *Iraqi Postgrad Med J.* 2007; 6:190-3.
- Barui S, Prosenjit G, Parikshit S, Niloy P. Study of diagnostic accuracy of fine needle aspiration cytology of lymph nodes over 6 years in a tertiary care hospital. *Int J Res Med Sci.* 2017; 5:4013-4016.
- Adhikari P, Sinha B, Baskota D. Comparison of fine needle aspiration cytology and histopathology in diagnosing cervical lymphadenopathies. *Australas Med. J.* 2011; 4:97-9.
- Kollur SM, El Hag IB. Fine needle aspiration cytology of metastatic nasopharyngeal carcinoma in cervical lymph nodes: comparison with metastatic squamous cell carcinoma and Hodgkin' and Non Hodgkin' lymphoma. *Diagn Cytopathol.* 2003; 28:18-22.
- Mendon ME. Fine needle aspiration cytology of lymph nodes. *Prog Diagn Cytol.* 1999; 32:410-1.
- AlAlwan NA, AlHashimi AS, Salman MM, AlAttar EA. Fine needle aspiration cytology

- versus histopathology in diagnosing lymph node lesions. *East Mediterr Health J.* 1996; 2:320–5.
18. Brandao GD, Rose R, McKenzie F. Grading of follicular lymphoma in fine needle aspiration biopsies: The role of thin preparation of slide and FCM. *Cancer.* 2006; 108:319–23.
 19. John M, “Lymph nodes” Chapter 5 in Orell, S. R., Sterrett, G. F., & Orell, S. R. Orell and Sterrett's fine needle aspiration cytology 2012 Edinburgh: Churchill Livingstone.
 20. Ustun M, Risberg B, Davidson B, Berner A. Cystic change in metastatic lymph nodes: a common diagnostic pitfall in fine-needle aspiration cytology. *Diagn Cytopathol.* 2002; 27: 387–392.