Original Article

The efficacy of lymph node fine needle aspiration cytology

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Abstract

Introduction: Fine needle aspiration cytology (FNAC) of lymph nodes is a safe, easy, cheap and quick diagnostic tool, which involves the examination of a random sample of cells from a lymph node.

Aim: To assess the distribution of diagnostic categories and the efficacy of lymph node fine needle aspiration cytology at our institution. These were compared to the literature.

Methodology: All of lymph node FNAC cases taken between the 1st January 2012 and the 31st December 2013 were retrieved from our Laboratory Information System. A total of 300 cases were retrieved and then placed into one of six categories; Category 1: Non-diagnostic, 2: Reactive, 3: Probably reactive but lymphoma cannot be excluded, 4: Non-Hodgkin lymphoma, 5: Hodgkin lymphoma, and 6: Metastasis. These were then correlated with the histology of the lymph node excision specimens.

Results: The proportion of diagnoses placed under categories 1, 2, 3, 4, 5 and 6 represent 14%, 53%, 4.3%, 5.7%, 1.7% and 21.3% of the total respectively. The overall efficacy of FNAC showed a sensitivity of 84.5%, specificity of 99.3%, a false negative rate of 10%, a false positive rate of 0.7%, accuracy of 93.1%, positive predictive value of 98.8% and negative predictive value of 89.9%.

Conclusions: FNAC of lymph nodes is a very useful and effective tool in triaging patients with lymphadenopathy.

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Introduction

Fine needle aspiration cytology (FNAC) is a safe, easy, quick, cheap technique for diagnosing benign as well as malignant enlarged lymph nodes.[1-2] This technique involves taking a random sample of cells from a potentially pathological lymph node using a needle.[3] The indications for lymph node FNAC are: for the diagnosis of reactive lymphadenopathy, metastatic and lymphoid malignancy, staging and monitoring for relapse or the effects of treatment.[1] Lymph node FNAC is excellent in the diagnosis of metastatic malignancy, reducing the need for diagnostic excision biopsy in many patients.[4-5] The diagnosis of lymphoid neoplasms on FNAC remains controversial and is often followed by tissue biopsy.

In this study, we present our lymph node FNAC experience encompassing all diagnostic categories.

Materials and methods

All lymph node FNAC cases taken between the 1st January 2012 and the 31st December 2013 were retrieved from our Laboratory Information System via the Cognos search engine by inputting the specimen type using SNOMED codes. The reports were then reviewed and categorised as follows:

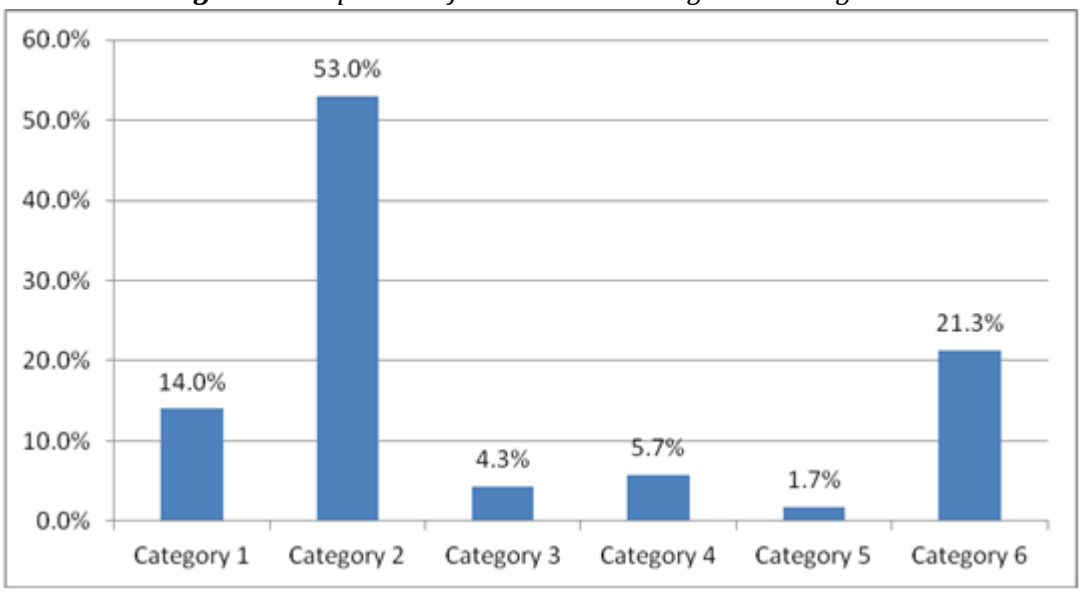
Category **1**: Non-diagnostic
Category **2**: Benign reactive lymphoid hyperplasia
Category **3**: Although favouring a reactive process, lymphoma cannot be excluded
Category **4**: Suspicious for non-Hodgkin lymphoma
Category **5**: Suspicious for Hodgkin lymphoma
Category **6**: Metastatic malignancy

The cytological findings were then correlated with the histological findings of the lymph node excision specimens when these were subsequently submitted to the histopathology department. The aim was to assess the overall efficacy of the test.

Results

A total of three hundred (300) lymph nodes were sampled by FNA in the period under review. The diagnoses designated under categories 1, 2, 3, 4, 5 and 6 represented 14.0%, 53.0%, 4.3%, 5.7%, 1.7% and 21.3% of all lymph node FNACs respectively (see figure 1).

Figure 1: *Proportion of cases in the six diagnostic Categories*



Category 1: Non Diagnostic

In our study, 73.8% (32 out of 42) of all of cases categorised as non-diagnostic did not have follow up histology. One case (2.38%) was followed up by core biopsy; however the two core biopsies submitted were composed of fibrous connective tissue and skeletal muscle with no evidence of lymphoid tissue on histology. This biopsy was therefore considered inadequate for diagnostic purposes. In four cases (9.52%), subsequent histology showed benign lymphoid hyperplasia. Three cases of Hodgkin lymphoma and three cases of metastatic carcinoma (each representing 7.14%) were diagnosed on histology of the subsequently excised lymph nodes.

These results are summarised in Table 1.

Cases in this FNAC diagnostic category are inadequate and hence histologic correlation is not appropriate. We have therefore opted to exclude this category from our efficacy statistics.

Category 2: Benign lymphoid hyperplasia

In our study, 78.6% (125) of cases were not followed up by histology. From a clinical perspective and for the purpose of this study, these are assumed to represent reactive lymph nodes. The 21.4% cases which did have subsequent histology can be divided into two groups, namely true negative cases (52.9%) and false negative cases (47.1%). The false negative cases were 6 cases of non-Hodgkin lymphoma, 1 case of Hodgkin lymphoma and 9 cases of metastatic carcinoma.

These results are summarised in Table 2.

Category 3: Although favouring a reactive process, lymphoma needs to be excluded

Six cases in this category showed benign lymphoid hyperplasia on subsequent histology whilst two cases were diagnosed as non-Hodgkin lymphoma and four cases as Hodgkin lymphoma on subsequent histology. One case did not have follow up histology.

The thirteen cases in this diagnostic category were excluded from the overall efficacy statistics in view of the higher degree of uncertainty inherent in the cytologic diagnosis.

Category 4: Suspicious for non-Hodgkin lymphoma

There were seventeen cases in this category. Two cases did not have follow up histology however they were confirmed with ancillary tests; using cell block and immunohistochemistry. Fourteen cases were confirmed to be cases of non-Hodgkin lymphoma on follow up histology. One case was a false positive and was diagnosed as a pilomatrixoma on subsequent histology.

Category 5: Suspicious for Hodgkin lymphoma

All five cases diagnosed on FNAC were confirmed on subsequent histology.

Category 6: Metastatic malignancy (see Table 3)

Of these, twenty two cases did not have a follow up histology. From a clinical perspective and for the purpose of this study, these are assumed to represent metastasis to lymph nodes. Fifteen cases were confirmed using ancillary tests. Twenty seven cases were confirmed on subsequent histology.

These results are summarised in Table 5.

The overall efficacy of lymph node fine needle aspiration cytology is summarised in table 4.

Table 1: *Category 1: Non Diagnostic*

Number of patients	Histopathological report	Number of patients
42 (14%)	No follow up histology	31(74%)
	Non diagnostic histology	1(2%)
	Benign lymphoid hyperplasia	4(10%)
	Hodgkin lymphoma	3(7%)
	Metastatic carcinoma	3(7%)

Table 2: *Category 2: Benign Reactive Lymphoid Hyperplasia*

Number of patients	Histopathological report	Number of patients
159 (53.0%)	No follow up histology	125(79%)
	Benign lymphoid hyperplasia	18(11%)
	Non-Hodgkin Lymphoma	6(4%)
	Hodgkin Lymphoma	1(1%)
	Metastatic carcinoma	9(5%)

Table 3*: Category 6: Metastatic malignancy*

Number of patients	Histopathological report	Number of patients
64 (21.30%)	No follow up histology	22(34%)
	Metastatic carcinoma*	42(66%)

*Of these, 27 cases had follow up histology and 15 cases were confirmed using cell block and immunohistochemistry.

Table 4: The overall efficacy of lymph node FNAC

True negative	143
False negative	16
True positive	87
False positive	1
Sensitivity	84.5%
Specificity	99.3%
False positive rate	0.7%
False negative rate	10.0%
Accuracy	93.1%
Positive Predictive Value	98.8%
Negative Predictive Value	89.9%

Discussion

The proportion of cases in the different categories and the efficacy of FNAC at our institution were compared to those reported in the literature (summarised in Tables 5 and 6).

Category 1: Non Diagnostic

A non-diagnostic diagnosis occurs when the specimen is found unsatisfactory either because of low cellularity or due to difficulty in assessment e.g. obscuring blood.

After a literature review, we could not find a standardised system for assessing the adequacy of a lymph node aspirate and in practice this appears to be based on the cytologist's interpretation. The adequacy rate of lymph node FNAC in our institution (14%) compares well with that reported in the literature (5.6% –21.7% [2, 7]). The wide variability depends on the size and location of the lymph node, and on the operator's and cytologist's experience.

Table 5*: Comparison of the relative frequency of the different categories*

	C1	C2	C3	C4	C5	C6
Our results	*14%*	*53%*	*4.3%*	*5.7%*	*1.8%*	*21.3%*
Mitra et al	5.6%	-	2.8%	13.7%		
Nasuti et al	12%	13%		17%		52%
Gilani et al	21.7%	-	-	-	-	-
Jing et al	8%	-	-	-	-	-
Steel et al	10.9%					
Rammeh et al	20.6%	-	-	-	-	-
Lioe et al	15.9%	52.7%	6.1%	25.1%		
Stani J	-	23.5%	-	-	-	-

Table 6: *Comparison of the efficacy of fine needle aspiration cytology of lymph nodes*

	Sensitivity	Specificity	False negative	False positive	Accuracy	Positive Predictive Value	Negative Predictive Value
Our results	*84.5%*	*99.3%*	*10%*	*0.7%*	*93.1%*	*98.8%*	*89.9%*
Gilani et al	91.7%	100%	4.3% [1]	11% [2]	93.5%	100%	77.8%
Jing et al (for metastasis)	77.5%	100%	-	-	82.2%	100%	53.7%
Steel et al	-	-	3.4%	0.9%	-	-	-
Thierauf et al	85%	87%	5%	15%	-	64%	92%
Hall et al (for melanoma)	97%	98%	-	-	-	-	-
Lioe et al	85.4%	100%	12.5% [3]	0%	94.4%	100%	91.8%
Marti et al (for metastasis)	86%	100%	29%	0%	91%	100%	78%
Fung et al (for metastasis)	75%	100%	-	-	95.6%%	100%	79%

[1] Micrometastasis on histology.
[2] The patients had undergone preoperative neoadjuvant chemotherapy, with no residual tumour present.
[3] The false negative rate fell to 3.5% after excluding lymphomas.

Category 2: Benign lymphoid hyperplasia

A diagnosis of benign lymphoid hyperplasia is conferred when the cytology specimen is cellular, is not obscured by blood or other material and is composed of a polymorphic population of lymphoid cells. The proportion of cases in this category in our institution is considerable, amounting to 53% of all cases. This is higher than reported by Nasuti et al and Stani (13% and 23.5% respectively) [6, 15], and comparable to Lioe et al (52.7%). [14] The high percentage of cases in category 2 in this study could possibly be accounted for by a lower clinical threshold to perform fine needle aspiration cytology at our institution.

Category 3: Although favouring a reactive process, lymphoma needs to be excluded

In this category, the cytological picture is cellular and unobscured and is composed of a relatively monomorphic population of small to intermediate-sized lymphocytes. This category is reserved for those cases where the cytological picture is equivocal and has overlapping features. One of the limitations of fine needle aspiration cytology of lymph nodes is in differentiating between reactive lymphoid proliferations and lymphoma, especially low grade lymphoma.[5] The proportion of cases in this category (4.3%) lies in between that observed in the study by Mitra et al (2.8%) and Lioe et al (6.1%).[2, 14]

Category 4: Suspicious or diagnostic of non-Hodgkin lymphoma

The cytological picture of this category is characterised by a cellular, unobscured monomorphic population of intermediate-sized to large atypical lymphoid cells and with variable mitosis. At our institution, non-Hodgkin lymphoma holds an overall specificity of 94.1% and sensitivity of 66.7%. This rises to 72.7% if the cases in categories 1 and 3 are excluded.

Category 5: Suspicious for Hodgkin lymphoma

In this category, the diagnosis relies on the identification of Reed-Sternberg or Hodgkin cells, on a background of small monomorphic lymphocytes, eosinophils and other inflammatory cells, in the absence of tingible body macrophages. At our institution, Hodgkin lymphoma holds a specificity of 100% and sensitivity of 38%. If the cases in categories 1 and 3 are excluded, the sensitivity rises to 83%. According to Chhieng et al.[10], Hodgkin lymphoma has a high false negative rate due to typical scarcity of Reed-Sternberg or Hodgkin cells in aspirates, the presence of fibrosis (in the nodular sclerosis type), sampling error and misinterpretation of the diagnostic cells.

Category 6: Metastatic malignancy

In this category, the cytological diagnosis relies on the presence of single cells or clusters of malignant cells with a morphology which is alien to that of the normal lymphoid milieu. This often occurs on a background of a normal lymphoid FNAC specimen. The overall specificity at our institution was 100%. The overall sensitivity was 84%, which rises to 88% after excluding the cases in categories 1 and 3. Our data compares well with that in the reported literature which shows a specificity of 100% across all studies and a sensitivity which ranges from 75 to 86%.[8, 16-17] The lower specificity in some cases can be explained by the small size of metastatic deposits. [17]

There overall efficacy of lymph node fine needle aspiration cytology is tabulated in table 4.

This study has a number of limitations which were taken into consideration:

- This is a retrospective study.
- A number of lymph node FNAC cases were submitted by the clinicians as a lesion or mass in the head and neck region. These were thus encoded using the 'Head and neck cytologic material' SNOMED code and were not included in this study.
- This study assumed that all lymph nodes classified as benign reactive lymphoid hyperplasia, which did not have a subsequent diagnosis of lymphoma within one year, were truly reactive.
- This study assumed that all lymph nodes classified as metastatic malignancy were truly involved.
- Lymph node excisions performed in the private sector following a FNA performed at our institution could not be assessed.
- The lymph node excised may not be the same lymph node that was sampled by fine needle aspiration.
- The numbers in categories 3,4,5 are small. These can introduce a wide margin of error in statistical comparisons.

In spite of these limitations, this study has been able to demonstrate the clinical usefulness of this test.

Conclusion

The overall efficacy of lymph node FNAC diagnosis compares very well with that quoted in the literature. This test's greatest strength lies in triaging reactive from neoplastic lymph nodes, principally high grade non-Hodgkin's lymphoma and metastasis. Its weakness lies in sampling issues and differentiating between certain patterns of reactive lymphoid hyperplasia and low grade non-Hodgkin's lymphoma. Our comparatively high rate of cases in the benign category could possibly be explained by a higher index of suspicion among our clinicians with a consequent lower threshold to biopsy. The proportion of cases with a non-diagnostic cytology result could be possibly

brought down by ensuring that operators and cytologists are properly trained and retrained. Fine needle aspiration cytology of lymph nodes remains a very important and valid tool in the management of patients with lymphadenopathy.

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